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Editorial

We are indeed living in very interesting times. Usually, “Interesting times“ and “case reports“ are found on the same sentence or pharagraph. In the world of medecine, intersting case repots connote further studies, a tone of research and aportal to an entire body of treatment strategies, It is said that no two patients are alike, but these case reports represent an entire universe of truths and remonstrance that behooves as all to change: change in mindset, change in physical assesment, change in diagnostic strategies. all in all, case reports are interesting because they lead to imporved strategies and development of the science.

Dear reader, I know you will enjoy thes compendiuum. My prayer is that each case you will read here will humanized and lead you to more compassion and therefore, to more excellence.

Cheers!

GILBERT C. VILELA, MD
Deputy Executive Director
Education, Training and Research Services

Coronary Artery Fistula Associated With Mitral Valve Regurgitation in a Young Symptomatic Patient

Jenny-Lynn V. Juhuri, MD; Delfin Barrion, MD

Congenital coronary artery fistulas are rare cardiac defects. A fistula associated with other cardiac anomalies, like valvular heart disease, is an extremely rare condition. We report a young symptomatic patient who presented with a continuous murmur heard along second right intercostal space and a systolic murmur at the apex on clinical examination. Chest x-ray showed left ventricular prominence and transthoracic echocardiography with doppler studies showed right coronary fistula draining into the right atrium and moderate mitral regurgitation. She is being followed up with medical management at the outpatient department. We recommend coronary angiography with cardiac catheterization, and if patient will give her consent, surgical repair of the fistula with possible mitral valve surgery is recommended. We conclude that diagnosis of coronary artery fistula should be considered when patient presents with continuous murmur. A non-invasive test, like transthoracic echocardiography with Doppler studies, can demonstrate dilated coronary arteries and their receiving chambers or vessels. ***Phil Heart Center J 2021;24(1):1-4.***

Key Words: ■ Coronary artery fistula ■ coronary artery malformation ■ coronary artery anomaly ■ congenital heart disease ■ continuous murmur

A coronary artery fistula (CAF) is an abnormal communication between a coronary artery and a cardiac chamber, great vessel, or other vascular structure.[1] The incidence of CAF is estimated at 1 in 50,000 live births, and it is detected in approximately 0.2% of the adult population during coronary angiography.[2] The most common origin is the right coronary artery (RCA) and a single termination is found in the majority of patients.[3] The right ventricle is the most common site of drainage (45%) followed by the right atrium (25%), pulmonary artery (15–20%) and coronary sinus (7%).[3] These can be symptomatic or asymptomatic because the hemodynamic consequences of the fistula vary and depend on the shunt dimensions.[4] In general, symptoms of angina, palpitations and cardiac failure may occur in patients aged over 30 years, with the cardinal clinical finding of a continuous murmur similar to a patent ductus arteriosus (PDA)[3] but the diagnosis of CAF may be suggested by the finding of a continuous murmur in a precordial location, which is atypical for PDA.[1]

Doppler echocardiography is currently used as the noninvasive method to establish the diagnosis and evaluate management of CAF.[3] Magnetic resonance imaging has become an alternative method to evaluate anatomy, flow and function.[3] In most instances the diagnosis is made during heart catheterization for coronary or congenital heart disease.[5] Cardiac catheterization is usually performed in order to confirm anatomy and plan surgical treatment.[3]

Gurbuz et. al. reported a case of CAF with mitral valve stenosis and they mentioned that reports of the coincidence of mitral stenosis and CAF are rare in the literature. A fistula opening into the right atrium is rare in patients with coronary artery anomalies and mitral valve disease.[2] Now, for its rarity, we report a case of a symptomatic young patient with concomitant mitral valve regurgitation and CAF, with the fistula draining into the right atrium.

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Case: A 25 years old female reported dyspnea and easy fatigability for 1 year already. There was no cough, fever, chest pain, orthopnea or edema. Symptoms progressed and she also noted palpitations, so she sought consult and was given unrecalled medications. 2D echocardiography was advised and she was told to have a 'hole in the heart'. Symptoms persisted, thus, she was referred to Philippine Heart Center. Medical or surgical history was unremarkable, as well as, family history. On physical examination, she had dynamic precordium, displaced apex beat, continuous murmur at second right intercostal space radiating to the mid right parasternal border area and grade 3/6 systolic murmur at apex radiating to the back.

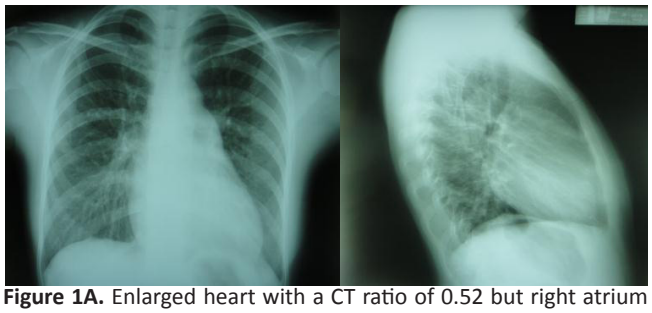

Figure 1A. Enlarged heart with a CT ratio of 0.52 but right atrium is not enlarged and right cardiac border is not prominent with the lateral border of the cardiac silhouette measuring 2 cm from the lateral border of the spine. The aorta and MPA are prominent. The lungs are hypervascular. B. Right ventricle is not prominent. Hoffman-rigler measurement is 1.6cm indicative of LV prominence

We proceeded with diagnostic evaluation. 12-lead electrocardiogram (ECG) was normal. Chest x-ray revealed an enlarged heart with prominent aorta, prominent main pulmonary ar tery and increased pulmonary vascularity *(Figure 1A*). On lateral view, it showed LV prominence (*Figure 1B*). 2-dimensional trans-thoracic echocardiography (TTE) with Doppler studies showed a dilated RCA draining into the right atrium, with noted continuous turbulent flow most likely the fistulous connection, and a mosaic color flow display across the mitral valve during systole denoting mitral regurgitation. (*Figure 2. A, B and C*).

She was managed medically on an outpatient basis. Further diagnostic tests were discussed and if patient will give her consent, surgical repair of the CAF and possible mitral valve surgery is being contemplated.

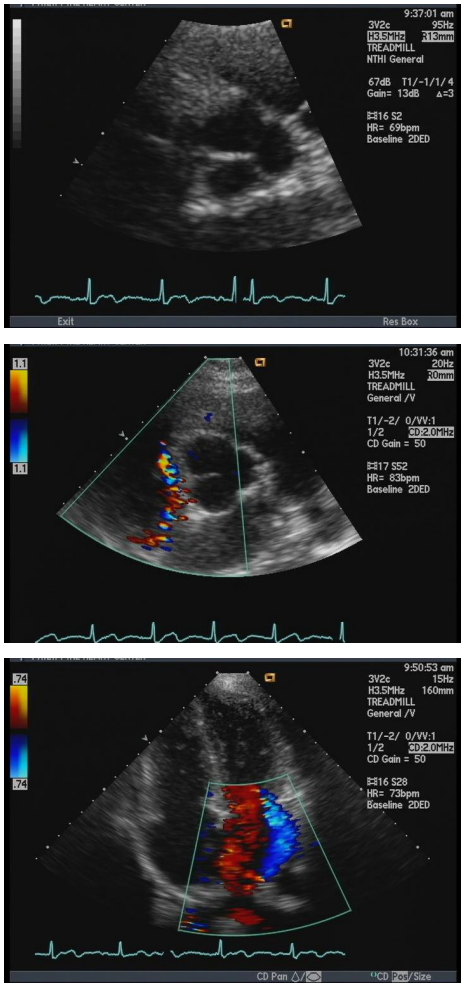

Figure 2. A. Dilated right coronary artery (green arrow). **B.** Continuous turbulence noted from the right coronary artery to superior aspect of the right atrium denoting the fistulous connection. **C.** Mosaic color flow display noted across the mitral valve during systole denoting mitral regurgitation.

DISCUSSION

Congenital CAFs, a subgroup of anomalies of the coronary arteries, are an extremely rare cardiac defect.[6] It is an infrequent but potentially important abnormality that can affect any age group.[1] In an article by Chu et. al., the ages of the patients, who underwent surgical treatment for CAF, ranged from 4 months to 50 years.[7] Our case is a 25 years old female which falls near the mean age of this report, which is 22 years.[7] In general, symptoms are rare under the age of 20 years.[3] The pathophysiologic mechanisms

resulting in symptoms include cardiac volume overload due to the shunting of blood and reduction of the myocardial blood supply due to "coronary steal."[1] Dyspnea and chest pain represented a frequent (71%) clinical symptom in CAFs in adults while in the pediatric age group, the majority was silent (79%) and dyspnea and chest pain accounted for only 8% of the symptoms.[8] Liu and his colleages reviewed fourteen patients with congenital CAF and only one was asymptomatic, but diagnosis was suspected from clinical presentation of a continuous murmur. In the symptomatic patients, angina and exertional dyspnea were the most common symptoms.[9] Also, Hong and his colleagues reviewed fifteen cases of congenital CAF, and twelve patients were symptomatic at the time of the diagnosis.[10] Parga et. al. mentioned the cardinal clinical finding of continuous murmur, usually heard at the middle left or right sternal border or even at the lower sternal border. Even Chu and his colleagues mentioned that continuous heart murmurs was heard in all the cases they reviewed except one. Our patient presented with dyspnea and easy fatigability since she was 24 years old, consistent with these reports [3, 8-10] and she had a continuous murmur at the 2nd right intercostal space, radiating to the mid right parasternal border area which is also consistent with these reports.[3,7]

The diagnosis may be established non-invasively by echocardiography, demonstrating the dilated coronary artery and the fistula (including its entry site into the chamber or vessel).[3] But according to Bauer et. al., in most instances the diagnosis is made during heart catheterization for coronary or congenital heart disease. Likewise, Said and his colleagues stated that the diagnostic modalities for CAF, from the literature between 1993 and 2004, were mainly cardiac catheterization and coronary angiography. However, the CAF in our case was demonstrated by TTE, as a dilated RCA draining into the superior aspect of the right atrium (RCA fistula).

Several reports reviewing congenital CAF cases have different views regarding the origin and drainage of CAF. Bauer et. al. showed that there was equal affectation of the right and left coronary artery (LCA). According to Tirilomis and his colleagues, CAF originated mostly from the left coronary system (proximal left descending artery, left main stem, circumflex artery) which was also the same with the reports of Liu et. al. and Abdelmoneim et.al, showing the left anterior descending coronary artery (LAD) as the most commonly involved. In contrast, the findings of Parga et. al. revealed that 55% to 65% of congenital CAFs arise from the RCA. The right ventricle is the most common site of drainage (45%) followed by the right atrium (25%), pulmonary artery (15–20%) and coronary sinus (7%).[3] This report regarding drainage of CAF was also affirmed by the article of Chu et. al., which mentioned that all the drainage sites of the CAF were on the right side of the heart (right atrium, right ventricle, pulmonary artery) as well as these other reports.[9-11] Our finding of RCA fistula proves that RCA is still the most common origin of CAF, as mentioned by Parga et. al. Also, its drainage to the right atrium is consistent with these previous reports.[3,7,9,10]

Meanwhile, Chu et. al. noted that only one of the patients with CAF had associated cardiac disease while the report of Hong et. al showed that six patients with CAF had associated cardiac anomalies. Gurbuz and his colleagues reported a rare case of CAF and mitral valve stenosis in a patient with dyspnea and fatigue before valve replacement and surgical radiofrequency ablation. They mentioned that CAF can be diagnosed more frequently if coronary angiography is performed simultaneously with cardiac catheterization to evaluate valve functions or nonatherosclerotic myocardial ischemia in each valvular heart disease case. Our patient also presented with a grade 3/6 systolic murmur at the apex radiating to the back. On TTE, there was presence of moderate mitral regurgitation. Hence, it is a rare finding to see patients with CAF and associated cardiac disease, like in our case, RCA fistula with mitral regurgitation, which was confirmed by TTE.

The management of CAF is complicated and recommendations are based on anecdotal cases or very small retrospective series.[12] Correction of CAF is indicated if the patients are symptomatic or if other secondary complications develop.[12] Early surgical treatment for coronary artery fistulas is safe and effective. The risk of operative

correction appears to be considerably less than the potential for development of serious and potentially fatal complications, even in asymptomatic patients.[10] The report of Hong and his colleagues showed that out of fifteen CAF patients, for whom six had associated cardiac anomalies, all received surgical correction. All patients had stable condition and were asymptomatic during a mean postoperative follow-up of 13.3 years.[10] Also in the case reported by Gurbuz et. al., the patient with CAF and mitral stenosis had coronary angiogram one month after surgical repair which showed normal coronary anatomy and occluded fistula. In this case, our recommendation is for coronary angiography which is to be performed simultaneously with cardiac catheterization to confirm the anatomy, evaluate the valves and to plan the surgical treatment. We recommend surgical repair of the CAF with possible mitral valve surgery, since patient is symptomatic and it is proven from literatures that the surgical risk is less than the adverse events from the procedure itself.

CONCLUSION

In patients presenting with continuous murmur, especially if symptomatic, a diagnosis of coronary artery fistula should be considered. Non-invasive diagnostic tests, particularly two-dimentional transthoracic echocardiography with doppler studies, can demonstrate a dilated coronary artery, with flow in the fistula and identification of its receiving chamber, vessel or other vascular structures. From the previous reports cited, our recommendation is to proceed with coronary angiography with cardiac catheterization to confirm the anatomy, evaluate the valves and to plan the surgical treatment, if the patient will give her consent. Surgical repair of the RCA fistula and possible mitral valve surgery is recommended since correction of CAF is indicated if patients are symptomatic and knowing that early surgical treatment for CAF is safe and effective.

REFERENCES

1. Sapin P, Frantz E, Jain A, Nichols TC, Dehmer GJ. Coronary artery fistula: an abnormality affecting all age groups. Medicine (Baltimore). 1990 Mar;69(2):101-13. PubMed PMID: 2319939.
2. Gürbüz A, Yetkin U, Tetik O, Kestelli M, Yesil M. Right coronary artery fistula draining into the right atrium and associated with mitral valve stenosis: a case report. Heart Surg Forum. 2007;10(4):E325-8. PubMed PMID: 17599885.
3. Parga JR, Ikari NM, Bustamante NP, Rochitte CE, Dea Vila LFR, Oliveira SA. Case report: MRI evaluation of congenital coronary artery fistulae. The British Journal of Radiology. 2004 june; 77: 508-511. DOI: 10.1259/bjr/24835123.
4. Fazio G, Pipitone S, Mongiovì M, Sutera L, Zito R, Novo S. A coronary right fistula canalized in a small accessory right atrial chamber. J Cardiovasc Med (Hagerstown). 2007 Sep;8(9):759. Erratum in: J Cardiovasc Med (Hagerstown). 2007 Nov;8(11):following 980. PubMed PMID: 17700415.
5. Bauer M, Bauer U, Alexi-Meskishvili V, Pasic M, Weng Y, Lange PE, Hetzer R. [Congenital coronary fistulas: the most frequent congenital coronary anomaly]. Z Kardiol. 2001 Aug;90(8):535-41. German. PubMed PMID: 11565208.
6. Tirilomis T, Aleksic I, Busch T, Zenker D, Ruschewski W, Dalichau H. Congenital coronary artery fistulas in adults: surgical treatment and outcome. Int J Cardiol. 2005 Jan;98(1):57-9.
7. Chu JJ, Chang JP, Lin PJ, Lee MC, Shieh MJ, Chang CH. Surgical management of congenital coronary artery fistula. Taiwan Yi Xue Hui Za Zhi. 1989 Oct;88 (10):1046-52. PubMed PMID: 2634728.
8. Said SA, Lam J, van der Werf T. Solitary coronary artery fistulas: a congenital anomaly in children and adults. A contemporary review. Congenit Heart Dis. 2006 May;1(3):63-76.
9. Liu PR, Leong KH, Lee PC, Chen YT. Congenital coronary artery-cardiac chamber fistulae: a study of fourteen cases. Zhonghua Yi Xue Za Zhi (Taipei). 1994 Sep;54(3):160-5. PubMed PMID: 7954056.
10. Hong GJ, Lin CY, Lee CY, Loh SH, Yang HS, Liu KY, Tsai YT, Tsai CS. Congenital coronary artery fistulas: clinical considerations and surgical treatment. ANZ J Surg. 2004 May;74(5):350-5.
11. Abdelmoneim SS, Mookadam F, Moustafa S, Zehr KJ, Mookadam M, Maalouf JF,Holmes DR. Coronary artery fistula: single-center experience spanning 17 years. J Interv Cardiol. 2007 Aug;20(4):265-74.
12. Raju MG, Goyal SK, Punnam SR, Shah DO, Smith GF, Abela GS. Coronary artery fistula: a case series with review of the literature. J Cardiol. 2009 Jun;53(3):467-72.

Congenital Absence of the Right Coronary Artery with Septal Perforators Supplying the Right Side of the Heart

Jericho C. De Leon, MD

Congenital absence of a coronary artery is a rare condition that may be clinically silent or may produce fatal conditions such as myocardial infarction or sudden cardiac death. A case of a 41-year old hypertensive female presenting with chest pain was reviewed. Work-up done to the patient include coronary angiography revealing an absent right coronary artery. The right side of the heart is supplied by the septal perforators coming from the left anterior descending artery. Accurate knowledge of the anatomy of the coronary vessels in patients with anomalous arteries is crucial in the management of such patients. ***Phil Heart Center J 2021;24(1):5-8.***

Key Words: ■ Congenital absence ■ anomaly ■ right coronary artery ■ single coronary artery ■ absent coronary artery

Coronary artery anomalies are relatively common conditions that may or may not present with signs or symptoms. These anomalies may be in the form of anomalous origins and distribution of vessels, ectopic or inappropriate course and location, or the presence of fistula. These conditions, if asymptomatic, are usually detected only in autopsies or as incidental findings in conventional angiography or in radiologic examinations such as CT angiogram.

A single coronary artery (SCA) however is a rare condition with an incidence of only 0.024% to 0.066% in the general population.[1] These conditions are usually benign, with majority of cases detected only incidentally during angiogram. However, this condition is also associated with congestive heart failure, angina, myocardial infarction, syncope, arrhythmias and sudden cardiac death.[1,2]

It is thus important to note cases involving anomalies of the coronary arteries especially cases of congenital absence of one of its branches as they have clinical implications. Secondary prevention of complications can be done in order to prevent morbidity in those patients with the abnormality.

Case: We are presented with a 41 year old female, who came for consult in the outpatient department due to chest pain. History revealed the she had been experiencing chest pain described as substernal heaviness for the past 1 year associated with exertional dyspnea. One month prior to her consult, she noted to have increased frequency of chest pain and sometimes observed at rest. This prompted her to seek consultation to our institution.

She is a known hypertensive, a non-diabetic, non-smoker, with no family history of coronary artery disease. She has a history of acute cerebral infarct, with a left sided weakness residual.

Pertinent physical examination include a blood pressure of 120/70 mmHg, cardiac rate at 50-60 beats per minute. Examination of the cardiovascular system showed an adynamic precordium, apex beat at the 5th intercostal space, left midclavicular line, bradycardic, with regular rhythm, normal S1 and S2, no murmurs appreciated. The rest of the physical examination was essentially normal. She was admitted for work-up and managed as a case of chronic stable angina.

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Laboratory exams were done, showing elevated low density lipoprotein (LDL) and decreased high density lipoprotein (HDL). Fasting blood sugar was normal. Electrocardiogram was done revealing normal sinus rhythm without ST-segment abnormalities. (*Figure 1)*. Echocardiogram was done, revealing concentric left ventricular remodelling with segmental abnormality, with hypokinesia of the posterior interventricular septum from mid to apex.

The patient then underwent coronary angiogram. Fluoroscopy showed absence of calcifications. Pressure recordings showed a normal systemic arterial pressure, LVEDP of 12 mmHg, and absence of systolic pressure gradient across the aortic valve. Coronary arteriography showed a good-sized normal left main artery, angiographically free of disease, bifurcating into an LAD and LCX, both of which are likewise free of disease and appearing normal. The right coronary artery however was not able to be cannulated and was not visualized on aortic root injection. (*Figure 2*) The septal perforators were supplying the right coronary artery distribution. (*Figure 3*)

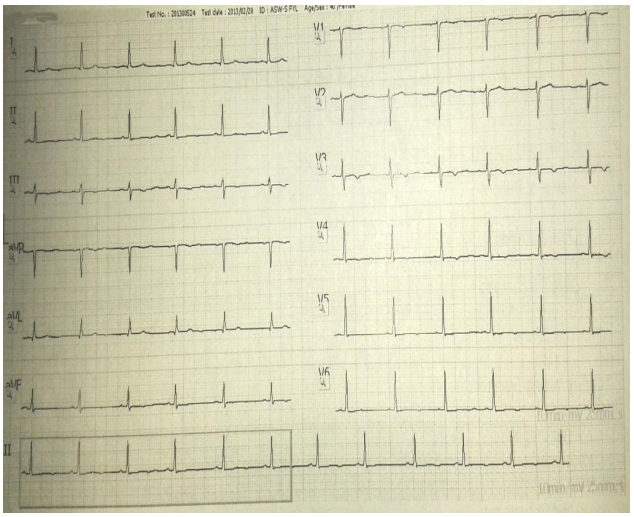

Figure 1. ECG of the patient showing normal sinus rhythm without significant ST-segment abnormalities

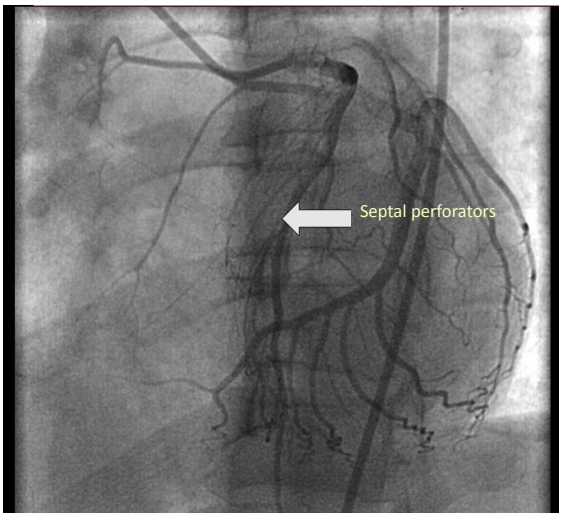

Figure 3. Arteriography of the left anterior deascending artery showing the septal perforators supplying the right coronary artery distribution

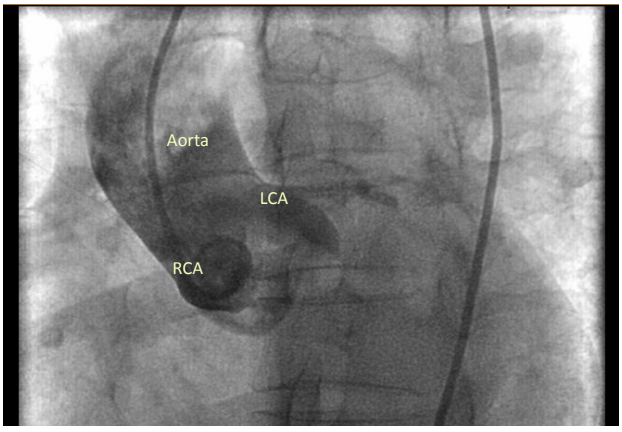

Figure 2. Aortography showing the absence of the right coronary ostium on its supposed location. (LCA- left coronary artery; RCA- right coronary artery)

DISCUSSION

Coronary artery anomalies occur in about 0.2%-1.3% of the general population.[1,3] As mentioned, these anomalies can be in the form of absence of a coronary artery, anomalous origins and distribution of vessels, ectopic or inappropriate course and location, interarterial commu nications or the presence of fistula. The congenital absence of a coronary artery is a more uncommon condition occuring in 0.024%-0.066% of the population.

A single coronary artery is defined as an artery that arises from the aortic trunk from a single coronary ostium and supplies the entire heart.[4] It is suggested that the reason for the single artery to form is because of the under-

development of the proximal portion of the coronary artery which is expected to grow into the aorta during the final stages of the coronary artery formation during organogenesis in utero.[5] Several classification schemes have been devised for this condition in order to facilitate communication among health professionals and for prognostication. They may be the only anomaly found in the patient's heart, or it may be associated with other congenital anomalies.

In a report by Shirani and Roberts,[5] they classified solitary coronary arteries into 20 categories on the basis of the origin in the aorta of the solitary coronary ostium, presence or absence of an aberrant-coursing coronary artery, and the distribution of the aberrant-coursing coronary artery. They correlated each category with the cause of death of the patients with the specific anomaly type. Using their classification, our patient falls into the IA category, with a low correlation of death caused by cardiovascular disease. Most of their studied patients falling in Type IA category dead of infections, pulmonary cause, or trauma.

Presence of an anomalous anatomy of the coronary vessels can be "silent", meaning patient being asymptomatic and the anomalies detected only during autopsy, or as incidental findings during ancillary procedures. However, these anomalies can produce symptoms ranging from angina to myocardial infarction and even sudden cardiac death. Mechanisms postulated for the causes of the development of symptoms include compression of the anomalous artery because of its abnormal course, or sporadic spasm of the anomalous coronary artery. With the case of our patient, she presented with symptoms of angina aggravated by exertion. With the right side of her heart supplied only by the small septal perforators coming from the left anterior descending artery, and considering her abnormal lipid profile, there is a possibility that myocardial ischemia due to stenotic vessels is the cause of her angina.

Coronary angiography is the gold standard in evaluating coronary artery disease. However in this case, we need other diagnostic modalities in order to further visualize the coronary arteries and to confidently conclude that the patient's symptoms are caused by the anomalous coronary arteries. Further evaluation by cardiac magnetic resonance imaging or CT angiography is recommended, which can also prognosticate our patient.

Our patient was managed medically. According to the previously mentioned classification scheme, our patient is at low risk for suffering death caused by cardiovascular disease based on the anatomy of her coronary arteries. Lifestyle modification was also promoted in order to control or lessen her other risk factors for coronary artery disease.

However, it is important to highlight in this report the combination of an anomalous coronary anatomy and the possibility of atherosclerotic disease. Even though the patient has a low risk of developing cardiovascular event based on her coronary anatomy, she is susceptible to the deleterious effects of atherosclerotic occlusive disease as the heart and the conduction system entirely depend on the SCA for oxygenated blood supply. Optimal medical treatment including antiplatelets, ACE inhibitor and a beta-blocker was given, since the patient is vulnerable to myocardial ischemia, with her right coronary artery distribution supplied only with the septal perforators coming from the left anterior descending artery.

CONCLUSION

In cases of congenital anomalies of the coronary vessels, it is important to take note of the specific anomaly or anatomy in order to prognosticate and manage the patient well. A single coronary artery is an extremely rare condition that may be clinically "benign" producing no symptoms, or it may cause fatal arrhythmias, myocardial infarction or sudden cardiac death. It is also important to consider other risk factors such as the presence of atherosclerotic disease like in the case of our patient. In such cases, secondary prevention is extremely recommended in order to prevent cardiovascular events and complications of those congenital anomalies.

REFERENCES

1. Blaschke F, Zimmermann E, Greupner J, Zohlnhoefer D, Krackhardt F, Haverkamp W, et al. A rare case of a congenital single coronary artery: right coronary artery originating from the distal left circumflex artery. Vasc Disease Management. 2013;10(11):E244-E247.
2. Malhorta S, Landolfo C, Kapoor D. Congenital absence of right coronary artery without any other associated anomalies. Cardiology Review. 2008; 17 (13):12-16.
3. Lipton MJ, Barry WH, Obrez I, Silverman JF, Wexler L. Isolated single coronary artery: diagnosis, angiographic classification, and clinical significance. Radiology. 1979;130(1):39-47.
4. Liesting C, Brugts JJ, Johannes M, Kofflard M., Dirkali A. Acute coronary syndrome in a patient with a single coronary artery arising from the right sinus of Valsalva. World J Cardiol. 2012 August 26; 4(8): 264-266.
5. Shirani J, Roberts W. Solitary coronary ostium in the absence of other major congenital cardiovascular anomalies. J Am Coll Cardio. 1993 January; 21 (1): 137-43.
6. Elliot G., Martin A. Congenital absence of the right coronary artery with a unique origin of the artery to the sinu-atrial node: A case study. Int J Anat Var. 2012; 5: 120–125.

Hypertrophic Cardiomyopathy with Absent Major Septal Perforator Coronary Artery Successfully Treated with Dual-Chamber Pacing as an Alternate Strategy to Alcohol Septal Ablation and Surgical Myectomy

Bernard Benjamin P. Albano, MD; Erdie C. Fadreguilan, MD; Ed Gabitoya, MD; Dr. Jeffrey M. Chua, MD; James Ho, MD; Ana Beatrice Medrano, MD

Background --- Hypertrophic Cardiomyopathy (HCM) is the most common of the genetic cardiovascular disease characterized by a thickened non-dilated ventricle in the absence of another cardiac or systemic condition. Its most important hemodynamic consequence is left ventricular outflow tract (LVOT) obstruction. Its primary management strategy is surgical septal myectomy, but an acceptable alternative treatment in patients who are not suitable for (or who refuse) surgery is alcohol septal ablation (ASA). However, in patients with unfavorable coronary anatomy which precludes ASA (i.e. absence of major septal perforator branch of the left anterior descending artery), another reasonable option is dual chamber pacemaker implantation to decrease LVOT outflow gradient.

Case --- A 77 year-old female, known hypertensive, diabetic with a history of coronary artery disease presented with one week history of worsening chest pain and shortness of breath. She was admitted as a case of acute coronary syndrome and pneumonia. On work-up, 2DED revealed hypertrophic obstructive cardiomyopathy (HCM) with a demonstrated systolic anterior motion (SAM) of the mitral valve with a peak instantaneous gradient of 194 mmHg across the basal left ventricular cavity. The patient refused surgical myectomy, and alcohol septal ablation was the preferred treatment option. On coronary angiography, there was incidental finding of absent major septal perforator branch of the left anterior descending coronary artery (LAD), rendering her unsuitable for septal ablation. She was referred to electrophysiology for evaluation. She underwent dual chamber pacemaker implantation and documented significant decrease in the peak instantaneous gradient from 194 mmHg to 37 mmHg; with complete obliteration of systolic anterior motion (SAM) and improvement in overall wall motion. She remained stable and asymptomatic after pacemaker insertion until her recent outpatient follow-up (5 months post implantation).

Conclusion --- We present a case of hypertrophic cardiomyopathy with congenitally- absent major septal perforator branch coronary artery treated with dual chamber pacemaker implantation. To our knowledge, this is the first reported angiographically-absent first (major) septal perforator coronary anatomy in the setting of hypertrophic cardiomyopathy, and also the first description of dual chamber pacemaker implantation to relieve the LVOT obstruction. Although the role of dual-chamber pacing has become limited in HCM because surgical myectomy and septal ablation has resulted to better decrease in LV outflow gradient and symptom improvement, this modality remains essential and may still be considered as the treatment strategy-of-choice in patients who are unsuitable for surgical myectomy and alcohol septal ablation. ***Phil Heart Center J 2021;24(1):9-14.***

Key Words: ■ Hypertrophic cardiomyopathy ■ hypertrophic obstructive cardiomyopathy ■ surgical myectomy ■ alcohol septal ablation ■ dual chamber pacemaker implantation ■

Hypertrophic Cardiomyopathy (HCM) is the most common genetic cardiovascular disease characterized by a thickened non-dilated ventricle in the absence of other cardiac or systemic condition.[1] It is a global disease with a reported prevalence of 0.2% in the general

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population.[2] Its clinical diagnosis is made by imaging with two-dimensional echocardiography. The most important hemodynamic consequence of this condition is left ventricular outflow tract (LVOT) obstruction in which 70% of patients develop dynamic LV outflow gradient of 30 mmHg or greater. In the obstructive form, there is subaortic mechanical impedance to LV outflow, producing markedly increased intraventricular pressures that, over time, may be detrimental to LV function as a result of increased myocardial wall stress and oxygen demand. Most common obstructive mechanism (90%) is the systolic anterior motion (SAM) of the mitral valve, the remaining cause (10%) include intraventricular obstruction caused by systolic contact of septum with a papillary muscle that is anomalously positioned and may insert directly into anterior mitral leaflet.

In patients with severe drug-refractory NYHA class III and IV symptoms, the preferred primary management is surgical septal myomectomy.[2,3] In patients who are not candidates for surgery, an alternative treatment option is alcohol septal ablation (ASA).[1,4,5] This modality involves injection of alcohol into a major septal perforator coronary artery to create necrosis and permanent transmural myocardial infarction localized to the proximal ventricular septum which results in progressive thinning of the LV wall and a resultant decrease in LV outflow gradient.[6] However, in patients with congenitally-absent major septal perforator branches of the left anterior descending (LAD) coronary artery, the performance of ASA may be ineffective. Implantation of a dual-chamber pacemaker was proposed as an alternate treatment for these patients with severe symptomatic obstructive HCM.[7-9] By pacing the right ventricular apex with maintenance of atrioventricular synchrony, this results in a decrease in the LVOT gradient and improvement of symptoms. Importantly, however, its role in HCM has become limited due to lack of evidence of efficacy.[10]

This is a case of a symptomatic HCM in an elderly who refused surgical myectomy, and was planned for alcohol septal ablation but did not push through due to incidental finding of absent major septal perforator branch of the left anterior descending artery (LAD). Due to persistent refusal of surgery, she was referred to electrophysiology and underwent dual chamber pacemaker implantation. There was noted significant improvement of symptoms and she was discharged hemodynamically stable. To our knowledge, this is the first reported case of congenital absence of septal perforator artery in the setting of HCM and also the first description of successful treatment of LVOT gradient using dual chamber pacing.

Case: This is a case of a 77 year-old Filipino, female, diabetic, hypertensive with a history of coronary artery disease who underwent percutaneous coronary angioplasty of the right coronary artery (RCA) in 2000. One week prior to consult, she complained of occasional chest heaviness aggravated by effort and worsening shortness of breath. She was admitted in the wards and initially managed as a case of acute coronary syndrome and community-acquired pneumonia. Pertinent physical examination findings include the following: BP 100/60 mmHg, CR 77 bpm, RR 22, no neck vein engorgement, bibasal rales, with a systolic ejection murmur heard over the lower left sternal border with no radiation to the carotids. 12 –lead electrocardiography showed sinus rhythm, normal axis, with left atrial abnormality, and LV hypertrophy with secondary ST-T wave abnormalities; chest radiography revealed enlarged heart with LV prominence with mild congestion. Two-dimensional transthoracic echocardiogram was done which showed markedly thickened walls of the left ventricle (*Figures 1 and 2)* with a peak instantaneous continuous wave Doppler gradient across the basal left ventricular segment of 194 mmHg; concentric left ventricular remodeling with segmental wall motion abnormality with preserved systolic function and presence of systolic anterior motion (SAM) of the mitral valve with an LV ejection fraction of 57% by Simpson's. Surgical myectomy was advised but she refused any surgical treatment. Alcohol septal ablation was then the treatment option.

On the second hospital day, she underwent coronary angiogram which showed patent stent on the right coronary artery (RCA) with absence of a major septal perforator branch of the left anterior descending artery (LAD) (*Figures 3-5*). Septal ablation was deferred and she was

referred to electrophysiology for evaluation. On the third day, electrophysiologic/ventricular tachycardia (VT) studies was done which revealed a sinus rhythm, with a cardiac rate of 77 bpm, and a maximum rate of 140 bpm; no significant sinus pause, atrioventricular blocks, intraventricular conduction delays; on isoproterenol infusion, she had atrial tachycardia and atrial fibrillation with rapid ventricular response and developed congestion and hypoxia. She was given with one shock of synchronized cardioversion, 150J and was transferred to coronary care unit for close monitoring. Electrolytes were corrected accordingly. After she was stabilized, she was transferred to regular room and was scheduled for dual chamber (DDD) pacemaker implantation. After implantation of pacemaker, she remained stable and symptom-free. A repeat transthoracic echocardiogram was done which revealed significant decrease in peak instantaneous gradient basal left ventricular segment from 197 mmHg to 37 mmHg, the systolic anterior motion of the mitral valve shown before was no longer appreciated, and there was overall improvement in wall motion. The presence of pacemaker lead in place was identified. She was discharged on the 10th hospital day stable and asymptomatic.

She had regular outpatient follow-up and up to 5-months post-pacemaker implantation, she remained asymptomatic.

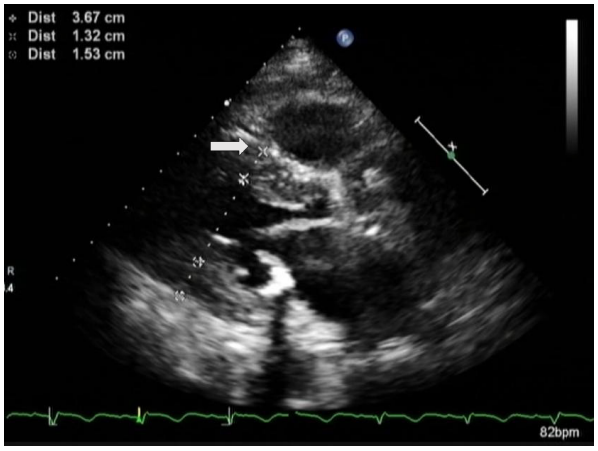

Figure 1. Parasternal long axis echocardiographic image of the patient showing hypertrophied septum (red arrow) and reduced left ventricular cavity size

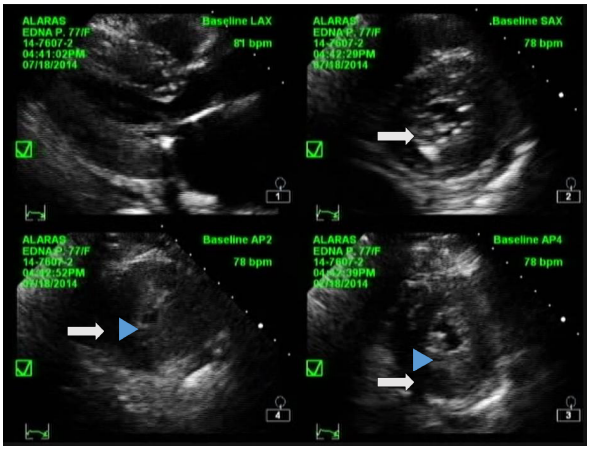

Figure 2. Short axis echocardiographic image of the patient showing concentric hypertrophy of the left ventricular wall (red arrows) and reduced LV cavity (yellow arrowhead).

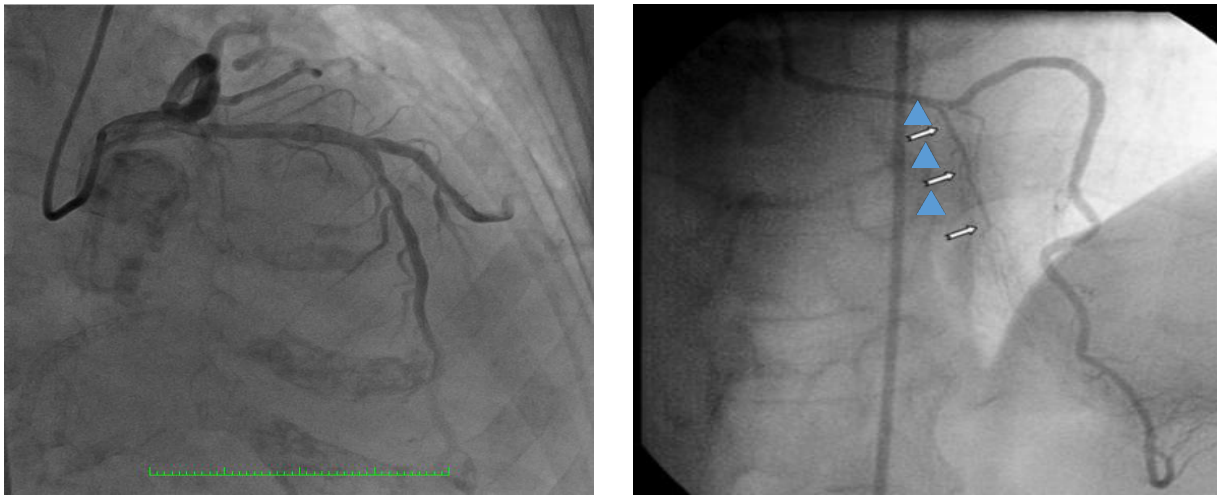

Figure 3. (A) Coronary angiography of the patient showing the left anterior descending artery (arrow) which was a good-sized vessel, with no significant stenosis but with absent first (major) septal perforator branch. (B) Normal major septal perforator (yellow arrowheads) originating from the long LAD from a 52 year-old female (11).

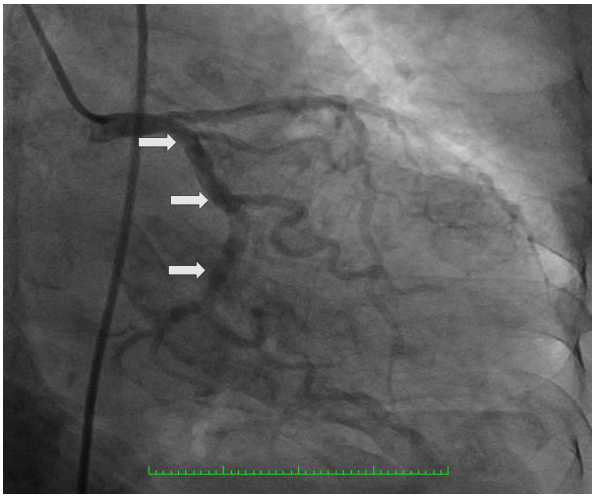

Figure 4. Coronary angiography showing the left circumflex coronary artery which was a good-sized vessel with no significant stenosis (arrows)

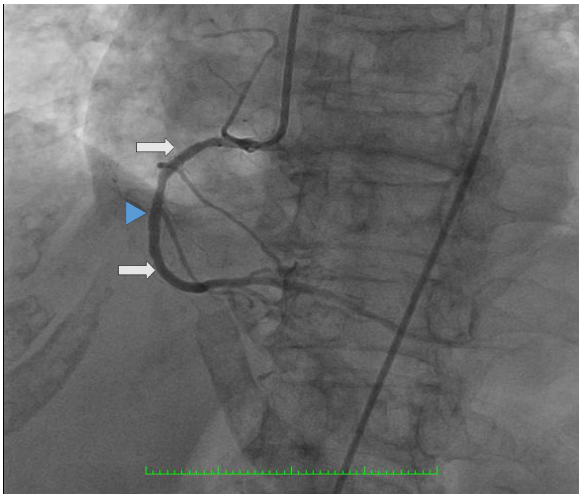

Figure 5. Coronary angiography showing the right coronary artery (RCA) (red arrows) which was a good-sized vessel with patent stent at the proximal to mid segment (arrowhead) with good flow and with no significant stenosis

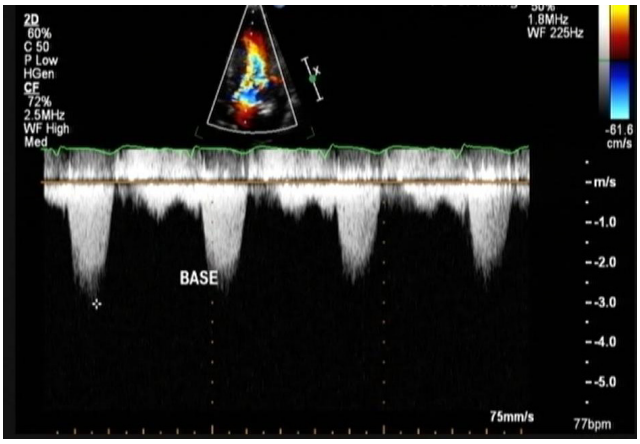

Figure 6. Color flow Doppler study of the patient showing a peak instantaneous gradient of 37 mmHg at post-implantation of dual chamber pacemaker. (This was previously described as 194 mmHg before implantation of pacemaker)

DISCUSSION

Treatment Strategies in Hypertrophic Cardiomyopathy. The American College of Cardiology/European Society of Cardiology, and American Heart Association has recommended surgical septal myectomy as the preferred primary management option for patients with HCM with severe drug-refractory NYHA class III/IV symptoms and those with obstruction to LV outflow under basal conditions with physiologic exercise (±50 mmHg).[2,3,10] The objective of surgery is the reduction in heart failure symptoms and improved quality of life, by virtue of relieving the SAM and outflow obstruction, and normalizing LV pressures. In patients who underwent surgery, 95% of patients experienced permanent eradication of the basal outflow gradient and 85% experienced symptom relief during periods of up to 25 years. [2,3,10] Surgery is not recommended in patients who are asymptomatic or mildly symptomatic because of the lack of conclusive evidence that prophylactic relief of obstruction is advantageous. Its operative mortality has decreased steadily and is now less than 1% at selected myectomy centers.[12]

Alcohol septal ablation is an alternative to myectomy and involves injection of 1 to 3 ml of 95% alcohol into a major septal perforator coronary artery to create necrosis and a permanent transmural myocardial infarction localized to the proximal ventricular septum which leads to progressive thinning and restricted basal septal excursion, and reduction in LV outflow tract gradient. ASA is considered an alternative treatmetn modality to septal myectomy in the following settings: (1) patients whose symptoms limit daily activities (functional class III or more, or exercise-induced syncope) despite medical therapy or if medical therapy cannot be tolerated; (2) patients with a significant level of outflow obstruction (i.e. pressure drop >50–60 mmHg with provocation by a Valsalva maneuver, bicycle stress, or postextrasystolic augmentation); (3) patients with a suitable left

ventricular and coronary morphology, that is, those with a "classical," subaortic obstruction produced by the protruding septum and the "SAM" of the mitral valve and one or more septal perforator arteries that serve the septal area. Several published studies on alcohol septal ablation demonstrated immediate reductions in the mean resting LVOT gradient from 65 to 17 mmHg and the mean post-extrasystolic gradient from 125 to 53 mmHg, with persistence of reduction even after 12 months of treatment (16 and 32 mmHg, respectively).[13] Meta-analyses have indicated no difference between septal ablation and myectomy in the medium-term incidence of SCD or all-cause mortality.[13]

Dual-chamber pacemaker implantation was proposed as an alternative treatment for patients with severe symptomatic obstructive HCM. Although the exact mechanism of improvement with pacing remains unknown, the decrease in gradient may be caused by timing of septal contraction but may also reflect long-term remodeling. Although there was an initial enthusiasm for dual-chamber pacing as a primary treatment for patients with obstructive HCM, subsequent RCTs demonstrated long-lasting beneficial results in only a small minority of patients.[14,15] The overall success rate in symptom relief and gradient reduction is significantly lower compared to those patients who undergo septal myectomy.[14,15] The mean residual gradient after septal myectomy is 10 mmHg compared with a 40 to 50 mmHg gradient after dual-chamber pacing.[14,15] Patients >65 years of age may be a subgroup who achieve the greatest benefit.[14]

Individualizing Treatment Options. In our case, the patient was appraised for surgical myectomy. However, she refused surgery and opted for an alternative, less invasive option – alcohol septal ablation. Unfortunately, on coronary angiography, there was absence of major septal perforator coronary anatomy rendering her unsuitable for ASA. Consequently, an alternate option (dual chamber pacing) was offered with the goal of reducing the LV outflow tract gradient and improvement of symptoms. The absence of septal perforator branches of the left anterior descending artery was described by Angelini et al. in 1999 and classified under "other anomalies" with an incidence of 0.27% using 1950 coronary angiograms.[16] While the first septal perforator branch of the left anterior descending artery (LAD) is the typical channel for ASA, HCM patients with severe septal hypertrophy may rarely present with unusual septal perforator anatomy.[17] The absence of septal perforator coronary arteries in these patients render them unsuitable for ASA.[3]

Outcome and Follow-up. She underwent the dual chamber pacemaker implantation as alternate to ASA and documented immediate significant reduction in the peak instantaneous gradient across the basal segment and obliteration of the systolic anterior motion of the mitral valve. There was also noted improvement in overall systolic function. These hemodynamic changes were coupled with symptomatic improvement as the patient remained stable and asymptomatic after implantation. Five months post-implantation of dual chamber pacemaker, the patient had an outpatient follow-up and was reported to have absence of symptom recurrence since she was discharged.

CONCLUSION

We presented a case of hypertrophic cardiomyopathy with angiographically-absent major septal perforator branch of the left anterior descending coronary artery (LAD) treated with dual chamber pacemaker implantation to reduce the LV outflow gradient. To our knowledge, our case is not only the first reported angiographically-absent first septal perforator coronary anatomy in the setting of hypertrophic cardiomyopathy, but also the first description of dual chamber pacemaker implantation to relieve the LVOT obstruction.

Although the role of dual-chamber pacing has become limited in HCM because surgical myectomy has set the standard for therapy and alcohol septal ablation has been accepted as suitable alternative, this modality remains essential and may still be considered as the the treatment strategy of choice in patients who refuse surgery and who are not suitable for alcohol septal ablation.

REFERENCES

1. Mann DL, Zipes DP, Libby P, Bonow RO. Braunwald's heart disease: a textbook of cardiovascular medicine. 10th ed. Philadelphia: Elsevier; 2014. p.1574-88.
2. Maron BJ, Maron MS. Hypertrophic cardiomyopathy. Lancet. 2013 Jan 19; 381(9862):242-55.
3. Maron BJ, McKenna WJ, Danielson GK, Kappenberger LJ, Kuhn HJ, Seidman CE, et al. Task Force on Clinical Expert Consensus Documents. American College of Cardiology; Committee for Practice Guidelines. European Society of Cardiology. American College of Cardiology/European Society of Cardiology. clinical expert consensus documents of hypertrophic cardiomyopathy. A report of the Americal College of Cardiology Foundation Task Force on Clinical Expert Concensus Documents and the European Society of Cardiology Committee for Practice Guidelines. J Am Coll Cardiol. 2003 Nov 5;42(9):1687-713.
4. ten Cate FJ, Soliman OI, Michels M, Theuns DA, de Jong PL, Geleijnse ML, et al. Long-term outcome of alcohol septal ablation in patients with obstructive hypertrophic cardiomyopathy: a word of caution. Circ Heart Fail. 2010 May; 3(3):362-9.
5. Nishimura RA, Ommen SR. Septal reduction therapy for obstructive hypertrophic cardiomyopathy and sudden death: what statistics cannot tell you. Circ Cardiovasc Interv. 2010 Apr;3(2):91-3.
6. Valeti US, Nishimura RA, Holmes DR, Araoz PA, Glockner JF, Breen JF, et al. Comparison of surgical septal myectomy and alcohol septal ablation by cardiac magnetic resonance imaging in patients with hypertrophic obstructive cardiomyopathy. J Am Coll Cardiol. 2007 Jan 23;49(3):350-7.
7. Fananapazir L, Epstein ND, Curiel RV, Panza JA, Tripodi D, McAreavey D. Long-term results of dual-chamber (DDD) pacing in obstructive hypertrophic cardiomyopathy. Evidence for progressive symptomatic and hemodynamic improvement and reduction of left ventricular hypertrophy. Circulation. 1994 Dec; 90(6):2731– 42.
8. Jeanrenaud X, Goy JJ, Kappenberger L. Effects of dual-chamber pacing in hypertrophic obstructive cardiomyopathy. Lancet. 1992 May 30;339(8805): 1318–23.
9. McDonald K, McWilliams E, O'Keeffe B, Maurer B. Functional assessment of patients treated with permanent dual chamber pacing as a primary treatment for hypertrophic cardiomyopathy. Eur Heart J. 1988 Aug; 9(8):893–8.
10. Gersh BJ, Maron BJ, Bonow RO, Dearani JA, Fifer MA, Link MS, et al. American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines; American Association for Thoracic Surgery; American Society of Echocardiography; American Society of Nuclear Cardiology; Heart Failure Society of America; Heart Rhythm Society; Society for Cardiovascular Angiography and Intervention; Society of Thoracic for Surgeons. 2011 ACCF/AHA guideline for the diagnosis and treatment of hypertrophic cardiomyopathy: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2011 Dec 13;124(24):e783-831.
11. Moreno-Martínez FL, Vega L, Fleites H, Ibargollin R, Gonzalez R, Lopez O. Dual left anterior descending coronary artery. Internet J Thorac Cardiovasc Surg. 2004 [cited 2015 Mar 25];7(1). Available from: URL: https://ispub.com/IJTCVS/7/1/11944
12. Maron BJ. Controversies in cardiovascular rmedicine. Surgical myectomy remains the primary treatment option for severely symptomatic patients with obstructive hypertrophic cardiomyopathy. Circulation. 2007 Jul 10;116(2):196-206.
13. Leonardi RA, Kransdorf EP, Simel DL, Wang A. Meta-analyses of septal reduction therapies for obstructive hypertrophic cardiomyopathy: comparative rates of overall mortality and sudden cardiac death after treatment. Circ Cardiovasc Interv. 2010 Apr;3(2):97–104.
14. Maron BJ, Nishimura RA, McKenna WJ, Rakowski H, Josephson ME, Kieval RS. Assessment of permanent dual-chamber pacing as a treatment for drug-refractory symptomatic patients with obstructive hypertrophic cardiomyopathy. A randomized, double-blind, crossover study (M-PATHY). Circulation. 1999 Jun 8; 99 (22):2927–33.
15. Nishimura RA, Trusty JM, Hayes DL, Ilstrup DM, Larson DR, Hayes SN, et al. Dual-chamber pacing for hypertrophic cardiomyopathy: a randomized, double-blind, crossover trial. J Am Coll Cardiol. 1997 Feb; 29 (2):435– 41.
16. Angelini P, Villason S, Chan AV Jr, Diez JG. Coronary artery anomalies: a comprehensive approach [online]. Philadelphia: Lippincott Williams & Wilkins; 1999 [cited 2015 Mar 25]. Available from: URL: http://digitalcommons.library.tmc.edu/cgi/viewcontent.cgi?article=1005&context=angelini.
17. Choi D, Dardano J, Naidu SS. Alcohol septal ablation through an anomalous right coronary septal perforator: first report and discussion. J Invasive Cardiol. 2009 Jun;21(6):e106–9.

A Case of Pulmonary Embolism Presenting as Transient Loss of Consciousness

Jeru Faisal L. Usman, MD

Background --- Venous thromboembolism encompasses pulmonary embolism and deep vein thrombosis. Pulmonary embolism increase in frequency with age but can afflict both young and elderly persons. Such occurrence with a previously healthy young adult without any known risk factor is very isolated.
Case Study --- A 26 year old male was admitted due transient loss of consciousness lasting for 1-2 minutes while playing basketball, this was associated with dyspnea and hemoptysis. No other signs and symptoms were noted such as chest pain, palpitation or seizure episode. Patient works as a company electrician, non-smoker, non alcohol drinker, no known comorbids, denies any history of elicit drug use or sexually transmitted infection. Upon examination, patient was tachypneic, tachycardic, with neck vein engorgement, JVP of 10 cm-H2O with RV heave and a palpable P2. 2D echo with doppler was done and revealed a dilated right ventricle withhypokinesia of the right ventricular free wall and depressed systolic function, flattening of the interventricular septum during systole, dilated main pulmonary artery and echogenic density was noted at the main pulmonary artery before the bifurcation measuring 3.5 x 1.8 cm. Findings were consistent with pulmonary embolism with thrombus at the main pulmonary artery. Subsequent Computed Tomography of the pulmonary arteries revealed acute bilateral pulmonary embolism. Patient was then started on anticoagulation and workup for hypercoagulopathy and Malignancy will be done.
Conclusion--- In patients presenting with transient loss of consciousness, it is important to rule out pulmonary embolism even when there is a non-high probability (Wells score < 4). Together with the history and physical examination, ancillary procedures such as 12L – ECG, 2D echo with Doppler, CT- scan and biomarkers, PE can be diagnosed accurately in order to start early appropriate therapy and eventually decrease mortality among VTE. ***Phil Heart Center J 2021;24(1):15-17.***

Key Words: ■ Venous Thromboembolism ■ Pulmonary Embolism ■ Deep Venous Thrombosis

Pulmonary Embolism (PE) and Deep Vein Thrombosis (DVT) together constitute one of the "big three" cardiovascular diseases, the other two being myocardial infarction (MI) and stroke. PE and DVT increase infrequency with age but afflict children and teenagers as well as elderly persons.[1] Intertwining risk factors and pathophysiology linking Venous Thromboembolism (VTE) and atherosclerosis.[2] This is a case of a 26 year old male presented with transient loss of consciousness due to pulmonary embolism, apparently healthy with no known risk factors for VTE.

Case: A case of a 26 year old male, single, electrician, Filipino. The present condition started 1 month prior to admission when the patient experienced dyspnea and transient loss of consciousness while playing indoor basketball for around 15 minutes. On the subsequent days patient notes exertionaldyspnea and easy fatigability, palpitations and hemoptysis. No other signs and symptoms were noted such as chest pain, fever or other signs and symptoms. Patient is a non-smoker, non-alcohol drinker, no known comorbids and with family history of hypertension. Upon examination, patient was tachypneic, tachycardic, with neck vein engorgement, JVP of 10 cmH_2O with RV heave and a palpable P2. 12 L ECG revealed sinus tachycardia, biatrial abnormality, right axis deviation, right ventricular hypertrophy, persis-

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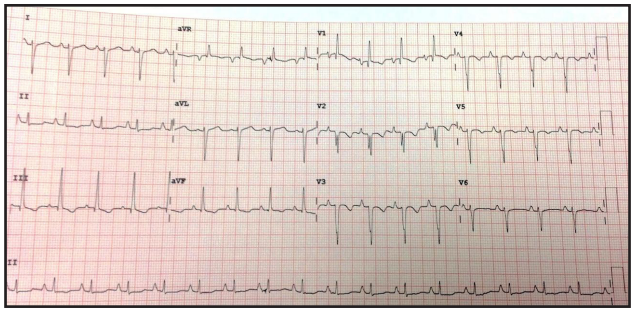

Figure 1. 12 L ECG revealed sinus tachycardia, Right axis deviation, Biatrial abnormality, Right ventricular hypertrophy, persistent posterobasal forces, with a deep s wave at lead I, q wave and t wave inversion at lead 3 and V1 to V4.

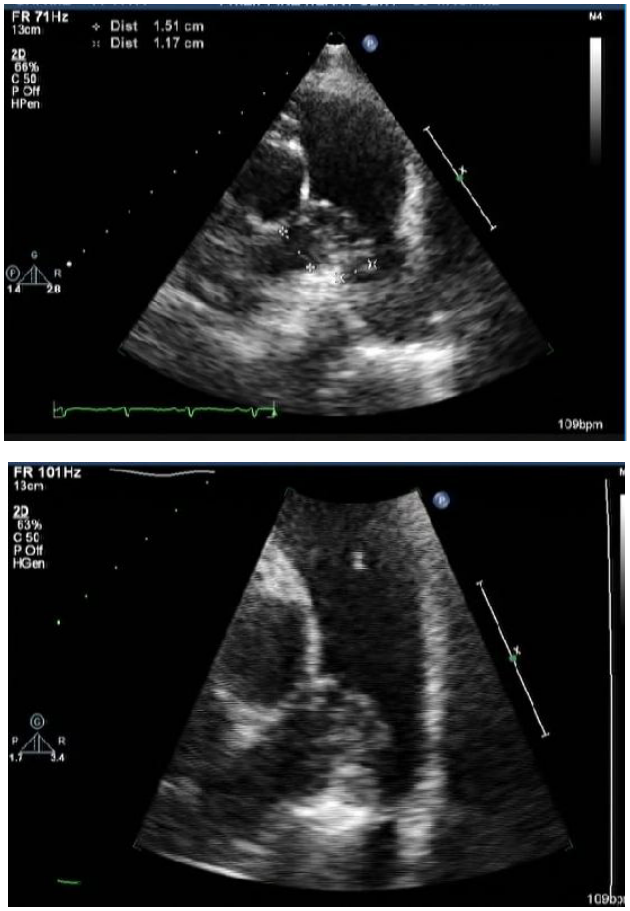

Figure 2 and 3. Dilated main pulmonary artery and echogenic density was noted at the main pulmonary artery before the bifurcation measuring 3.5 x 1.8 cm.

tent posterobasal forces, with a deep s wave at lead I, Q wave and t wave inversion at lead 3 and V1 – V4. (*Figure 1*). 2D echo with doppler was done and revealed a dilated right ventricle with hypokinesia of the right ventricular free wall and depressed systolic function, flattening of the interventricular septum during systole, dilated main pulmonary artery and echogenic density was noted at the main pulmonary artery before the bifurcation measuring 3.5 x 1.8 cm. *(Figure 2 and 3*). Findings were consistent with pulmonary embolism with thrombus at the main pulmonary artery. Subsequent Computed Tomography of the pulmonary arteries revealed acute bilateral pulmonary embolism. Patient was started on anticoagulation with unfractionated heparin and titrated to target INR. Workup for hypercoagulable states will be done 3 months after treatment.

DISCUSSION

We deal with transient loss of consciousness everyday at our clinical practice, at the clinic, at the emergency room or even during in hospital admission. In order to diagnose properly we need to do a systematic history taking and physical examination and emphasis must be done on the risk factors that accompany our patient in order to narrow down or differential diagnosis. Regarding our patient, no pertinent risk factors for thromboembolism is present, but due to thorough physical examination and with the help of ancillary procedures we came up with a correct diagnosis. The incidence of VTE is approximately 1.5 cases per 1000 person-years, and DVT cases are approximately twice as numerous as PE cases. Incidence increases with age and equally affecting men and women. VTE aggregates in families. Clinical predictors of fatal PE include black race[3], obesity, anatomically massive PE, neurologic disease, age older than 75 years, and cancer.[4]

Classification of acute PE can assist with prognostication and clinical management.[3] Massive PE accounts for 5% to 10% of cases. Submassive PE is more common, occurring in approximately 20% to 25% of patients. Low-risk PE constitutes the majority of PE cases - approximately 70%. Anticoagulation usually with unfractionated heparin is the cornerstone

in medical therapy for pulmonary embolism. Advance therapy should be considered such as systemic thrombolysis, surgical embolectomy, pharmacomechanical catheter directed theraphy or inferior vena cava filter. Risk stratification is very important in order to come-up with an appropriate management.

The Pulmonary Embolism Severity Index score (PESI) is used in order to stratify patient with P.E. Our patient has a PESI score of 80 (Class 2) and is considered as low risk. High risk patients is best managed by thrombolysis or embolectomy plus anticoagulation and low risk patient are managed by anticoagulation alone. As for the duration of anticoagulation, it is important to label patient with VTE as provoked and unprovoked. For provoked patient the duration of anticoagulation is 3 months and for unprovoked like in our patient, it recommended to extend the duration of anticoagulation to more than 3 months. Above all it is important to rule out the possible cause of the occurrence of PE in our patient in order to minimize or to prevent the reccurence of VTE. But it is important to note that approximately half of the cases are idiopathic, occurring without antecedent trauma, surgery, immobilization, or cancer.

CONCLUSION

In patients presenting with transient loss of consciousness, it is important to rule out pulmonary embolism even when there is a non-high probability (Wells score < 4). Together with the history and physical examination, ancillary procedures such as 12L – ECG, 2D echo with Doppler, CT- scan and biomarkers, PE can be diagnosed accurately in order to start early appropriate therapy and eventually decrease mortality among VTE.

REFERENCES

1. Patocka C, Nemeth J: Pulmonary embolism in pediatrics. J Emerg Med 42:105, 2012.
2. Piazza G, Goldhaber SZ: Venous thromboembolism and atherothrombosis: An integrated approach. Circulation 121:2146, 2010.
3. Tang Y, Sampson B, Pack S, et al: Ethnic differences in out-of-hospital fatal pulmonary embolism. Circulation 123:2219, 2011.
4. Laporte S, Mismetti P, Decousus H, et al: Clinical predictors for fatal pulmonary embolism in 15,520 patients with venous thromboembolism: Findings from the RegistroInformatizado de la EnfermedadTrombo Embolicavenosa (RIETE) Registry. Circulation 117:1711, 2008

Yamaguchi Syndrome: Apical Hypertrophic Cardiomyopathy Initially Presenting as Acute Atrial Fibrillation in a 38 Year Old Filipino Male

Jason Roy M. Bacani, MD; Myla Gloria Salazar-Supe, MD

Background --- Yamaguchi Syndrome or apical hypertrophic cardiomyopathy is an autosomal dominant disease that is common among Japanese but relatively rare among Caucasians and non-Japanese population, however its exact incidence among Filipinos is not yet established. Its clinical manifestation is due to impaired ventricular relaxation. It has a relatively benign course but it is still associated with morbidities dictated by three adverse pathways: sudden cardiac arrest, congestive heart failure with preserved ejection fraction or atrial arrhythmias and its complications including stroke.[1]

Case --- We are presenting a case of a 38 year old Filipino male who initially presented as acute atrial fibrillation complicated by transient ischemic attack and on further work up revealed the presence of apical hypertrophic cardiomyopathy or known as Yamaguchi Syndrome.

Conclusion --- This case report is not just to emphasize the rarity of the case but also endeavours to establish a registry for Filipino patients with Yamaguchi Syndrome in order to determine the natural course of this disease among the Filipino population. ***Phil Heart Center J 2021;24(1):18-20.***

Key Words: ■ Yamaguchi Syndrome ■ Apical Hypertrophic Cardiomyopathy (AHCM) ■

Apical hypertrophic cardiomyopathy is an uncommon phenotype of hypertrophic cardiomyopathy (HCM), it is otherwise called as Yamaguchi's disease earliest reported by Sakamoto in 1976.[1,2] It is an autosomal dominant disease with variable penetration. It is common in Japan and estimated to represent 25% of Japanese patients with HCM. However, it has been identified in only 0.2-2% of HCM patients among Caucasians and non-Japanese population.[2,3]

The incidence of Yamaguchi Syndrome is not yet well established among Filipinos, at the time of this writing, no locally published data supports its prevalence. In order to prospectively monitor the outcome patients it is relevant to establish a local registry that will compare if the incidence is tantamount to that of the Japanese population or to the Western race.

Case: This is a case of a 38 year old Filipino male who complained of tolerable exertional dyspnea of about 1 year duration, until 3 months prior to consult, patient had left-sided weakness prompting consult and was admitted in a tertiary hospital with an initial impression of CVD, Acute Infarct probably cardioembolic. Pediatric and family histories are unremarkable. Physical examination on admission are as follows - BP: 110/70 HR: 120' s irregularly irregular, RR: 18, cardiac examination revealed apex beat at the 5th intercostals space left midclavicular line, variable SI and a grade 2/6 holosystolic blowing murmur at the apex. Neurologic examination revealed 5/5 motor strength in all extremities and other parts of the physical examination are unremarkable.

Baseline diagnostics are as follows: Head CT Scan was unremarkable; 12L EKG revealed atrial fibrillation in rapid ventricular response,

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left ventricular hypertrophy with deep T-wave inversion at V3-V5, and initial 2D echocardiogram revealed concentric LVH with normal wall motion, systolic function and contractility. There was no residual weakness and was discharged improved. However, he still had bouts of worsening exertional dyspnea becoming more intolerable. Due to the incongruence of symptoms in relation to previous diagnostics, a repeat 12L ECG was requested and dobutamine stress echocardiography was preferred over treadmill stress test due to the presence of LVH with the following results: hypertrophied apical anterolateral left ventricular free wall with obliteration of the apical lumen during systole, normal ejectionfraction, with normal wall motion, contractility and systolic function. He was referred to the Electrophysiology Team and started on Amiodarone for rate and rhythm control. He clinically improved and presently is NYHA Class 1. He is maintained on oral anticoagulant for stroke prevention (CHADS2: 2). He was further worked up with a 24-hour holter monitoring to document atrial or ventricular ectopies, but was unremarkable.

DISCUSSION

The symptomatology of patients with apical HOCM is explained by impaired ventricular relaxation resulting in a reduced rate and volume during the rapid filling period of diastole, thus a resultant compensatory increase in atrial systolic filling occurs. Thus with the progressive increase in size of the left atrium, the propensity to develop atrial fibrillation also increases, eventually resulting to severe hemodynamic deterioration.[1]

Electrocardiograms reveal left ventricular hypertrophy and giant T-waves defined as T inversion >10mm[2,4] that could be mistaken or mimic an acute coronary syndrome.[5] Transthoracic echocardiogram which will reveal "ace-of-spades" configuration, is universally accepted as the first-line imaging modality in investigation of patients with suspected apical hypertophic cardiomyopathy, due to its non-invasiveness, versatility, and well-established cost benefit ratio.[4]

Apical HCM has a typically benign course with average age of presentation of 41.4 ± 14.5 years.[5] Unlike patients with hypertrophic obstructive cardiomyopathy, patients with AHCM generally have benign outcomes, and sudden cardiac death is rare. In the study by Eriksson et.al., they were able to note that on long term follow-up of the following, cardiovascular mortality was 1.9% (2/1 05); annual cardiovascular mortality was 0.1, and a good overall survival rate of 95% at 15 years. North American patients with AHCM have low long term cardiovascular mortality but nearly one third of patients have increased cardiovascular morbidity. Major morbid events were identified in 30% of the study population, the most frequent being atrial fibrillation (12%) and myocardial infarction (10%). Three predictors of cardiovascular morbidity were identified: age at presentation <41 years, left atrial enlargement, and New York Heart Association (NYHA) class > or = II at baseline[5] In the case report of Imdad et.al, they reported 2 patients went into cardiac arrest due to occurrence of malignant arrhythmias.[1] These isolated cases shed light that AHCM might also predispose malignant arrhythmias thus the rationale of doing 24-hour holter monitor in our patient.

Generally, no treatment is needed.[3] Symptoms of angina and exertional dyspnea are well controlled with medical therapy like beta blockers and calcium channel blockers, but still are debatable.[6]

CONCLUSION

We reported a case of Yamaguchi Syndrome in a 38 year old Filipino male who initially presented with acute atrial fibrillation that was complicated with a transient ischemic attack. He had the typical symptoms of having diastolic dysfunction that was aggravated because of the concomitant atrial fibrillation. Apical HCM is still relatively rare among Filipinos. It should be considered as a differential diagnosis in patients initially presenting as atrial arrhythmias with associated giant inverted T waves. However,

these ECG findings may also be seen in other clinical conditions thus further elucidating the need to search for an underlying cause. 2D echocardiogram is still valuable in diagnosing apical HCM but warrants keenness in its identification. Indeed most literatures state that this type of cardiomyopathy has a benign course, but its natural history has not been established in the Filipino population. No definitive management has been documented, but the present management for our patient is directed in ameliorating the symptoms to improve his quality of life and to prevent associated complications.

Therefore this report was done not just to emphasize the rarity of the case but also endeavours to establish a registry for Filipino patients with Yamaguchi Syndrome that will influence the counseling and management of Filipino patients with AHCM.

REFERENCES

1. Ahmed I, Smalley SJ, Zhu DX, Dahiya R, House, CM, Nelson WB. Findings that shed new light on the possible pathogenesis of a disease or an adverse effect sudden cardiac arrest in apical hypertrophic cardiomyopathy. BMJ Case Rep. 2009 Sept.
2. Sakamoto T, Tei C , Murayama M, Ichiyasu H, Hada Y. Giant T wave inversion as a manifestation of asymmetrical apical hypertrophy (AAH) of the left ventricle. Echocardiographic and ultrasonocardiotomographic study. Jpn Heart J. 1976 Sept;17(5):611-29.
3. Suwa K, Hiroshi Satoh H, Sano M, Nobuhara M, Saitoh, T, Saotome M. Functional, morphological and electrocardiographical abnormalities in patients with apical hypertrophic cardiomyopathy and apical aneurysm: correlation with cardiac MR. BMJ. 2014 March; 1(1): 1-9.
4. Yusuf K, Manne JR, Epperla N, Bapani S, Garcia-Montilla R. Apical hypertrophic cardiomyopathy presenting as recurrent unexplained syncope. Clin Med Res. 2012, February; 10(1): 2-31.
5. Lakshmanadoss U, Kulkarn A, Balakrishnan S, Shree N, Harjai K, Jagasia D. All that glitters is not gold: apical hypertrophic cardiomyopathy mimicking acute Coronary Syndrome. Cardiology Research, 2012, June;3(3):137-139.
6. Eriksson MJ, Sonnenberg B, Woo A, Rakowski P, Parker TG, Wigle ED, Rakowski H. Long-term outcome in patients with apical hypertrophic cardiomyopathy. J Am Coll Cardiol. 2002 Feb 20;39(4):638-45.

Diagnosis and Treatment of Ruptured Mycotic Infrarenal Aortic Aneurysm Secondary to Salmonella Species

Bryan Rene Toledano, MD; Emily Mae Yap, MD; Warren S. Rondilla, MD; Joel Paz, MD

Background --- Ruptured infected aortic (mycotic) aneurysm is a rare and life-threatening condition, early and proper initiation of antibiotics aside from aneurysmal repair is of paramount importance. The typhidot IgG and IgM as a supportive test might help with this dilemma, especially in negative blood culture and while waiting for aortic sample result.

Case --- A 47-year-old male Filipino with type 2 diabetes mellitus presented with severe back pain for 1 month and intermittent fever for 3 weeks. There was worsening of the back pain prompting consult. Complete blood count showed anemia and leukocytosis with predominance of neutrophils. On Computed Tomography Aortogram a segmental calcification and wall discontinuity in the right posterolateral wall of the infrarenal abdominal aorta with heterogenous collection in the retroperitoneal region was seen and aortic rupture secondary to mycotic aneurysm was considered. He underwent emergency abdominal aortic aneurysm repair with debridement, antibiotic lavage, aortoiliac grafting, anastomosis and omental packing. The typhidot IgG and IgM test was positive and was given Ceftriaxone 2gm/IV every 24 hours for six weeks. Blood cultures did not reveal significant growth of any pathogen. The aortic wall culture showed heavy growth for salmonella species sensitive to the antibiotic used, confirming and guiding the management. He was then discharged improved.

Conclusion --- Aside from the standard blood, aortic wall cultures, the typhidot test can also be a valuable tool for supportive diagnosis of salmonella as a cause for mycotic aortic aneurysm which can lead to early and proper initiation of antibiotics. ***Phil Heart Center J 2021;24(1):21-25.***

Key Words: ■ Mycotic aneurysm ■ abdominal aortic rupture ■ typhidot

Salmonella is an intracellular gram-negative bacteria that commonly affects the intestines. It may spread to the bloodstream and to other body sites. The aortic vasculature may be affected, notably the infrarenal aorta. Although uncommon, Salmonella has been reported in literature to cause aortic rupture with aneurysm.[1-2]

The prevalence of mycotic aneurysm is only 0.7 to 2.6% (3) and 40% is secondary to Salmonella[4,5] highlighting its rarity. The current epidemiology typically involves diabetic men who are between 50-70 years old with an atheromatous or aneurysmal aortas.[6]

Case: We report a case of a 47-year-old Filipino male engineer who was admitted due to severe tearing back pain associated with abdominal pain for about a month. He has also been complaining of on-and-off fever for three weeks. He has no known comorbid illnesses. He has been a 30-pack year cigarette smoker and regularly indulges in street food. Consult was sought at a local clinic. Complete blood count showed a normal leukocyte count (WBC 8.14, Neutrophils 74.5%, lymphocytes 16%), normal haemoglobin and hematocrit levels (14.4 g/dL and 43.4% respectively) and a normal platelet count (274 x103uL). Chest x-ray revealed hazy densities in the left lower lung suggestive of pneumonia. Lumbar spine x-ray showed spondylosis at L3-L4. Urinalysis showed pyuria (WBC 33/HPF), hematuria (RBC 42/HPF). Urine culture was taken which did not reveal any growth. Whole abdominal ultrasound was unremarkable.

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He was managed as a case of complicated urinary tract infection and community acquired pneumonia. Levofloxacin 750mg/tab 1 tab once a day was given for one week and Paracetamol 325 mg/tab, Tramadol 37.5 mg/tab thrice a day were given for pain. Morphine 15mg tablet 1 tablet 3x a day was added for breakthrough pain. HBA1C was taken which was high (9.8%). Oral anti-diabetic medications were started. There was persistence of pain, which prompted further work-up.

Whole abdominal CT scan was done which revealed a saccular aneurysm arising from the infrarenal abdominal aorta with evidence of rupture. A CT angiogram of the aorta was then done which showed segmental calcification and wall discontinuity in the right posterolateral wall of the infrarenal aorta at the prebifurcation level with active extravasation of contrast material in the retroperitoneal region (extending from L3 level down to L5-S1 level) measuring 16.8 x 6.8 x 7.4 cm with approximate volume of 440 cc. (*Figure 1*). Because of these findings, he was then immediately transferred to our institution.

On admission, the patient complained of severe back and abdominal pain. He was in respiratory distress with the following vital signs: BP 100/70 mm Hg, HR104 bpm, RR 28 cpm, T 38.3, O2 sat 99% at room air. He had pale palpebral conjunctivae. The abdomen was soft with direct tenderness at the right lower quadrant. Complete blood count revealed anemia (Hgb 85g/L, Hct 26%), leukocytosis with neutrophilic predominance (WBC 14.7 neutrophil 75%) and 693 platelet count. He was started on Piperacillin-Tazobactam 4.5gm/IV every 6 hours. He underwent emergency abdominal aortic aneurysm repair, debridement, antibiotic lavage, aortoiliac grafting, anastomosis and omental packing of aneurysmal sac space. (*Figure 3*). Operative findings include an infrarenal pseudoaneurysm with point of rupture at the right posterolateral aspect. There was hematoma and fibrinous material within. Tissue samples were taken from the aortic wall for histopathology and for culture.

Post-operatively, septic work-up was done. Blood cultures did not reveal any significant growth. Treponema pallidum particle agglutination test was negative. Typhidot was positive for both IgM and IgG antibodies, the antibiotic was then shifted to Ceftriaxone 2gm/IV every 24 hours. Salmonella infection was considered the likely cause of the prolonged history of fever. Gram stain of the aortic wall did not show any microorganisms. However, there was heavy growth of Salmonella species on the tissue culture, which was sensitive to Ceftriaxone, Amoxicillin, Ciprofloxacin and Trimetophrim sulfamethoxazole, which confirmed our diagnosis. Histopathology showed severe atherosclerosis with calcification. Defervescence ensued after Ceftriaxone was started. He was then discharged improved on out-patient antibiotic therapy. He completed a total of 6 weeks of antibiotic.

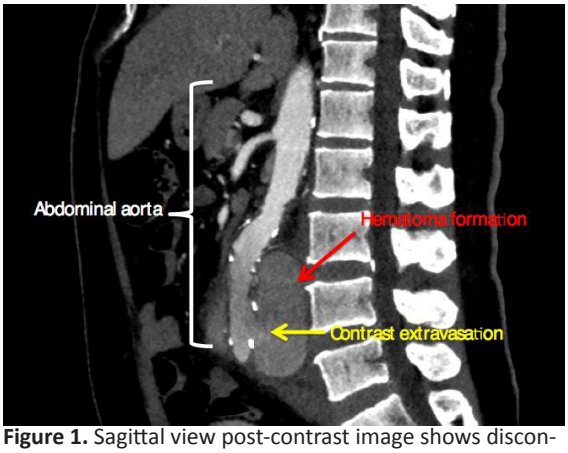

Figure 1. Sagittal view post-contrast image shows discontinuity of the wall of the infrarenal abdominal aorta and active contrast extravasation

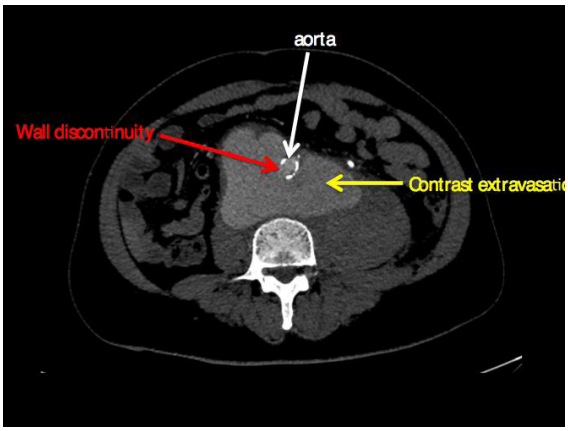

Figure 2. Axial view image shows discontinuity of the infrarenal aorta with active extravasation of contrast in the retroperitoneal region

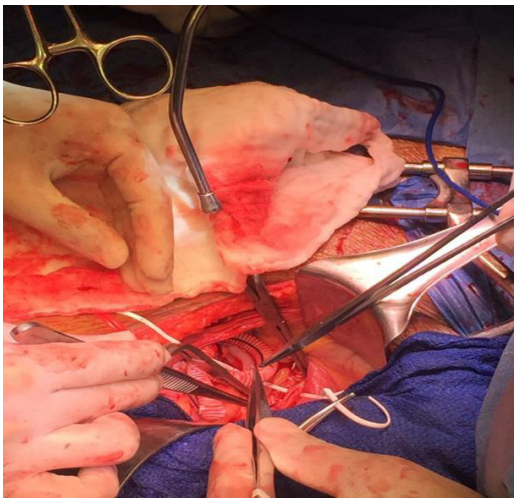

Figure 3. Axial view image shows discontinuity of the infrarenal aorta with active extravasation of contrast in the retroperitoneal region

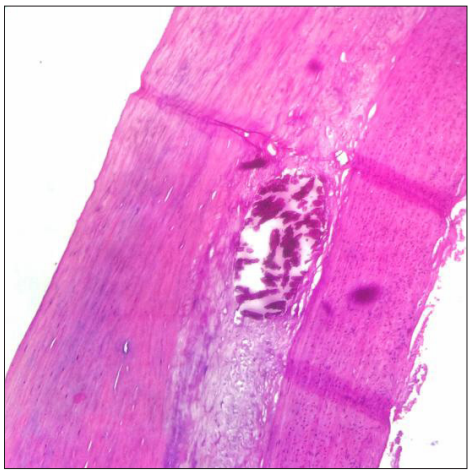

Figure 4. Vessel wall with areas of fibrosis, calcified atherosclerotic plaque and patchy areas of smooth muscle nuclei loss (H&E 100x)

Figure 5. Fragmentation and splitting of elastic fibers (Von Gieson Elastic 100x)

DISCUSSION

Infected aortic aneurysm accounts for less than 1% of all aneurysm undergoing surgery. It can have a fulminant course with frequent aneurysm rupture (>50%) and a high mortality rate of up to 50%.[1] The classic triad includes fever abdominal, back or chest pain and a pulsatile tender mass.[7] A high index of suspicion is needed in order to diagnose and treat patients before complications arise. Blood cultures are requested when an infectious cause of aortitis is considered. Staphyloccous aureus, Streptococcus species and Salmonella typhi are the most commonly isolated organisms.[8] Culture-negative cases can confound the diagnosis. This setting is common among those who were given empiric antibiotics before blood cultures were taken, similar to our case. Many studies have already reported cases of mycotic aneurysms with negative blood culture results.[14-16] These cases may account for misdiagnosis and deaths confirmed through autopsy. Furthermore, the sensitivity of blood culture was reported to be only 66 % (95 % CI 56–75 %) compared to bone marrow culture as reference standard in diagnosis of salmonella infection in the study of Mogasale et al.[9] In our case, Typhidot was used to support our suspicion, the positive IgM and IgG antibodies are consistent with a recent salmonella infection. This test, which has been recommended by the Philippine Society for Microbiology and Infectious Disease, is a rapid dot-enzyme immune assay, which detects antigen of Salmonella enterica serotype Typhi.[10,11] The utility of this test was also supported by studies done by Dinkar et al.[12] and Sanjeev et al.,[13] in which the Typhidot test showed a high sensitivity and good specificity for the diagnosis of Salmonella infection, with blood cultures used as the reference standard. It is important to note that in both studies, the Typhidot test has the highest positive result in relation to the total number of patients with a clinical diagnosis of typhoid fever and offers an advantage of early and rapid diagnosis.[12,13]

For mycotic aneurysm, the isolation of the organism from the aorta or aortic thrombus is still the confirmatory test.[1] As of known, no studies compared the sensitivity and specificity of typhidot and blood culture to aorta or aortic

thrombus culture in the diagnosis of this kind of case. Soravia-Dunand et al. reported early surgical intervention as the treatment of choice since it greatly increases survival.[17] A mortality rate of 40% was reported in their study among those who underwent both medical management and surgical intervention, compared to medical management alone which has a significantly higher mortality rate of 96%.[17] Endovascular aortic repair was done in one case report on a patient with severe comorbidities with good outcome. This was performed on a patient who had good response to antibiotics and did not present with signs of gross purulence or fistula.[18]

Hsu et al. studied the clinical outcomes and risk factors of infected aortic aneurysm. Advanced age, non-salmonella infection and no operation were reported to be the major determinants of mortality.[3] All reported cases recommend the prompt initiation of empiric antibiotics, which should be continued for 6-8 weeks with frequent follow-ups.[19-21]

CONCLUSION

A ruptured mycotic aneurysm, although rare should be considered as one of the differential diagnosis in an adult diabetic male presenting with the usual symptoms of fever, abdominal and back pain with or without tender pulsatile mass. The typhidot test can also be a valuable tool for the rapid diagnosis of salmonella as the etiologic agent for the rupture of the mycotic aortic aneurysm. It can lead to early and proper initiation of antibiotics aside from the standard blood, aorta and aortic thrombus cultures.

REFERENCES

1. Mann DL. Zipes DP. Libby P. Bonow RO. and Braunwald, E. Braunwald's heart disease: a textbook of cardiovascular medicine. 11th ed. PA: Elsevier Saunders, c2015.
2. Gou Y, Xu T, Wang C, Wang J. Aortic Dissection with aneurysm associated with Salmonella infection. Euro J Inflammation. 2017. July 26;15(2):98-101.
3. Hsu RB, Chen RJ, Wang SS, Chu SH. Infected aortic aneurysms: clinical outcome and risk factor analysis. J Vasc Surg. 2004 Jul;40(1):30-5.
4. Aerts PD, van Zitteren M, Kotsopoulos AM, van Berge Henegouwen DP, Vriens PW, Heyligers JM. Infected abdominal aneurysm due to Salmonella sepsis: report of a unique case treated using the superficial femoral vein. Ann Vasc Surg. 2012 Feb;26(2):279.e5-7.
5. Brossier J, Lesprit P, Marzelle J, Allaire E, Becquemin JP, Desgranges P. New bacteriological patterns in primary infected aorto-iliac aneurysms: a single-centre experience. Eur J Vasc Endovasc Surg. 2010 Nov; 40(5):582-8.
6. Stephens CT, Pounds LL, Killewich LA. Rupture of a nonaneurysmal aorta secondary to Staphylococcus aortitis. Angiology. 2006 Aug-Sep;57(4):506-12.
7. Kao CJ, Chang WH, Choi WM. Salmonella aortic aneurysm: a patient with nonspecific type of low back and abdominal pain. Int J Gerontology. 2007 September; 1(3): 134-137.
8. Bennet JE. Dolin R, Blaser MJ. Mandell, Douglas and Bennett's principles and practice of infectious diseases. PA: Elsevier Saunders, c2015.
9. Mogasale V, Ramani E, Mogasale VV, Park J. What proportion of Salmonella Typhi cases are detected by blood culture? A systematic literature review. Ann Clin Microbiol Antimicrob. 2016 May 17;15(1):32.
10. Task Force on the Philippine clinical practice guidelines on the diagnosis, treatment and prevention of Typhoid Fever in adults. 2017.
11. Choo KE, Oppenheimer SJ, Ismail AB, Ong KH. Rapid serodiagnosis of typhoid fever by dot enzyme immunoassay in an endemic area. Clin Infect Dis. 1994 Jul; 19(1):172-6.
12. Dinkar JK, Kumar N, Chandrkishore. A comparable study of Widal and Typhidot (IgM and IgG specific assay): test in the diagnosis of enteric fever. IAIM, 2017;4(7): 126-130.
13. Sanjeev H, Nayak S, Pai Asha KB, Rekha R, Karnaker V, Ganesh HR. A systematic evaluation of rapid Dot-EIA, blood culture and Widal test in the diagnosis of Typhoid Fever. Nitte Univ J Health Science. 2013 March; 3(1):21-24.
14. Bennett DE. Primary mycotic aneurysms of the aorta. Report of case and review of the literature. Arch Surg. 1967 Jun;94(6):758-65.

15. Oderich GS, Panneton JM, Bower TC, Cherry KJ Jr, Rowland CM, Noel AA, et al. Infected aortic aneurysms: aggressive presentation, complicated early outcome, but durable results. J Vasc Surg. 2001 Nov; 34(5):900-8.
16. Maeda H, Umezawa H, Goshima M, Hattori T, Nakamura T, Umeda T, et al. Primary infected abdominal aortic aneurysm: surgical procedures, early mortality rates, and a survey of the prevalence of infectious organisms over a 30-year period. Surg Today. 2011 Mar;41(3):346-51.
17. Soravia-Dunand VA, Loo VG, Salit IE. Aortitis due to Salmonella: report of 10 cases and comprehensive review of the literature. Clin Infect Dis. 1999 Oct; 29 (4):862-8.
18. Strahm C, Lederer H, Schwarz EI, Bachli EB. Salmonella aortitis treated with endovascular aortic repair: a case report. J Med Case Rep. 2012 Aug 15;6:243.
19. Carnevalini M, Faccenna F, Gabrielli R, Irace L, Dell'isola S, d'Ettorre G, et al. Abdominal aortic mycotic aneurysm, psoas abscess, and aorto-bisiliac graft infection due to Salmonella typhimurium. J Infect Chemother. 2005 Dec;11(6):297-9.
20. Alioti M, Alioti R, Campos Soares de Faria R, de Camargo O, Geiger MA. Infected abdominal aneurysm due to Salmonella species. J Vasc Bras. 2016 Jan/ Mar;15(1):74-77.
21. Hela B, Sayda M, Hassen J, Tarak B, Makram K, Sahar E, et al. Mycotic aneurysm of the abdominal aorta caused by Salmonella non-typhi treated surgically. J Clin Exp Cardiolog. 2016; 7(2):1-3.

A Case Report on Hypoplastic Aortic Arch

Kristine Gay S. Tria, MD

Although anatomically independent, aortic arch hypoplasia is said to be part of coarctation of the aorta.[1] It is a rare occurrence in the Philippine Heart Center with only 3 patients diagnosed from 2004 to 2015. This reports a case of a 9-year-old female who presented with a murmur and was diagnosed of congenital heart disease during infancy; however due to financial constraints, surgical management was delayed until childhood. Patch Aortoplasty using a glutaraldehyde-treated pericardium was performed. Aortic arch or tubular hypoplasia presents with a vast array of clinical symptoms from infancy, childhood to adolescence. Definitive management is surgical, which include different techniques and expertise.***Phil Heart Center J 2021;24(1):26-28.***

Key Words: ■ aortic arch hypoplasia ■ tubular hypoplasia ■ coarctation of the aorta ■ arch repair

Aortic arch hypoplasia is defined as narrowing of more than two segments of the arch of the aorta. The aortic arch is divided into a proximal segment between the brachiocephalic artery and the left carotid artery; the distal segment from the left carotid to the left subclavian artery and the isthmus between the left subclavian artery and the ductus arteriosus. In relation to the ascending aorta, the proximal segment is considered to be hypoplastic if it is measured to be less than 60%, the distal segment if it is 50% less and isthmus if it is less than 40%.[2] In some studies however, a segment is defined to be hypoplastic if measured to be less than 50% of the descending aorta.[3] In a study by Poirier, et al. isolated aortic arch lesions were seen in 20 out 37 patients while 13 out of 37 patients had an associated intracardiac lesion.[2] There are two theories which hypothesized the development of hypoplastic aortic arch and coarctation of the aorta. Associated anomalies included those that decrease left ventricle outflow such ventricular septal defect, aortopulmonary window, and atrioventricular septal defect, or those with left ventricular outflow obstruction such aortic or mitral stenosis and bicuspid aortic valve.[4] Hypoplastic aortic arch is also associated with patients who have hypoplastic left heart syndrome.[5]

In infants, aortic arch hypoplasia may present with congestive heart failure including tachypnea, diaphoresis, hepatomegaly and poor perfusion. In children, they usually present with a murmur while adolescents present with arterial hypertension. Clinical hallmark are discrepant arterial pulses and systolic blood pressures in the upper and lower extremities. Normal to increased vascularity can be seen in chest radiograph and electrocardiogram would show a left atrial enlargement and left ventricular hypertrophy. Electrocardiography and cardiac CT angiogram can confirm the diagnosis, however, cardiac catheterization is the gold standard for evaluation of aortic arch anatomy.[6]

Surgical management of aortic arch hypoplasia include different approaches including resection and end-to-end anastomosis, end-to-side anastomosis, subclavian free flap method[6] and a patch aortoplasty.[7] Each of which have their own advantages and disadvantages. Post-operative complications would include restenosis of the distal arch anastomosis and hypertension warranting repair of the lesion.

Case: The patient is a 9-year-old female who presented with incidental finding of a murmur. The patient was apparently well until 1 week old

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when she was noted to have decreased weight and diaphoresis. At 1 month old, she was noted to have cough and colds and was admitted as a case of Pneumonia; however, there was note of an incidental finding of a murmur. Work-up was done and she was diagnosed to have a Congenital Heart Disease. She was referred and seen at our institution at 7 months at which she had regular follow-up. She was maintained on Digoxin, Furosemide and Captopril. She was advised surgery but was not immediately done due to financial constraints and recurrent infections. On review of systems, the patient was noted to have diaphoresis, and easy fatigability. On physical examination, the patient was noted to be not cyanotic with a systolic blood pressure gradient of 30mmHg between the upper and lower extremities.

There was note of bounding pulses on both upper extremities and weak pulses on the both lower extremities. Moreover, there was a Grade 3/6 systolic-diastolic murmur at the left upper sternal border. A clinical diagnosis of coarctation of the aorta was considered. Chest x-ray showed normal vascularity with right ventricular prominence. A 15-lead electrocardiogram showed right axis deviation with left ventricular hypertrophy. Suprasternal view of the echocardiography showed narrowing of the distal segment and isthmus of the aortic arch, and a subpulmonic type of a ventricular septal defect. Cardiac CT angiogram was requested and revealed a short segment narrowing of the proximal descending aorta and suspicious high-lying ventricular septal defect. The patient underwent Aortic Arch Repair (Patch Aortoplasty) and VSD repair.

Figure 1. 2D echocardiogram of the patient. (a) Suprasternal long-axis view showing the narrowed aortic arch with measurements of the proximal, distal and isthmic segments (b) Continuous wave doppler flow across the hypoplastic segment showing two superimposed signals representing the low-velocity flow proximal to the narrowed segment and higher-velocity flow across the narrowed segment itself.

Figure 2. Cardiac CT angiogram of the patient showing the narrowed segment noted at the proximal descending aorta measuring 1.8cm.

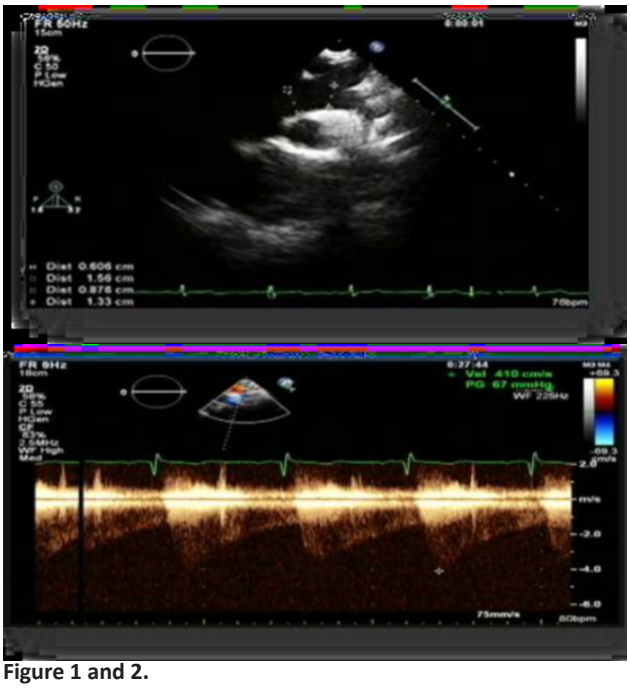

Figure 1 and 2.

DISCUSSION

A child with an incidental finding of a murmur is one of the presenting features of hypoplastic aortic arch or coarctation of the aorta.[5] She was acyanotic and noted to have blood pressure and arterial pulses gradient between the upper and lower extremities. On echocardiogram, there was note of a ventricular septal defect. The presence of a ventricular septal defect diminishes outflow through the left ventricle and in turn reduces volume flowing through the fetal aortic arch leading to narrowing of an arch segment.

The patient underwent patch aortoplasty. Patch aortoplasty can be done using a Cryopreserved homograft, Gortex or polytetrafluoroethylene, Dacron or a glutaraldehyde-treated autologous pericardial patch, which was what was used in the patient. According to one of the studies, on long-term follow-up of 37 patients, none develop cardiac symptoms and all reported normal functional status after patch aortoplasty. The patient did not develop hypertension postoperatively and is being monitored for development of restenosis.

CONCLUSION

In different age groups, hypoplastic aortic arch may have various clinical presentations. It can present as an infant with signs of heart failure, a child with a murmur or an adolescent with systemic hypertension.[6] It can be diagnosed clinically however confirmatory procedures include echocardiogram, cardiac CT angiogram and cardiac catheterization. Management is mainly surgical and includes different approaches to the narrowed segment. Long-term follow-up is important to screen patients for development of hypertension or restenosis.

REFERENCES

1. Kiraly L, Kòrnyei L, Mogyorossy G, Szatmari A. Hypoplastic aortic arch in newborns rapidly adapts to post-coarctectomy circulatory conditions. Heart. 2005 Feb 1;91(2):233-4.
2. Moulaert AJ, Bruins CC, Oppenheimer-Dekker AR. Anomalies of the aortic arch and ventricular septal defects. Circulation.1976 Jun;53(6):1011-5.
3. Poirier NC, Van Arsdell GS, Brindle M, Thyagarajan GK, Coles JG, Black MD, Freedom RM, Williams WG. Surgical treatment of aortic arch hypoplasia in infants and children with biventricular hearts. Ann Thorac Surg. 1999 Dec 1;68(6):2293-7.
4. Kau T, Sinzig M, Gasser J, Lesnik G. Rabitsch E, Celedin S, Eicher W, Illiasch H, Hausegger KA. Aortic development and anomalies. Sem Intereventional Radiol 200 7 Jun;24(2):141.
5. Allen HD, Driscoll DJ, Shaddy RE, Feltes TF. Moss & Adams' heart disease in infants, children and adolescent including the fetus and young adult. 9th ed. PA: Lippincott Williams & Wilkins, c2013.
6. Kubota H, Camilleri L, Legault B, Miguel B, El Youssoufi AT, Bailly P, Brazzalotto I, Helfter S, Lusson JR, de Riberolles C. Surgical correction of the hypoplastic aortic arch by the subclavian free flap method in the neonate. J Thorac Cardiovasc Surg. 1998 Sep 1;116(3):519-21.

Total Anomalous Pulmonary Venous Return in Pediatrics: a case series

Sheryl Dell Carag-Reyes, MD

Total anomalous pulmonary venous connection (TAPVC) is a very uncommon cyanotic anomaly comprising 1% of all congenital heart diseases. Since pulmonary veins drain into the systemic venous circulation, TAPVC is incompatible with life unless a communication between the right and left sides of the heart exists; usually via a patent foramen ovale or atrial septal defect. As the right to left shunt is usually small, right heart dilatation and failure ensues owing to a volume overload. Stenosis and obstruction of varying degree at the junction of the anomalous trunk with the vena cava leads to severe pulmonary hypertension which further worsens right heart failure. Patients presenting early infancy with bluish discoloration exaggerated by activity and symptoms of heart failure. They are usually severely acidotic and cyanotic. Without surgery most infants die by 12 months of age. However, post-operative mortality is also high owing to increased pulmonary vascular resistance and inadequate repair due to obscure anatomy, the purpose of this case report is to highlight the fact that best postoperative care is the key element of thankful outcome. Even with best of care misdiagnosis can happen. The main objective of this paper is to present 3 cases of patients who presented with a complaint of cyanosis and difficulty of breathing on admission. ***Phil Heart Center J 2021;24(1):29-34.***

Key Words: ■ Mycotic aneurysm ■ abdominal aortic rupture ■ typhidot

Case 1: Patient is a 3 months old female, came in due to difficulty of breathing, was born term to a 24 years old G3P3 mother with unremarkable maternal history, at a lying in assisted by a midwife via NSD. At birth patient was noted to be cyanotic hence was referred for work-up but parents did not comply. At one month of age patient was noted to have respiratory tract infection consulted a paediatrician and was referred in our institution. Consulted at two months of age with cardiac rate of 101, peripheral O2 saturation of 77-86%, noted dusky lips and mucosa, a murmur grade 3/6 systolic ejection on the left upper sternal border was noted, on ECG presence of biventricular prominence and x-ray with increase vascular markings suggestive of pulmonary congestion. Echocardiography revealed all pulmonary veins drain to the coronary sinus with ASD secundum measuring 0.53 -0.87 cms with right to left shunting. A dilated right atrium, right ventricle and a dilated main pulmonary artery were seen (*Figure 4*). Patient was admitted and on the 11th hospital stay, with pre-op antibiotics of vancomycin and amikacin, patient underwent surgery on cardio pulmonary bypass with total bypass time of 2 minutes and 4 seconds and total cross clamp time of one hour and 31 minutes. Surgically, dissection was done to expose the right pulmonary veins, tracing it towards the transverse sinus behind the aorta and SVC. The vertical vein was identified and opened and its course traced into the coronary sinus. The coronary sinus was unroofed, creating a connection into the left atrium. The vertical vein was patched by an autologous pericardium; the ASD was likewise patched Intraoperative findings of all veins draining to coronary sinus with ASD of 0.5 cms, TAPVR correction and ASD closure done. Post-op echocardiograph showed no ASD leak , all veins draining to Left Atrium, LV= 1.84 (1.55- 2.3) , LA= 2.9 (0.85- 1.6), aorta = 0.7 (0.85- 1.35) , LVEF = 70% , RVEF = 1.5 by TAPSE , PAP = 91 mmhg by PAT. Patient was discharged on the 19th hospital stay.

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Case 2: This is a case of a one month old female delivered full term by a G1P1 mother via caesarean section due to failure in dilatation. Maternal history revealed that mother had cough and colds at first trimester of pregnancy with no medications taken. At two weeks of life patient was noted to have tachypnea with associated poor feeding. Consultation was done to a private MD and was given salbutamol nebulization and cefaclor as home medications. After one week at home, symptoms persist hence consulted again and were admitted for Pneumonia. On the third day of admission patient was noted to have circumoral cyanosis referred to a paediatric cardiologist 2Decho was requested showed CHD, TAPVR to Superior Vena Cava. Patient was started with lanoxin and spironolactone. Then was referred in our institution for surgical management.

At 1½ months of age patient was admitted in our institution for surgical management. On physical examination was focused on the chest/ lungs with harsh breath sounds on both lung fields, noted adynamic precordium, PMI at 4th ICS LMCL, normal S1, Split S2, irregular rhythm, with thrill, with grade 4/6 PSM LMSB. Vital signs revealed: BP: 90/P Cardiac Rate: 130 bpm RR: 40 T: 37' with oxygen saturation of 83%. He was admitted, chest x-ray are within normal limits. ECG showed right atrial deviation with right ventricular hypertrophy, 2D-echo revealed Patent foramen ovale measuring 0.40 to 0.46 cms with obligate right to left shunting, with the interatrial septum bulging to the left. Intact interventricular septum. All 4 pulmonary veins forming common pulmonary veins and draining to superior vena cava with noted turbulence, a maximum gradient of 16 to 21 mmHg. Right atrial enlargement Right ventricular enlargement (*Figure 5*). On the 9th hospital stay underwent TAPVR correction with pre-operative antibiotics of Vancomycin and Amikacin. The procedure was the heart flipped over towards the right side, confluent of the pulmonary veins identified, incision along the confluent of pulmonary vein and continuous suturing done between the pulmonary vein and the left atrial appendage. Right atrium was opened to check for the patent foramen ovale and close. Intra-operatively all four veins drain to the superior vena cava. Total bypass time 2 hours and 45 minutes and total cross clamp time of 2 hours and 55 minutes. On the 22nd post-op day with unremarkable hospital stay with good oral intake patient was discharged.

Case 3: A 4 month old female was admitted in our institution due to difficulty of breathing and noted murmur. Patient is born to a 31 years old G2P2 mother via Caesarean section secondary to previous CS (placenta previa) noted tachypnea at birth and was observed for 4 days then patient was discharged for home. No cyanosis was noted. Maternal history revealed regular prenatal check-ups at a health center, had cough and colds on first trimester of pregnancy and given amoxicillin for 5 days. At 1 month of age with interrupted feeding and associated occasional fast breathing. No consult was done, patient was observed at home. Not until 2 weeks prior to admission, persistence of the above symptoms consulted a private MD, admitted and treated for pneumonia. On auscultation murmur was noted hence referred to a pediatric cardiologist, 2Decho was done showed Congenital Heart Disease, started on furosemide, aldactone and lanoxin. Consulted our institution, ECG showed right axis deviation with right ventricular hypertrophy, 2D echocardiography was done showed ASD secundum type PAH severe, and hence patient was admitted. On PE, awake, irritable, mildly tachypneic with CR = 142 RR = 65 peripheral O2 saturations = 85-88%, with subcostal retractions, adynamic precordium, PMI at 4th ICS left midclavicular line, no thrill, no heave, grade 3/6 SEM LUSB, slightly globular abdomen, soft, non palpable liver, full pulses, no clubbing and non-cyanotic nail beds.

Patient was admitted at Pediatric ICU was hooked to venoclysis and laboratory work-ups were done, showed xray with increase pulmonary vascular markings, CBC showed anemia hence was transfused with PRBC, other laboratory results are within normal limits. Few hours at PICU she was noted to have laboured breathing and grunting, patient was then intubated and hooked to mechanical ventilator and was placed under sedation and paralysis. On the second to fourth hospital stay medications were continued. Feeding started via OGT and was tolerated; gradual weaning from the mechanical

ventilator was instituted. Repeat chest x-ray showed further increase in congestion with beginning pulmonary edema hence furosemide was shifted to drip. 2D echocardiography was done, on further review results showed CHD TAPVR to right atrium, atrial septal defect, and secundum. All pulmonary veins drain to right atrium. Pulmonic Regurgitation moderate, gradient 47 mmHg and Tricuspid Regurgitation, moderate to severe, maximum grad. = 91 mmHg.

From the seventh to 13th hospital stay, management continued with gradual weaning from the mechanical ventilator, repeat x-ray showed clearing of pulmonary edema, other medications were continued. Repeat diagnostics were done and are within normal limits hence on the 14th hospital stay patient underwent TAPVR correction under cardiopulmonary bypass, surgically a Buffle was created over the Pulmonary vein towards the left atrium. The enlarged ASD was likewise patched with autologous pericardium.

Intaroperatively all pulmonary veins were seen draining to the RA with ASD of 0.5 cms, TAPVR correction with ASD closure was also done. Total bypass time of 2 hours and 51 minutes and total cross clamp time of 2 hours and 6 minutes. Immediately post–operative patient was directed to surgical intensive care unit for close monitoring. Additional echo view was done showed No ASD leak, TR trivial, all veins draining to left atrium with RVEF of 74% and LVEF of 62%, no pericardial effusion, PAP of 73 mmHg by PAT. Furosemide drip was increased due to repeat x-ray of increasing pulmonary edema and other medications were continued. On the fifth post-operative day with continued management, repeat x-ray showed clearing of congestion and pulmonary edema, with favourable arterial blood gas result patient was extubated. The rest of the hospital stays were unremarkable, medications and management were continued, vital signs were stable, on the 20th post-operative day patient was discharged.

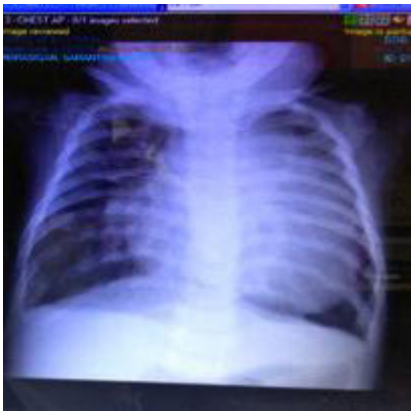


Figure 1. Case 1: TAPVR to Coronary Sinus

Preoperative x-ray: significant clearing of congestion
Same degree of cardiomegaly and biventricular prominence
-MPA remains prominent

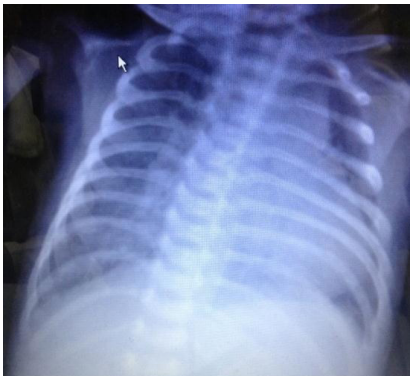


Figure 2. Case 2: TAPVR to Superior Vena Cava

Preoperative x-ray: Chest study shows normal pulmonary vascularity. No active parenchymal infiltrates are seen. Heart is magnified but appears enlarged. Diaphragm and costophrenic sulci are intact.

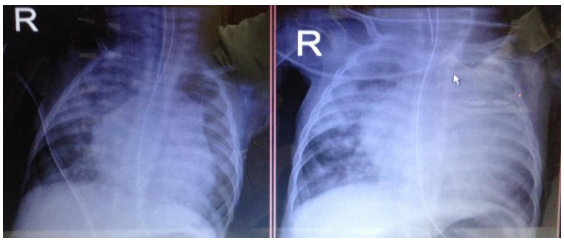


Figure 3. Case 3: TAPVR to Right Atrium

Preoperative x-ray: Pulmonary congestion to edema.
Overall pulmonary vascularity is increased
Some degree of cardiomegaly with right ventricular prominence
MPA segment appears to be prominent

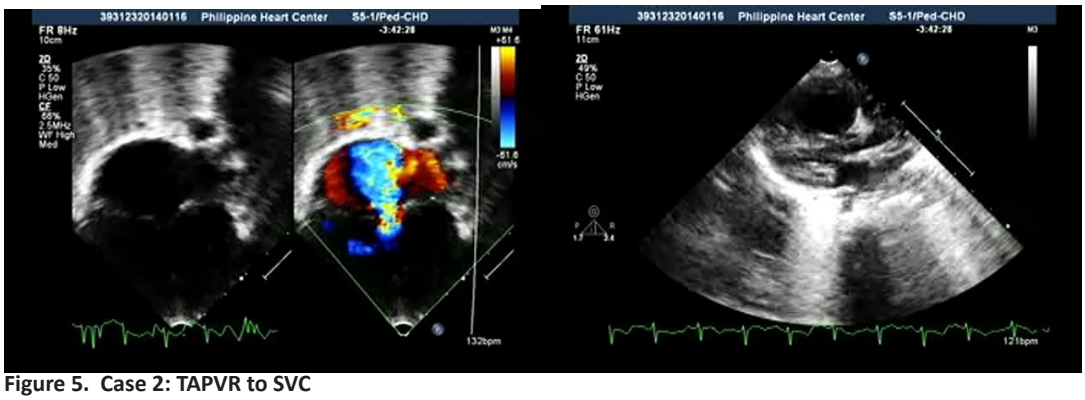
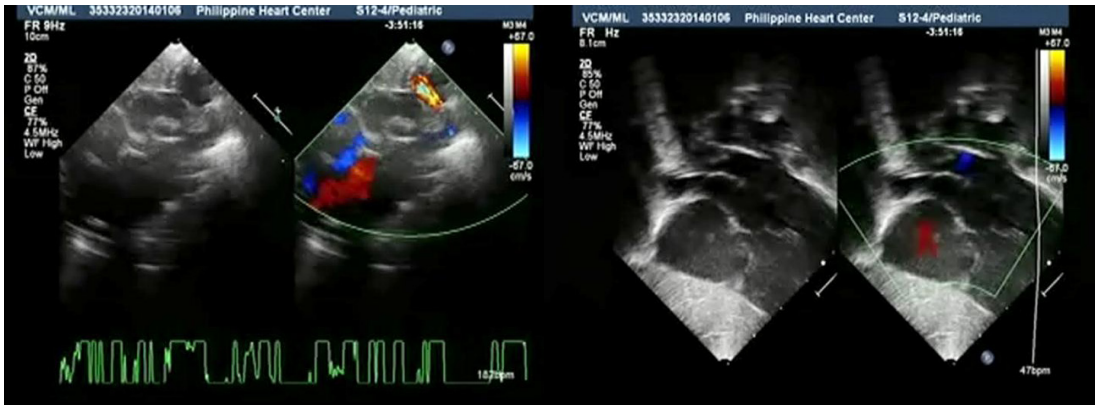


Figure 5. Case 2: TAPVR to SVC



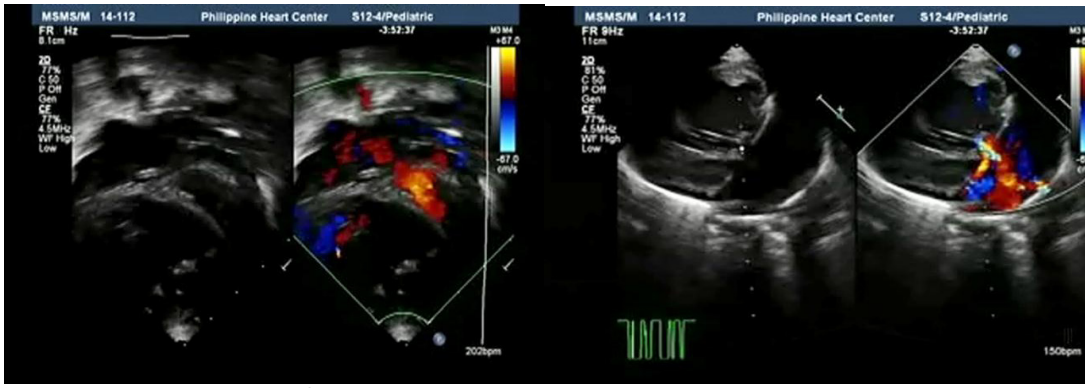


Figure 6. Case 3: TAPVR to Right Atrium

DISCUSSION

Total Anomalous Pulmonary Venous Connections represents a group of congenital heart defects with an array of anatomic and physiologic variants in which the pulmonary veins connect to the remnants of the embryologic venous circulation rather than to the left atrium. It is a rare congenital anomaly corresponding to only 2% of the congenital anomalies.[2] It has no sexual predilection but some studies would state that it has a slight male preponderance.[1]

The mechanism of transmission of TAPVC has not been elucidated. The Baltimore-Washington Infant Study, however, showed a possible association with exposure to lead, paint or paint-stripping chemicals, and pesticides. Although there is no known genetic pattern of transmission of TAPVC, a monogenic pattern of inheritance has been suggested from the number of reported family cases in the literature.

Numerous classifications of TAPVC have been advanced. Darling et al. divided them as

follows: Type I, anomalous connection at the supracardiac level; type II, anomalous connection at the cardiac level (to the coronary sinus); type III, anomalous connection at the infracardiac level; and type IV, anomalous connection at two or more of the above levels. Burroughs and Edwards suggested a classification with prognostic implications based on the length of the anomalous channel (i.e., long, intermediate, or short); however, the prognostic and physiologic implications suggested by these classifications are not always true. Smith et al. provided an alternative classification for TAPVC: Supracardiac (without pulmonary venous obstruction) and infradiaphragmatic (with pulmonary venous obstruction). The most common type according to Darling et al. and based on the anatomic site of abnormal connection is the supracardiac type comprising 40 -50%.

Embryologically, if the connection to the right common cardinal system becomes dominant, all the pulmonary veins will drain into the SVC or azygous veins. If the left common cardinal vein connection persists, the pulmonary veins will drain into the left innominate vein or with the coronary sinus persistence of the communication with the umbilicovitelline system will result in drainage into the portal venous system, the ductus venosus or rarely, the hepatic veins.[1]

The symptoms and signs of TAPVR are variable usually depending on the pathological anatomy and change of hemodynamics as to the presence and absence of obstruction. Patients are usually asymptomatic at birth. In patients without pulmonary venous obstruction, tachypnea and feeding difficulties were the initial symptoms, usually manifesting by the first few weeks of life. Some would have repeated respiratory infections, and usually had cardiorespiratory failure by 6 months of age. Cyanosis may be so mild as to be clinically inapparent, except in the presence of cardiac failure. This was manifested by our patients.

In patients with TAPVC with pulmonary venous obstruction, symptoms usually will not appear in the first 12 hours of life, a finding that differentiate these patients from patients with respiratory distress syndrome. Once symptoms began there will be rapid progression to dyspnea, feeding difficulties and cardiorespiratory failure. The clinical course in severely obstructed patients such as the infradiaphragmatic type might be stormy with rapid development of acidosis and severe respiratory distress.

As the advent of echocardiography, TAPVR can be readily diagnosed without much difficulty. The sensitivity and specificity for diagnosis by echocardiography including cross-sectional and color. Doppler flow mapping have been reported to be up to 97-99%.[3] MRI and CT angiogram are also included as tools for diagnosis. Diagnostic cardiac catheterization is currently not so desirable due to its invasive nature; it has been reserved in patients with complex heart lesions or mixed connections of pulmonary veins.

The treatment for TAPVR is surgical correction and should be performed as soon as possible. The operative results have been improving over the past decades. The technique of trans atrial exposure of common venous chamber, interrupted suturing of the common veins to the left atrium and pericardial patch augmentation significantly improves survival and decreases the risk of restenosis.[5]

In a study conducted by Tara Karamlou et al, showed that mortality after total anomalous pulmonary venous connection repair has decreased but remains highest in young patients and in those with cardiac connection type or pulmonary venous obstruction. Unfavourable anatomic characteristics remain important determinants of post repair survival despite improved perioperative care. Historically the risk factors for operative mortality are young age, the anatomical type, and presence of pulmonary hypertension, presence of obstruction to the venous drainage, metabolic acidosis and the urgency of the operation.[6] Another study by Husain et al. concluded that mortality after repair of TAPVC is highest in patients presenting with obstruction at the time of repair, longer cardiopulmonary bypass and cross clamp time are associated with recurrent pulmonary venous obstruction requiring intervention. [4]

CONCLUSION

Tachypnea, difficulty of breathing and cyanosis are usually the presenting symptoms of patients who have Total Anomalus Pulmonary Venous Return. Cyanosis is a significant clinical manifestation and is more common in in-patients with pulmonary venous obstructions hence caregivers should have the sense of alertness in the early detection. TAPVR are rare and high-risk congenital cardiac abnormality that needs early diagnosis and surgical treatment with special care in the intensive care unit. Successful results are obtained with comprehensive multidisciplinary team effort in specialized centers.

REFERENCES

1. Allen HD, Driscoll DJ, Shaddy RE, Feltes TF. Moss & Adams' heart disease in infants, children and adolescent including the fetus and young adult. 9th ed. PA: Lippincott Williams & Wilkins, c2013.
2. Khan MA, Waqar Tariq. Total anomalous pulmonary venous connection: management and outcome, experience from Children's Hospital , and Ittefaq Hospital Lahore, Pakistn. Ann. Pak. Inst. Med. Sci. 2012;8(3):196-199.
3. The normal examination and echocardiographic measurements. 2nd ed. MGA Graphics, c2007.
4. Husain SA, Maldonado E, et al., Total anomalous pulmonary venous connection: factors associated with mortality and recurrent pulmonary venous obstruction. Ann Thorac Surg. 2012 Sep;94(3):825-31
5. Wilson WR Jr, Ilbawi MN, et. al. Technical modifications for improved results in total anomalous pulmonary venous drainage. J Thorac Cardiovasc Surg. 1992 May; 103(5):861-70.
6. Tara Karamlou, MD. et al. Factors associated With mortality and reoperation in 377 children with total anomalous pulmonary venous connection. Circulation 2007;115:1591-1598.

Case Report -
Pulmonary and Critical Care Medicine

MÉNAGE À TROIS: a Case of Obesity, Kyphoscoliosis and Obstructive Sleep Apnea

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Association between obesity and hypersomnolence has long been recognized. We know of Joe, the fat boy, from the work of Charles Dickens, The Pickwick Papers, who was markedly obese and tended to fall asleep uncontrollably during the day. The understanding on obesity hypoventilation syndrome has increased since Auchincloss first described the syndrome in 1955 eventually being known as Pickwickian syndrome. In 1981, Guilleminault described how severe kyphoscoliosis resulted in alterations in sleep states, coining the term Quasimodo Syndrome. Fast forward to present, these syndromes collide, we have a new face nobody has seen before, severe obesity, kyphoscoliosis and obstructive sleep apnea all occurring in a single patient. Here we will present a preternatural mix of severe obesity, severe kyphoscoliosis and severe obstructive sleep apnea. We have a ménage a trois. A threesome so to speak of three distinct disease entities overlapping to cause profound pathologic alterations.

Case: PD is a 29 year-old, male, known hypertensive, known diabetic, morbidly obese, with kyphoscoliosis. He was referred to our institution for polysomnography. The same scenario occurred six months prior to admission. One month prior to admission, he was again readmitted due to pneumonia, presenting as productive cough and difficulty of breathing. Laboratory exams revealed increased hemoglobin and hematocrit; normal thyroid function tests. Echocardiography revealed normal pulmonary artery pressure, and normal RA, RV and main pulmonary artery dimensions, ejection fraction of 65%, with eccentric LV hypertrophy. He was discharged and was referred to our institution for polysomnography.

Significant past medical history revealed, hypertension and diabetes, childhood medical history revealed, meningocele at birth; had meningocele repair surgery at 4 months; diagnosed with kyphoscoliosis at 8 years, work-up done; advised surgery but did not comply; no history of accidents, serious physical injuries or trauma.

He is a previous six pack year smoker, quit 4 years ago and an occasional alcoholic beverage drinker. He has easy fatigability, dyspnea on exertion, chest pain. The patient is morbidly obese with a BMI of 40.8 kg/m^2, he has a short neck, neck circumference of 48 centimeters or 18.9 inches (*Figure 1)*; normal sized tongue with no retrognathia, Mallampati 4 with only the hard palate is visible *(Figure 2*). Angulated shoulders with hip tilt *(Figure 3)*, asymmetrical chest expansion with lagging on the left hemithorax, prominent rib hump at right posterior chest, exaggerated by forward bending *(Figure 4)*, percussion was technically difficult, vesicular breath sounds on both lung fields. Heart examination revealed an accentuated P2. Abdomen is globularly enlarged, waist circumference of 140 cm or 55.1 inches *(Figure 5)*. No edema, no cyanosis, no clubbing, hyperpigmentation of the distal aspect of both legs, arm span 168 cms (66.1 inches) which is a surrogate of his true

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height with an arm span to height ratio: 1.1. Neurologic examination was unremarkable.

With that presented, we had an admitting impression of Obstructive Sleep Apnea, Severe Kyphoscoliosis, and Severe Obesity.

DISCUSSION

Sleep related breathing disorders are characterized by abnormal respiration during sleep. The three major sleep related breathing disorders are central sleep apnea syndromes, obstructive sleep apnea syndromes, and sleep related hypoventilation/hypoxemia syndromes. Central sleep apnea syndrome is characterized by a lack of drive to breathe during sleep, resulting in insufficient or absent ventilation and compromised gas exchange. The following are the types of central sleep apnea. Obstructive Sleep Apnea Syndrome is a disorder that is characterized by obstructive apneas and hypopneas caused by repetitive collapse of the upper airway during sleep. The third category is sleep related hypoventilation-hypoxemia syndromes. We considered obstructive sleep apnea, obesity-hypoventilation syndrome, central sleep apnea, and sleep disordered breathing due to kyphoscoliosis.

Next we will compare and contrast the three main considerations OSA, OHS, and CSA. Generally speaking, the three present similarly. With their symptoms mainly related to disrupted sleep. Nocturnal symptoms are the following *(Figure 6)*. Checked are those seen in our patient. Daytime symptoms are enumerated *(Figure 7)*. Checked are those seen in our patient.

With most symptoms similar to OSA, OHS patients commonly present with symptoms of pulmonary hypertension and right sided heart failure. Dyspnea on exertion is a clue that OHS is present because patients with OSA - alone generally do not develop dyspnea on exertion. Next is central sleep apnea, the most common reported symptoms are insomnia and excessive daytime sleepiness. In general, the degree of daytime hypersomnolence is less than that observed with obstructive sleep apnea, and insomnia is more prominent. Patients with secondary CSA also have features of the underlying disease.

On to physical examination, OSA patients commonly show the following. PD was obese, a neck circumference of 18.9 inches, Mallampati 4 and hypertensive. In OHS, physical examination shows plethoric obesity, enlarged neck circumference, crowded oropharynx, and prominent pulmonic component of the S2. All of which are seen in our patient. For central sleep apnea, no physical findings are predictive and patients usually have a normal body habitus. For the risk factors, OSA has definite and potential risk factors. Obesity is the best documented risk factor. Craniofacial and upper airway soft tissue abnormalities, current smokers, but not past smokers, and diabetes. Our patient was obese, Mallampati 4 and is diabetic. OHS, shares most of the risk factors of OSA, with obesity being the main risk factor. For central sleep apnea, risk factors are increased age, male gender, heart failure and stroke.

Another consideration is sleep disordered breathing secondary to a chest wall disorder. Our patient has severe; kyphoscoliosis. Sleep related breathing disorder among them commonly present as obstructive sleep apnea or nocturnal hypoventilation. Daytime respiratory symptoms are more common when the angle of the spinal deformity approaches 100 degrees.

We move on to the diagnostic criteria. The diagnosis of OSA is confirmed if the number of obstructive events, apneas, hypopneas or respiratory event related arousals on PSG is greater than 15 events per hour or greater than 5 per hour in a patient that reports any of the following symptoms *(Figure 8)*. OHS is diagnosed when the following criteria are confirmed: Obesity or BMI of more than 30, awake alveolar hypoventilation that cannot be attributed to other conditions such as pulmonary disease, skeletal restriction, neuromuscular weakness, hypothyroidism, or pleural pathology *(Figure 9)*. The absence of an alternative cause of hypoventilation is an important requirement for the diagnosis of OHS. For central sleep apnea, the individual must fulfil A, B, and C for a diagnosis *(Figure 10)*. With that presented, the

differential diagnoses cannot be ruled out by the patient's history and physical examination. For findings invariably overlap among the considered forms of sleep related breathing disorders. Polysomnography is essential. However, other workup is necessary, arterial blood gas testing to document hypercapnia and or hypoxemia, a high serum bicarbonate level is a clue of chronically hypercapnia. Pulmonary function tests for evidence of obstructive or restrictive disease. Radiographs to look for parenchymal lung disease and chest wall disease. Echocardiography to document right sided heart failure and/or pulmonary hypertension.

Examination revealed an increase in neck circumference, Obese 2, and Mallampati 4. All of these are features suggestive of Obstructive Sleep Apnea. Obesity, hypertension, and Type 2 diabetes puts at him as high risk for OSA as stated in the latest AASM Guidelines. From the same article, patients deemed high risk should have the diagnosis confirmed and severity determined with objective testing. The patient was evaluated for his daytime sleepiness through Epworth Sleepiness Scale. He had a score of 19 out of a maximum 24 which means that the patient has excessive daytime sleepiness and opted him to undergo polysomnography (Figure 11). Polysomnography is a diagnostic test used in the evaluation of sleep disorders. Various physiological sensors are connected to the patient. Sensors on the face and scalp measure eye movement and brain activity. Sensor at the nose to measure airflow. Sensor on the finger measures the amount of oxygen saturation. Elastic belt sensors around chest and abdomen measures amount of effort to breathe. Wires transmit data to the computer generating an epoch. Showing you a 120 second epoch. Zooming into a 30 second epoch in REM stage of sleep characterized by rapid eye movements in electro-oculogram. In this epoch an obstructive apnea was noted. Defined as a drop in peak signal excursion by >90% of pre-event baseline, in duration of more than or equal to 10 seconds. Hypopneas were also noted which is defined as Peak signal excursions drop by more than or equal to 30% of pre-event baseline, with duration of more than or equal to 10 seconds, and with more than or equal to 3% oxygen desaturation from pre-event baseline. During this period, desaturation was also noted. Our patient was noted to have hypopnea, apnea, and desaturation *(Figure 12)* with an Apnea-Hypopnea Index of 59.8 per hour of sleep which according to AASM classification denoted a severe state. Hence, he was signed out as a case of Severe Obstructive Sleep Apnea-Hypopnea Syndrome. Therapeutic Study was done. CPAP at pressure of 17 cm H20 abolished apnea and hypopnea. Therefore, nightly use of CPAP at 17 cm water was recommended other remarkable physical finding was the presence of prominent rib hump on the right posterior chest *(Figure 4)*. An x-ray of the thoracolumbar spine showed a rightward deviation with T4 as the upper end vertebra and L3 as the lower end vertebra yielding a Cobb angle of 100 degrees *(Figure 13)*. He was diagnosed with severe kyphoscoliosis. Kyphoscoliosis is a disease of the spine and its articulations. The deformation of the spine consists of kyphosis which is an anteroposterior angulation of the spine and scoliosis which is lateral displacement of the curvature. It occurs 1 in 1000 for mild deformity to 1 in 10,000 for severe spinal deformity. This is a representation of how Cobb angle is measured. It is used to determine the prognosis, predicts the effects of disease to lung function, and the risk of developing respiratory failure. Arterial Blood Gas showed, Hypoxemia with pO2 of 56, oxygen saturation of 85.6%, hypercapnia with pCO2 of 66.5, and bicarbonate of 36, interpreted as chronic respiratory acidosis with moderate hypoxemia. Rom and associates presented patients with severe kyphoscoliosis that showed hypercapnia with mild to moderate hypoxemia. Comparing his subjects with our patient, our patient is much younger at age 29 with a more deranged hypercapnea and hypoxemia. This led us to think whether the kyphoscoliosis is aggravated by sleep disorder of this patient. A study by Mezon and associates, presented 5 patients with kyphoscoliosis and sleep disorder. However, his subjects presented with central sleep apnea in contrast to our patient who presented with obstructive sleep apnea. Mezon's subjects showed that during REM sleep, physiologic disturbance was greatest, being the time of greatest desaturations. This proves to be the same with our patient. Another study made by Guilleminault presented 5 patients with kyphoscoliosis and obstructive sleep apnea. He coined

the term Quasimodo Syndrome. His subjects were older with weight ranging 57-71 kgs compared to our patient who is much younger at age 29 and heavier with weight of 92kg. He found his subjects to have a predominantly obstructive type of apnea which is consistent with our patient. Similar to Guilleminault's finding, our patient has lowest oxygen saturation during REM sleep. However, comparing the degree of hypoxemia and hypercapnea, our patient has more deranged values than those found in Guilleminault's subjects. Is this because our patient is also obese? How will obesity affect the respiratory function? With the presence of obesity, should we consider him still as a case of Quasimodo Syndrome? On further work-up.

CBC showed polycythemia which could be secondary to previously mentioned hypoxemia. Chest x-ray showed a right lung base subsegmental atelectasis and marked thoracolumbar dextroscoliosis *(Figure 14)* as previously discussed. Pulmonary Function test was done with a flow-volume loop narrowed due to decrease lung volume. The FEV1/FVC ratio was normal, FVC and FEV1 *(Figure 15)* were decreased suggestive of a probable moderately severe restrictive ventilatory defect. Lung volume study done showed decreased total lung capacity, vital capacity and FRC *(Figure 16)*, confirming the finding of moderately severe restrictive ventilatory defect. Diffusion study is moderately reduced. These findings are consistent with those found in patients with kyphoscoliosis. A study by Caro and associates showed 38 kyphoscoliotic patients with restrictive ventilatory defect. All have decreased total lung capacity, vital capacity, and functional residual capacity. Hoffstein, on the other hand found no direct relationship between pulmonary function studies and obstructive sleep apnea. Hence, the findings of severe restrictive ventilatory defect in our patient was primarily due to kyphoscoliosis. Echocardiography showed an EF of 65%, normal LV dimension with good wall motion and contractility, High normal RV dimension, normal main pulmonary artery, and pulmonary arterial pressure. Is this an early finding of increased RV workload that would eventually result to cor pulmonale? Our patient is hypertensive, diabetic, with central obesity and hypertriglyceridemia, satisfying the diagnosis of metabolic syndrome. Despite substantial evidence from several studies to suggest an independent link between obstructive sleep apnea and metabolic syndrome, the issue still remains controversial. A study made by Lam and associates among Chinese volunteers showed an association with OSA and metabolic syndrome. He found that OSA has five-fold risk of having metabolic syndrome. So, is there really a connection between obstructive sleep apnea and metabolic syndrome? A study made by Palaniappan showed that obesity is main precursor of the metabolic syndrome. From the study of Young, obesity is also a significant factor in the development of obstructive sleep apnea. These studies prompted Parish and associates to hypothesize obesity as the association between OSA and metabolic syndrome. The BMI cut-points from the 1998 WHO Consultation on obesity are generally accepted, however the International Obesity Taskforce developed cut-off points appropriate for Asians. Thus, based on that classification, our patient is categorized as Obese II. With the data at hand, we think: Is this a case of Obesity and obstructive sleep apnea giving us Obesity hypoventilation syndrome? However with Kyphoscoliosis coming into the picture, does it rule out obesity hypoventilation syndrome? Or does it make this case a Quasimodo Syndrome? If you recall, they do not present with obesity making our case even more unique *(Figure 17)*. The ménage à trois of the three diseases in a single individual will come to a common end point. To bridge the gaps, we must first discuss each entity by itself. It all started with the patient having severe kyphoscoliosis. The rotation of the spine disrupts the respiratory mechanics by decreasing the chest wall compliance and increasing elastic recoil of the chest wall, thereby decreasing the lung compliance. This results to a restrictive ventilator pattern as shown by the decreased TLC, VC, FEV1, FVC with a normal FEV1/FVC ratio, also presenting as micro-atelectasis, as seen in our patient *(Figure 18)*. adults, the severity of the restrictive process is directly proportional to the severity of the spinal deformity. The relationship can be computed from the following equation, yielding a predicted vital capacity *(Figure 19)*.

Thus curves of 10 to 25 degrees are considered mild, with a decline in predicted vital capacity of 84 to 79%. Curves of 25 to 45 degrees are considered moderate with a decline in predicted vital capacity of 79 to 72%. Curves of more than 45 degrees are considered severe with a decline in predicted vital capacity of less than 72%. However, starting at 65 degrees, V/Q mismatch occurs, leading to hypoxemia. At angles more than 100 degrees, respiratory failure occurs. Our patient has a Cobb angle of 100 degrees with a predicted vital capacity of 46, which may account for the recurrent hospital admissions due to respiratory failure. Our patient was later diagnosed with obstructive sleep apnea. Can kyphoscoliosis affect sleep? Is there a connection? In kyphoscoliosis, the stiffened chest wall leads to increased elastic load leading to a heightened respiratory drive, so that diaphragm activation increases, also there is greater recruitment of the inspiratory muscles of the rib cage. When the patient goes in to non-REM sleep, the neural drive to the intercostal muscles is diminished and may be absent in REM sleep. Hence the burden of expanding the non-distensible chest wall falls more on the diaphragm, thereby causing hypotonia leading to hypoventilation *(Figure 20)*. Inspiratory activation of upper airway muscles occurs earlier than activation of the diaphragm, which stabilizes the upper airway and counter-balances the collapsing force exerted on the upper airway by diaphragm. Any reduction or delay in upper airway inspiratory muscle contraction, relative to diaphragm activity, predisposes to upper airway narrowing or collapse during sleep. The combination of kyphoscoliosis and obstructive sleep apnea is Quasimodo syndrome as coined in the study of Guilleminault as presented earlier. He attributed the OSA to the collapse of the upper airways to the mechanism previously discussed. On the other hand, a study done by Al-Kattan and associates using bronchoscopy in kyphoscoliotic patients showed that OSA and nocturnal hypoxemia could be due to the secondary twisting of the extra-thoracic trachea *(Figure 21)*. Unfortunately, bronchoscopy was not done in our patient. So to answer the first question of Dr. Mampao, does our patient have the complex of kyphoscoliosis and OSA called the Quasimodo syndrome? The answer is yes. However, as mentioned earlier, our patient presented much earlier than expected. Furthermore, a more deranged hypercapnea and hypoxemia were noted compared to the subjects in the study. Could there be another factor that is causing the earlier symptoms, resulting to a more deranged clinical picture? We are dealing with a patient who has morbid obesity and OSA. These two can work in concert to produce a third disease entity, Obesity Hypoventilation Syndrome. A study by Mohkhlesi showed a close relationship between BMI and OHS. As the BMI increase to 40 and above, the likelihood of OHS increases in parallel *(Figure 22)*. Likewise, 90% of OHS patients also have OSA. In OSA, post-apneic hyperventilation after arousal in an important factor for decreasing PCO2 and increasing oxygenation. However, patients with OHS are unable to normalize their PCO2 between such respiratory events. With the failing pH, the kidney buffers by decreasing bicarbonate excretion. and serum bicarbonate accumulates. Eventually the serum bicarbonate level becomes high enough to depress ventilation, causing chronic hypoventilation and hypercapnea *(Figure 23)* both during sleeping and waking hours. This explains the blood gas of our patient. So does our patient have obesity hypoventilation syndrome? The answer to the question would have been straightforward. We cannot fulfill all the criteria for OHS due to the presence of kyphoscoliosis. The absence of an alternative cause of hypoventilation is an important criterion for the diagnosis of OHS. Patients may have other cause of hypoventilation such as obstructive airways disease, interstitial lung disease, chest wall disorders such as kyphoscoliosis, hypothyroidism, and neuromuscular diseases. If the other disease is mild and unlikely to cause hypercapnea, then it is reasonable to give the patient a diagnosis of OHS. But if the other disease is more severe and probably contributing to hypercapnea, the situation becomes more complicated. Thus, in this setting, pure OHS cannot be diagnosed with certainty. However, in a patient with severe obesity, severe sleep apnea and oxyhemoglobin desaturation during sleep, we generally presume that OHS may be a component of the disease complex of our patient. By the same token, there is a well-established relationship between OSA and obesity. Obesity

results in anatomic and functional changes like decreasing pharyngeal airway size, and increased leptin resistance that can result to the development of OSA in obese individuals. Likewise, OSA may predispose individuals to worsening obesity because of sleep deprivation, daytime somnolence and disrupted metabolism *(Figure 24)*. In OSA, the intermittent hypoxia and reoxygenation also induces the production of reactive oxygen species resulting to endothelial dysfunction thereby promoting systemic inflammation, causing cardiovascular events, impaired fasting glucose, and hypertriglyceridemia leading to metabolic syndrome. Which manifested in our patient. This vicious cycle explains the role of obesity in OSA and metabolic syndrome as mentioned by Dr. Mampao. As to the connection between obesity and kyphoscoliosis, a thorough search of the literature yielded no published data. Looking now at the bigger picture. Our patient has an ominous combination of obesity, obstructive sleep apnea and kyphoscoliosis. What would we name this syndrome? This merger of three diseases is indeed complex and unique and would require a multi-disciplinary management.

The ménage a trois of obesity, kyphoscoliosis and obstructive sleep apnea requires a long-term, multidisciplinary approach to management. Let us first discuss the management options of kyphoscoliosis. PD was diagnosed at 8 years old and was previously advised surgery but did not comply. The present state of his kyphoscoliosis is severe, with the angles of scoliosis and kyphosis both at 100 degrees. Operative treatment traditionally consists of spinal fusion and or insertion of rods with goals of prevention of curve progression and partial curve correction. Spinal surgery should be performed at an early age, ideally before the age of skeletal maturity, and it is rarely effective in adults. In a study by Tzelepis, spinal surgery in patients more than 20 years old did not result in significant improvement of vital capacity or gas exchange and posed a high, 20 percent complication rate. With our patient presenting with severe kyphoscoliosis at 100 degrees, and the presence of his comorbidities, he is not a good candidate for spinal surgery. Hence, supportive therapy should be maximized. Through immunizations – due to their predisposition to recurrent infections, supplemental oxygen for hypoxemia and for correction of polycythemia, adherence to smoking cessation, and weight reduction. Specific nonsurgical approach include, noninvasive ventilation and pulmonary rehabilitation. Indications for initiating NIV include, hypoventilation, hypercapnia, and oxyhemoglobin desaturation. All of which were present in our patient. Long term oxygen therapy combined with positive pressure ventilation in kyphoscoliotic patients results in significant increases in vital capacity, maximal inspiratory pressure, arterial oxygen and a decrease in carbon dioxide. Shown are the survival curves of kyphoscoliotic patients on long term oxygen alone versus long term oxygen plus positive pressure ventilation. After 1 year of treatment, survival was only 66% in the LTO group versus 100% in the NIPPV group. *(Figure 25)*.

Pulmonary rehabilitation can bring about improvements in patients with restrictive lung disease. A study by Bihiyga of 31 patients, 14 of which had kyphoscoliosis, a 24 week program showed significant improvements in exercise capacity, muscle force and scores on the chronic respiratory disease questionnaire. In another study by Ong-Cabrera and associates in our institution among non-COPD patients, an 8 week program showed improvements in exercise capacity. With the following improvements on 6 minute walk test distance and perceived breathlessness and muscle fatigue. On the other hand, obesity and OSA are best approached in tandem. The consensus initially focuses on patient education and support on the following points. It is in the process of education that interventional therapy can be introduced, such as positive pressure airway therapy or PAP, the primary treatment for OSA. Positive airway pressure therapy is the most effective treatment for OSA. It can be given in the form of continuous positive airway pressure or CPAP, the gold standard. It is indicated for moderate to severe OSA and for those with comorbidities. CPAP was initiated in our patient. Another form of PAP is bilevel positive airway pressure or BiPAP, used in patients requiring higher pressures and for those intolerant to CPAP. Lastly, the auto-titrating positive airway pressure or APAP, used in moderate to severe OSA with no comorbidities. The following images show the effects of progressive

increases of CPAP pressure from zero to 15 centimeters water, the upper airway progressively enlarges with increasing pressure of CPAP *(Figure 26)*. CPAP is like a pneumatic splint for the airway preventing collapse during sleep. It eliminates apneas and hypopneas, decreases arousals, and normalizes oxygen saturation. In a study by Ueno among 70 OSA patients, CPAP has been shown to improve AHI from a mean of 51.9 to 4.2. Optimal CPAP pressure, is defined as the level that will abolish apneas and hypopneas, snoring and desaturation in all positions and during REM sleep. It is variable and patient dependent. For our patient, with an initial AHI of 59.8, respiratory events were abolished at CPAP level of 17 centimeters water to an AHI level of 2.8.

In another study by Antic on moderate to severe OSA patients on CPAP for 3 months. 70% exhibited normal sleep latency, and 60% had normal ESS scores, and 35% had normal functional outcomes of sleep questionnaire or FOSQ. In a study at our institution, CPAP treatment in moderate to severe OSA patients resulted in significant improvements in ESS and FOSQ scores.

In our patient, CPAP for eleven months achieved the following, a decrease in FOSQ score from 80 to 87 and normalization of ESS from 19 to 9. Other than improvements of symptoms of disrupted sleep, CPAP provides benefits on the patient's comorbidities. In the study by Sharma and associates, 86 metabolic syndrome patients on CPAP for 3 months showed statistically significant reductions in FBS, triglycerides, hemoglobin A1C, and HDL. On follow-up, our patient showed the following. Should compliance to CPAP therapy be inadequate, alternative therapy can be instituted. It involves behavioral strategies, oral appliances and surgery. Behavioral strategies include – weight loss, exercise, and sleep positional therapy. Oral appliances such as the Mandibular Repositioning Splint -- to protrude the mandible forward and hold the tongue more anteriorly. Surgery is indicated if PAP is inadequate or if the patient exhibits intolerance and when obstructive anatomy compromise other therapies. The common surgical procedures are the following, with uvulopharyngoplasty being the most commonly performed. The management of obesity primarily focuses on weight reduction.

In a study by Peppard on moderate weight change in patients with sleep disordered breathing, a 10% weight loss causes a 26% decrease in AHI with an increase of 32% if the patient had 10% weight gain. Weight loss can be approached non-surgically and surgically. Non-surgical therapy consists of behavioral therapy, low caloric diet, medications and promotion of physical activity. While surgical management centers on bariatric surgery. In this case, can we recommend bariatric surgery for our patient? The answer could be answered by. A study published by Dixon, where bariatric surgery compared with conventional weight loss therapy showed no statistically significant greater reduction in AHI. Hence, we will not recommend bariatric surgery.

With the management we have given, what lies ahead for PD? Long term outcomes for OSA patients were studied by Young and associates. In a study on sleep disordered breathing and mortality with an eighteen year follow-up *(Figure 27)*. All-cause mortality adjusted for age, sex, and BMI was significantly increased with SDB severity. The findings also showed a significant high mortality in untreated SDB. In another study published by Marti on the effects of CPAP on moderate to severe OSA, the data showed a reduction of 40% in all-cause mortality in the treated group against those who did not received treatment *(Figure 28)*. A search on the prognosis of his other comorbidities, a BMI of 40-45 reduces life span by 8-10 years, and for untreated early-onset severe kyphoscoliosis, there is significantly increased mortality from respiratory failure or cardiovascular diseases compared to the general population with increased risk of death after 40 years of age. Presented was a ménage a trois of obesity, kyphoscoliosis and obstructive sleep apnea. Add to the mix the other comorbidities – hypertension, diabetes and dyslipidemia. An unfortunate mix, but a challenge. There are no published data on the prognosis of patients like ours, all his illnesses will eventually take their toll. But we will not be deterred, we will continue patient education, weight reduction, proper nutrition, control of blood pressure, hyperglycemia,

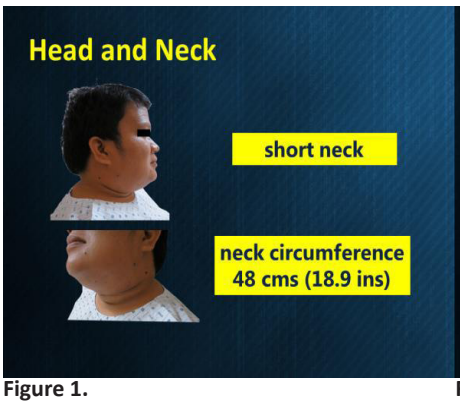
and dyslipidemia and continued adherence to CPAP therapy. Which for now, has had significant effects on the well-being of the patient.

CONCLUSION

In medicine, we live by a rule of William of Ockham, "pluritas non-esponenda sin necessitas" which translates as "plurality should not be posited without necessity." That means that most of the time, a variety of symptoms can be explained by a single diagnosis.

But we have come across with Hickam's dictum, by Dr. John Hickam, a 20th-century American physician born in the Philippines that simply states "Patients can have as many diseases as they damn well please." At no stage should a particular diagnosis be excluded solely because it doesn't appear to fit the principle of Occam's razor.

Here we have unfolded a ménage a trois of kyphoscoliosis, obesity, and obstructive sleep apnea. In time, the fateful mix will carry a much worse prognosis than any of the three entities alone. We can only hope that our interventions for this young man will carry him through.



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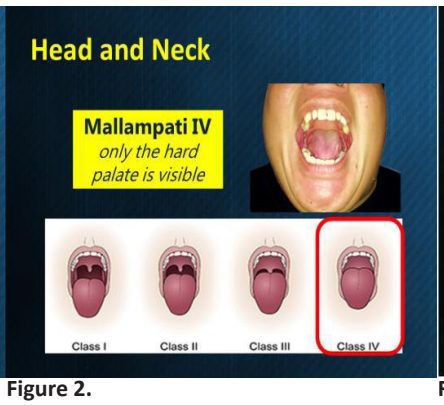

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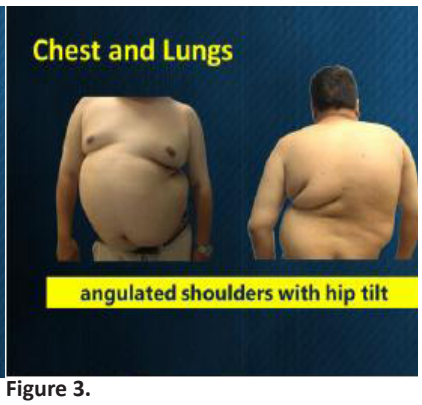

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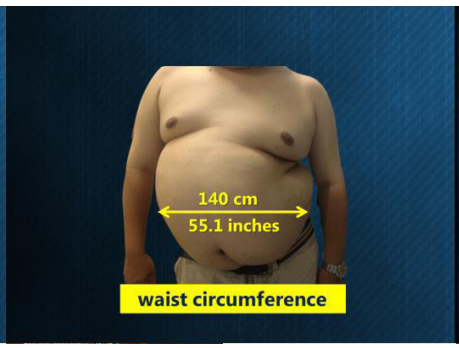

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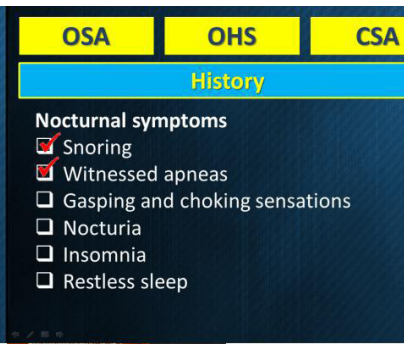

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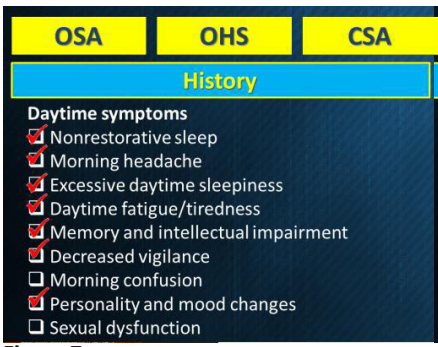

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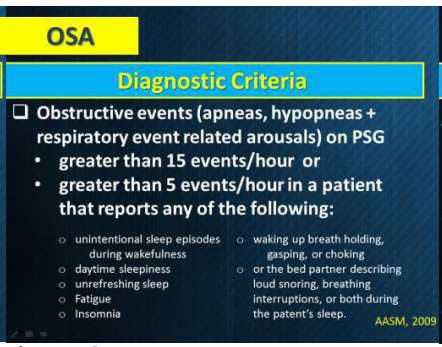

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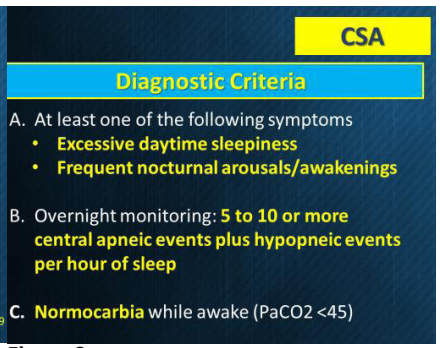

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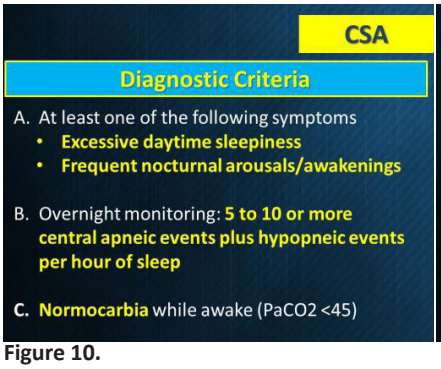

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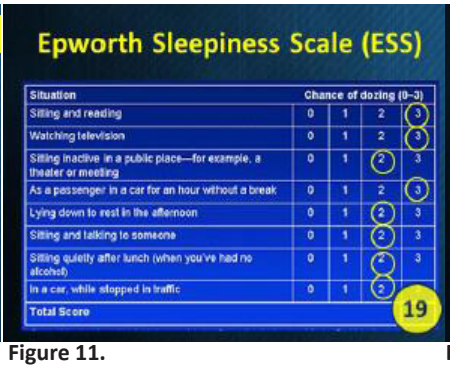

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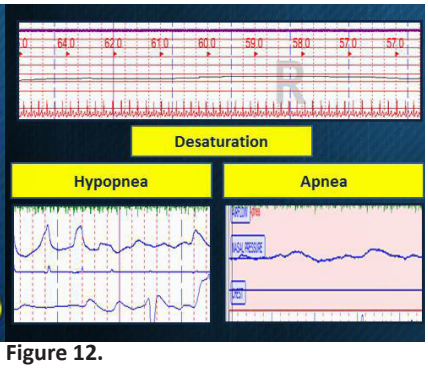

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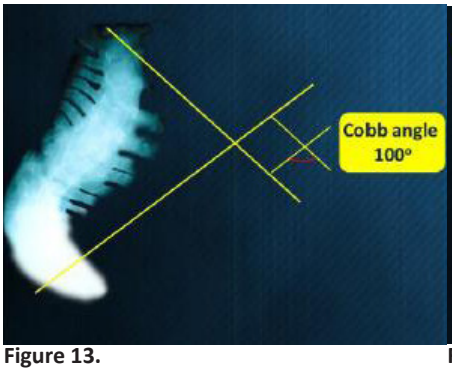

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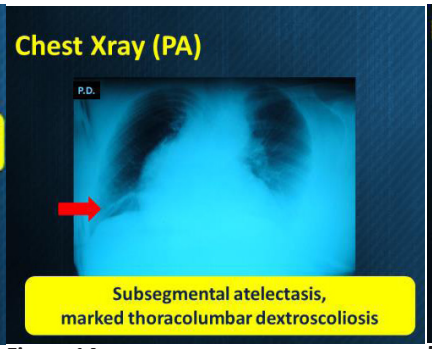

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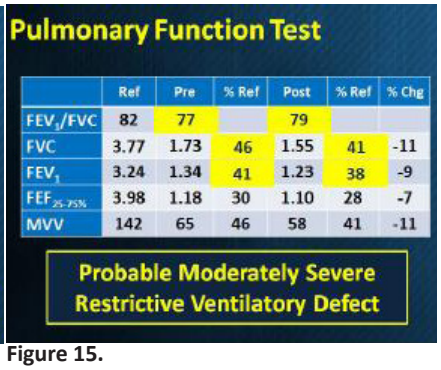

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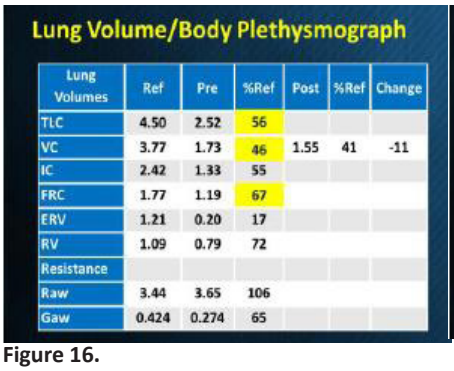

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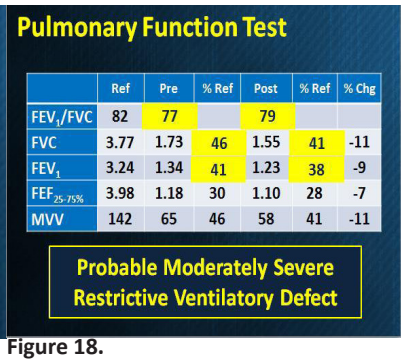

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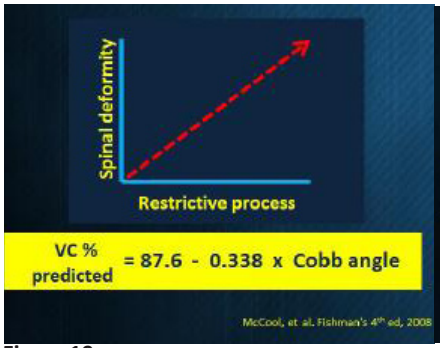

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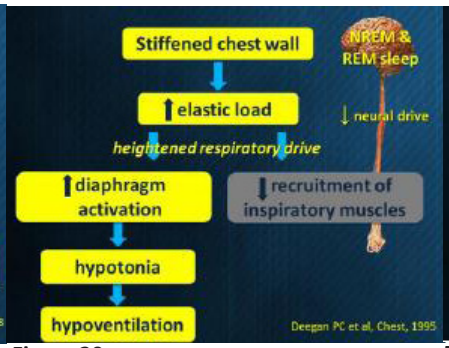

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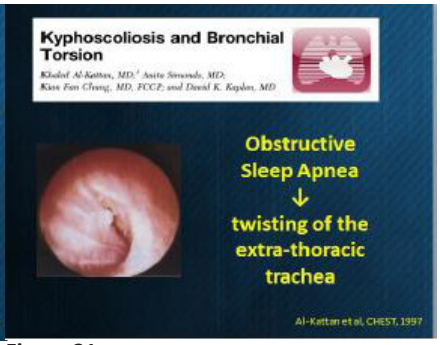

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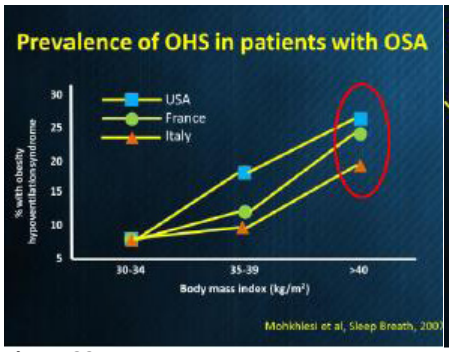

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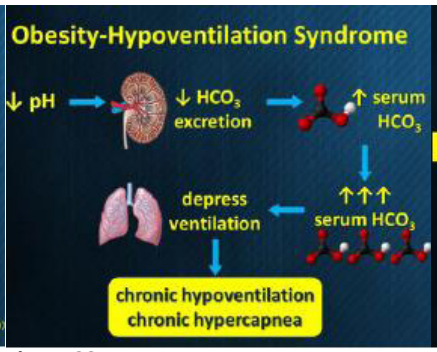

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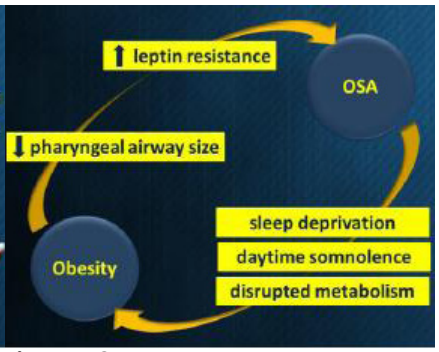

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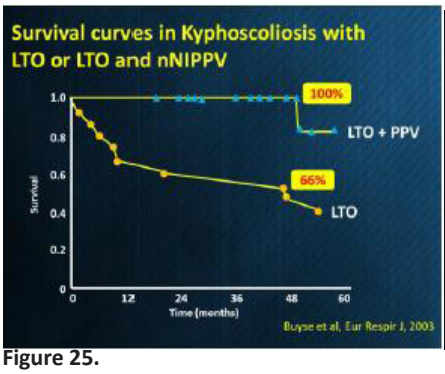

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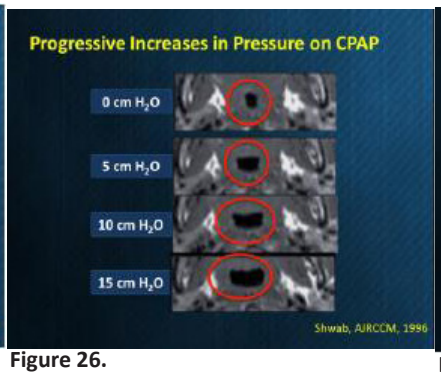

Figure 26.

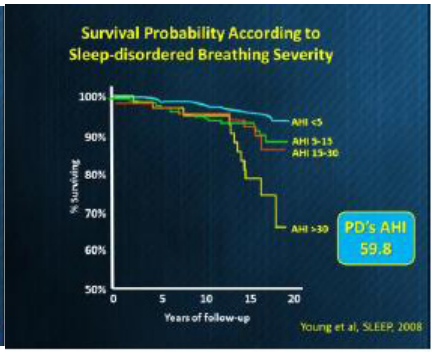

Figure 27.

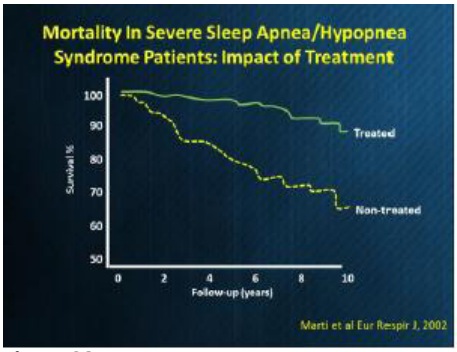

Figure 28.

Case Report -
Pulmonary and Critical Care Medicine

A Primary Malignant Melanoma of the Anterior Mediastinum

Cristia Maysol T. Maderazo-Morales, MD; Ma. Encarnita Blanco-Limpin, MD

A twenty three (23) year old male presented with cough and chest discomfort associated with intermittent fever for 5 months. This was associated with shortness of breath on exertion and weight loss. Family history was significant for breast cancer in the mother and sister. CT scan of the chest with contrast was done and showed an anterior mediastinal mass. Histopathologic diagnosis of CT scan guided biopsy revealed malignant melanoma, confirmed by immunohistochemical stains. Resection of the mass with lymph node dissection was done and the procedure was tolerated. Primary malignant melanoma of the anterior mediastinum is extremely rare. Definite diagnosis is through histopathologic yield of malignant melanoma and an immunohistochemistry staining of pleomorphic melanocytes with prominent nucleoli and melanin pigment which was present in our patient. Adjuvant chemotherapy after resection is the treatment of choice. ***Phil Heart Center J 2021;24(1): 45-48.***

Key Words: ■ Malignant Melanoma ■ Anterior Mediastinum ■

Primary malignant melanoma (MM) is a rare tumor. It is originating from the uncontrolled growth of melanocytes found in the basal stratum of the oral mucous membranes.[1] The pathogenesis of MM is associated with both environmental and genetic factors. Melanoma most commonly occurs in the skin and mucous membranes.[3] Primary malignant melanoma of the anterior mediastinum is extremely rare, accounting for 0.1-0.5% of all primary malignant neoplasms. These tumors may be mistakenly diagnosed as lymphomas, thymic carcinomas and malignant germ-cell tumors of the mediastinum.[2] Early diagnosis and treatment are important for reducing morbidity and mortality. Malignant melanoma cells stain positively with antibodies to human melanoma black 45 (HMB-45), S-100 protein, and vimentin. Hence, immunohistochemistry has an important role for evaluating the depth of invasion and the location of metastases. Exclusion of other primary melanoma sites is mandatory to confirm a primary mediastinal melanoma.

Case: A 23 year old Filipino male with no known co-morbidities presented to the emergency department with complaints of worsening dyspnea on exertion associated with chest pain and intermittent fever for approximately 5 months. He did not have chills, night sweat, cough or sputum production. On physical examination, patient had the following vital signs, with blood pressure of 120/70 mmHg, pulse rate 96 beats/min, and respiratory rate of 22 breaths/min and temperature of 38.2C. Tenderness was noticed on anterior chest wall. Examination of abdomen and pelvis was normal. There was no abnormality noticed in the scrotal examination. Examination of lungs revealed right mid posterior egophony and decreased breath sounds in the right lung base with muffled heart sounds. His complete blood count revealed leukocytosis of 16×109 cells/L with predominance of segmenters at 75%. Chest radiograph showed mediastinal widening with a bulky lobulated mass lesion. Patient was subjected to plain chest CT scan which showed a bulky anterior mediastinal mass measuring 18x14x16 cm. Patient

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was advised to undergo surgical resection of the mass and was eventually done. The procedure was tolerated well by the patient. The gross specimen showed several, brown, firm to friable tissues measuring 18 x 14 x 4 cm (*Fig. 1*). The histopathologic report showed mainly of multiple nodules of neoplastic cells divided by scant fibrous septa (*Fig. 3A*). The individual neoplastic cells are enlarged and exhibit round to ovoid, vesicular nuclei, abundant eosinophilic cytoplasm with prominent eosinophilic nucleoli. Frequent mitosis is observed (*Fig. 3B*). Extensive areas of hemorrhage and necrosis identified. Immunohistochemical studies done with good working positive controls show the neoplastic cells with strong and diffuse cytoplasmic and nuclear reactivity against S100, strong cytoplasmic reactivity against vimentin, strong cytoplasmic reactivity against Human Melanoma Black (HMB45) and Melan-A. Proliferation index using Ki-67 is at 60%. (*Fig. 2*) These findings are compatible with melanoma, anterior mediastinum. Patient was referred to an Oncologist. Patient received Cisplatin-based chemotherapy with no complications noted. Patient was then discharged improved.

Figure 1. Gross specimen of the anterior mediastinal mass. The mass consists of several fragments of brown friable material and aggregately measures 18 x 14 x 4 cm.

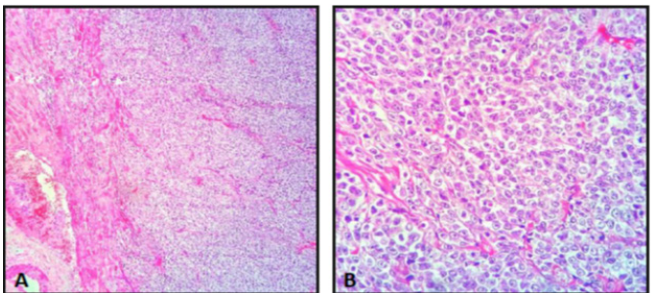
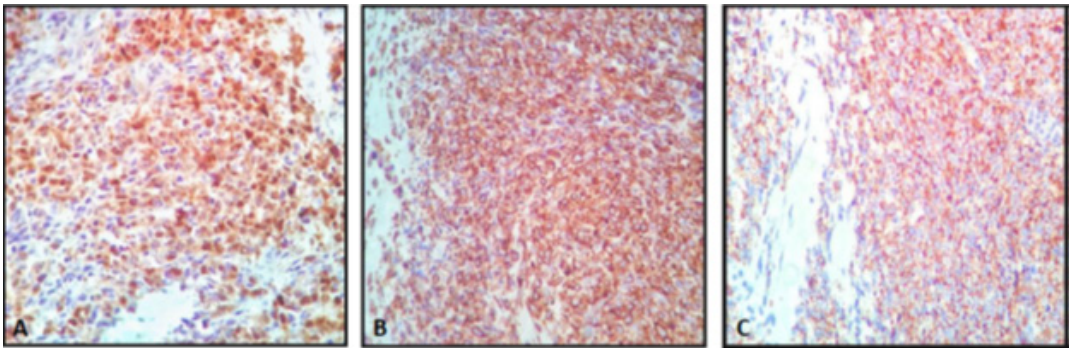


Figure 2. A. Microscopic sections of the mediastinal mass show multiple nodules divided by fibrous septa. (H&E 100X)



B. Neoplastic cells showing enlarged, vesicular nuclei, prominent eosinophilic nucleoli, with abundant amount of eosinophilic cytoplasm. (H&E 400X)

DISCUSSION

Mediastinal tumors account for 50% of mediastinal masses and the most common primary mediastinal tumors include thymoma, teratoma, and lymphoma.[4] Histopathological features and immunohistochemical staining are helpful for the diagnosis of this disease and are also the primary means to identify other MM tumors. Histologically, primary MM exhibits significant heterogeneity, with a growth pattern consisting of isolated clusters and the pathological features of mediastinal MM are the same as those of MM tumors in other parts of the body. The main features observed by light microscopy of tumor tissue sections include a large number of spindle shaped cells and coarse pigment granules. The tumor cells can be arranged in nests, sheets, and cords, and exhibit obvious cellular atypia, with cells ranging in size and morphology, including rounded or polygonal cells with distinct boundaries, abundant and red-stained cytoplasm, melanin granules in the cytoplasm, centered or deviated nuclei, clearly identifiable nucleoli, and apparent pathological mitosis. There are abundant vessels among the extracellular matrix. The immune phenotype is investigated using the monoclonal antibody, S-100, which is the most sensitive marker for melanoma; however, it has low specificity, while HMB-45 can identify melanoma cells with a high specificity, and Ki67 is the most useful marker for differentiating benign from MM. Combined with Melan-A, these markers can effectively prevent misdiagnosis.

There is no consensus regarding the treatment of metastatic mediastinal or primary mediastinal MM; therefore, current treatment guidelines for cutaneous melanoma are generally followed. If possible, complete surgical resection to reduce the tumor mass is advocated for patients with early stage disease, before chemotherapy or radiotherapy.[1,9] Although chemotherapy or radiation therapy can be used to treat advanced MM.[1,10] Dacarbazine is only proven to have a 3.7% rate of effectiveness as first line chemotherapy.[11] Radiotherapy has been administered to control the local spread of melanoma, but does not prolong survival rates.[12] Given the clear immunogenicity of MM, immunotherapy is considered the most promising current treatment. Research to develop small molecule targeting drugs has greatly improved the survival rate of patients with MM and is a topic of intense investigation. The cytokines interleukin 2 and interferon alpha were the earliest immune agents to be approved by the US Food and Drug Administration for the treatment of unresectable or metastatic MM. In recent years, the use of immune regulatory antibodies has been a breakthrough in the immunotherapy of MM. An antibody (ipilimumab) targeting cytotoxic T lymphocyte-associated antigen 4 (CTLA-4) was also approved by the US Food and Drug Administration for the treatment of metastatic MM in March 2011, and its use significantly improves overall patient survival.[13] Pembrolizumab and nivolumab, drugs targeting programmed death protein-1, which are expected to be approved for the treatment of metastatic MM in the near future, have also shown to produce high and persistent objective response rates when applied in the clinic.

CONCLUSION

Primary mediastinal MM is a rare tumor of uncertain histogenesis, associated with morbidity concealment. With no specific clinical manifestations or imaging features, preoperative diagnosis of this disease is difficult and it is easily misdiagnosed. Immunohistochemical examination is the main method to distinguish primary mediastinal MM from other tumors. The histopathological features of mediastinal MM are the same as those of MM in other parts of the body, and extensive clinical and radiological investigation to rule out possible metastases, and to search for another potential primary tumor, is essential. Despite the low chances of cure, if possible, complete surgical resection to reduce the tumor mass is advocated for early stage patients before chemotherapy or radiotherapy. With a fast progression and poor prognosis, timely and effective systemic treatment is necessary to improve the survival rates of patients with advanced disease. Immunotherapy and targeted therapy are the most promising treatments for unresectable or advanced stage patients; however, their effectiveness is unknown due to the rarity of the disease and evidence from additional clinical cases is required.

REFERENCES

1. Gondivkar SM, Indrkar A, Degwekar S, Bhowate R. Primary oral malignant melanoma--a case report and review of the literature. Quintessence Int. 2009;40:41–46.
2. Kuzur ME, Cobleigh MA, Greco FA, Einhorn LH, Oldham RK. Endodermal sinus tumour of the mediastinum. Cancer 1982;50:766-74.
3. Karuppiah SV, Buchan KG. Primary malignant melanoma: a rare cause of mediastinal mass. Jpn J Thorac Cardiovasc Surg. 2006;54:396–398.
4. Laurent F, Latrabe V, Lecesne R, et al. Mediastinal masses: diagnostic approach. Eur Radiol 1998;8:1148–1159.
5. Park SY, Kim MY, Chae EJ. Primary malignant melanoma of the mediastinum: radiologie and pathologic correlation in two case. Korean J Radiol 2012;13:823–6.
6. Ueno T, Tanaka YO, Nagata M, et al. Spectrum of germ cell tumors: from head to toe. Radiographics. 2004; 24:387-404.
7. Trousse D, Avaro JP. Mediastinal tumors: introduction. Rev Pneumol Clin 2010;66:13–6.
8. Park SY, Kim MY, Chae EJ. Primary malignant melanoma of the mediastinum: radiologie and pathologic correlation in two case. Korean J Radiol 2012;13:823–6.
9. Cormier JN, Xing Y, Feng L, et al. Metastatic melanoma to lymph nodes in patients with unknown primary sites. Cancer 2006;106:2012–20.
10. Feldman L, Kricun M. Malignant melanoma presenting as a mediastinal mass. JAMA 1979;241:396–7.
11. Cordina E, Assouline PS, Krespine C, et al. Primary malignant mediastinal melanoma. Apropos of a case. Rev Pneumol Clin 1997;53:203–6.
12. Kalra A, Kalra A, Palaniswamy C, et al. Primary malignant melanoma presenting as superior mediastinal mass. Int J Surg Case Rep 2011;2:239–40.
13. Kim HR, Lee JS, Kim YT, et al. Primary malignant melanoma presenting as an anterior mediastinal mass. Korean J Thorac Cardiovasc Surg 2002;35:697–700.
14. Cui C, Mao L, Chi Z, et al. A phase II, randomized, double-blind, placebo-controlled multicenter trial of Endostar in patients with metastatic melanoma. Mol Ther 2013; 21:1456–63.
15. Bastiaannet E, Beukema JC, Hoekstra HJ. Radiation therapy following lymph node dissection in melanoma patients: treatment, outcome and complications. Cancer Treat Rev 2005;31:18–26.
16. Maio M, Grob JJ, Aamdal S, et al. Five-year survival rates for treatment-naive patients with advanced melanoma who received ipilimumab plus dacarbazine in a phase III trial. J Clin Oncol 2015;33:1191–6.

Case Report -
Pulmonology a Critical Care Medicine

Diaphragmatic Hernia in 6 Months Old Infant

Jay G. Ylanan, MD; Dulce Requiron-Sy, MD; Beverly Dela Cruz, MD

Congenital diaphragmatic hernia is an anatomical defect of the diaphragm, which allows protrusion of abdominal viscera into the chest, causing serious pulmonary and cardiac complications in the neonate. However, the presentation of Congenital Diaphragmatic Hernia in older children and adults is rare, and, therefore, little is known concerning its symptoms, operative management, and postoperative complications. We report a six month old, female who presented with tachypnea due to diaphragmatic hernia. This patient was initially managed as pneumonia. Late presenting diaphragmatic hernia can present with acute or chronic gastrointestinal, or less frequently, respiratory symptoms. Misdiagnosis can result in significant morbidity. Favorable outcome is expected when the correct diagnosis is made. ***Phil Heart Center J 2021;24(1):49-52.***

Key Words: Tachypnea ■ Congenital Diaphragmatic Hernia ■

In surgical causes of respiratory distress in neonates, the underlying mechanisms include airway obstruction, pulmonary collapse or displacement and parenchymal disease or insufficiency; one of the most common causes is congenital diaphragmatic hernia (CHD), with an incidence of 1:2500-5000 live births.[1] Congenital diaphragmatic hernia is an anatomical defect of the diaphragm, which allows protrusion of abdominal viscera into the chest, causing serious pulmonary and cardiac complications in the neonate.

On the opposite side of the CDH clinical spectrum, there is an uncommon subset of patients who present symptoms beyond the neonatal period: these cases with late presenting CDH represent 10-13% of all CDH cases.[2-6] The symptoms in this late-onset group are non-specific and may commonly include recurrent chest infections, failure to thrive, vomiting, diarrhea, anorexia and abdominal pain. For these reasons, late-presenting CDH is quite frequently misdiagnosed.

Case: The patient is a six month old female who presented with tachypnea. The mother had fever and subchorionic hemorrhage at 2 months age of gestation and took paracetamol and other unrecalled medication. She was born fullterm via normal spontaneous delivery at a lying-in clinic with good cry and activity. There was no claim of recurrent illness. She has no exposure to tuberculosis. The patient was apparently well until 3 months of age, the patient was noted to be tachypneic with gurgly chest, constipation. Consulted with a local health physician and was advised to observe the patient and was said that infants are fast breathers by nature. A month prior to admission, consulted at their provincial hospital due to persistence of tachypnea which was now associated with fever and rashes. She was diagnosed to have Roseola Infantum. Eleven days prior to admission, persistence of tachypnea noted now associated with high grade fever and cough. She was admitted in the provincial hospital. Chest x-ray was done and was signed out as Pneumonia with pleural effusion and thickening in the right lung; bullous changes with bronchiectasis, left lung. The patient was managed as a case of Pneumonia and Pulmonary Tuberculosis with pleural effusion. However, patient was in respiratory distress despite the management. A referral to a tertiary hospital was

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made. She was then transferred to another hospital. The patient was seen by a pediatric pulmonologist. Chest xray was done (*Figure 1*) and showed multiple cystic lucencies with thick walls replacing the left hemithorax sparing the apical region, the heart and mediastinal structures are displaced to the right and a note of paucity of bowel gas in the upper abdominal quadrant. referred to this institution for further management. Chest examination showed decreased movement on the left with dullness on percussion, and bowel sounds on the left hemithorax. There was a noted of scaphoid abdomen (*Figure 2*). Plain chest CT scan revealed large hiatal hernia with mainly herniated large colon; Pneumonia, right lower lobe. Prior surgery, a 2D echocardiography was done and revealed no intracardiac lesion with normal pulmonary artery pressure. Arterial blood gas blood gas taken showed metabolic acidosis. Repair of diaphragmatic hernia was done. Operative findings were 3 cm left posterolateral hernia with sac, small and large intestines protruding into the left pleura, hypoplastic lung with milky white fluid noted over the left pleura (*Figure 3*). A repeat chest xray was done after the repair of diaphragmatic hernia showed expansion of the left lung (*Figure 4*). At present, patient is still at surgical intensive care unit. She is being monitored for any post-operative complications. Plan is to ventilate the patient for 3 days to open up the left lung.

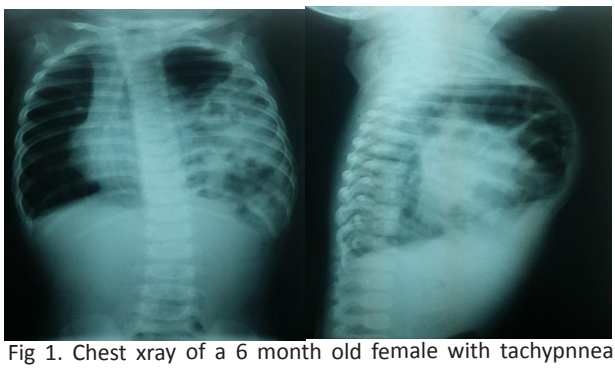

Fig 1. Chest xray of a 6 month old female with tachypnnea shows multiple cystic lucencies with thick walls replacing the left hemithorax sparing the apical region, the heart and mediastinal structures are displaced to the right and a note of paucity of bowel gas in the upper abdominal quadrant

Fig 2. Patient showed scaphoid abdomen on examination

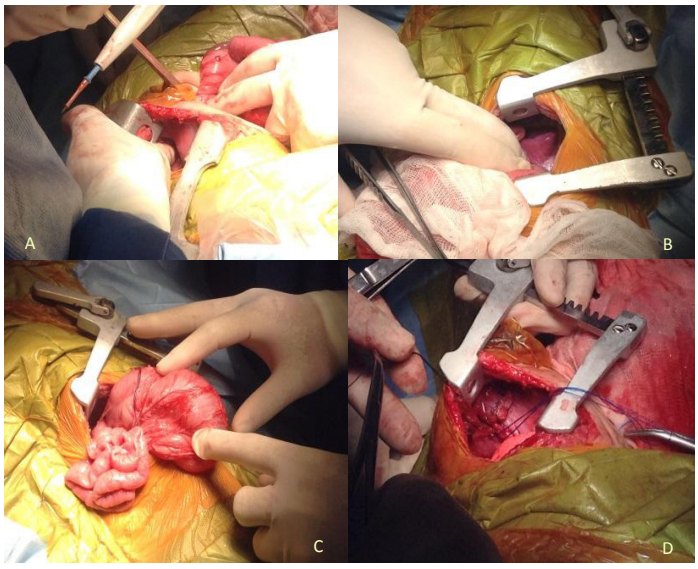

Figure 3. Intra-operative finding. (A) 3 cm left posterolateral hernia (B) hypoplastic lung (C) small and large intestines protruding into the left pleura (D) repair of diaphragmatic hernia

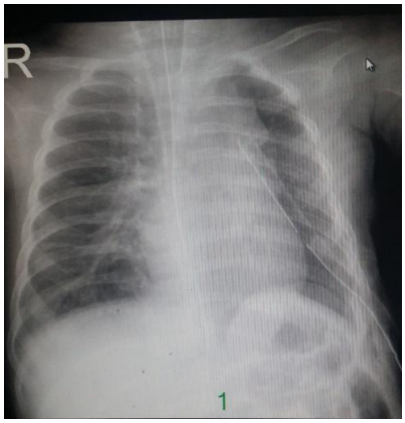

Figure 4. Chest x-ray after repair of congenital left diaphragmatic hernia

DISCUSSION

The anomaly underlying CDH is the failure of normal diaphragm development during embryogenesis.[7] Between the fourth and sixth weeks of gestation, failure of formation or fusion of pleuroperitoneal membranes results in a posterolateral diaphragmatic defect that is often referred to as Bochdalek's foramen.[8] This defect occurs five times more frequently on the left side than the right, probably because of earlier closure of the right pleuroperitoneal canal than the left. Bochdalek DH usually presents in the neonatal period as severe respiratory distress. However, late presenting DH has been described in the literature, and is usually associated with a better outcome. Incidence varies between 5% and 25% of all Bochdalek DH.[3,9,10] In 349 late-presenting CDH children recently reviewed, the male-to-female ratio was close to 2:1.4. Among late-presenting CDH cases, unilateral postero-lateral defects constituted more than 96%, with 79.4% and 20.6% left and right-sided hernias, respectively. Eighty percent of cases of delayed onset diaphragmatic hernia present with acute symptoms.[11] As most of the cases presenting late do not have associated anomalies, the etiopathology of diaphragmatic defect is less likely to be similar to the usual congenital diaphragmatic hernia.[11,12]

Late onset diaphragmatic hernia is often intriguing. Today, late-presenting CDH is regarded by pediatric surgeons merely as a clinical variant of CDH. Taking into account the larger series published in the last two decades, the occurrence of late-presenting CDH can be estimated to be 10-13% of all CDH cases[13-16] An important epidemiological feature of late presenting CDH is the very low incidence of major associated anomalies, which stands in great contrast to neonatal hernia.[12-14] This patient doesn't have any congenital anomaly based on the physical examination and diagnostics done.

Misdiagnosis of late presenting DH is often reported. Although pneumonia is frequently the initial incorrect diagnosis in these children, and was previously reported in up to 62% of patients with DH,[15] it is usually not associated with severe morbidity. Likewise, this patient was initially diagnosed as pneumonia.

CONCLUSION

We report a case of a 6 month old female with left congenital diaphragmatic hernia without any other congenital anomaly. Children presenting with tachypnea and gurgly chest should be investigated. The importance of sound physical examination, correct interpretation of imaging as surgical correction is life saving and curative. All pediatricians and pediatric surgeons should be aware of this condition in their routine practice.

REFERENCES

1. Van Meurs K, Lou Short B. Congenital diaphragmatic hernia: the neonatologist's perspective. Pediatr Rev 1999; 20: e79-87.
2. Weber TR, Tracy T Jr, Bailey PV, Lewis JE, Westfall S. Congenital diaphragmatic hernia beyond infancy. Am J Surg 1991; 162: 643-646.
3. Berman L, Stringer D, Ein SH, Shandling B. The late-presenting pediatric Bochdalek hernia: a 20-year review. J Pediatr Surg 1988; 23: 735-739.
4. Malone PS, Brain AJ, Kiely EM, Spitz L. Congenital diaphragmatic defects that present late. Arch Dis Child 1989; 64: 1542-1544.
5. Numanoglu A, Steiner Z, Millar A, Cywes S. Delayed presentation of congenital diaphragmatic hernia. S Afr J Surg 1997; 35: 74-76.
6. Mei-Zahav M, Solomon M, Trachsel D, Langer JC. Bochdalek diaphragmatic hernia: not only a neonatal disease. Arch Dis Child 2003; 88: 532-535.
7. Gosche JR, Islam S, Boulanger SC. Congenital diaphragmatic hernia: searching for answers. Am J Surg 2005; 190: 324-332.
8. Skarsgard ED, Harrison MR. Congenital diaphragmatic hernia: the surgeon's perspective. Pediatr Rev 1999;20: e71-78.
9. Osebold WR, Soper RT. Congenital posterolateral diaphragmatic hernia past infancy. Am J Surg 1976;131:748–54.
10. Newman BM, Afshani E, Karp MP, et al. Presentation of congenital diaphragmatic hernia past the neonatal period. Arch Surg 1986;121:813–69.
11. Bagłaj M. Late-presenting congenital diaphragmatic hernia in children: a clinical spectrum. Pediatr Surg Int 2004 Sep;20(9):658-669.
12. Tibboel D, Gaag AV. Etiologic and genetic factors in congenital diaphragmatic hernia. Clin Perinatol 1996 Dec;23(4):689-699. J.

13. Butler MW, Stolar CJ, Altman RP. Contemporary management of congenital diaphragmatic hernia. World J Surg 1993; 17: 350-355.
14. Kitano Y, Lally KP, Lally PA. Late-presenting congenital diaphragmatic hernia. J Pediatr Surg 2005; 40: 1839-1843.
15. Berman L, Stringer D, Ein SH, et al. The late-presenting pediatric Bochdalek hernia: a 20-year review. J Pediatr Surg 1988;23:735–9.
16. Weinstein S, Stolar CJ. Newborn surgical emergencies. Congenital diaphragmatic hernia and extracorporeal membrane oxygenation. Pediatr Clin North Am 1993 Dec;40(6):1315-1333.

Case Report -
Pulmonology a Critical Care Medicine

Giant Pulmonary Bulla in a 2 Year-old Child

Brenda Lou Lovely H. Noel-Abanilla MD; Ma. Dulce Requiron Sy, MD

Pulmonary bulla in children represent interesting entities. Mostly congenital bronchopulmonary foregut malformations and acquired cysts. This paper will present a case of a 2 year old child with recurrent cough but with no signs of respiratory distress. On further investigation the patient was harbouring a huge pulmonary cyst resulting in mediastinal deviation. Following initial work-up, a giant pulmonary bulla was considered and thoracotomy with bullectomy was done. There was no post-operative complication thus patient was discharged improved. ***Phil Heart Center J 2021;24(1):53-56.***

Key Words: Large bullae ■ Cystic lesion ■ Bullectomy ■

Cystic anomalies of the lung in the pediatric population represent entities with several differentials-mainly divided into congenital and acquired lesions. It can be caused by a diverse array of pathologic processes. A lung cyst or cystic airspace viewed by chest radiograph and chest computed tomography, is a parenchymal space with well-define, thin wall usually less than 2-mm thick. A cystic lesion lesion is an air-fluid or fluid-containing lesion, measuring 1 cm or more in diameter. Their manifestations remain constant with features of respiratory distress and mass effects predominantly.

The purpose of this paper is to present a rare case of a giant pulmonary bulla in a 2 year old child with no signs of respiratory distress but with mediastinal deviation on CT scan.

Case: A two year old, female child from Laguna was admitted due to recurrent cough. Her condition started 5 weeks prior to admission when patient had non-productive cough but without fever. Unrecalled antibiotic was given with persistence of symptoms thus four weeks prior to admission, chest x-ray (*Figure 1)* was done which revealed Koch's pneumonia, massive pneumothorax, left; minimal hydrothorax left. A repeat chest x-ray (*Figure 2)* 19 days prior to admission showed large bulla formation and interval decrease in the pneumonic infiltrates. Patient was given cefuroxime, oxacillin and metronidazole. Mantoux test was O mm. CT-scan of the chest (*Figure 3*) resulted large pulmonary bulla vs. pneumatocoele with deviation of the mediastinal structures to the right.

Patient was born to a 28 year old G2P2 mother with unremarkable prenatal history. Patient was delivered full term weighing 3 kilograms via normal spontaneous delivery. No complications were noted at birth. Past medical history include recurrent cough since 6 months of age with no history of pulmonary tuberculosis exposure nor treatment. She is non-asthmatic with no known food and drug allergies. Developmental history was at par with age.

Patient was seen awake, comfortable and not in respiratory distress with normal vital signs. Chest and lung findings include chest asymmetry, positive chest lag on left hemithorax, no retractions, hyperresonant and decrease tactile fremitus as well as decrease breath sounds on the left. No adventitious sounds noted. All other physical findings were unremarkable.

On admission, patient was stable. Antibiotics were continued. A repeat chest x-ray (*Figure 4*) showed lucency on the left with shifting of mediastinal structures to the right. Patient was referred to TCVS service for co-management.

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Laboratory tests which include CBC, electrolytes, Protime and APTT were normal. Tidal breathing analysis showed small airway disease with no significant response to bronchodilator. Patient underwent thoracotomy and left bullectomy (*Figure 5*). Intra-op findings was a large mass arising from a segment of the left lower lobe with multiple cysts within the cystic mass with bronchial connection. Chest x-ray (*Figure 6*) post-operative revealed interval resolution of previously noted cystic lucency and rightward mediastinal shift. Pleural fluid analysis revealed an exudative fluid with no growth on culture, no fungal and negative AFB seen. Cell count revealed 255 WBC with lymphocytic predominance. Patient had no complications noted post-operatively. Lung biopsy results fragments of lungs tissue with focal intra-alveolar hemorrhages and mild emphysematous changes and thin fibrous cyst wall favor pulmonary bulla. Negative for significant inflammation, granuloma or malignancy. Patient was then discharged improved on the eleventh hospital day with final diagnosis of giant pulmonary bulla, left s/p thoracotomy and bullectomy, left, pneumonia, bacterial community acquired Category C.

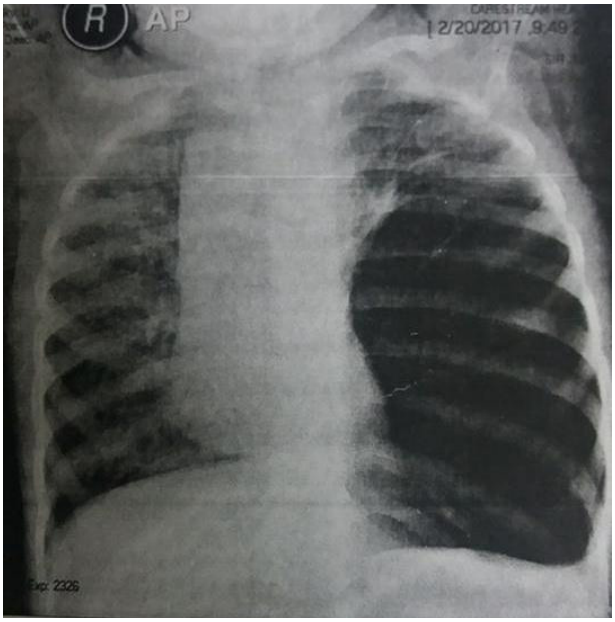

Fig 1. Koch's pneumonia, massive pneumothorax, left; minimal hydrothorax left

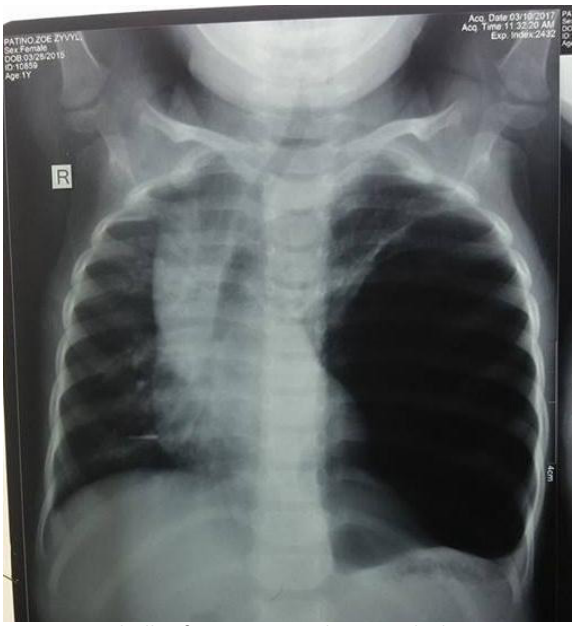

Fig 2. Large bulla formation and interval decrease in the pneumonic infiltrates

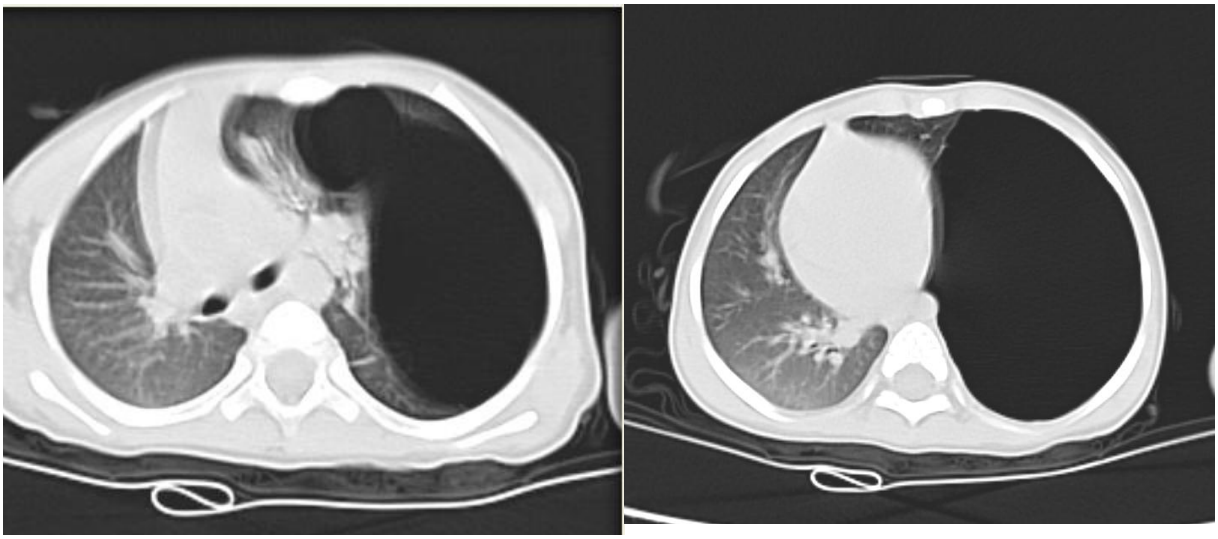

Fig 3. Large pulmonary bulla vs. pneumatocoele with deviation of the mediastinal structures to the right

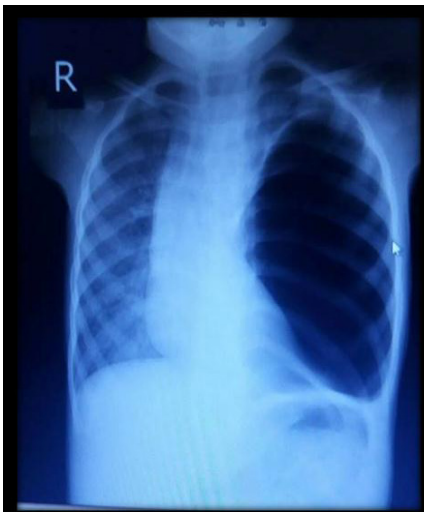

Fig 4. Lucency on the left with shifting of mediastinal structures to the right

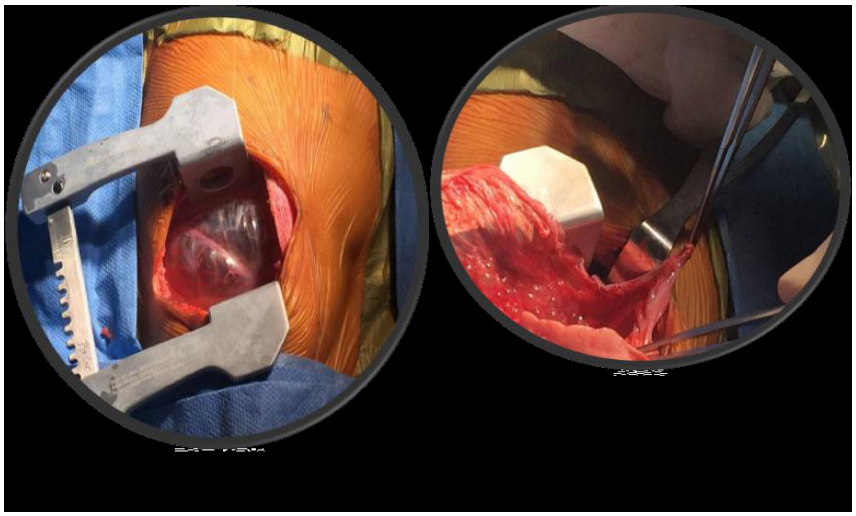

Fig 5. Thoracotomy and left bullectomy

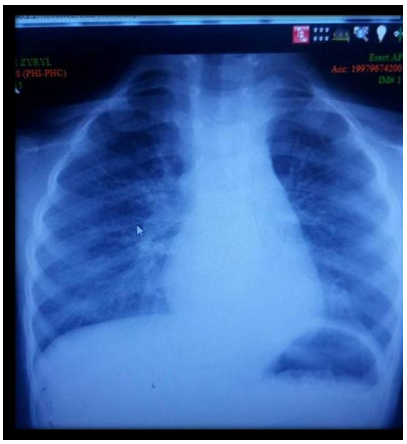

Fig 6. Resolution of previously noted cystic lucency and right ward mediastinal shift

DISCUSSION

Pulmonary cystic and cavitary lesions caused by diverse etiologies are commonly encountered in chest imaging. The terms "cyst" and "cavity" are used to describe air-filled regions in the center of a nodule or consolidation of the lung. To date, only radiologic aspects of these lesions have been addressed. The morphologies of pulmonary cystic and cavitary lesions exhibit a broad spectrum, ranging from benign to malignant pulmonary diseases of acquired or congenital origin, including variable infectious diseases.[1] In children, etiology of cystic lesions differs from that in adults, with congenital lesions being more prominent.[1] A pulmonary cyst is a round, circumscribed space surrounded by an epithelial or fibrous wall of variable thickness. Cysts vary in wall thickness but usually have a thin wall (< 2 mm). On CXR and computed tomography, a cyst appears as a round parenchymal lucency with a well-defined interface with normal lung.[2] The initial step in the diagnosis of a bulla is to identify wether a true cyst exist in CT scan. Bulla can be considered when a true cyst is found in subpleural location base on HRCT. Bulla is an air space in the lung measuring more than one centimeter in diameter in the distended state.[3] Giant bulla is used for bullae that occupy at least 30% of the hemithorax which is the case in the patient presented. A single bulla is rare as they are usually multiple in number and occupy portions of the lung most movable and least subject to continuous pressure of the chest wall, hence they are most frequently found in the upper anterior as well as along the mediastinal aspect of the lung.[4] Normal alveoli communicate with each other by means of minute perforations in the inter-alveolar walls. Bulla formation begins when there is confluence of two or more of the terminal elements of the bronchial tree.[4] Any acute but more often chronic intraalveolar pressure sufficiently great to stretch the inter-alveolar-walls will eventually lead to the formation of bulla. Most lung cysts are acquired as a result of bronchial inflammation and obstruction and very few are truly congenital in origin.[5] When a large cyst is found in a child with history of pulmonary infection, it is probable that the cyst was caused by bronchial inflammation and obstruction.[6] Secretions associated with infection blocked respiratory passages especially in young children

whose airways are small and coughing reflex is not yet-developed. This obstruction increases intraalveolar pressure leading to cyst/bulla formation.[6] Patient presented had recurrent cough thus a history of chronic pulmonary infection was established.

Patients with giant bullae may be asymptomatic, dyspneic on exertion or dyspneic at rest and exertion. Physical examination of the patient presented were consistent with a bulla as it may present with a normal chest or may reveal tachypnea, barrel-shaped chest, hyperresonance on chest percussion and decreased breath sounds.[7] Regardless of the patient's age and presenting signs and symptoms, the family history should be explored in detail for cancers and cystic lesions that might suggest familial pleuropulmonary blastoma syndrome.[7]

Pulmonary cysts are mostly diagnose with the help of chest radiography, CT examination has greatly to the appropriate diagnosis as well as management of such cysts. The prominent complications include repeated infections, haemorrhage, erosion into other adjacent structures or spontaneous pneumothorax. Hemoglobin concentration is assessed to exclude anemia as a contributor to dyspnea and to evaluate for secondary polycythemia due to chronic hypoxemia. Pulmonary Function Tests (PFTs) are indicated in all patients with a giant bulla to assess airflow limitation and air trapping.

The management of giant bulla depends on the degree of symptoms and development of complications. For asymptomatic patients medical and surgical therapy is usually deferred pending development of symptoms or other complications. However for patients whose dyspnea and exercise intolerance persist despite optimization of medical therapy bullectomy may be beneficial.[7] Bullectomy involves the surgical removal of one or more giant bullae by thoracotomy or video-assisted thoracoscopic surgery. Indications for bullectomy aside from a symptomatic patient includes a bulla that occupies greater than 30% of the hemithorax and a radiographic evidence that the bulla is compressing adjacent structures.[7] Following bullectomy, expansion of surrounding healthy lung tissue and improvement in chest mechanics by remodeling of the thorax and diaphragm occurs. Symptomatic improvement (dyspnea, exercise capacity, need of oxygen) and functional improvement occurs.

CONCLUSION

This is a rare case of a 2 year old female child presented with recurrent cough who had a large pulmonary cystic lesion in the left lung. Cystic and cavitary lung lesions can be caused by a diverse array of pathologic processes. In evaluating a patient with such lung lesions, it is helpful to distinguish cysts from cavities and to categorize focal or multifocal vs. diffuse distribution. These characteristics correlated with the tempo of the disease process and the clinical context provide the basis for prioritizing the diagnostic possibilities that will guide the subsequent evaluation and management. Patient was eventually diagnosed with a giant pulmonary bulla and underwent bullectomy with no noted complications and patient was discharged improved.

REFERENCE

1. Kim NR, Han J. Pathologic review of cystic and cavitary lung diseases. Korean J Pathol. 2012 Oct;46(5):407-14.
2. Liao SL, Lai SH, Hsueh C, Wong KS. Comparing late-onset and neonatally-diagnosed congenital cystic adenomatoid malformation of the lung. Chang Gung Med J. 2010 Jan-Feb;33(1):36-43.
3. Ryu JH, Swensen SJ. Cystic and cavitary lung diseases: focal and diffuse. Mayo Clin Proc. 2003 Jun;78(6):744-52.
4. Marti-Bonmati L, Catala FJ, Ruiz Perales F. Computed tomography differentiation between cystic bronchiectasis and bullae. J Thorac Imaging. 1991 Dec;7(1):83-5. Wiese ER. Bulla of the lung. Chest. 1946 May-June; 12 (3): 238-241.
5. Couriel J. Assessment of the child with recurrent chest infection. British Med Bull. 2002. March;61(1):115-132.
6. Raoof S, Bondalapati P, Vydyula R, Ryu JH, Gupta N, Raoof S, et al. Cystic lung diseases: algorithmic approach. Chest. 2016 Oct;150(4):945-965.

Case Report -
Pulmonology and Critical Care Medicine

Pulmonary Intralobar Sequestration with Congenital Pulmonary Airway Malformation Type II (CPAM Type II)

Florangel P. Avellana, MD

Intralobar sequestration (ILS) associated with congenital cystic adenomatoid malformation (CCAM) is a well-known entity. This hybrid form has many considerations for an appropriate management. This is a case of a month old male who presents with respiratory distress at birth. ***Phil Heart Center J 2021;24(1):57-60.***

Pulmonary sequestration is an uncommon congenital abnormality in which non-functioning lung tissue is supplied by an anomalous systemic artery. Both the extralobar and intralobar forms probably develop from an accessory lung bud from the primitive foregut.[1] Their etiology is far from understood, with various proposed theories. Some have suggested that intralobar sequestration is acquired when a focus of infection or scarring acquires its blood supply from a systemic collateral, basing this on the relative sparsity of other malformations associated with this type of sequestration and its rarity in perinatal autopsies.[2]

This case report aims to discuss a case of a 1-month old male who presented with persistent respiratory distress since birth and to discuss the epidemiology, pathogenesis, diagnosis and management for pulmonary sequestration.

Case: The patient was born to a 36y/o G3P2 (3012) mother, full term, cephalic, via repeat CS. The mother had regular prenatal check-up at a private OB-Gyne. The mother denied illnesses, intake of teratogens nor exposure to radiation. At birth, the patient had good cry and activity. However, tachypnea was noted hence was admitted at Lipa Medix Medical Center as a case of neonatal pneumonia. On the third day of admission at the said institution there was persistence of tachypnea despite IV antibiotics hence a chest CT scan was done which showed congenital thoracic malformation possible CCAM. He was transferred at our institution for further evaluation and management. Family medical history and review of systems were unremarkable.

On physical examination, the patient was awake, with good cry, suck and activity. Vital signs were within normal limits. There were no skin lesions or active dermatoses. Chest examination showed symmetrical chest expansion with the presence of subcostal retractions. There is no suprasternal retraction. Clear breath sounds was appreciated on the left with decreased breath sounds on the right. There were no wheeze, rhonchi or crackles. The rest of the physical examination was unremarkable.

Upon admission, the patient's vital signs were monitored. Chest CT scan (contrast-enhanced) was done which showed intralobar sequestration in the right lower lobe with adjacent cysts, which may represent Congenital Pulmonary Airway Malformation Type 2. 2D echocardiography was done which showed patent foramen ovale.

On the 7th hospital day, patient underwent posterolateral thoracotomy, right lower lobectomy. Intraoperative findings showed large arterial branch from the aorta connected to the

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right lower lobe, with right lower lobe consolidation and cystic areas. The patient was intubated and hooked to mechanical ventilator. He stayed at Pediatric Intensive Care Unit for 20 days, wherein gradual weaning from mechanical ventilator and completion of medications were done. On the 15th hospital day, he was extubated. However, milky drain was noted on chest tube on the 18th hospital day. Pleural fluid was analyzed which revealed chylothorax. The patient was put on Total Parenteral Nutrition (TPN) for 1 week. Milk feeding was resumed with recurrence of milky drain that was noted on chest tube. The patient was then put on NPO. TPN was resumed. Persistence of chylothorax was noted, hence Ocreotide was started.

On the 43rd hospital day, he remained to have stable vital signs without signs of respiratory distress. Ocreotide (Day 15) and TPN were continued. Trial of breastmilk was started. Monitoring of chylothorax was done. However, chylous drain persisted, thus, thoracic duct ligation was done. He was transferred to PICU on day 61th of hospital stay. At that time he developed decreased in activity with persistent hypoglycemia. Septic work-up was done revealing blood culture growth of *Serratia Marcescens.* Meropenem was given for 10 days and was shifted to Ciprofloxacin. Gradual introduction of milk feeding was done and chest x-ray monitoring of chylothorax were done with improving results. CTT was removed and increasing increments of Alfare was given.

On day 92nd day of hospital stay he remained to have stable vital signs with no significant change of chest x-ray. He was discharged with improved condition.

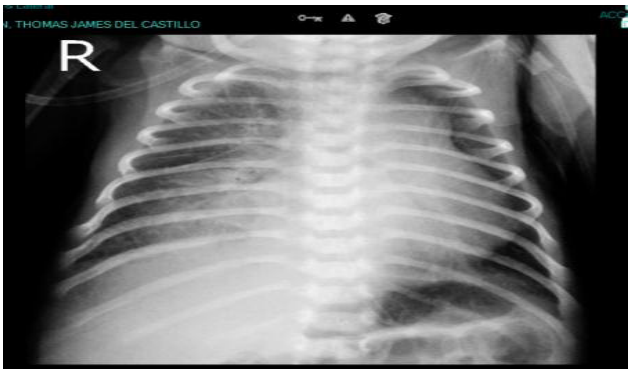

Fig.1**.** Chest x-ray AP view showing heterogeneously enhancing lesions at the right lower lobe without mediastinal shift

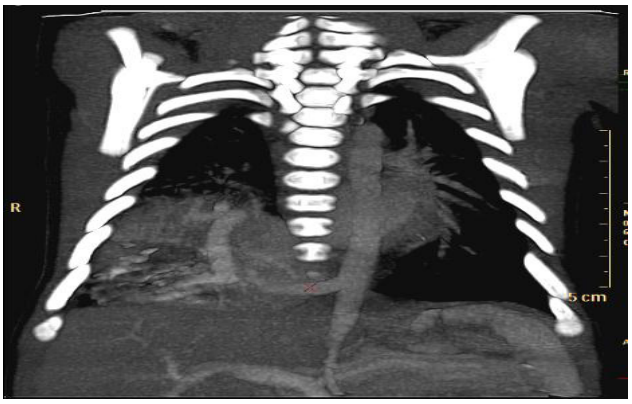

Fig. 2

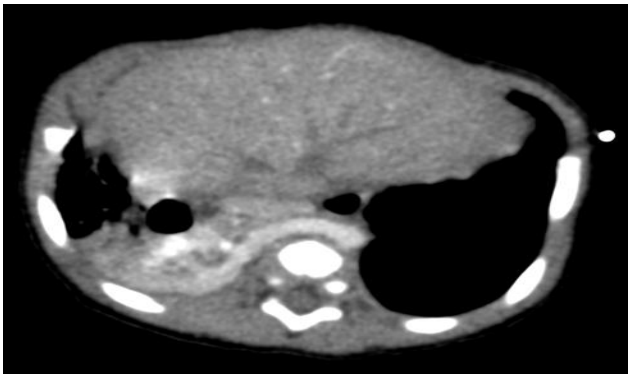

Fig. 3

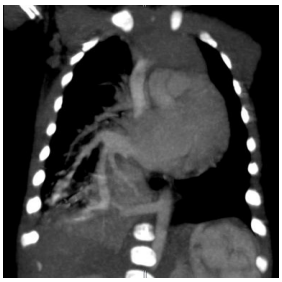

Fig. 4

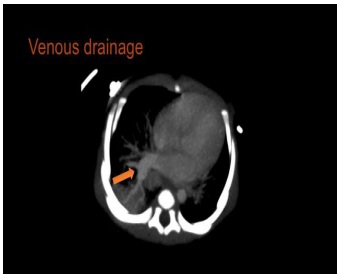

Fig. 5

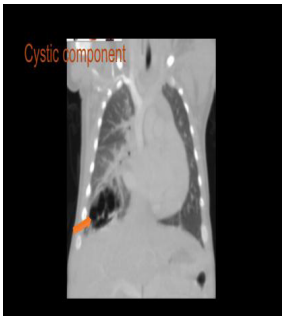

Fig. 6

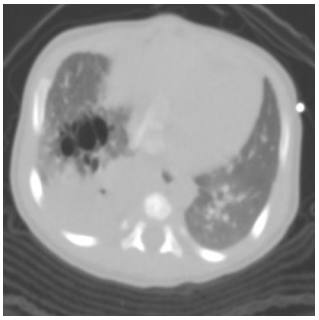

Fig. 7

Figure 2 and 3: CT scan of the chest revealing the arterial supply from the distal branch of descending aorta which supplies the posterior segment of the right lower lobe without communication to the tracheobronchial tree

Figure 4 and 5: CT scan of the chest showing the venous drain age (right inferior pulmonary vein to the left atrium) of the lesion

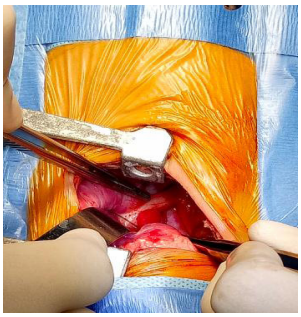

Fig. 8

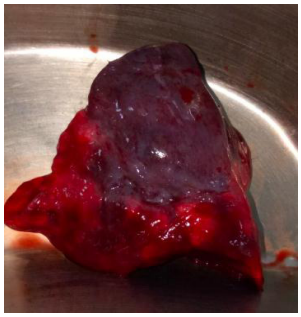

Fig. 9

Figure 6 and 7: CT scan of the chest showing the cystic structures at the right lower lobe

Figure 8: Intraoperative finding showing the arterial supply of the lesion coming from the descending aorta

Figure 9: Gross specimen of the sequestered lobe taken adjacent to the right lower lobe

DISCUSSION

Pulmonary sequestration consists of 2 types. Intralobar sequestration is usually found in the posterior basal segment of the left lower lobe. It is encircled by visceral pleura and has no pleural separation from the rest of the lobe. More than half the cases of intralobar sequestration are diagnosed after adolescence, and symptoms in neonates and infants are uncommon. Systemic arteries are likely to be large, and the veins drain into the pulmonary system. The extralobar type on the other hand is usually found beneath the left lower lobe. It is generally detected in infancy because of associated malformations. It affects males four times more frequently than females. The systemic arteries are small and the venous drainage is likewise systemic through the azygos.[2] Both types of sequestration have certain similar pathologic characteristics as well as clear-cut differences. In both types, the pulmonary tissue is largely cystic and contains disorganized, airless alveoli, bronchi, cartilage, respiratory epithelium, and a systemic artery. It is often secondarily infected, bronchiectatic, or atelectatic, and may show histology of a CCAM, particularly type 2 CCAM in extralobar variants.

In 1861, Rokitansky introduced the first description of the disease, and proposed that PS occurs when pulmonary tissue separates from the lung during embryogenesis; this was later known as "the fraction theory". Since then, many theories were introduced to explain the possible underlying pathophysiologic mechanisms producing the malformation.

In 1946, Pryce was the first to use the term "pulmonary sequestration", and classified the disease into intralobar and extralobar types. An intralobar sequestration is the most common form of the disease where the lung malformation remains within the visceral pleura of its lobe, whereas the extralobar type corresponds to a true accessory lung, with a separate pleural envelope and an aberrant venous drainage.

As the ectopic accessory bud arise from the primitive foregut, during the fourth week of gestation, a lung-resembling structures develops without communicating with the main bronchial tree, it becomes enveloped by its separate visceral pleura and derives its arterial supply from the systemic circulation. An extralobar sequestration can be sub-classified depending on the level at which the accessory bud branches off the primitive foregut into and intrathoracic type (*supradiaphragmatic*), and abdominal type (*subdiaphragmatic*).

Intralobar sequestration theories debate in defining the disease as either a congenital or acquired condition. Theories of the acquired aetiology state that chronic pulmonary infections of a lung tissue disconnected from the normal bronchial tree can cause hypertrophy of a regional systemic artery, hence the aberrant arterial supply. Despite being separated from the bronchopulmonary tree, infections may spread to the sequestered segment from adjacent aerated lung tissue via accessory inter-alveolar or broncho-alveolar connections, e.g. pores of Kohn, and canals of Lambert. These theories are supported by the low incidence of other congenital anomalies in association with intralobar sequestration, as opposed to the extralobar type. Additionally, more than half of intralobar sequestrations are diagnosed in later childhood or adulthood, while the majority of extralobar types are diagnosed during infancy.[3]

In a case series done by Basheer in 2015, pulmonary sequestration consists of about 0.1–6% of all structural lung diseases and developmental malformations.[3] The Philippine Pediatric Society noted 11 cases of sequestered lung among pediatric age group while 3 of which was on ages 28 days and below.

There is a greater male prevalence for the extralobar sequestration, approximately 3-4 times more common in males than in females. The extralobar type was only slightly more common in males 54% vs. females 46%. The main clinical manifestations are recurrent respiratory tract infections, and respiratory symptoms that often mimic other common pulmonary diseases, such as pneumonia, asthma, interstitial and obstructive pulmonary diseases. It should be noted that the patient is a one month old male who initially presented with respiratory distress at birth and was noted to have intralobar sequestration upon histologic examination. This makes the case a rare occurrence since the location of the lesion is more commonly found at the left lower lobe in contrast to our patient wherein the location is at the right lower lobe. The extralobar type is also more common in males and not the intralobar lesions. Furthermore, most of intralobar sequestration are diagnosed during late childhood or adolescence as opposed to extralobar types.

The misdiagnosis rate was reported as high as 87%, due to the wide array of nonspecific symptoms, delaying treatment and limiting therapeutic options. The main CT findings in this large group of patients included a mass lesions (49%), cystic lesions (29%), cavitary lesions (12%), and pneumonic lesions (8%).[3] The patient presented with cystic lesions upon CT scan.

The ILS-CCAM association is a hybrid lesion with CCAM histology and a systemic arterial supply. The diagnosis should be considered when prenatal explorations show a macrocystic lesion with an aberrant systemic vessel. The hybrid lesion enters into the differential diagnosis of fetal lung malformations, especially when the mass location is contiguous to the diaphragm. Prenatally, it is difficult to detect the association of ILS with CCAM. The main difficulty lies in identifying the aberrant vessel. Chest CT at 1 month of life is considered the most accurate examination in the postnatal radiologic investigations of prenatally diagnosed pulmonary lesions. Its sensitivity is estimated to be 100%. CT is recommended as the first-line postnatal investigation for all babies with a suspected prenatal diagnosis of CCAM (including the prenatal resolved lesions).[4] Surgical resection remains the standard of care for all patients with pulmonary sequestration, as it serves to establish the diagnosis, differentiate anomalous pulmonary tissue from malignancies, and prevent recurrent infectious or haemorrhagic complications.

FINAL DIAGNOSIS

1. Congenital Pulmonary Airway Malformation type 2 with Pulmonary Intralobar Sequestration, Right Lower Lobe
2. S/P Right Posterolateral Thoracotomy, Right lower lobectomy
3. Chylothorax S/P CTT insertion (9/6/2017)
4. Hospital Acquired Pneumonia (S. marcescens)
5. Congenital Heart Disease, Patent Foramen Ovale

CONCLUSION

Pulmonary sequestration is a rare disease with multiple theoretical etiologies, often misdiagnosed due to its variable and non-specific presentation. CT scan/angiography and other imaging modalities which can accurately identify the arterial supply and venous drainage of the sequestered segment, are essential for diagnosis and preoperative planning

REFERENCE

1. Corbett HJ, Humphrey GM. Pulmonary sequestration. Paediatr Respir Rev. 2004 Mar;5(1):59-68.
2. Wilmott R, Bush A. Boat T, Deterding R, Ratjen F, Chernick V. Kendig and Chernick's disorders of the respiratory tract in children. 8th ed. Mo: Elsevier, c2012.
3. Tashtoush B, Memarpour R, Gonzalez J, Gleason JB, Hadeh A. Pulmonary sequestration: a 29 patient case series and review. J Clin Diagn Res. 2015 Dec;9(12): AC05-8.
4. Zeidan S, Hery G, Lacroix F, Gorincour G, Potier A, Dubus JC, et al. Intralobar sequestration associated with cystic adenomatoid malformation: diagnostic and thoracoscopic pitfalls. Surg Endosc. 2009 Aug;23(8): 1750-3.

Case Report -
Pulmonary and Critical Care Medicine

Recurrent Pnuemothorax in a Patient with a Rare Case of Sporadic Lymphangioleiomyomatosis

Karen Anne G. Bispo, MD

Lymphangioleiomyomatosis (LAM) is a rare progressive cystic lung disease of uncertain etiology that affects young women. It appears to involve one of the most bizarre pathogenic mechanisms in human disease: the metastasis of histologically benign cells. Pneumothorax is one of the complications and most common pulmonary manifestations of LAM. We present a case of a 49-year-old Filipino, female, non-smoker and no comorbidities with recurrent pneumothorax, which was diagnosed to be a sporadic LAM. Diagnostic procedures like chest x-ray, Chest CT scan, and tissue biopsy were done. Video Assisted Thoracoscopic Surgery (VATS) and pleurodesis were done and was maintained on Sirolimus, which is the only drug proven to stabilize lung function. Pneumothorax although common may have very rare associations. ***Phil Heart Center J 2021;24(1):61-67.***

Key Words: ■ Lymphagioleiomyomatosis ■ recurrent pneumothorax ■

Lymphangioleiomyomatosis (LAM) is a rare progressive cystic lung disease of uncertain etiology that affects young women. It appears to involve one of the most bizarre pathogenic mechanisms in human disease: the metastasis of histologically benign cells. Pneumothorax is one of the complications and most common pulmonary manifestations of LAM. We present a case of a 49-year old Filipino, female, non-smoker and no comorbidities with recurrent pneumothorax, which was diagnosed to be a sporadic LAM. Diagnostic procedures like chest x-ray, Chest CT scan, and tissue biopsy were done. Video Assisted Thoracoscopic Surgery (VATS) and pleurodesis were done and was maintained on Sirolimus, which is the only drug proven to stabilize lung function. Pneumothorax although common may have very rare associations.

CASE

We present a case of a 49-year old Filipino, female, non-smoker, with no co-morbidities presented in the Emergency Department with twelve days of progressive difficulty of breathing. Initially, patient had sudden onset of breathing while climbing two flights of stairs relieved after resting for several minutes with no other signs and symptoms. Four days prior to admission, the dyspnea recurred, noted to be persistent, progressive, and less relieved by rest; aggravated by doing even non-strenuous house hold chores; and now associated with occasional non-productive cough. She consulted at the Emergency Department of a private hospital wherein she was managed as a case of Community Acquired Pneumonia – Low Risk. She was given Salbutamol + Ipratropium nebulization with note of slight relief and was given oral antibiotic. Two days prior to admission, the dyspnea persisted but was relieved by rest. She was subsequently admitted as a case of spontaneous pneumothorax and was given oxygen inhalation at 5 liters nasal cannula. Due to the persistence of the aforementioned signs and symptoms, the patient transferred to our institution for further evaluation and management and was henceforth admitted.

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Her past medical history and family history are non-contributory to patient's current problem. Personal and social history is unremarkable and recently with an inactive lifestyle. Obstetric history is likewise unremarkable and denies shortness of breath during episode of menstruation.

On physical examination, she was in mild cardio-respiratory distress with respiratory system findings of asymmetric lung expansion, tachypnea with absent intercostal retractions, no mass or lesion noted, lagging in the right, decreased vocal and tactile fremitus at the right lung field with no crepitations. On auscultation, there was hyperresonance on the right lower lung field with decreased breath sounds on the right mid to base with no adventitious breath sounds. Cardiovascular system examination showed tachycardia with no murmur. Other systems were unremarkable.

Chest radiograph showed 30% pneumothorax on the right with minimal pleural effusion (*Fig. 1*). Chest CT-scan showed multiple, well circumscribed, diffusely distributed thin walled varisized cysts ranging from 1-30mm in size with intervening normal lung, without lobar predominance (*Fig. 2*). Other findings were pneumothorax in the right, atelectasis in the right middle and lower lobe with noted minimal pleural effusion (*Fig. 3-4*).

Cranial MRI revealed non-specific flair hyper-intensities in the subcortical frontal lobe. Abdominopelvic imaging showed liver cysts that are not compatible with the characteristic low attenuation materials seen in hepatic angiomyolipoma (*Fig. 5*). Arterial blood gas at 5LPM via nasal cannula revealed pH 7.47, PCO2 27.9, PO2: 121, HCO3: 20.3, CO2: 21.1, base deficit: -1.3, PO2: 97.4%.

2D echocardiography was unremarkable with normal mean pulmonary artery pressure of 19mmHg by right ventricular acceleration time. The patient had a 6-minute walk test done wherein she covered a total distance of 192 meters with no rest period and with episodes of desaturation necessitating oxygen supplementation of up to 4LPM via nasal cannula. Pulmonary function test with DLCO was done revealing a probable restrictive ventilatory defect with no bronchodilator response with decreased DLCO.

Patient was referred to a thoraco-vascular surgeon for insertion of chest tube and underwent mini-thoracotomy right to obtain specimen for biopsy. Intra-operative findings showed multiple cystic lesions on the exposed segments of the right, which are typical gross findings for Lymphangioleiomyomatosis (*Fig. 6a*). The patient's biopsy revealed varisized cystic spaces lined by alveolar epithelium, on higher magnification, there the slides showed clustered areas of spindle cells and cuboidal epithelioid cells which are characteristic histopathologic findings for LAM. (*Fig. 6b*) The patient's immunohistochemistry results were positive for Human Melanocyte Black – 45 (HMB45) and Smooth Muscle Actin (SMA) (*Fig.s 7a-7b*), definitive of LAM.

The patient's histopathologic findings and immunohistochemistry results confirms the diagnosis of Definite LAM. The patient's chest tube was eventually removed however she had an episode of tension pneumothorax necessitating intubation and insertion of bilateral chest tubes due to recurrence of pneumothorax this time bilateral. The patient had chemical pleurodesis done bilaterally using talc slurry, however she had another recurrence of pneumothorax this time on the left. The patient underwent Video-assisted thoracoscopy and bilateral mechanical pleurodesis. Our patient was started on Sirolimus 1mg/tablet once a day and through levels were checked after 2 weeks. She was referred to pulmonary rehabilitation and pneumococcal vaccine was given prior to her discharge.

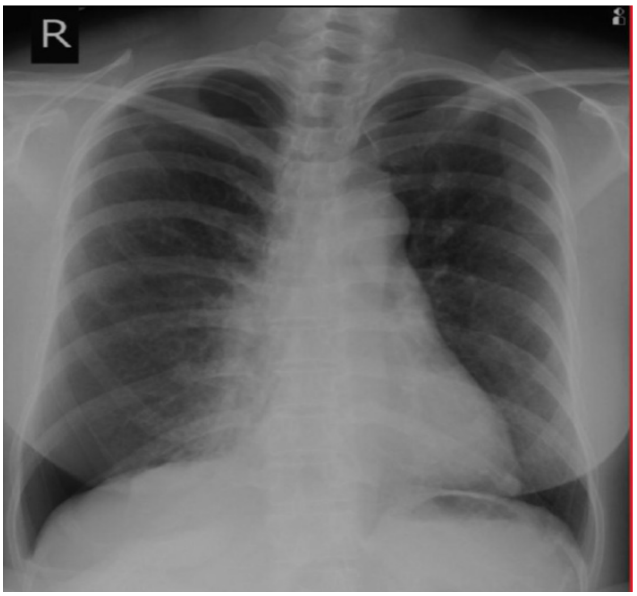

Figure 1. Chest radiograph with pneumothorax in the right with minimal pleural effusion

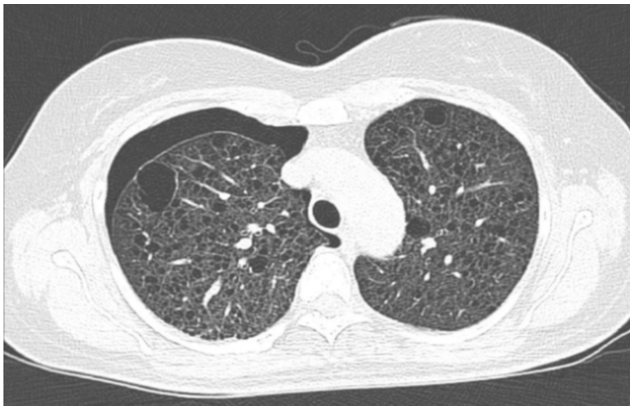

Figure 2. Chest CT scan showing multiple, well circumscribed, diffusely distributed thin walled varisized cysts ranging from 1-30mm in size with intervening normal lung, without lobar predominance.

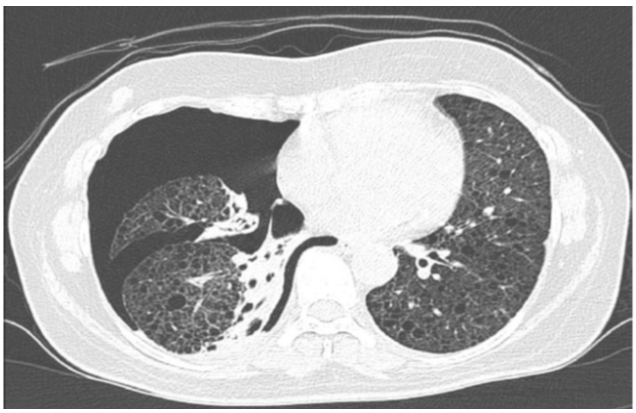

Figure 3. Chest CT scan showing multiple, well circumscribed, diffusely distributed thin walled varisized cysts with atelectasis on the right middle and lower lobe

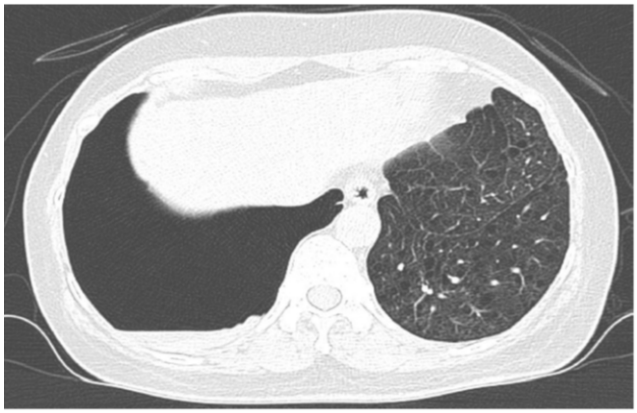

Figure 4. Chest CT scan showing minimal effusion right.

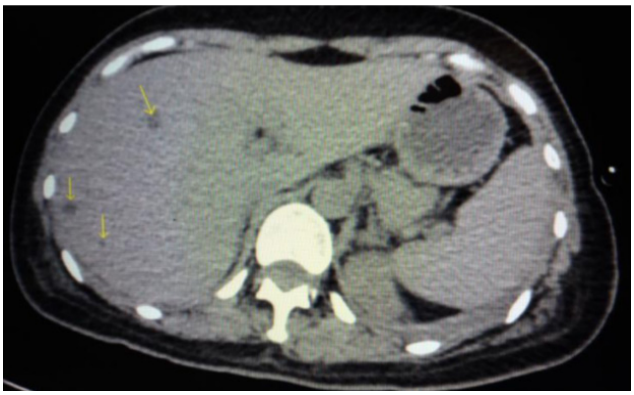

Figure 5. Whole abdominal CT scan showing multiple hepatic cysts

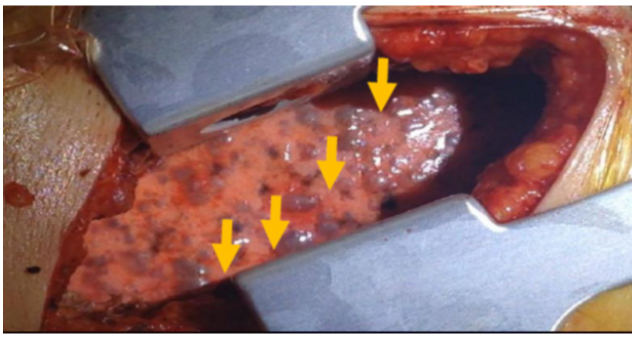

Figure 6a. Gross findings during the patient's mini-thoracotomy showing multiple cystic lesions on the exposed portions of the right lung

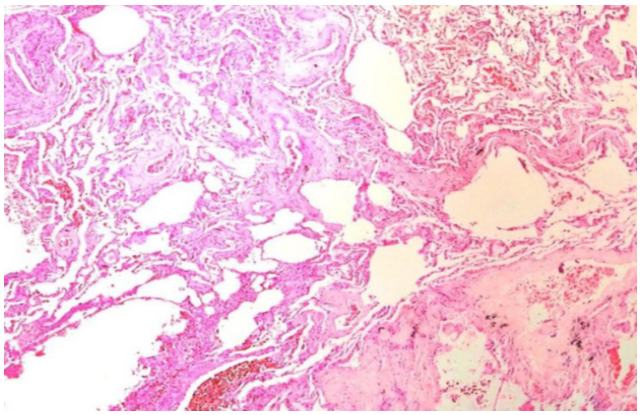

Figure 6b. Histopathologic images of our patient showed varisized cystic spaces lined by alveolar epithelium.

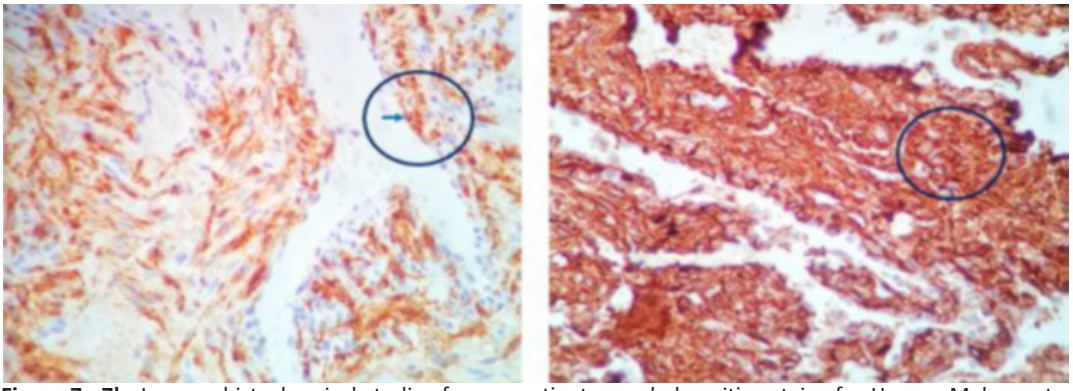

Figure 7a-7b. Immunohistochemical studies for our patient revealed positive stains for Human Melanocyte Black -45 (HMB 45) [figure 8-a] and smooth muscle actin (SMA) [figure 8-b]

DISCUSSION

Lymphangioleiomyomatosis (LAM) is a rare progressive cystic lung disease of uncertain etiology that affects young women. There are two types of LAM: the sporadic-LAM (S-LAM) and Tuberous Sclerosis Complex LAM (TSC-LAM). The term sporadic LAM is used for patients with LAM who do not have tuberous sclerosis complex (TSC). According to the LAM Foundation, the estimated number of patients with sporadic LAM (S-LAM) globally is around 30,000 – 50,000. TSC-LAM refers to LAM that occurs in patients with TSC and the estimated number of patients with TSC-LAM is around 250,000 globally.

Diagnostic criteria for LAM: The diagnosis of LAM is made by tissue biopsy (generally from the lung but occasionally from lymph nodes or lymphangioleiomyomas) and/or a combination of history and high-resolution computed tomography scanning (HRCT). Pathologic characteristic of LAM cell morphology and positive immunoreactivity to smooth muscle actin and HMB-45 antibodies confirms the diagnosis of LAM. Non-invasive procedures such as HRCT can also be utilized to diagnose LAM.[14]

According to the European Respiratory Society guidelines for the diagnosis and management of lymphangioleiomyomatosis, the diagnostic criteria for definite LAM include the following: 1) characteristic or compatible lung HRCT, and lung biopsy with pathologic characteristic for LAM; or 2) characteristic lung HRCT and any of the following: angiomyolipoma (kidney); thoracic or abdominal chylous effusion; lymphangioleiomyoma or lymph-node involved by LAM; and definite or probable tuberous sclerosis complex.[14]

Pathologic criteria for diagnosis: There are two lesions that are characteristic of LAM: cysts and a multifocal nodular proliferation of immature smooth muscle and perivascular epithelioid cells (LAM cells). There is a typical proliferation of immature smooth muscle cells and epithelioid cells outside the normal muscular structures, associated with cyst formation. Routine haematoxylin and eosin staining in combination with adequate clinical and radiological information is sufficient to make the diagnosis in most cases.[14] Immunohistochemistry for smooth muscle actin, desmin and HMB45 is an important adjunct to diagnosis.[1]

Vascular endothelial growth factor: Elevated serum VEGF-D (>800 pg/ml) has been utilized to establish the diagnosis of LAM.[13] It was found elevated among women patients with LAM compared to women patients with other cystic lung diseases, such as pulmonary Langerhans cell histiocytosis, emphysema, follicular bronchiolitis, lymphoid interstitial pneumonia, and Birt-Hogg-Dub´e syndrome. The optimal threshold for discriminating cystic lung disease due to LAM from cystic lung disease due to another cause varied across studies, with most estimates falling between 600 and 800 pg/ml.[13] Studies showed that VEGF-D predicts LAM with a sensitivity greater than 70% and a specificity greater than 90%, again with results varying on

the cut-off levels done in different studies.[13]

Characteristic features of pulmonary LAM on HRCT: HRCT is used for the diagnosis, assessment and follow-up of diffuse infiltrative lung disease. Characteristic of LAM on HRCT are multiple (>10) thin-walled round well-defined air-filled cysts with preserved or increased lung volume with no other significant pulmonary involvement specifically no interstitial lung disease except those with possible features of multifocal micronodular pneumocyte hyperplasia in patients with TSC.[14]

Abdominal Imaging: Abdominal CT scanning is also of value in detecting angiomyolipomas, lymphangioleiomyomas or lymphadenopathy to support the diagnosis.[14] Abnormal abdominopelvic imaging findings in patients with LAM are found in up to two thirds of patients.[19]

Lung Function Testing: Spirometry, bronchodilator testing and DLCO are also performed. FEV1 and DLCO should be performed to assess disease progression and response to treatment. Disease progression may be evaluated by repeating lung function tests at 3–6 monthly intervals during the first year following diagnosis then at 3–12 monthly intervals depending on the severity and progression of the disease.[14]

Arterial Blood Gas: Arterial blood gases do not provide useful information above that obtained by pulse oximetry in the assessment of patients with mild to moderate disease. However, it is useful in providing baseline date in advanced disease and in providing long term oxygen therapy, especially for transplant evaluation and to exclude hypercapnia.[20]

2D Echocardiogram: Estimation of pulmonary artery pressure by echocardiography may be performed in patients with LAM, especially with severe disease and those requiring long-term oxygen therapy.[14]

6-minute walk test (6MWT): The 6MWT may be performed to evaluate the disability, the progression of the disease and response to treatment.[14]

Pathophysiology: Early investigators recognized a striking similarity between the pulmonary lesions seen in otherwise healthy women with LAM, and those seen in patients with tuberous sclerosis and lung involvement, which led to the hypothesis that these disorders share common genetic and pathogenetic mechanisms.[6,3] Linkage analysis led to the discovery of 2 tumor suppressor genes: TSC1 and TSC2. Hamartin is a protein product of TSC1 and tuberin is a protein product of TSC2. LAM cells develop through the classic two-hit model originally proposed by Knudson. Series of meticulous experiments demonstrated that germline mutations in TSC1 and TSC2 are not present in patients with S-LAM; in contrast, TSC-LAM is characterized by germline mutations in TSC2. However, LAM cells in both TSC-LAM and S-LAM carry mutations. These findings explain why LAM occurs frequently in patients with TSC with a prevalence of approximately 33%, while S-LAM like this case is extremely rare requiring 2 acquired mutations (typically in TSC2) for it to occur.[3]

Understanding the genetic basis of LAM has been crucial to progress in pathogenesis. There are several pathways for which the pathogenesis can be postulated but we focused on four mechanisms: inappropriate cell growth and proliferation which is regulated by MTOR (mammalian target to rapamycin), hormone-stimulated growth and migration as it may be linked to estrogen-mediated signaling effects, cytoskeleton reorganization which is regulated by the hamartin-tuberin complex; and invasion, angiogenesis and lymphangiogenesis resulting to replacement of the normal lung parenchyma with thin-walled cysts, which result in the respiratory manifestations of the disease, including progressive dyspnea, recurrent pneumothorax, and chylous effusions.

Our patient presented with pneumothorax which is one of the complications and the most common pulmonary manifestation leading to the diagnosis of LAM in 86.5% of cases.[11] LAM has the highest recurrence rate for pneumothorax, therefore should undergo appropriate surgical procedure with pleurodesis such as Video Assisted Thoracoscopic Surgery (VATS) or open thoracotomy because this intervention

has the lowest recurrence rate of pneumothorax in LA. Our patient underwent mini-thoracotomy with lung biopsy and subsequently VATS with pleurodesis.[12]

The pathogenesis in LAM primarily involves inappropriate activation of mammalian target of rapamycin (mTOR) signaling. The standard therapy for LAM is Sirolimus, it is not a cure but it's the only drug that is proven to stabilize lung function. The Miles Trial showed significant improvement favoring sirolimus in the change from baseline FEV1 and FVC, the score on the EuroQuality of life visual-analogue scale and in serum vascular endothelial growth factor-D level.[13]

There are other therapeutics of unclear benefit such as statin, hormonal therapy and doxycycline because of the variability in the result of the studies.

In the past two decades, continuous research have been made in search of a cure for this rare disease, new discoveries in the molecular pathogenesis of LAM have been established such that future therapies including simvastatin, interferon, tyrosine kinase and immunotherapy as single and in combination with mTOR inhibitor is now undergoing study.

The definitive treatment for advanced LAM is lung transplantation. These are the following criteria for lung transplantation among LAM patients: NYHA Functional Class III/IV, hypoxemia at rest, FEV1 of 25%, DLCO of 27% and maximal oxygen consumption of 50% predicted.[14] Our patient has a functional class of 2, with oxygen saturation of 93% at rest, FEV1 of 47% and a DLCO of 34% hence she is not a candidate for lung transplantation.

Supportive management is similar to other chronic airway disease and this includes smoking cessation, vaccination, inhaled bronchodilator, supplemental oxygen, pulmonary rehabilitation.

LAM has a slower progression and a better prognosis than previously thought with a mean annual decline in FEV1 of 60–120 mL per year in different retrospective studies of referral centers. The median transplant-free survival for LAM was 29 years from the time of onset of symptoms, and 23 years from the time of diagnosis. The criteria that predicts a worse prognosis are the following: (a). dyspnea as the presenting symptom, (b) weight loss, (c) supplemental oxygen therapy, (d) reversible airflow obstruction and (e) elevated VEGF-D.[16]

CONCLUSION

Pneumothorax although common may have very rare associations.

REFERENCES

1. Bonetti F, Pea M, Martignoni G, Zamboni G, Iuzzolino P. Cellular heterogeneity in lymphangiomyomatosis of the lung. Hum Pathol 1991;22:727–728.
2. Goncharova EA, Goncharov DA, Eszterhas A, Hunter DS, Glassberg MK, Yeung RS, et al. Tuberin regulates p70 S6 kinase activation and ribosomal protein S6 phosphorylation: a role for the TSC2 tumor suppressor gene in pulmonary lymphangioleiomyomatosis. J Biol Chem 2002;277:30958– 30967.
3. Juvet S, McCormack F, Kwiatkowski D, Downey G. Molecular pathogenesis of lymphangioleiomyomatosis: lessons learned from orphans. Am J Respir Cell Mol Biol 2007;36:398-408.
4. Krymskaya V. Smooth muscle-like cells in pulmonary lymphangioleiomyomatosis. Proc Am Thorac Soc 2008; 5:119-126.
5. Finlay G. The LAM cell: what is it, where does it come from, and why does it grow? Am J Physiol Lung Cell Mol Physiol 2004;286:L690– L693.
6. Cornog JL Jr, Enterline HT. Lymphangiomyoma, a benign lesion of chyliferous lymphatics synonymous with lymphangiopericytoma. Cancer 1966;19:1909–1930.
7. Harari S, Torre O, Cassandro R, Moss J. The challenging face of a rare disease: lymphangioleiomyomatosis. Eur Respir J 2015;46:1471-1485.
8. Finlay GA, York B, Karas RH, Fanburg BL, Zhang H, Kwiatkowski DJ, Noonan DJ. Estrogen-induced smooth muscle cell growth is regulated by tuberin and associated with altered activation of platelet derived growth factor receptor-beta and ERK-1/2. J Biol Chem 2004;279:23114–23122.
9. Goncharova E, Goncharov D, Noonan D, Krymskaya VP. TSC2 modulates actin cytoskeleton and focal adhesion through TSC1-binding domain and the Rac1 GTPase. J Cell Biol 2004;167:1171–1182.

10. Kumasaka T, Seyama K, Mitani K, Sato T, Souma S, Kondo T, et al. Lymphangiogenesis in lymphangioleiomyomatosis: its implication in the progression of lymphangioleiomyomatosis. Am J Surg Pathol. 2004 Aug;28(8):1007-16.
11. Ryu JH, Beck GJ, Brown KK, Chapman JT, Finlay GA, Olson EJ, et al. The NHLBI Lymphangioleiomyomatosis Registry. Characteristics of 230 Patients at Enrollment. Am J Respir Crit Care Med. 2006 Jan 1; 173(1): 105–111.
12. Almoosa KF, McCormack FX, Sahn SA. Pleural disease in lymphangioleiomyomatosis. Clin Chest Med. 2006 Jun;27(2):355-68.
13. McCormack FX, Inoue Y, Moss J, Singer LG, Strange C, Nakata K, et al. Efficacy and safety of sirolimus in lymphangioleiomyomatosis. . N Engl J Med. 2011 Apr 28;364(17):1595-606. doi: 10.1056/NEJMoa1100391. Epub 2011 Mar 16.
14. Johnson SR, Cordier JF, Lazor R, Cottin V, Costabel U, Harari S, et al. European Respiratory Society guidelines for the diagnosis and management of lymphangioleiomyomatosis. Eur Respir J. 2010 Jan;35(1):14-26. doi: 10.1183/09031936.00076209.
15. Baldi BG, Freitas CS, Araujo MS, Dias OM, Pereira DA, Pimenta SP, et al. Clinical course and characterisation of lymphangioleiomyomatosis in a Brazilian reference centre. Sarcoidosis Vasc Diffuse Lung Dis. 2014 Jul 8;31(2):129-35.
16. Oprescu N, McCormack FX, Byrnes S, Kinder BW. Clinical predictors of mortality and cause of death in lymphangioleiomyomatosis: a population-based registry. Lung. 2013 Feb;191(1):35-42.
17. Bonetti F, Chiodera PL, Pea M, Martignoni G, Bosi F, Zamboni G, et al. Transbronchial biopsy in lymphangiomyomatosis of the lung. HMB45 for diagnosis. Am J Surg Pathol. 1993 Nov;17(11):1092-102.
18. Avila NA, Kelly JA, Chu SC, Dwyer AJ, Moss J. Lymphangioleiomyomatosis: abdominopelvic CT and US findings. Radiology. 2000 Jul;216(1):147-53.
19. Boehler A, Speich R, Russi EW, Weder W. Lung transplantation for lymphangioleiomyomatosis. N Engl J Med. 1996 Oct 24;335(17):1275-80.
20. McCormack FX, Gupta N, Finlay GR, Young LR, Taveira-DaSilva AM, Glasgow CG, et al. Official American Thoracic Society/Japanese Respiratory Society Clinical Practice Guidelines: Lymphangioleiomyomatosis Diagnosis and Management. Am J Respir Crit Care Med. 2016 Sep 15;194(6):748-61.

Case Report - Thoracic CV Surgery

Posterior Mediastinal Tumor

Sheila Rose A. Embolterio, MD

Posterior mediastinal tumors are rare type tumors that are most often neurogenic origin. Some of these tumors occur as soft tissue in origin. The typical manifestations are secondary to compression of the surrounding structures.

Case --- This is a case of a 70 year old female who presented with non-productive cough, previously underwent surgical resection for a posterior mediastinal tumor. This patient underwent complete resection of the posterior mediastinal tumor. Final histopathology report revealed a Leiomyosarcoma with adipocytic component.

Conclusion --- The complete surgical resection of the tumor is the treatment of choice for this patient. Close monitoring should be undertaken to check for tumor recurrence. ***Phil Heart Center J 2021;24(1):68-70.***

Key Words: ■ Mediastinal Tumor ■ Sarcoma ■

Posterior mediastinal tumors are rare tumors, more so are tumor recurrences in this area. This is a case of a 70 year old female presenting with recurrent, non-productive cough.

Posterior mediastinal tumors are usually neurogenic in origin in presents most commonly in children, although in adults the most common type of posterior mediastinal tumors are also neurogenic.[1] In some cases, mediastinal tumors can be mesenchymal in origin. These types of tumors are usually asymptomatic and are noted only through incidental radiographic findings. In symptomatic patients, this signifies that the tumor is more likely to be malignant in origin.

There are a handful of studies reporting the occurrence of posterior mediastinal tumors. Most of which are neurogenic in origin. This report will showcase the case of a posterior mediastinal tumor in a patient previously operated on, for a tumor classified to be neurogenic in origin and is currently mesenchymal in origin.

Case: This is the case of a 70-year old female who present with recurrent cough and episodes of dyspnea. Patient previously diagnosed with posterior mediastinal tumor (neurofibroma) 14 years prior to admission. She underwent left thoracotomy for total excision of the tumor. No complaints were noted until 6 weeks prior to admission when she had recurrent cough. She was initially given antibiotics with temporary relief of symptoms. She had episodes of dysphagia prompting consult. Chest x-ray was done which revealed a large, ovoid soft tissue mass density in the bilateral retrocardiac areas compressing the heart anteriorly. She was then advised to undergo MRI. MRI revealed a large middle and posterior mediastinal mass with soft tissue and fat components with mass effect. Mass was measured to be approximately 5.6 x 13.0 x 10.6 cm (APWCC). She was advised biopsy.

Two weeks prior, patient was admitted for CT scan guided biopsy. CT scan study done revealed a large, complex, solid mass lesion with well marginated border in the inferior, middle and posterior mediastinum. Fine needle aspiration was done, however, the results only revealed rare atypical cells with few fibrous tissue and adipose tissue. Thus patient was admitted for excision of the mass.

She underwent excision of posterior mediastinal mass via left posterolateral thoracotomy with pleuropericardial window. Intraoperative findings revealed a 10 x 12 x 10 cm firm lobular mass located in the posterior mediastinum extending from the left pleura to the right pleura. Final histopathologic report revealed Leiomyosarcoma with an adipocytic component.

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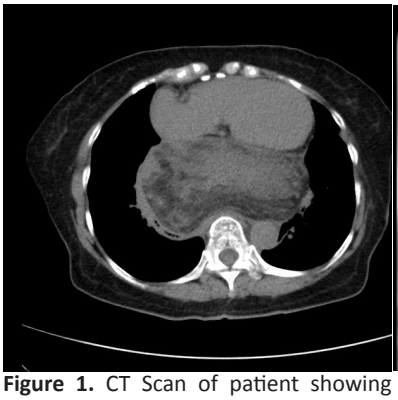

Figure 1. CT Scan of patient showing the posterior mediastinal tumor

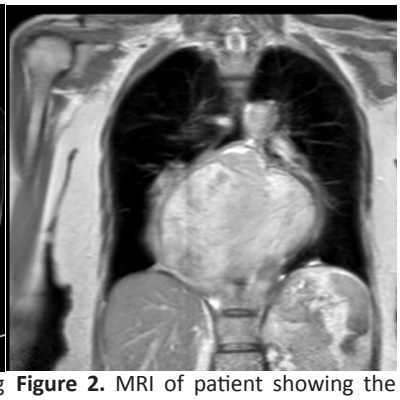

Figure 2. MRI of patient showing the posterior mediastinal tumor

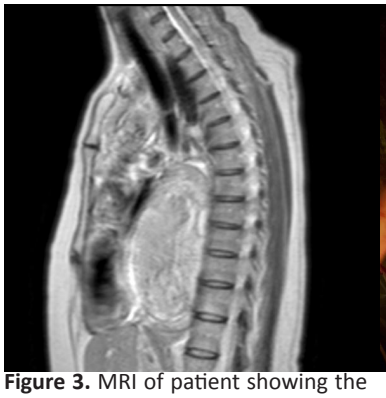

Figure 3. MRI of patient showing the posterior mediastinal tumor

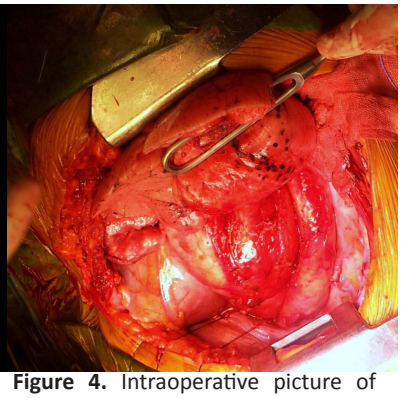

Figure 4. Intraoperative picture of posterior mediastinal tumor

DISCUSSION

Mediastinal tumors are often benign and asymptomatic. Symptoms usually occur in patients secondary to their compressive nature. In some instances, symptoms occur due to their malignant origin.

The posterior mediastinum, otherwise known as the paravertebral sulci bilaterally technically contains the descending aorta, the esophagus, thoracic duct, azygos and hemiazygos veins and the lymphatics.[1] Tumors arising in this area are rare. The most common tumors are neurogenic in origin. It occurs on about 52% of all posterior mediastinal tumors.[2] The presence of mesenchymal tumors occur in 10% of patient with posterior mediastinal tumors. Of this small amount of population, one specific subtype is Leiomyosarcoma which is about 12% of the total population.[3]

Throughout the years, there is only a handful of cases recorded of tumors arising from the mediastinum diagnosed to be Leiomyosarcoma. In a report done by A. Eroglu et. al, it was noted that up to 1993, only 6 cases have been recorded.[4] These tumors arise from the different areas of the mediastinum.

Leiomyosarcoma is an aggressive type of soft tissue sarcoma of smooth muscle origin. It occurs in about 1 in every 100 cancers. It mostly affects individuals of more than 50 years of age. Only a handful of reported cases involving Leiomyosarcoma in the mediastinum have been reported. This type of tumors in the lung and mediastinal cavity occurs during the 6th decade of life with male preponderance[5] during the 6th decade of life with male preponderance.[5]

Leimyosarcomas are such tumors that recur even in the advent of complete surgical resection. There still is no consensus on the effects of radiation and/or chemotherapy on the complete remission of the disease.[6,7]

The presence of such tumors in the mediastinum causes a mass effect due to its bulky size thus the late presentation. It is usually manifested as cough, pain and in some cases superior vena cava syndrome. The prognosis of such tumors is more often poorer due to its higher rate of recurrence secondary to tumor invasion on the time of diagnosis and resection.[5]

As such in our patient, she was initially diagnosed to have a benign tumor of the posterior mediastinum that was completely excised. However, she later developed a tumor in the same area which was identified to be Leiomyosarcoma that is malignant. No previous records have shown that there is a conversion of one type of tumor that is benign to a more aggressive tumor of different origin in the life span of an individual.

The treatment of such tumor is complete surgical resection. In symptomatic patients, the prognosis is poorer due to a higher frequency of local invasion and recurrence.

CONCLUSION

In the case of this 70 year old patient, the tumor is a primary mediastinal tumor arising from the soft tissues within the posterior mediastitum. It is a rare type of tumor that may have manifested late due to the large size of the tumor causing compression symptoms. Even though complete resection has been done on this patient, it is still prudent to do aggressive follow-up due to the natural history of the disease. There is a high rate of recurrence in the presence of microinvasion to the surrounding structures.

The use of chemo and or radiotherapy is still controversial, thus complete resection is still the recommended choice in the management of Leiomyosarcoma of the mediastinum. In the case of this patient, complete resection was done with close monitoring. Follow after 4 months revealed no tumor recurrence on this patient.

REFERENCES

1. Brunicardi FC et al. Schwartz's principle of surgery, 9th ed. McGraw-Hill Companies, Inc.; 2010: Ch 19.
2. Brunicardi FC et al. Schwartz's principle of surgery. 9th ed. McGraw-Hill Companies, Inc. 2010: Ch 36.
3. Skandalakis, J.E., ed., et. al., Skandalakis' surgical anatomy, Paschalidis Medical Publication Ltd. International Student Edition, 2004: Ch 04.
4. Eroğlu A, Kürkçüoğlu C, Karaoğlanoğlu N, Gürsan N. Primary leiomyosarcoma of the anterior mediastinum. Euro J of Cardiothorac Surg. 2002 May, 21(5):943–945.
5. Gladish GW, Sabloff BM, Munden RF, Truong MT, Erasmus JJ, Chasen MH. Primary thoracic sarcomas. RadioGraphics 2002; 22:621–637.
6. Lee DH, Park CK, Keum DY, Kim JB, Hwang I. Leiomyosarcoma of the posterior mediastinum extending into the adjacent spinal canal. Korean J Thorac Cardiovasc Surg 2012; 45:192-195.
7. Gonzalez RL. Primary eiomyosarcoma of mediastinum which compromises the vein system SVC. Surgical resection associated with venous reconstruction. Rev. Chilean surgery. 2011 Aug. 63(4):404-410.

Coronary Artery Fistula

Stewart S. Santos, MD

Coronary artery fistula (CAF) is a rare disease that often diagnosed incidentally in coronary angiogram. Untreated coronary fistula may lead into detrimental complications such as bacterial endocarditis, arrhythmias, congestive heart failure and even sudden death. In the case we are reporting a 61 year old female who presented with numbness of face and chest pain. Patient was worked up as a case of ACS, patient underwent coronary angiogram which revealed severe 3 vessel disease and an incidental findings of coronary artery fistula coming from left anterior descending artery draining into main pulmonary artery. Patient underwent CABG and ligation of coronary artery fistula. Patient was discharged improved. ***Phil Heart Center J 2021;24(1): 71-73.***

A coronary artery fistula is one of the congenital anomaly of the coronary system. It is an abnormal communication between one of the coronary arteries draining into one of the cardiac chamber or a great artery, caval system or in the pulmonary vascular system. Early detection of signs and symptoms of CAF and prompt surgical intervention is warranted to prevent its detrimental complications.

This is a case report of a 61 year old male diagnosed with coronary artery fistula of the left anterior descending artery draining into the main pulmonary artery who underwent a successful surgical closure of CAF.

Case: A 61-year-old male was admitted in our institution with a one week history of dizziness accompanied with numbness over the left side of the face, accompanied by difficulty of breathing and chest pain. Physical examination revealed 110/80 mmHg, 89bpm, 19rr, pertinent findings was a presence of 3/6 continuous murmur at the left parasternal area. Initial impression at that time was coronary artery disease ruled out congenital heart disease, patent ductus arteriosus. Laboratories requested were within normal limits except for the electrocardiogram (ECG) which revealed sinus rhythm, left axis deviation and lateral wall ischemia. Coronary angiogram was done which showed severe 3 vessel disease and incidental findings of, left anterior descending coronary artery (LAD) was connected to the pulmonary artery through a congenital fistula *(Figure 1)*.

The patient was operated on through a midline sternotomy. After opening the pericardium, a tortuous CAF was seen to course from the proximal segment of the LAD to the entrance of the proximal part of the main pulmonary artery (MPA). *(Figure 2)* Because of the pulmonary artery orifice, it was decided to ligate the fistula under cardiopulmonary bypass (CPB) surgery prior to CABG. The extracardiac fistula was ligatured with 5/0 monofilament transfixion sutures. The postoperative course was uneventful, and the patient was discharged eight days after the operation.

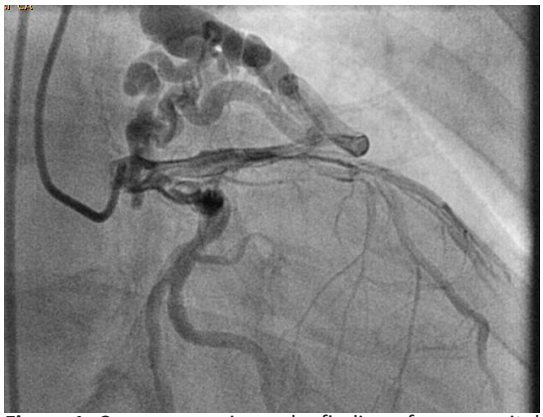

Figure 1. Coronary angiography finding of a congenital artery fistula

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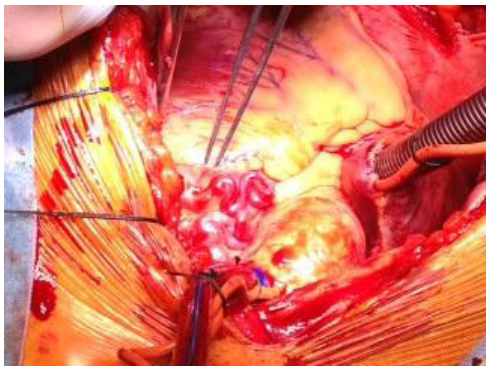

Figure 1. Intraoperative finding of tortuous fistulous communication between the proximal left anterior coronary artery and the pulmonary artery and collaterals

DISCUSSION

A coronary arteriovenous fistula is a congenital abnormal communication between a coronary artery draining to one of the four cardiac chambers or the great arteries or veins adjacent to the heart.[1] It was the first by describe Krause in 1865,[2] and it is seen in 0.002% of the general population, and visualized in 0.25% of patients undergoing cardiac catheterization.[3] In 50% of the cases, they have been reported to arise more commonly from the right coronary artery (RCA) followed by left anterior descending artery (LAD 25%), the circumflex coronary artery (CCA 18.3 %), diagonal branch (1.9%), and the left main coronary artery (LMCA) or the circumflex-marginal branch (both 0.7%) connections between the coronary system and a cardiac chamber appear to represent persistence of embryonic intratrabecular spaces and sinusoids.[4]

The coronary arteriovenous fistula mostly drain into the pulmonary artery in 29.8-43% of patients followed by the right ventricle in 14-40%, right atrium in 19-20.2%, left ventricle in 5.8-19%, and the left atrium in 5%. The coronary artery fistula also associated with other congenital cardiac anomalies (20-45%) such as tetralogy of fallot, atrial septal defect, patent ductus arteriosus and ventricular septal defect.[5]

Presenting signs and symptoms of coronary artery fistula in elderly patients will have shortness of breath in 71% and right ventricular failure as a result of the progressive enlargement of the fistula and increased left-to-right shunt. Nineteen percent will have congestive heart failure develops and some while have a 20% risk of developing bacterial endocarditis.[6] In rare instances, sudden death, arrhythmias, and conduction defects may be the first manifestation of CAF. Although overall morbidity and mortality from anomalously terminating coronary arteries are low, most patients who do not have surgery for this condition develop symptoms and fistula-related complications as they get older.

Various cardiac imaging modalities are utilized for diagnosis and for planning before surgical or percutaneous interventions if closure of the coronary fistula is indicated. The electrocardiogram may be normal or may show changes consistent with ischemia or myocardial infarction. Doppler echocardiography demonstrates a dilated coronary artery, turbulent flow in the fistula and the recipient chamber[7] but the coronary catheterization remains the gold standard for the evaluation of coronary fistula. It can be used to reliably identify the size and anatomical features of the fistulous tract.[7]

Treatment of symptomatic CAF is surgical closure of the fistula by ligation. The overall survival and closure rate were 100%. No reported data regarding recurrence rate after surgical closure of CAF.[5]

Patients with asymptomatic fistulas, however, the timing and indications for surgical closure is still debatable. According to Fernandes, et al. There are alternative surgical techniques for CAF closure, including internal cameral closure via CPB, tangential arteriography, distal ligation, and saphenous vein/internal mammary artery bypass.[3] If technically possible, a catether-based closure has become the preferred treatment option and are increasingly being used, especially in the pediatric population.[8]

In summary, coronary artery fistula is a rare congenital coronary malformation that will lead to heart failure if not treated accordingly. Surgical closure of CAF should be done as soon as the diagnosis is made to prevent complications and symptoms just like developed in our patient. Surgical closure of CAF remains the gold standard compared to percutaneous closure and has a low morbidity and mortality.

REFERENCES

1. Masood Sadio, FL. Manangment of coronary arteriovenous fistula by device., Pakistan Heart Journal, 2000;(33):1-2.
2. Garcia-Rinaldi R. Von Koch L, Howell JF. Successful repair of a right coronary artery sinus fistula with associated left coronary arteriosclerosis. Bol Asoc Med PR 1977;69:(156-9).
3. Fernandes ED, Kadivar H. Hallman GL, et al. congenital malformation of the coronaries: the Texas Heart Institute experience. Ann of Thorac Surg. 1999;(54): 732-74.
4. Cohn, LH. Cardiac surgery in the adult. 3rd ed. McGraw-Hill Companies, Inc; 2010.
5. Yaliniz HM, Topcuoglu S. Surgical treatment of congenital coronary artery-pulmonary artery fistula: a case report, Cardiovascular surgery, Medical Faculty University of Cukurova, Adana, Turkey. 2013; 21.
6. Tkebuchava T. Von Segesser LK, congenital coronary fistula in children and adults: diagnosis, surgical technique and results. Cardiovascular Surgery (Torino) 1996; 37:29-34.
7. Jayanth Koneru et al. Coronary anomaly and coronary artery fistula as cause of angina pectoris with literature review. Journal of Clinical Medicine and Research. 2012; 4:74.
8. Mavroudis C, Backer CL. Coronary artery fistula in infants and children: a surgical review and discussion of coil embolization. Ann Thoracic Surgery 1997; 63: 1235-42.

Right Atrial Myofibroblastic Sarcoma with Multiple Pulmonary Metastases in a 65-Year Old Male: a Case Report and Review of the Literature

Glenn Nathaniel SD. Valloso, MD; Othaniel Philip R. Balisan, MD

Background --- Myofibroblastic tumor is a relatively new nosologic entity sharing similar features with a smooth muscle tumor. The low-grade myofibroblastic sarcoma (LGMS) is an intermediate or low-grade malignant myofibroblastic neoplasm.

Case --- The patient was a 63-year-old Asian male whose cardiac imaging revealed a right atrial mass suggestive of myxoma measuring 8.70 cm in widest diameter and with a chest CT-scan that showed bilateral pulmonary masses. The atrial mass was excised and a subsequent fine needle aspiration of the right pulmonary mass was performed. Within two months of presentation, patient's disease progressed and eventually died.

Results --- Microsections of the atrial mass revealed a tumor composed of fascicles and sheets of spindle cells in a variable fibromyxoid matrix with mitoses of 1-5/10 HPF and necroses. The abundance of myxoid stroma simulated features of myxoma. Immunohistochemistry showed focal reactivity to smooth muscle actin (SMA) and desmin, and non-reactivity to *H*-caldesmon. Proliferation studies using Ki-67 and p53 were 40% and 10% respectively. The histologic findings of the atrial mass were compatible with a low-grade myofibroblastic sarcoma. The CT-scan guided fine needle aspiration of the pulmonary mass showed similar spindle cells in myxoid matrix. Immunohistochemistry showed non-reactivity to thyroid transcription factor-1 (TTF-1), pancytokeratin, and synaptophysin, and with a proliferation index of 20-25% using Ki-67. The aspirate findings were consistent with a tumor metastatic from the cardiac tumor.

Conclusion --- The application of the panel of immunohistochemical stains can aid in the diagnosis of a myofibrolastic sarcoma in particular *H*-caldesmon, which when negative, rules-out smooth muscle tumors. The proliferation index is a vital clue in the disease course even if the histology appears low grade. ***Phil Heart Center J 2021;24(1):74-81.***

Key Words: ■ Myofibroblastic sarcoma ■ pulmonary metastases ■ h-caldesmon ■

Myofibroblastic tumor is a new nosology more commonly used in pediatric tumors and later in adult cases wherein the tumor cells exhibit histologic, ultrastructural and immunohistochemical features seen in myofibroblasts. The categories range from benign tumors to inflammatory myofibroblastic tumors (IMT) and its neoplastic counterparts. Low-grade myofibroblastic sarcoma (LGMS) is an intermediate-or low-grade malignant myofibroblastic neoplasm composed of cells displaying well-developed myofibroblastic differentiation, which frequently express actin-associated proteins. More than 90% of low-grade malignant myofibroblastic neoplasms express calponin, smooth muscle actin, muscle-specific actin, and fibronectin. Generally, these neoplasms are negative for h-caldesmon.[1] We present a case of a right-atrial histologically low-grade myofibroblastic sarcoma with bilateral pulmonary metastases in a 63 year old Asian male. Its immunoprofile and proliferation indices are discussed.

***Clinical History*:** The patient was a 63 year old Asian male who presented with chest heaviness. 2D echocardiography revealed a right atrial mass suggestive of myxoma measuring 8.74 x 4.26 cm and extending into the inflow of the right ventricle with further prolapse during diastole. (*Fig. 1*)

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His coronary angiography showed insignificant coronary artery disease. He was initially managed as a case of atrial myxoma, rule-out malignancy. He underwent open heart surgery for debulking of the mass, which was subsequently sent for histopathologic examination. Further work-up of the chest due to persistence of chest heaviness post-operation, revealed two demarcated, non-calcified, mildly enhancing, homogenous, oval densities in the right lower lobe by CT-scan. The largest is located in the lateral segment measuring 3.2 cm and the smaller in the posterobasal segment measuring 2.0 cm. An oval nodule of similar characteristic in the posterobasal segment of the left lower lobe is also seen approximately measuring 2.5 cm (*Fig. 2*). The right lung mass was subsequently biopsied through CT-scan guided fine needle aspiration. Immunohistochemical studies of the right atrial mass revealed low-grade myofibroblastic sarcoma. The pulmonary mass revealed similar histomorphologic features as the atrial mass. Subsequent immunohistochemical studies of the pulmonary mass are consistent with metastases from the right atrial tumor as primary. He was discharged after the lung biopsy, eight days post-surgery. After 10 days, he was re-admitted due to left leg swelling accompanied by increased fatigability on exertion and diagnosed with acute to subacute deep venous thrombosis involving the left leg. Within two months after presentation, patient's disease progressed and eventually died.

Gross, Histopathologic, Histochemical, and Immunohistochemical Findings. On gross examination, the right atrial mass consisted of several fragments of tan, irregular, soft to firm tissues, and aggregately measured 8.3 x 7.0 x 3.1 cm. Cut-sections showed tan, predominantly solid tissues surrounded by grainy, soft, and friable peripheral tissues. Microsections show tumor cells of variable cellularity composed of fascicles and storiform groups of spindle to plump neoplastic cells with mild variation in size, embedded in a collagenous to fibromyxoid matrix with prominent hyalinization, in places surrounding several scattered thin-walled mildly dilated vascular channels, and with geographic areas of necroses (*Fig. 3*). The tumor cells exhibited oval to elongated enlarged nuclei with hyperchromasia, irregular nuclear membranes, evenly distributed fine to coarse chromatin, inconspicuous nucleoli, with moderate amount of pale, eosinophilic, elongated to stubby cytoplasm (*Fig. 4*). Mitoses of 1-5/10 HPF are identified (*Fig. 5*). Tumor cells with a myxoid background, composed of clear, mucoid substance are seen (*Fig. 6*). Based on histomorphology (necroses, nuclear atypia, and mitoses), the tumor grade is from low-to-intermediate grade. Special stain using trichrome stain showed uptake of red and light-blue stains by the tumor cells and collagen background, respectively (*Fig. 7*). Immunohistochemistry showed reactivity to desmin, variable reactivity to smooth muscle actin (SMA), and non-reactivity to *H*-caldesmon. There is strong staining with CD99 as well. Proliferation studies using Ki-67 and p53 were 40% and 10%, respectively (*Fig. 8*). The evaluation of the margins cannot be fully ascertained due to specimen fragmentation.

The CT scan-guided fine needle aspiration of the pulmonary mass showed similar spindle to plump cells in two-dimensional sheets, some with crush-artifact exhibiting small to medium-sized, round to ovoid hyperchromatic nuclei with a granular chromatin pattern, inconspicuous nucleoli, and scant to moderate amounts of pale eosinophilic cytoplasm (*Fig. 9)*. Immunohistochemistry showed focal reactivity to smooth muscle actin and non-reactivity to thyroid transcription factor-1 (TTF-1), pancytokeratin, and synaptophysin. Proliferation studies using Ki-67 was 20-25% (*Fig. 10*). The aspirate findings were consistent with a tumor metastatic from the cardiac tumor.

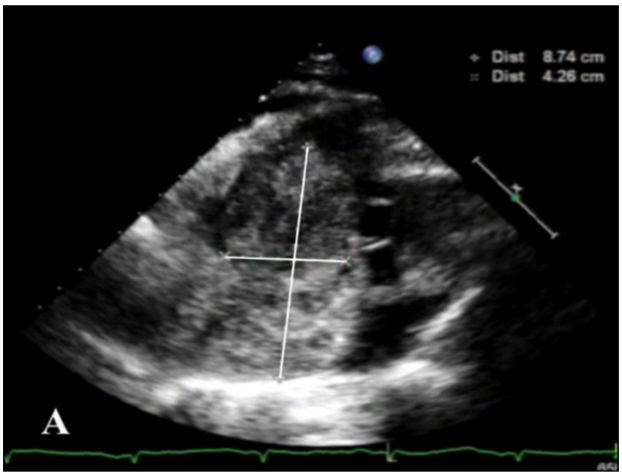

Figure 1. 2D echocardiography revealed a right atrial mass suggestive of myxoma measuring 8.74 x 4.26 cm and extending into the inflow of the right ventricle with further prolapse during diastole.

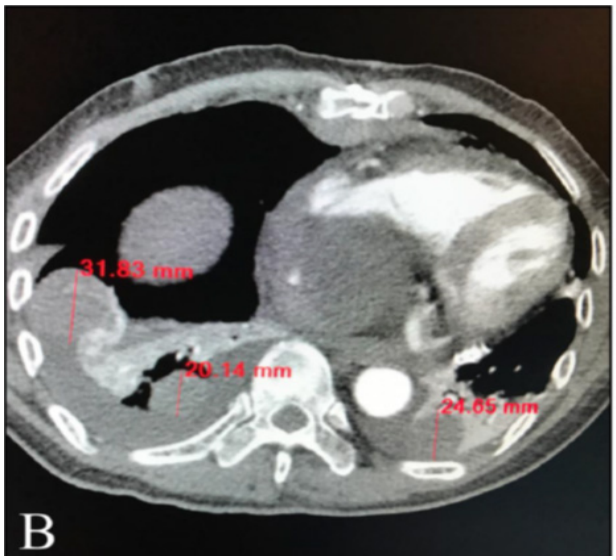

Figure 2. CT scan of the chest post-debulking revealed are two fairly demarcated, non-calcified, mildly enhancing, homogenous, oval densities in the right lower lobe. The largest is located in the lateral segment measuring 32.0 mm and the smaller in the posterobasal segment measuring 20.0 mm. An oval nodule of similar characteristic in the posterobasal segment of the left lower lobe is also seen approximately measuring 25.0 mm. Likewise seen is the atrial mass as described.

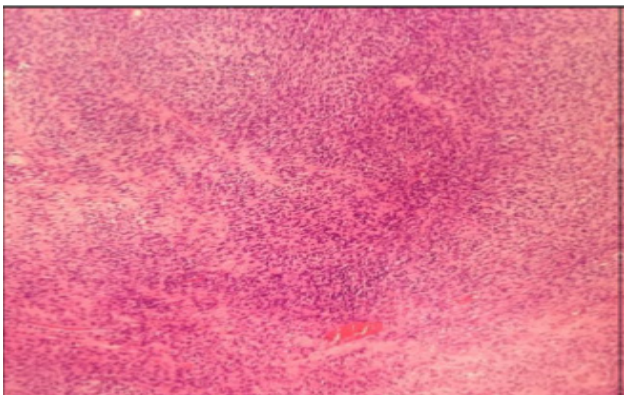

Figure 3. Microscosection of the tumor revealed fascicles and storiform groups of spindle to plump neoplastic cells with mild variation in size, embedded in a collagenous to fibromyxoid matrix (H&E 40x).

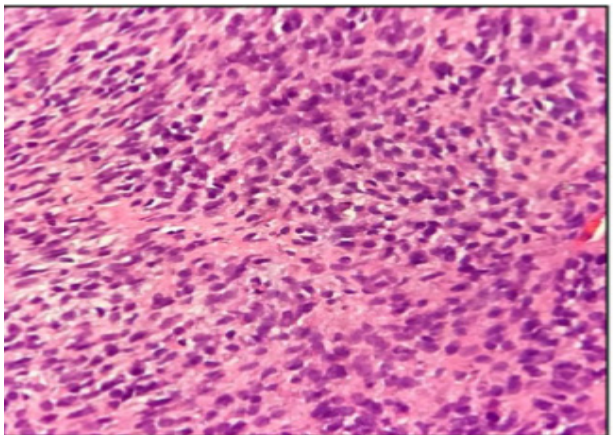

Figure 4. The tumor cells exhibited oval to elongated enlarged nuclei with hyperchromasia, irregular nuclear membranes, evenly distributed fine to course chromatin, inconspicuous nucleoli, with moderate amounts of pale eosinophilic elongated to stubby cytoplasm (H&E 400x)

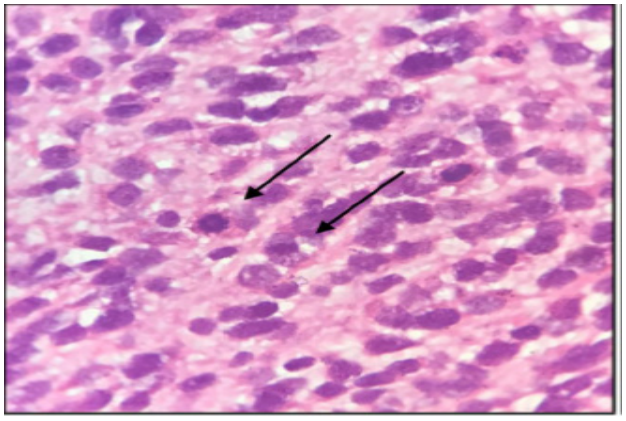

Figure 5. Mitoses of 1-5/10 HPF (H&E 1000x).

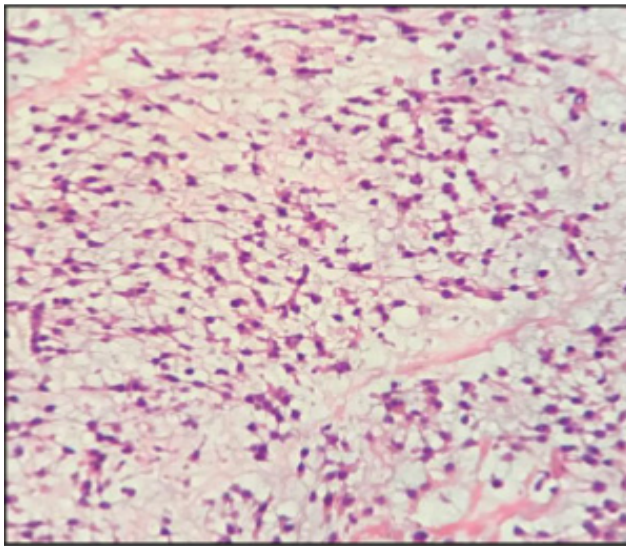

Figure 6. Tumor cells with a "myxoid" background, composed of clear, mucoid substance (H&E 400x).

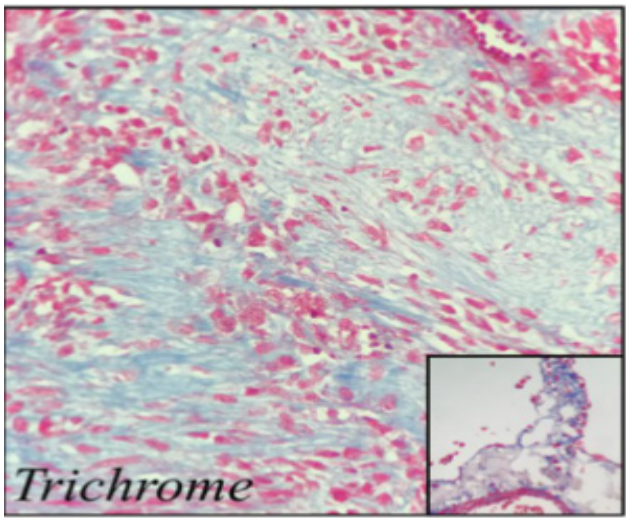

Figure 7. Tumor cells are stained red and embedded in a light-blue-stained collagen background (Trichrome 200x).

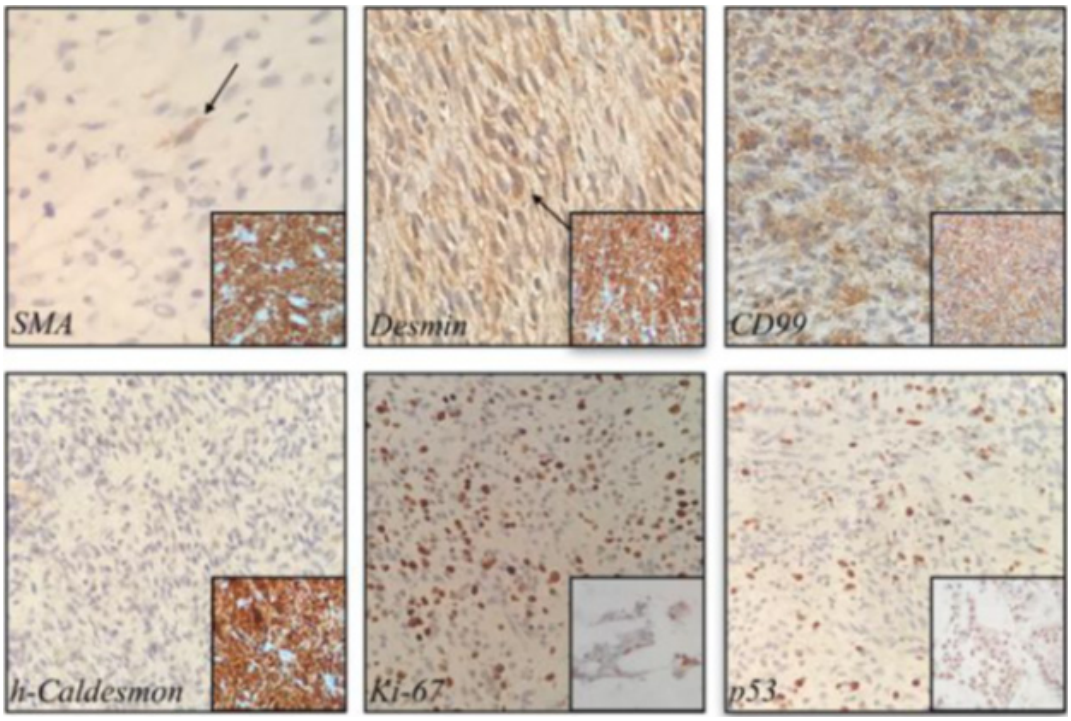

Figure 8. Immunohistochemistry showed reactivity to smooth muscle actin, desmin, and CD99 (400x) and non-reactivity to h-caldesmon (200xferation studies using ki-67 and p53 were 40% and 10% respectively (200x).

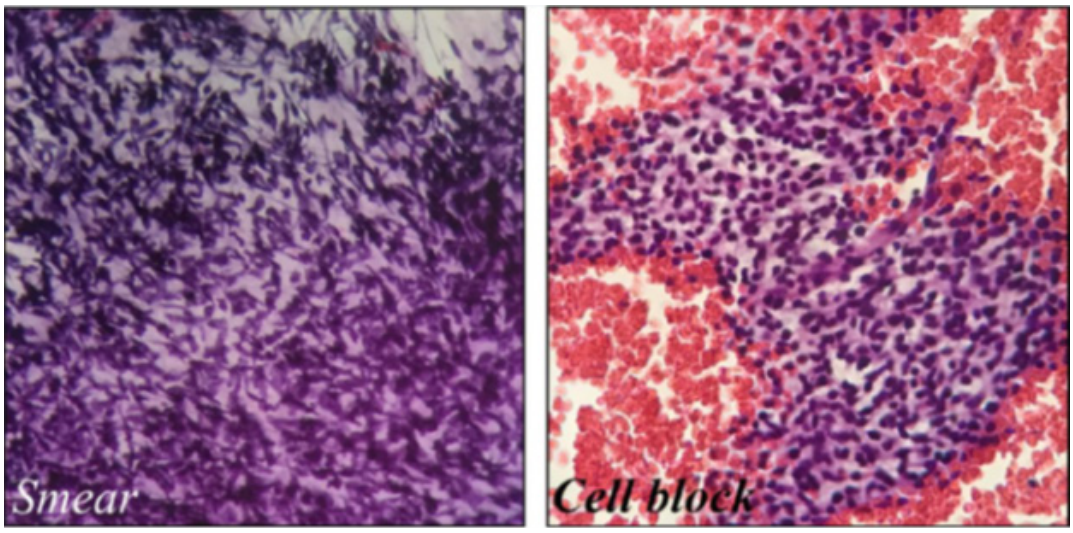

Figure 9. The CT scan-guided fine needle aspiration smear of the pulmonary mass showed similar spindle to plump cells in 2-dimensional group with crush-artifact (Diff-Quik, 400x). In the cell block, the cells exhibited small to medium-sized, round to ovoid hyperchromatic nuclei with a granular chromatin pattern, inconspicuous nucleoli and scant to moderate amounts of pale pink cytoplasm (H&E, 400x).

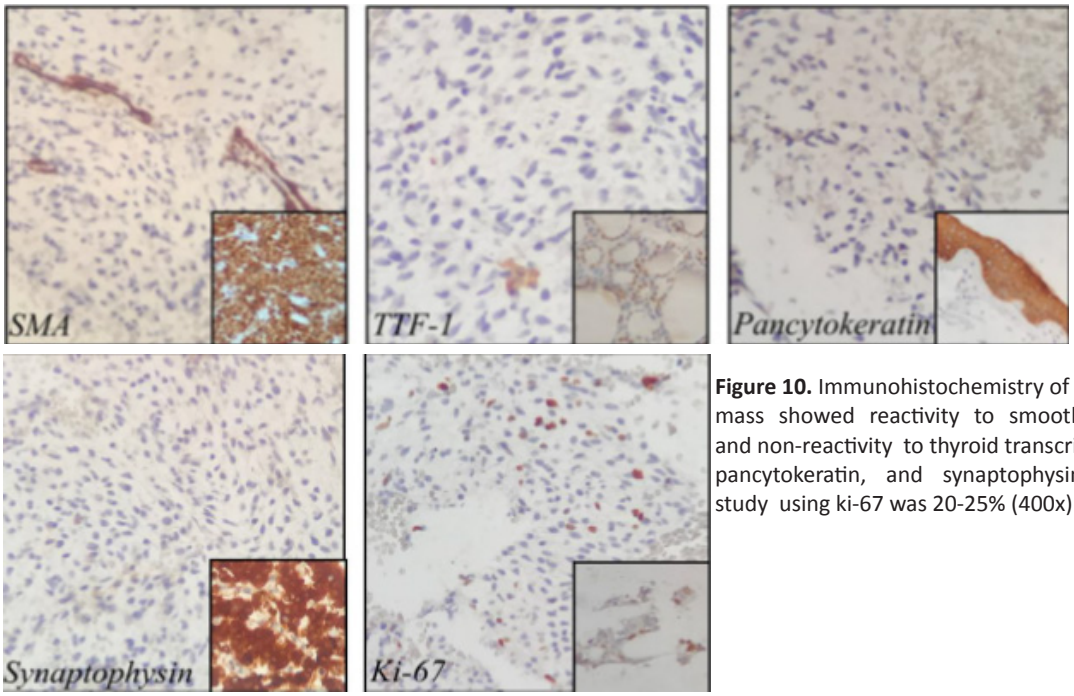

Figure 10. Immunohistochemistry of the pulmonary mass showed reactivity to smooth muscle actin and non-reactivity to thyroid transcription factor-1 , pancytokeratin, and synaptophysin. Proliferation study using ki-67 was 20-25% (400x)

DISCUSSION

We presented a case of a right-atrial histologically low-grade myofibroblastic sarcoma with bilateral pulmonary metastases in a 63 year old Asian male. Its immunoprofile and proliferation indices are discussed.

Primary cardiac tumors are uncommon (incidence in autopsy series, 0.001–0.03%). Majority of primary cardiac tumors (~75%) are benign; atrial myxoma being the most common tumor encountered. About 25% of primary cardiac tumors are malignant and 95% of these are sarcomas; the remaining 5% are lymphomas. Prognosis of cardiac sarcomas remains poor because of distant metastases at the time of diagnosis. The World Health Organization 4th edition (2015) in nomenclature of tumors of the heart and pericardium emphasize that the most common site of sarcoma is the left atrium.[2]

The concept of myofibroblast is relatively new, and is a continuing controversy for the past decade. Myofibroblasts are spindle cells having ultrastructural features common with smooth muscles and fibroblasts. Tumors of myofibroblast, based on phenotypic features, fall into four main groups. The myofibroblastic sarcoma, also the inflammatory myofibroblastic tumor, belongs to the sarcomas showing myofibroblastic differentiation. Other groups are reactive fasciitis-like lesions, benign lesions like mammary and intranodal myofibroblastoma, angiomyofibroblastoma, and dermatomyofibroma, and, lastly, fibromatoses lesions which are locally aggressive.[3]

In the recent years, based on the clinicopathologic features, myofibroblasts have been described as a true neoplastic component termed as "myofibroblastic tumors" which can be benign or rarely malignant. A third tumor type with borderline biologic course, named "inflammatory myofibroblastic tumor" (IMT), has been identified, a condition that has been thought to be purely benign in nature.[4]

An analysis of eighteen cases of low-grade spindle cell sarcoma described it as a distinct entity in the spectrum of low-grade myofibroblastic neoplasms and is distinguishable from fibromatosis, solitary fibrous tumor, fibrosarcoma, and leiomyosarcoma. Mentzel T et. al.[5] described low-grade myofibroblastic sarcomas as a cellular tumor with diffusely infiltrative pattern, and is composed of spindle-shaped tumor cells arranged mainly in fascicles. Immumohistochemically, all cases stained positively for at least one myogenic marker (desmin, alpha alpha-smooth muscle actin, and muscle actin). Ultrastructural examination in five cases showed characteristics features of myofibroblasts.

Reported cases are described in the skin, head and neck, lungs, heart, extremities, perifascial tissues of the abdomen and pelvis, and bones. Similar in this case report, the tumor cells had poorly defined, pale eosinophilic cytoplasm, and fusiform nuclei, which were either tapering and wavy or plumper and vesicular with indentations and small inconspicuous nucleoli. The tumor cells were set in a collagenous matrix often with prominent hyalinization. Likewise noted were nuclear atypia and mitoses of 1-5/10 HPFs.

Diagnosis of low-grade and pseudosarcomatous spindle cell lesions of skin and soft tissue can sometimes be problematic; in particular, distinction between fibroblastic, myofibroblastic, and smooth muscle proliferations. The study of Perez-Montiel assesed the utility of the differential expression of smooth muscle and myofibroblastic-associated marker, a panel of immunohistochemical markers consisting of smooth muscle actin (SMA), smooth muscle myosin (SMMS), calponin, and high-molecular weight caldesmon (h-caldesmon) were used to a series of spindle cell lesions of skin and soft tissue. The results demonstrate remarkably consistent pattern of reactivity of myofibroblastic-associated markers in lesions predominantly composed of myofibroblastic spindle cells characterized by positive staining for SMA and calponin and non-reactivity for SMMS and h-caldesmon.[6] This panel of immunohistochemistry was also utilized in this case with result yield compatible as mentioned.

A negative immunohistochemistry staining does not rule-out anything. However, the morphology may be supported by the panel of immunohistochemistry to strengthen the diagnosis. In a recent study by Ceballos KM et. al.,[7] they also included *H*-caldesmon in myoid immunohistochemical panel consisting of desmin, smooth muscle actin, and muscle actin. Out of the 72 tumors studied, diffuse staining for *H*-caldesmon was noted only within the leiomyosarcomas whereas malignant fibrous histiocytomas, malignant peripheral nerve sheath tumors, synovial sarcomas, and nodular fasciitis were all focally stained involving less than 1% of lesional cells. The negative *H*-caldesmon, in this case is consistent with myofibroblastic sarcoma and ruled-out smooth muscle tumor.

Zhao-Gen Kai et. al.[8] compared the clinicopathologic features of low grade and middle to high grade of myofibroblastic sarcoma of 15 cases. They found that the mean mitotic count /10 HPF and mean Ki-67 index for low grade were 1.9 ± 0.8 and 6.0 ± 2.2 and for moderate-to-high grade were 6.2 ± 1.2 and 20.0 ± 7. I. The proliferation index in the current case was 40% and almost twice the count in the high-grade category of Zhao-Gen Kai et al. The behavior of the tumor in this case was signaled by a very high proliferation than the histologic grade with a mitotic count of 1-5/10 HPF.

Immunohistochemistry is presently the most important adjunct tool in the evaluation of soft tissue tumors because of its practicability and relatively low cost. Some authors state that there is no universally accepted criteria for diagnosis of low-grade myofibroblastic sarcoma, and others suggest electron microscopy may be the gold standard. By electron microscopy, the characteristic findings include a lack or incomplete basal or external lamina and presence or incomplete fibronexus.

Chemotherapy and radiation therapy have limited benefit. Surgery with negative resection margins is the only mainstay of successful treatment. Chemotherapy and radiation therapy have limited value. Early recognition and treatment have important prognostic and therapeutic implications. In the present case, patient had mass resection with uncertain status of the margin due to specimen fragmentation. Neither chemotherapy nor radiotherapy was done.

In the Philippine Heart Center pathology cardiac registry, the malignant cardiac tumors after review and reclassification by Ribo et. al. in 2009,[9] enumerated 6 cases of myofibroblastic sarcoma. The current case is the 7th case which histologically appeared low grade but presented already with metastasis.

CONCLUSION

Ninety-five percent of malignant primary cardiac tumors are sarcomas. The features of myofibroblastic tumors are similar to smooth muscle tumors. The immunohistochemical staining pattern with desmin, SMA may be characteristic, and there is no staining with *H*-caldesmon. Thus, application of the panel of immunohistochemical stains may be of aid in the diagnosis of myofibroblastic sarcoma. Anti-*H*-caldesmon is an immunohistochemical reagent for more specific smooth muscle differentiation and not for myofibroblastic tumors. The low histologic grade by morphology alone may not represent the behavior of the tumor. Proliferation indices such as ki-67 and p53 should be included in the evaluation of the tumor.

We presented this case of a right-atrial myofibroblastic sarcoma with bilateral pulmonary metastases which was histologically low to intermediate grade but had a high proliferation index and a clinical behavior which was rapid or that of high grade.

REFERENCES

1. Qiu X, Montgomery E, Sun B. Inflammatory myofibroblastic tumor and low-grade myofibroblastic sarcoma: a comparative study of clinicopathologic features and further observations on the immunohistochemical profile of myofibroblasts. Hum Pathol. 2008 Jun;39 (6):846-56.
2. Burke A, Tavora F. The 2015 WHO Classification of tumors of the heart and pericardium. J Thorac Oncol. 2016 Apr;11(4):441-52.
3. Biselli R, Boldrini R, Ferlini C, Boglino C, Inserra A, Bosman C.Myofibroblastic tumours: neoplasias with divergent behaviour. Ultrastructural and flow cytometric analysis. Pathol Res Pract. 1999;195(9):619-32.
4. Fletcher CD. Myofibroblastic tumours: an update. Verh Dtsch Ges Pathol. 1998; 82:75-82.
5. Mentzel T, Dry S, Katenkamp D, Fletcher CD. Low-grade myofibroblastic sarcoma: analysis of 18 cases in the spectrum of myofibroblastic tumors. Am J Surg Pathol. 1998 Oct;22(10):1228-38.
7. Perez-Montiel, Plaza JA, Dominguez-Malagon H, Suster S. Differential expression of smooth muscle myosin, smooth muscle actin, h-caldesmon, and calponin in the diagnosis of myofibroblastic and smooth muscle lesions of skin and soft tissue. Am J Dermatopathol. 2006 Apr;28(2):105-11.
8. Ceballos KM, Nielsen GP, Selig MK, O'Connell JX. Is anti-h-caldesmon useful for distinguishing smooth muscle and myofibroblastic tumors? An immunohistochemical study. Am J Clin Pathol. 2000 Nov;114(5):746-53.
9. Cai ZG, Pan CC. Yu DH, Feng ZZ, Ma L, Zhao Y, Xu HB. Myofibroblastic sarcomas: a clinicopathologic analysis of 15 cases and review of literature. Int J Clin Exp Pathol 2016;9(2):1568-1577.
10. Ribo M, De Luna AM et. al., Epidemiological and pathological characteristics of cardiovascular tumors and tumor-like lesions: a 10-year study Philippine Heart Center. Manila: Philippine Heart Center. 2009. (unpublished paper).

Pulmonary Cryptococcosis in a 62 Year-Old Patient Diagnosed by Fine Needle Aspiration Cytology: A Case Report

C Philip Teomar A. Radin, MD

Background --- Pulmonary cryptococcosis is a disease occurring worldwide. The patient's immune status is the main factor determining the pathogenicity and histopathologic features of lung infection. Majority of normal hosts with cryptococcal infections are usually asymptomatic and only a small proportion has pulmonary symptoms. This report is prepared to present a pulmonary infection, its clinical presentation, histopathologic findings and course of the disease as a relatively rare case in this institution.

Case --- This patient is a 62 year-old male, known case of diabetes mellitus and chronic kidney disease who experienced non-productive cough, fever and difficulty of breathing. Few hours prior to admission, patient had episode of fever and difficulty of breathing which warranted admission. CT scan of the chest revealed a pulmonary artery aneurysm in the medial basal right lower lung measuring 1.6x1.1 cm with an impression considering mycotic aneurysm in the peripheral right pulmonary artery in the medial basal right lower lung. Subsequent CT Scan guided biopsy of the lesion was done. The patient was treated as a case of cryptoccocosis in an immunocompromised state and cytologic examinations revealed positive for Cryptococcus neoformans.

Findings --- On gross examination, the specimen consists of 2 ml of mucoid to bloody right lung aspirate and the smears prepared show numerous yeast cells with thick mucoid capsular halos frequently in monolayers and "honeycomb" pattern, admixed with several macrophages, some lymphocytes and neutrophils, some in vague granuloma formation, in a background of several red blood cells. The cell block shows scattered fungal yeast cells closely associated with macrophages and lymphocytes. No definite malignant cells identified. Special stain (PAS) done in the cell block show bright red color of the yeasts and pale red color of the capsule with spiney formation. The final diagnosis was chronic inflammation with granuloma formation; numerous fungal microorganisms morphologically consistent with Cryptococcus neoformans.

Conclusion --- Pulmonary cryptococcosis is a relatively rare disease in the Philippines due to limited number of reported cases. This disease is commonly seen among immunocompromised individuals including patients with AIDS. Proper approach in early detection and diagnosis should be followed to ensure good patient outcomes. This case implies that incidence of a lung lesion in an immunocompromised should never be underestimated regardless of HIV status. The authors hereby present a rare case of pulmonary infection in this institution. ***Phil Heart Center J 2021;24(1):82-85.***

Key Words: ■ Pulmonay Cryptococcosis ■ Cryptococcus neoformans ■ Diagnosis of Cryptococcus ■

Cryptococcosis is a worldwide disease frequently seen among immunocompromised hosts including patients with AIDS, post-transplanted, malignancies and those who are in immunosuppressant drugs.[1] It is an infection brought about by a fungus (*Cryptococcus spp*) which is an encapsulated opportunistic pathogen commonly seen in tropical countries. [1,2] This fungus is commonly found in bird droppings (pigeons), decaying wood, and dust.[1] The main passage of entry of this organism is via the respiratory tract through inhalation of the yeast spores.[1,2] It has a wide array of clinical presentation including pulmonary cryptococcosis, cerebral cryptococcoma and meningitis. Among immunocompromised hosts, central nervous system and other extrapulmonary sites are the most commonly involved.[2] Other organs such as the eyes, skin and muscular system could also be affected.[1] Imaging of the chest frequently

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show well-defined nodules occasionally mistaken for malignancy.[2] We present a case of a 62 year-old immunocompromised male who was admitted due to difficulty of breathing and upon further investigation, chest CT scan revealed a pulmonary artery aneurysm in the medial basal right lower lung. Mycotic aneurysm was the primary consideration that appears to be progressive in size. The cytopathologic diagnosis was chronic inflammation with granuloma formation, numerous fungal organism consistent with *Cryptococcus neoformans*. We hereby present the cytopathology and clinical presentation of this case.

***Clinical History*:** The patient is a 62 year-old male, known case of diabetes mellitus and chronic kidney disease who experienced non-productive cough, fever and difficulty of breathing. Few hours before admission, patient had difficulty of breathing which warranted admission. During his stay in the hospital, CT scan of the chest was done and revealed a pulmonary artery aneurysm in the medial basal right lower lung measuring 1.6x1.1 cm **(Figure 1A and 1B)**. Loculated pleural effusion in the left hemithorax with mild thickening and calcifications was also seen **(Figure 1C)**. The impression was mycotic aneurysm in the peripheral right pulmonary artery in the medial basal right lower lung. Possibility of necrosis of the pulmonary artery intima/minimal contrast leakage that is focal is also considered in the immediate surrounding lung parenchyma and pneumonia on the right lower lobe was likewise considered. Subsequent CT scan-guided biopsy of the said lesion was done. The patient was treated as a case of cryptoccocosis in an immunocompromised state and cytologic examinations revealed positive for *Cryptococcus neoformans*.

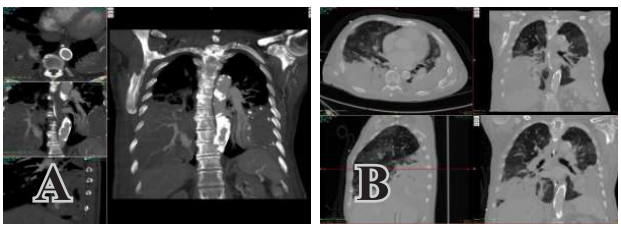

Figure 1. Chest CT Scan. Peripheral pulmonary artery aneurysm in the medial basal right lower lung **(A).** Right lower lung consolidation, patchy ground-glass opacities and interstitioalveolar infiltrates **(B).**

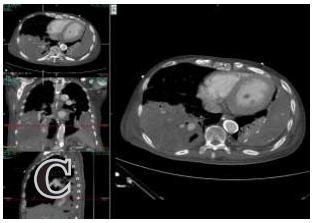

Figure 1. Loculated pleural effusion in the left hemithorax (white arrow) with mild thickening and calcifications on axial and lateral views **(C)**.

Cytology and special stains findings: On gross examination, the specimen consists of 2 ml of mucoid to bloody right lung aspirate and the smears prepared show numerous yeast cells with thick mucoid capsular halos frequently in monolayers and "honeycomb" pattern **(Figure 2A)** admixed with several macrophages, some lymphocytes and neutrophils, some in vague granuloma formation, in a background of several red blood cells **(Figure 2B)**. The cell block shows scattered fungal yeast cells closely associated with macrophages and lymphocytes. **(Figure 2C)**. No definite malignant cells were identified. Special stains (PAS and india ink) done in the cell block show bright red color of the yeasts and pale red color of the capsule with spiny formation **(Figure 2D)** and highlighted them against a darker background (2E). The final diagnosis was chronic inflammation with granuloma formation; numerous fungal micro-organisms morphologically consistent with *Cryptococcus neoformans*.

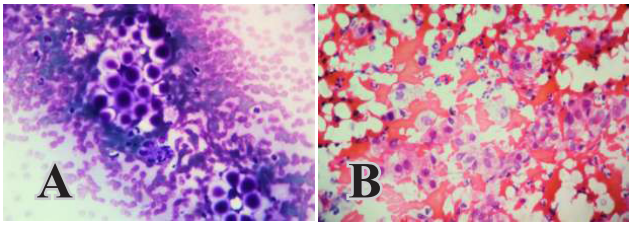

Figure 2. A. Smears reveal numerous yeast cells with thick mucoid capsular halos frequently in monolayers and "honeycomb" pattern. (Diff-Quik 40X) **B.** The yeast cells are admixed with several macrophages, some lymphocytes and neutrophils, occasionally in vague granuloma formation in a background of several red blood cells. (Papanicolaou stain 40X)

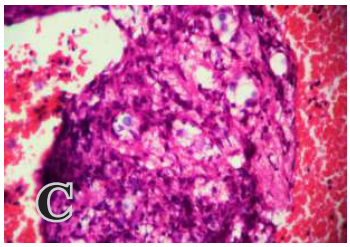

Figure 2. C. The cell block shows scattered fungal yeast cells closely associated with macrophages and lymphocytes.

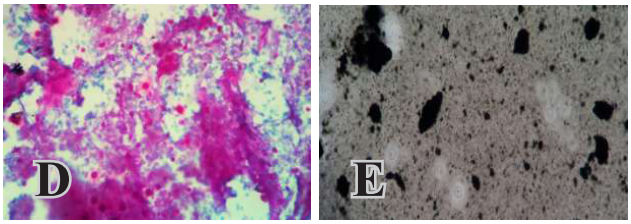

Figure 2. D. Special stain (PAS) show bright red color of the yeasts and pale red color of the capsule with spiny formation. **E.** India ink stain shows the encapsulated yeasts against a darker background.

DISCUSSION

Cryptococcosis is a disease with universal distribution affecting several organs in the body.[1] During the 1950s, less than 300 cases were told worldwide.[3] In a study conducted by *Salvana et al* in 2012 determining the most common opportunistic infections in Filipino HIV and AIDS patients, *Cryptococcal* infections ranked only 7th or 6 (3.9%) out of 155 cases.[15] In the USA, cryptococcosis was a rare infection up until the 1980s where cases rose to more than a thousand each year.[8] Habitually, the lung is the portal of entry for cryptococcal infections. But pneumonia due the causative agent of cryptococcosis is infrequently diagnosed.[13] The causative agent of this disease is from the *Cryptococcus species* which are facultative yeasts that can grow within the soil, in mammalian hosts' body fluids or tissues.[3] *Cryptococcus neoformans* (CN) is an opportunistic fungi which was first isolated from a bone infection in a young woman and described in 1894 by the pathologist Otto Busse and surgeon Abraham Buschke.[3] The cases were on the rise during the succeeding years together with the upsurge in immunocomprised patients and AIDS[3] including conditions affecting the cellular immunity such as organ transplantation, lymphoproliferative diseases and chronic users of immunosuppressive drugs.[6] A portion of the cases include individuals with no obvious disease.[3] An estimated 1 million cases of cryptococcal infections that occur among people with HIV/AIDS worldwide each year result to 625,000 deaths *(CDC 2015)*. In the Philippines, information on Cryptococcus infections is limited due to rarity of the disease in the local setting.

Cryptococcus neoformans (CN) usually resides in tropical regions commonly isolated in pigeon droppings, has a worldwide distribution and brings about opportunistic infections.[6] They rarely affect immunocompetent individuals.[5] The infirmities due to this fungi ranges from mild skin infections, cough, fever, pneumonia to systemic illnesses such as meningitis and spreads to distant sites.[3,12] Other organs such as the prostate, eyes, liver, spleen and adrenals are like wise susceptible.[11] The systemic disease is acquired by humans through the respiratory tract, by inhalation of scattered yeasts in the air.[4] Human-to-human transmission is not a characteristic of the disease.[11] The clinical presentation of pulmonary cryptococcosis (PC) is generic and varies among individuals, often times misdiagnosed as lung neoplasm, common pneumonia or other lung disease.[7] A low CD4+ T cell count among immunocompromised patients will pave way to high incidence of PC due to reduced production of cytokines impairing the anti-cryptococcal activity of monocytes.[10]

Presumptive and definitive diagnosis of PC can be done through various modalities including radiologic studies, fungal culture and histopatho logic examination.[1,12] By imaging, findings may vary among individuals and depend on their immune status. Among immunocompetent patients, PC appears as subpleural nodules (single or multiple) which can be unilateral or bilateral, no cavitations and well-circumscribed. On the other hand, immunocompromised individuals usually present with opacities in the interstitium and alveoli.[1] In the presented case, chest CT scan revealed a pulmonary artery aneurysm in the medial basal right lower lung with an impression considering mycotic aneurysm. Right lower lung consolidation, patchy ground-glass opacities and interstitio-alveolar infiltrates are also noted. Pleural effusions and lung consolidation can also be found among affected individuals and are like-wise apparent in our patient.[1]

The classical way of diagnosing PC definitively is by isolation of the causative agent from body fluids and preferably tissue samples by culture using Sabouroud and nigger seed agar media without without Cycloheximide due to its inhibitory effect on CN.[11,12]

The fungus may be identified by direct histopathological examinations including demonstration by hematoxylin and eosin (H&E), mucicarmine, PAS, alcian blue, Grocott-Gomori Methenamine silver and india ink preparation.[1,6] Under the microscope, cryptococcus appears as 5-10 mm yeast cells with spherical to ovoid shape covered by a virulence factor, polysaccharide capsule.[6] On H&E, fungi show pink cytoplasm with blue nuclei. The mucicarmine stains the capsule magenta and india ink preparation is useful by accentuating it against a dark background. The PAS technique is appreciated by visualization of basement membranes due to the presence of Schiff reactive glycoproteins within it.[6] Both the PAS and india ink stains were done on the patient's specimen and came out positive for CN. Latex agglutination test can also be used as a serological marker as a back-up in making a diagnosis of PC but due to constraints in analyzing it specially on vague cases, it has a limited use.[12]

CONCLUSION

Pulmonary cryptococcosis is a relatively rare disease in the Philippines due to limited number of reported cases. This disease is commonly seen among immunocompromised individuals including patients with AIDS. Proper approach in early detection and diagnosis should be followed to ensure good patient outcomes. This case implies that incidence of a lung lesion in an immunocompromised should never be underestimated regardless of HIV status. The authors hereby present a rare case of pulmonary infection in this institution.

REFERENCES

1. Labordac LS, Otochd JP, et al. Pulmonary cryptococcoma: a rare and challenging diagnosis in immunocompetent patients. Autopsy Case Rep [Internet]. 2015; 5(2):35-40. Available at http://dx.doi.org/10.4322/acr.2015.004.
2. Lee KT, Yong KY, Chua HH. Cryptococcal meningitis and pumonary cryptococcoma in a immunocompetent host - a rare case report. Asian Pacific J Trop Med.2020;13(1):46-48.
3. Srikanta D, Felipe H, Tirado S, Doering TL. Cryptococcus neoformans: historical curiosity to modern pathogen. Yeast. 2014 Feb;31(2):47-60.
4. Odashima K, Takayanagi N, Ishiguro T, Shimizu Y, Sugita Y. Pulmonary Cryptococcosis with Endobronchial lesions and meningitis. Intern Med. 2014;53(23):2731-5.
5. Fukuchi M, Mizushima Y, Hori T, Kobayashi M. Cryptococcal pleural effusion in a patient with chronic renal failure receiving long-term corticosteroid therapy for rheumatoid arthritis. Intern Med. 1998 Jun;37(6):534-7.
6. Gazzoni AF, Severo CB, Salles EF, Severo LZ. Histopathology, serology and cultures in the Diagnosis of Cryptococcosis. Rev Inst Med Trop Sao Paulo, Sep-Oct 2009;51(5):255-9.
7. Wang JM, Zhou Q, Cai HR, Zhuang Y, Zhang YF, Xin XY, et al. Clinicopathological features of pulmonary cryptococcosis with cryptococcal titan cells: a comparative analysis of 27 cases. Int J Clin Exp Pathol 2014;7(8):4837-4846.
8. Warnock DW. Cryptococcus neoformans. J. Antimicrobial Chemotherapy. 1999 July;44(1):139.
9. Mirza SA, Phelan M, Rimland D, Graviss E, Hamill R, Brandt ME, et al. The changing epidemiology of cryptococcosis: an update from population-based active surveillance in 2 large metropolitan areas, 1992–2000. Clin Infect Dis. 2003 Mar 15;36(6):789-94.
10. Wang J, Zeng Y, Luo W, Xie X, Li S. The Role of cryptococcus in the immune system of pulmonary cryptococcosis patients. PLoS One. 2015 Dec 4;10(12):e0144427
11. Othman N, Abdullah NA, Wahab ZA. Cryptococcal meningitis in an immunocompetent child: a case report and literature review. Southeast Asian J Trop Med Public Health. 2004 Dec;35(4):930-4.
12. Liew KL, Jee JM, Yap I, Yong PVC. In vitro analysis of metabolites secreted during infection of lung epithelial cells by cryptococcus neoformans. PLoS One. 2016 Apr 7;11(4):e0153356
13. Fisher JF, Valencia-Rey PA, Davis, WB. Pulmonary cryptococcosis in the immunocompetent patient-many questions, some answers. Open Forum Infect Dis. 2016 Sep 3;3(3):ofw167
14. Salvana, EM, Leyritana K, Alejandria M, Lim J, Destura R, Tenorio A. Opportunistic infections in Filipino HIV patients. Available from: https://idsa.confex.com/idsa/2012/webprogram/Paper36414.html

Abdominal Aortic Aneurysm in a Child with Severe Mitral Regurgitation

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This is an uncommon case of a 9-year old girl who was diagnosed as RHD with infective endocarditis presenting with a seven-week history of left sided weakness and concomitant suprarenal saccular abdominal aortic aneurysm measuring 5.3 x 6.6 x 6.5 cm in size. She underwent repair of the abdominal aneurysm on second hospital stay, and five days later, she had mitral valve replacement. Our objectives for submitting this case report are (1) to determine if all the clinical manifestations of this patient have arisen from the problem of infective endocarditis; (2) to analyze the proper timing and prioritization of surgical intervention needed by the patient, i.e., the repair of the suprarenal aneurysm or the open heart surgery for mitral regurgitation and (3) to discuss the anesthetic considerations of her current state of illness disease and what are the implications of these co-existing pathologies for the planned procedures. ***Phil Heart Center J 2021;24(1):86-91.***

Key Words: pediatric valvular heart disease ■ abdominal aortic aneurysm ■ infective endocarditis ■ cerebral infarct ■ mitral regurgitation ■

It is common knowledge that patients with congenital defects or those with valve lesions are vulnerable to infective endocarditis (IE). Infective Endocarditis occurs less often in children and accounts for approximately one in 280 pediatric admissions per year in developed countries, where the prevalence of rheumatic fever has declined.[1,2] Mycotic aneurysms are uncommon complications in children with IE and can develop in any systemic artery, but the aorta itself and the superior mesenteric artery are the most common sites.[3,4]

We report a nine year old female patient, diagnosed to have Rheumatic Heart Disease, who sought admission because of a left sided body weakness and an incidental finding of a suprarenal abdominal aortic aneurysm. It is interesting to analyze if all these disease entities are inter-related, and if the root cause of all these problems at hand are secondary to infective endocarditis.

The objective of the study is to; (1) determine if all clinical manifestations of the patient have arisen from the problem of infective endocarditis; (2) analyze the proper timing and prioritization of surgical intervention needed by the patient, ie, the repair of the suprarenal aneurysm or the open heart surgery for mitral regurgitation; (3) discuss the anesthetic considerations of the current state of illness disease and what are the implications of these co-existing pathologies for the planned procedures.

Case: This is a 9-year old girl, presenting with a left-sided body weakness and was admitted with a working diagnosis of RHD infective endocarditis, probably mycotic, severe mitral regurgitation, not in failure, and with concomitant suprarenal abdominal aortic aneurysm. History of present illness started 17 weeks prior to admission beginning with intermittent fever which persisted for 9 weeks until she developed joint pains, orthopnea and eventually left sided hemiparesis.

Upon admission, the vital signs were: BP 130/70 mmHg (left), 120/70 mmHg (right), 0/0 (both lower extremities); PR 115 bpm, RR 20 cpm, Temp 36.9 C; O2 sat 97%. She is severely malnourished, body weight 13kg, BMI 8. Physical examination revealed left sided hemipa-

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resis and her abdomen has a well circumscribed mass at the midline epigastric area about 6 x 7 cm. Auscultation of the heart revealed the pansystolic heart murmur, and she has clear breath sounds. The pulses on both upper extremities are full, but there no palpable pulses on both lower extremities (dorsalis pedis, popliteal and femoral).

2D TTE (Transthoracic echocardiography): Rheumatic Heart Disease, severe mitral regurgitation, with multiple echogenic mobile vegetations noted attached to the anterior and posterior mitral valve leaflets and there seemed to be a ruptured chordae of the posterior mitral valve producing mitral regurgitation, with estimated PAP of 64 mmHg by PAT. EF 43%, RVFAC 48; LVED 4.92 cm, LA 3.3cm.

Imaging Studies

- Cranial CT scan showed a sub-acute infarct at the right temporo-parietal area.
- Cranial MRI revealed a chronic infarction in the right lentiform nucleus and a complete occlusion of the right MCA. There as no acute territorial infarct, intracranial hemorrhage, mass lesion or midline shift. Incidental finding of a distal left posterior cerebral artery 2.0 mm saccular aneurysm was also noted.
- Abdominal CT scan showed a large para-aortic cystic mass closely related to the abdominal aorta, consisting of a thrombotic abdominal saccular aneurysm probably mycotic in origin. The abdominal CT aortogram showed a saccular suprarenal abdominal aneurysm (5.3 x 6.6 x 6.5 cm) with probable transection or compression of the infrarenal aorta.

Laboratory Tests: CRP: 76.5 mg/L, ESR 22 mm/hr, Protime: 88%, INR 1.06, APTT 37.4 sec Hgb 112 g/L; Hct 0.34, WBC 11.5 x103/µl, platelet 230 x103/µl Creatinine: 0.04 mmol/L, BUN: 4.7 mmol/L Total Calcium: 2.39, Magnesium: 0.70, Potassium: 2.9 mmol/L, Sodium: 126 mmol/L. SGPT: 17 U/L, SGOT: 28 U/L

Medications: Protocol for infective endocarditis was applied. Oral penicillin V and Propranolol were then started.

Patient Management: Because of the saccular nature of the aneurysm, ie, with risks for dissection or rupture, the patient was scheduled for AAA repair on the 2nd hospital day. Nutritional build-up was optimized by giving micronutrients.

Hence, the patient was referred to other specialties for preoperative evaluation and optimization, namely: TCVS, vascular medicine, pediatric nephrology, pediatric neurology, pediatric infectious disease and cardiovascular anesthesia. She was classified as ASA class III and the anesthesia plan was to do a combined general anesthesia with epidural anesthesia and catheter-based epidural postoperative analgesia.

Preoperative Preparation: On the night prior to surgery, Pen V was temporarily discontinued. Instead, Amphotericin B, Vancomycin and Amikacin were started. The proposed surgical plan was to do the aneurysm repair with CPB on standby, just in case the patient becomes hemodynamically unstable intra-operatively. If the aneurysm repair shall be done on CPB, the mitral valve would then be replaced as well.

Anesthesia Management for Repair of Abdominal Aneurysm: Basic minimum monitoring requirements for cardiac surgery were applied, to include continuous ECG, pulse oximetry and capnography and direct BP monitoring with a radial arterial line, a central venous access on the right internal jugular vein for CVP monitoring and drug administration, and a cerebral oximeter.

Patient was induced to sleep with 1 mg Midazolam and 3.2 mcg/kg/cc of Fentanyl, and endotracheal intubation facilitated with Rocuronium at 1 mg/kg. The epidural catheter was carefully inserted on a lateral decubitus position at L3-L4 interspace. Test dose was done and 5 cc of Bupivacaine 0.25% was administered for analgesia. Anesthesia was maintained with Propofol via TCI at a plasma level of 1.5 mcg/ml. Infusion of Albumin 5% was started to maintain intravascular volume.

Intraoperative Events: Intra-operatively, the initial vital signs were stable. However, upon

release of the compression on the infrarenal aorta, the blood pressure started to decline and epinephrine infusion was started at 0.10 mcg/kg/min. During clamping and repair of the aorta, the vital signs remained stable, with a low dose of nitroglycerine maintained at 1 mcg/kg/min. On declamping, the patient became severely hypotensive, followed by bradycardia. CPR was immediately initiated, with ROSC. From hereon, the vital signs remained stable until the end of the procedure. Patient was transferred to our SICU intubated. Her post-operative recovery post aneurysm repair was unremarkable and was extubated on the first post-operative day. She was given IV Acetaminophen for analgesia together with 0.8 mg Epidural Morphine given every 12 hours. On the 4th post-operative day, epidural catheter was removed.

Anesthesia Management for the Mitral Valve Replacement: Five days after the aneurysm repair, patient underwent mitral valve replacement under general anesthesia with oxygen – sevoflurane – fentanyl anesthesia. All monitoring parameters done in the first surgery were continued. The intra-operative course was unremarkable, with a total bypass time of 2 hours 35 min, and total ischemic time of 2 hours.

Post-operatively patient remained stable, was weaned successfully from the mechanical ventilator and was extubated on post operative days. Intravenous acetaminophen was given for analgesia. The rest of the hospital stay was unremarkable and was discharged home on the 22nd hospital day.

DISCUSSION

Undoubtedly, this 9-year old patient needs urgent medical management and surgical intervention both for her cardiac problem of severe MR secondary to ruptured chordae and for the co-existing suprarenal saccular abdominal aortic aneurysm with risks of dissection or rupture because of its size. The existing Infective Endocarditis (IE) supports the probable mycotic nature of the abdominal aneurysm. The IE also underlies the cause of the ruptured chordae.

Focal neurological deficit is rare in children and generally results from a cerebral infarction that most commonly occur as a result of embolization from endocardic vegetation.[5] Heiro et al[5] reviewed 218 episodes of IE and reported that in most IE episodes (76%) a neurological manifestation was evident before the start of antimicrobial treatment, being the first sign in 47% of episodes and also that 9 of 13 embolic brain infarctions were located in the region supplied by the middle cerebral artery.

Our patient had a seven week history of left-sided body weakness and this is due to the sub-acute infarct seen on cranial CT Scan at the right temporo-parietal area brought about most probably by thromboembolism as a consequence of the IE. Of further significant finding was the 2mm saccular aneurysm at the distal posterior cerebral artery. Several series have reported incidence rates of 20% to 40% and mortality rates as high as 58% for neurological complications among patients with IE and these complications are more common when both aortic and mitral valves are involved.[3,5] This patient had a severe MR because of a ruptured chordae, again most probably due to the infective endocarditis.

All the existing clinical problems involving the three major organs - the brain, heart and aorta – would certainly pose a threat to the patient's life. Thus preoperative optimization is crucial. Multidisciplinary communication is essential and of highest priority is optimum antibiotic coverage to arrest the on-going infective endocarditis before any planned surgical intervention.

Infective Endocarditis in Pediatric Cardiac Patients: In adults, mitral lesions have been associated with higher rates of embolization than aortic vegetations; the highest rate of embolization (37%) occurs when vegetations are attached to the anterior rather than the posterior mitral leaflet and patients with large vegetations on echocardiography (>10 mm) have significantly higher incidence of embolic events than those with small ones (10 mm).[1,3]

IE occurs less often in children and accounts for approximately one in 280 pediatric admissions per year in developed countries, where the prevalence of rheumatic fever has declined.[3,8] Common organisms related to IE in children are *Streptococcus Viridans* type, gram-positive cocci, staphylococci and enterococci.[1] *Staphylococcus Aureaus* is the most common organism associated with neurological manifestations in IE, whereas mycotic aneurysms usually occur secondarily to infections caused by non-hemolytic Streptococcus.[3,4,5]

Mycotic aneurysms, developing from septic emboli of cardiac origin account for 2.5% of aneurysms among all age groups and 10% of infected aneurysms.[6,7] Mycotic aneurysms are uncommon complications in children with IE and can develop in any systemic artery, but the aorta itself and the superior mesenteric artery are the most common sites. [3,4]

Mycotic aneurysms tend to increase rapidly in size, and ruptures virtually rapidly in size, and ruptures virtually inevitable. Early diagnosis is often difficult. Exceptionally clear definition can be obtained by three-dimensional CT scanning, which facilitates surgical planning. Excision of the aneurysm with extra-anatomic bypass is the classical method of repair, but if gross sepsis is not present m situ prosthetic grafting has become acceptable.[6,8]

A variety of micro-organisms including *Streptococci, Pseudomonas*, and *Salmonella* have been implicated. Blood-borne infection lodges in the intima or vasa vasorum and results in inflammatory destruction of the arterial wall. There is often underlying vessel disease, eg, atheroma, cystic medial necrosis, congenital abnormalities, or trauma. Bifurcations and coarctations are sites of predilection.

Mitral valve surgery (repair or replacement) is indicated, preferably prior to elective intermediate-or high-risk non-cardiac surgery, for symptomatic severe chronic primary MR with left ventricular ejection fraction >30 percent or asymptomatic severe MR with impaired left ventricular ejection fraction (left ventricular ejection fraction 30 to 60 percent) and/or increased left ventricular end-systolic dimension (≥40 mm).[9]

The transthoracic echocardiography findings on this patient disclosed severe mitral regurgitation, with multiple echogenic mobile vegetations attached to the anterior and posterior mitral valve leaflets. and there is a ruptured chordae of the posterior mitral valve producing mitral regurgitation, with estimated PAP of 64 mmHg by PAT. EF 43%, RVFAC 48; LVED 4.92 cm, LA 3.3cm. These findings necessitate surgery. However, the suprarenal abdominal aortic aneurysm also needs urgent surgical intervention because it has been found to be leaking.

Hence the medical team of surgeons, anesthesiologists and cardiologists concurred to proceed first with repair of the aneurysm with standby CPB, and should there be a need to go on cardiopulmonary bypass during the aneurysm surgery, the mitral valve replacement shall be done as well in one set up.

Most asymptomatic patients with severe MR can undergo urgent or elective non-cardiac surgery at an acceptable risk with careful intraoperative and postoperative management, including careful attention to afterload control and fluid balance, which can affect the severity of MR (particularly if functional). The 2014 American Heart Association/American College of Cardiology (AHA/ACC) valvular heart disease guideline noted that intermediate-risk elective non-cardiac surgery with appropriate intraoperative and postoperative hemodynamic monitoring is reasonable to perform in adults with asymptomatic severe MR.[9] The 2014 ACC/AHA guideline on non-cardiac surgery includes a similar statement.[10]

Hence, the anesthetic management of this patient is guided by the following principles: (1) for patients with primary MR, the preload should be maintained or reduced, to maintain intravascular volume while avoiding fluid overload, taking into consideration increased left ventricular volumes and compliance; (2) excessive systemic afterload should be avoided, because marked increases in blood pressure can increase the MR and diminish forward flow.[11,12]

The successful perioperative management was achieved with careful conduct of GETA, using Sevoflurane, Fentanyl and Rocuronium and administration of 0.25% bupivacaine epidurally for the aneurysm repair. The timely use of dobutamine and nitroglycerin infusions titrated to effect, facilitated the aneurysm surgery on a background of severe MR, without having to go on cardiopulmonary bypass support. In five days, the timing for mitral valve replacement under CPB was at its best when the endocarditis is definitely fully controlled.

With perioperative vigilance of all involved and supported by proper use of technology for patient monitoring in both procedures, we circumvented the progression of the cardiac problem during the aneurysm repair and also avoided deterioration of neurologic deficits, not to mention the possibility of a rupture or leak of that saccular cerebral aneurysm in her posterior cerebral artery during the separate surgical interventions.

The use of albumin as part of intraoperative volume management is also essential because of her severely low BMI. And not to be overlooked is the importance of postoperative pain. Optimizing pain control with epidural morphine and IV acetaminophen is important so that she can be weaned early from mechanical ventilation.

CONCLUSION

This case report has shown the significant value of proper preoperative evaluation, teamwork, and communication amongst all the disciplines involved in the management of valvular heart disease in a child complicated by infective endocarditis that resulted in a cerebral infarct and abdominal aneurysm.

The decision as to which surgical intervention should come first, that is, operation for the leaking aneurysm or surgery for the severe MR, definitely requires careful evaluation and preparation. The surgical environment must be ready to handle both situations happening as one set-up.

Fortunately, in our patient, the aneurysm repair was successfully executed as planned and mitral valve surgery followed five days later when the IE has been fully controlled. The judicious use of anesthetic agents, inotropes and vasodilator drugs and the careful choice of anesthetic techniques, guided by management principles that suit the existing pathophysiologic picture of the cardiac problem at hand would have positively influenced the surgical outcome of this patient.

However, total care for this patient does not stop with this surgical management. Proper nutritional support and appropriate physical rehabilitation must be secured so that she can have a better quality of life as she grows. The patient and her family must be informed and educated about the holistic care that she truly needs.

REFERENCE

1. Ferrieri P, Gewitz MH, Gerber MA, Newburger JW, Dajani AS, Shulman ST, et al. Unique features of infective endocarditis in childhood. Circulation. 2002; 105: 2115-7.
2. Dajani AS, Ayoub E, Bierman FZ. Special writing group of the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease of the Council on Cardiovascular Disease in the Young of the American Heart Association. Guideline for the diagnosis of rheumatic fever. Jones criteria,1992 update. JAMA. 268: 2069-73.
3. Baddour LM, Wilson WE, Bayer AS, Fowler VG Jr, Bolger AF, Levison ME, et al. Infective endocarditis diagnosis, antimicrobial therapy, and management of complications: a statement for healthcare professionals from the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease in the Young, and the Councils on Clinical Cardiology, Stroke, and Cardiovascular Surgery and Anesthesia, American Heart Association. Circulation. 2005;111: e394-e433.
4. Lorelli DR, Caimbra RA, Seabrook GR, Towne JB. Diagnosis and management of aneurysms involving the superior mesenteric artery and its branches: a report of four cases. Vasc Endovascular Surg. 2003; 37: 59-66.
5. Heiro M, Nikoskelainen J, Engblom E, Kotilainen E, Marttila R, Kotilainen P. Neurologic manifestations of infective endocarditis: a 17-year experience in a teaching hospital in Finland. Arch Int Med. 2000; 160: 2781-7.

6. Lobe TE, Richardson CJ, Boulden TF, et al: Mycotic thromboaneurysmal disease of the abdominal aorta in preterm infants: Its natural history and its management. J Pediatr Surg 27:1054-1060,1992.
7. Pasic M, Carrel T, Vogt M, et al: Treatment of mycotic aneurysm of the aorta and its branches: The location determines the operative technique. Eur J Vast Surg 6:419-423, 1992.
8. Pasic M, Carrel T, Vogt M, et al. Treatment of mycotic aneurysm of the aorta and its branches: the location determines the operative technique. Eur J Vas Surg 1992; 6:419-423.
9. Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014; 63:e57.
10. Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. J Am Coll Cardiol 2014; 64:e77.
11. Bach DS, Eagle KA. Perioperative assessment and management of patients with valvular heart disease undergoing noncardiac surgery. Minerva Cardioangiol 2004; 52:255.
12. Frogel J, Galusca D. Anesthetic considerations for patients with advanced valvular heart disease undergoing noncardiac surgery. Anesthesiol Clin 2010; 28: 67.

Combined Carotid Endarterectomy and Coronary Artery Bypass Graft Surgery for a Critically Compromised Carotid and Coronary Disease Patient

Darwin James G. Alvarez, MD

Background --- Carotid endarterectomy (CEA) and coronary artery bypass (CABG) surgery as a single stage procedure has an increased risk for stroke and perioperative myocardial infarction. This is a case report on the anesthetic challenges and management of a patient undergoing combined CEA and CABG.

Case --- This is a case of a 63-year old man who came In for chest pain. Coronary angiography revealed a severe triple vessel disease with critical left main involvement. He was also diagnosed with a totally occluded left distal internal carotid artery and 70-99% right internal carotid artery stenosis with type V plaque morphology and a history of cerebral vascular accident (CVA) 2 years prior to this presentation. He underwent a combined CEA and CABG procedure under IABP and CPB pump support. He did not have any major adverse event and was discharged improved.

Conclusion --- The use of preoperative IABP, neurologic monitors and employing neuroprotective measures in combined CEAlCABG on patients withseverely compromised coronary and carotid arteries may improve the outcome. ***Phil Heart Center J 2021;24(1):92-95.***

Key Words: carotid endarterectomy ■ coronary disease ■ coronary artery bypass graft ■ intraortic balloon pump ■ anesthesia management ■

Multivessel coronary artery disease (CAD and coexistent carotid artery stenosis (CAS) is not infrequent. One in 5 patients with multivessel CAD has a severe CAS, and CAD incidence reaches 80% in those referred for carotid revascularization.[1] Current surgical guidelines indicate that CEA is usually recommended before or concomitant with CABG in patients with a symptomatic carotid stenosis or asymptomatic carotid stenosis of 80% or more (Class IIa/C).[2] However, CEA-CABG is associated with a high risk of MI (in those with CEA prior to CABG) or stroke (CABG prior to CEA), and the cumulative major adverse event rate reaches 10-12%.[1,3]

Anesthetic challenges in combined CEA-CABG include providing myocardial protection while undergoing CEA and maintaining cerebral perfusion while undergoing CABG.

The case is presented to report on the anesthetic challenges and management of a patient with CAD severe 3VD with critical LM involvement and severe bilateral ICA stenosis who underwent combined CEA and CABG surgery.

Case: FE is a 63 year old 62kg male, was admitted at the Philippine Heart Center for chest pain. Patient has been complaining of occasional on and off chest discomfort for the last 5 years responsive to nitrates. Chest pain gradually increased in frequency and duration and was not associated with physical activity. Chest pain was unbearable an hour prior to admission and not responsive to medication thus prompting patient to seek consult at our institution.

The patient has a documented history of cerebral vascular accident right middle cerebral

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artery with minimal residual neurologic deficits. Patient is a known hypertensive, non-diabetic, non-asthmatic, occasional alcohol beverage drinker and previous smoker with an estimated 80 pack years.

Coronary angiogram revealed a 90% obstructed LM. The LAD had proximal multiple luminal obstruction ranging from 60 to 80% becoming sub-totally occluded at the mid and distal portion. The LCx had a 90 -95% stenosis at the proximal segment followed by a 70% occlusion at the middle. It then becomes sub-totally occluded distally (*Figure 1*). The RCA is good sized, dominant vessel with 30-40% proximal to mid-narrowing. The RPDA has ostial mid and distal 70% stenosis while the RPL has 80% odtio-proximal and bifurcation occlusion (*See Figure 2*).

The carotid duplex scan study revealed a totally occluded left distal internal carotid artery, 70-99% right internal carotid artery stenosis with type V plaque morphology. Consider significant left external carotid artery stenosis. Insignificant right external carotid artery and right common carotid artery stenosis. Normal antegrade bilateral vertebral artery flow.

The surgical plan was to do a CEA and CABG as a single stage procedure. The patient was pre-medicated with Morphine 5mg and Diphen-hydramine 50mg given intramuscularly. In the OR, standard ASA monitors were attached along with an arterial line (GI8 abbocath) to the left radial artery, pulmonary artery pressure monitor (Swan Ganz 4L) via the right femoral vein and cerebral oximetery monitor (Nonin Equanox 7600). An IABP was inserted through the right femoral artery and maintained at 1:2 configuration. Anesthesia induction was with via midazolam 2mg, fentanyl 8ug/kg, and isoflurane. Tracheal intubation was facilitated with rocuronium 50mg. Anesthesia was maintained with air-oxygen mixture, isoflurane, propofol, rocuronium, fentanyl. The MAP was regulated at > 70mmHg with inotropes when appropriate.

Simultaneous midline sternotomy and saphenous vem graft was done. The ascending aorta was noted to be calcified. Right axillary artery cannulation was done. Right CEA (eversion technique) was started with a backflow pressure at the ICA of 50 mmHg. Carotid artery clamp time was 11 minutes. After adequate systemic heparinazition, cardiopulmonary bypass (CPB) was initiated as pump support. Perfusion pressure was maintained between 70 to 90 mmHg. CABG (LIMA to LAD, SVG to RPL and OM) commenced thereafter. The surgery was tolerated and the patient was admitted to the SICU post - operatively. Weaning from mechanical ventilation was initiated after 6 hours and was subsequently extubated the next morning. Neurologic functions were normal. He was transferred to the ward after 3 days. The rest of the hospital stay was uneventful and was subsequently discharged in a stable condition.

CHARACTERISTICS	PATIENT
Gender	Male
Age (yrs)	63
Diabetes Mellitus	No
HTN	Yes
Coronary anatomy	3 vessels with left main involvement
Renal function	Normal
LVEF%	36%
Carotid Anomaly	Totally occluded LICA 79-99% RICA
CEA DATA	
Backflow pressure	50s mmHg
RICA clamp time	11
CABG DATA	
LIMA	Yes
SVG	3
Cardioplegia	None
Aortic cross clamp	None
Bypass time (mins)	132
Post op complications	None
ICU stay (days)	3

DISCUSSION

Patients with significant CAD may have co-existent significant asymptomatic carotid disease as well, which can lead to serious preoperative complications.[4] To date, managing patients with concurrent carotid and cardiac disease remains controversial. National and international guide-lines provide no real consensus.[5] A recent

systematic review of 624 papers on asymptomatic significant carotid stenosis undergoing simultaneous carotid and cardiac surgery[6] reported that current evidence leans towards simultaneous CEA/CABG. A recent randomized study by lllluminati et al[7] showed that previous or simultaneous CEA/CABG prevented stroke better than delayed CEA.

The surgical choice of doing the CEA first prior to the CABG increases the risk for cardiac dysfunction and MI.[1] In an analysis by Byrne et al. of 758 patients who underwent combined CEA and CABG, 21 patients succumbed to cardiac dysfunction with an overall mortality rate of 3.1%.[8] The patient in the case had severely compromised coronary arteries. Brightwell RE and NashefSM[9] reported a case of using an IABP as a bridge between surgery for critical symptomatic carotid and coronary disease. The IABP use during the case had a significant cardioprotective function while the CEA was being performed.

General anesthesia for combined CEA and CABG procedure is preferred because of the long duration of surgery, better cardiopulmonary control and neuroprotection it provides.[10] Neurologic monitoring is an important part of safe CEA. The various methods of monitoring are electroencephalography (EEG), somatosensory evoked potential (SSEP), transcranial doppler (TCD), ICA stump pressure, regional cerebral O_2saturation ($rS0_2$), bispectral index (BIS) and serial neurologic assessments during regional anesthesia. Detection of cerebral hypoperefusion by any of these modalities will guide for immediate placement of intraluminal shunt.[ll] In the case presented, both $rS0_2$ and ICA stump pressure monitoring methods were used.

The aorta was grossly calcified increasing the risk for embolization on aortic cross clamping. However, aortic cross clamping was not done due to the surgical choice of doing the CABG on a beating heart on CPB support. Should on pump CABG be done, TEE is recommended to help identify the site of atheromatous plaque in the ascending aorta and thus can be avoided in aortic cross clamping.[12] At present, some surgeons prefer CEA and off pump coronary is safe, effective, and with less neurological complication compared to combined and staged on pump CABG approach.[13]

In anesthetic management, midazolam, fentanyl isoflurane and rocuronium were used to help blunt the hemodynamic response to intubation. Rocuronium was used for its hemodynamic stability.[14] Isoflurane produces a dose related reduction in cerebral metabolic rate of 0_2 ($CMR0_2$) with increased cerebral blood flow (CBF).[11] Arterial perfusion pressure during CPB was maintained at 70-90 mmHg to deliver adequate cerebral, renal, and peripheral perfusion.

CONCLUSION

Inpatients with severely compromised coronary and carotid arteries undergoing a combined CEA/CABG procedure, preoperative insertion of IABP may afford myocardial protection prior to CPB. Using neurologic monitoring like cerebral oximetry during the sugery will help monitor decreasing trends of cerebral perfusion during CEA. Neuroprotective measures by anesthetics and an increased MAP and increased perfusion pressure during CPB is essential for better neurologic outcomes.

REFERENCES

1. Dzierwa K, Pieniazek P, Musialek P, Piatek J, Tekieli L, Podolec P, Driwla R, et al. Treatment strategies in severe symptomatic carotid and coronory artery disease. Med Sci Monit. 2011 Aug;17(8):RA191-197.
2. Eagle KA, Guytno RA, Davidoff R, Edwards FH, Ewy GA, Gardneer TJ, Hart JC, et al. ACC/AHA 2004 guideline update for coronary artery bypass graft surgery: a report of he American College of Cardiology/ American Heart Association Task Force on Practice Guidelines (Committee to Update the 1999 Guidelines for Coronary Artery Bypass Graft Surgery). Circulation. 2004 Oct 5;110(14):e340-437
3. Naylor AR, Cuffe RL, Rothwell PM, Bell PRF. A systematic review of outcomes following staged and synchronous carotid endarterectomy and coronary artery bypass. Eur J Vasc Endovasc Surg. 2003 May;25(5):380-9
4. Ahmed WRY. Combined carotid endarterectomy (CEA) and coronary artery bypass grafting (CABG): impact on morbidity and mortality. Pakistan Heart J. 2009 December; 42.

5. Naylor AR. Managing patients with symptomatic coronary and carotid artery disease. Perspect Vasc Surg Endovasc Ther. 2010 Jun;22(2):70-6.
6. Ogutu P, Werner R, Oertel F, Beyer. Should patients with asymptomatic significant carotid stenosis undergo simultaneous carotid and cardiac surgery? Interact Cardiovasc Thorac Surg. 2014 Apr;18(4):511-8.
7. Illuminati G, Ricco JB, Calio F, Pacile MA, Miraldi F, Frati G, Macrina F, Toscano. Short-term results of a randomized trial examining timing of carotid endarterectomy in patients with severe asymptomatic unilateral carotid stenosis undergoing coronary artery bypass grafting J Vasc Surg. 2011 Oct;54(4):993-9; discussion 998-9.
8. Byrne J, Darling RC, Roddy SP, Mehta M, Paty PSK, Krienberg PB, Chang BB, Ozsvath KJ. Shah DM. Combined carotid endarterectomy and coronary artery bypass grating in patients with asymptomatic high-grade stenoses: an anlysis of 758 procedures. J Vasc Surg. 2006 Jul;44(1):67.72.
9. Brightwell R, SAN N. First Use of an Intra-aortic Balloon Pump as a Bridge Between Surgery for Critical, Symptomatic Carotid and Coronary Disease. 2013; 46(5): p. 607.
10. Das SN SCKU. Combined carotid endarterectomy and coronary bypass with associated peripheral artery disease and renal artery stenosis. Indian J of Anesthesia. 2006; 50(2): p. 139-142.
11. Allain R MLMJJG. Carotid Endarterectomy. Int Anesthsiol Clin. 2005; 43(1): p. 15-38.

The Use of Fibrinolytic Agent (r-TPA) in the Management of Loculated Pleural Effusion

Eva Marie M. Crismundo, MD

Background --- Loculated parapneumonic effusions cause increasing morbidity and mortality rate with increasing case fatality rate worldwide. The use of intrapleural administration of recumbinant tissue plasminogen activators (r-TPA) has been a rising trend in other countries. To date, there is no known case of intrapleural thrombolytic therapy that has been reported in the Philippines.

Case --- The management was done in Philippine Heart center with the collaboration of the Interventional Radiology and Adult Pulmonology department on September 2016 with a case of a 60 year-old patient having complaints of exertional dyspnea and easy fatigability. Findings showed recurrent pleural effusion with loculations in the right mid to lower hemithorax. Serial intrapleural administration of r-TPA was given to the patient with daily ultrasound imaging and drainage. Patient had a progressive clinical and diagnostic improvement and was concluded to have responded positively on the treatment provided.

Conclusion --- The use of fibrinolytic agents break loculations to facilitate pleural space drainage. ***Phil Heart Center J 2021;24(1):96-99.***

Key Words: r-TPA therapy ■ loculated pleural effusion ■

Loculated pleural effusions are most commonly due to complicated parapneumonic effusions and empyema followed by tubercular etiology, hemothorax and malignant effusions. The presence of loculations and thick viscous fluid leads to failed pleural space drainage in spite of tube being patent and correctly positioned.[1] The British Thoracic Society classified this as a complicated parapneumonic effusion (CPE) which corresponds to late fibrinopurulent stage. The most significant finding of this stage would be the development of fibrin strands with or without loculations which is evident on ultrasonography or computed tomography. The current recommendation during this stage is by pleural space drainage along with either instillations of intrapleural fibrinolytics or VATS apart from appropriate antibiotics.[2]

The fibrinolytic agents, if used early in the CPE, break loculations and early pleural peel thereby facilitating pleural space drainage.[3]

Although the use of fibrinolytics to promote pleural drainage in patients with parapneumonic effusions has been used in other countries, few cases applied in the adult setting has led to this management under debate. In the Philippines, intrapleural administration of rTPA and other thrombolytics has not been practiced and majority has resorted to surgical management for long term cases of loculated effusions which has poor outcome to chest tube drainage.[4]

This report is the first known case of intrapleural administration in treating loculated parapneumonic effusion in this institution. No other similar case management was reported in other areas of the Philippines noted.

Case: This is a case of 60-year old male who had a history of ESRD secondary to diabetes mellitus Type II, previously diagnosed with coronary artery disease s/p Coronary Artery Bypass Graft (CABG) and post pulmonary tuberculosis treatment who came in with a chief complaint of dyspnea on exertion.

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Two months prior to admission, patient had an onset of easy fatigability and dyspnea on exertion. Chest x-ray was taken which showed bilateral pleural effusion, more in the left. Recurrence of pleural effusion prompted a pigtail insertion of the left chest and diagnostic thoracentesis on the right. Patient had minimal relief. Upon follow-up, ultrasound revealed reaccumulation of the pleural effusion with loculations in the right mid to lower hemithorax, hence was admitted.

Upon admission, laboratory and diagnostic imaging was done and reviewed. Chest physiotherapy was done and maintenance medications continued. Following the British Thoracic Society Classification and corresponding management, the plan was to have an ultrasound-guided intrapleural administration of thrombolytics to the loculated pleural effusion hence patient was referred to interventional radiology.

Preliminary ultrasound scan was done revealing moderate pleural effusion on the left and moderate pleural effusion on the right with loculations. Thrombolytics (rTPA) was prepared with a stock of 50mg/50mL in 1 vial divided into 6 doses. Each dose contained 8mg of rTPA added with 50 cc of sterile water. Left pigtail was drained with 875 mL of serous fluid obtained. Pigtail was inserted aseptically on the right and attempted to drain fluid with only 10 cc of serousanguinous aspirate obtained. Samples of aspirate was sent for gram staining. r-TPA was administered through the pigtail catheter. The patient was then observed for 4 hours and was advised to frequently change position to aid distribution of medication (rTPA) on the affected side. After 4 hours, patient was re-evaluated and was able to drain 600 cc of serousanguinous fluid on the right. Intrapleural administration was given every 12 hours imaging before administration of thrombolytics.

Patient had progressive improvement of his condition with relief of dyspnea and increased to tolerance to daily acitivities without easily getting tired and without oxygen supplementation. He was discharged improved.

DISCUSSION

Tissue plasminogen activator (tPA) is a glycosylated protein with a rapid plasma half-life which is cleared within minutes. Recombinant material is used therapeutically.[5] Recombinant tPA, or alteplase, is a recognized systemic treatment for myocardial infarction, pulmonary embolism and thromboembolic stroke. Similar to other fibrinolytics, tPA converts plasminogen to the active protease plasmin, which degrades fibrin into soluble products. A unique characteristic of tPA is that it is fibrin-selective and preferentially activates plasminogen at the surface of a clot.[6]

Intrapleural fibrinolytic therapy was first described in the late 1940's.[7] Intrapleural fibrinolytics lyse pleural adhesions by activation of plasmin, aiding drainage of the effusion by breaking down fibrinous septations.[6] Given early in the fibrinopurulent phase they may also prevent ongoing fibrin deposition and reduce the severity of loculations by counteracting the profibrotic milieu found within the infected pleural space.[8]

Repeated systemic administration of streptokinase has been linked with a higher incidence of allergic reaction and formation of anti-streptokinase antibody which may reduce its therapeutic efficacy.[9] Bleeding is often a concern of intrapleural administration of fibrinolytics. Some retrospective reviews of PPE did not observe any bleeding episodes associated with intrapleural tPA administration in children, while others noted minor bleeding in drained pleural fluid in some patients.[10]

Contraindication of using fibrinolytic therapy includes history of bleeding diathesis, stroke or significant hemorrhage in the preceding six months and use of any thrombolytics in any route in the previous two years.[10]

Table 1. Shows decreasing amount of drainage during the course of the treatment

Day	Drain (Right hemithorax)	rTPA (Right hemithorax)
Day 0 - Initial (4pm)	---	8 mg : 50 cc sterile water
After 4 hours	600 cc, serousanguinous fluid	---
Day 1 4am	325 cc, serousanguinous fluid	8 mg : 50 cc sterile water
4pm	262 cc, serousanguinous fluid	8 mg : 50 cc sterile water
Day 2 4am	220 cc, serousanguinous fluid	8 mg : 50 cc sterile water
4pm	120 cc, serousanguinous fluid	8 mg : 50 cc sterile water

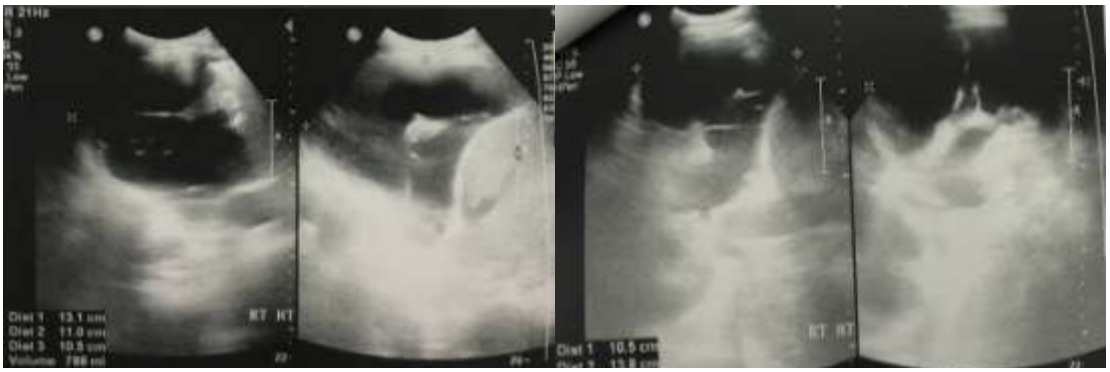

Figure 1. shows loculated pleural effusion in the right hemithorax

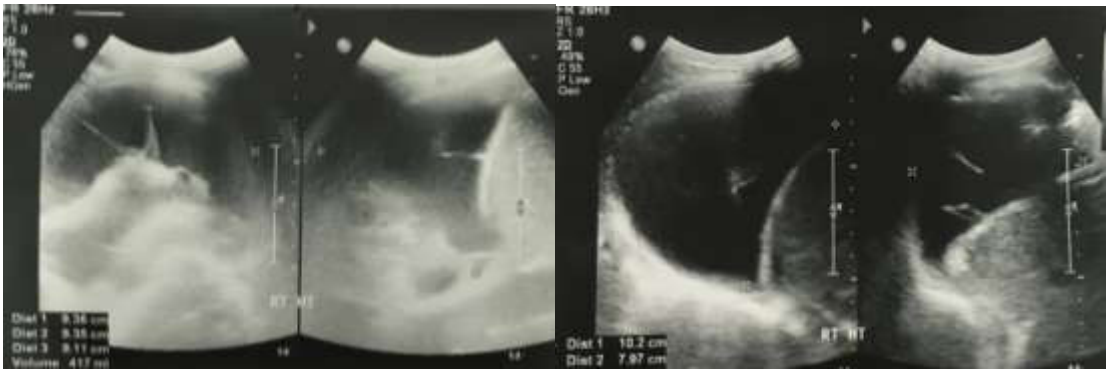

Figure 2. shows decreased loculations in the hemithorax

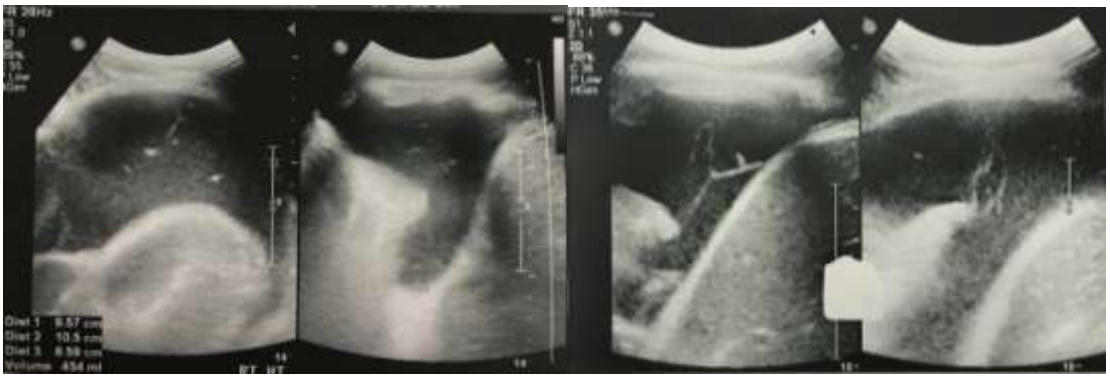

Figure 3. shows further decreased loculations **in** the right hemithorax

CONCLUSION

The use of fibrinolytic agents break loculations to facilitate pleural space drainage.

REFERENCES

1. Bouros D, Schiza S, Panagou P, Drositis J, Siafakas N. Role of streptokinase in the treatment of acute loculated para- pneumonic pleural effusions and empyema. Thorax 1994;49: 852e5.
2. Idell S, Girard W, Koenig KB, McLarty J, Fair DS. Abnormalities of pathways of fibrin turnover in the human pleural space. Am Rev Respir Dis 1991; 144: 187e94.

3. Philip-Joet F, Alessi MC, Philip-Joet C, Aillaud M, Barriere JR, Arnaud A, et al. Fibrinolytic and inflammatory processes in pleural effusions. Eur Respir J 1995; 8:1352e6.
4. Balfour-Lynn IM, Abrahamson E, Cohen G, et al; Paedi- atric Pleural Diseases Subcommittee of the BTS Standards of Care Committee. BTS guidelines for the management of pleural infection in children. Thorax. 2005;60(Suppl 1):i1-21.
5. Ray TL, Berkenbosch JW, Russo P, Tobias JD. Tissue plasminogen activator as an adjuvant therapy for pleural empyema in pediatric patients. J Intens Care Med. 2004;19(1):44- 50.
6. Bell WR. Present day thrombolytic therapeutic agents:pharmocotherapeutics and pharmocodynamics. Rev Cardiovasc Med.2002;2(suppl 2): S24–44.
7. Idell S, Girard W, Koenig KB, et al. Abnormalities of pathways of fibrin turnover in the human pleural space. Am Rev Respir Dis 1991;144:187-94.
8. Alemán C, Alegre J, Monasterio J, et al. Association between inflammatory mediators and the fibrinolysis system in infectious pleural effusions. Clin Sci (Lond) 2003;105:601-7.
9. Philip-Joët F, Alessi MC, Philip-Joët C, et al. Fibrinolytic and inflammatory processes in pleural effusions. Eur Respir J 1995;8:1352-6.
10. Chung CL, Chen CH, Sheu JR, et al. Proinflammatory cytokines, transforming growth factor-beta1, and fibrinolytic enzymes in loculated and free-flowing pleural exudates. Chest 2005;128:690-7.

Case Report - Nuclear Medicine

Utility of SPECT MPI in Assessing Myocardial Perfusion After Arterial Switch Operation

Michael Laurente Santos, MD

Pediatric MPI is not often done in our institution, because of difficulties performing these procedures and significant radiation exposure to the patient. This is a case report on a two (2) month old boy who was diagnosed with transposition of the great artery (TGA) and underwent an arterial switch operation (ASO) and tolerated procedure well but developed ST elevation in leads II, In and aVF but cardiac markers were negative. Patient was referred for myocardial perfusion scan which revealed a mainly scarred myocardium in the apical to basal to basal inferior and inferolateral LV segments. In conclusion, MPI is a safe and well-tolerated procedure for assessing left ventricular perfusion defects ill pediatric patients. ***Phil Heart Center J 2021;24(1):100-102.***

Key Words: myocardial perfusion imaging ■ arterial switch operation ■

Pediatric myocardial perfusion imaging is not a very popular procedure in our institution, with approximately 1-2 patients/year underwent this procedure. Several limitations and considerations are discussed prior to referring a patient to the Nuclear Medicine Division. Issues like exposure to radiation, difficulty in positioning the patient, probable attenuation due to patient motion are some concerns whenever a pediatric case is referred.

Our patient is the youngest case who underwent myocardial perfusion imaging (MPI) SPECT in this institution. Indication for the scan is an ST elevation in leads II, III and aVF after an arterial switch operation (ASO). The aim of this scan is to determine any post-operative perfusion defect in the left ventricular myocardium.

Case: We present a 2-month old boy, born to a G2P2 mother via NSD, meconium stained and cyanotic with good cry and activity. Patient eventually developed cyanosis and was diagnosed with transposition of the great arteries (TGA), underwent arterial switch operation (ASO) as definitive management.

A few days post-operatively, there was a development of ST segment elevation at leads II, III and, aVFTroponin I was requested but was negative. Patient was medically managed from then on. On the 35th hospital day the is ECG showed right bundle branch block and still with ST segment elevation. Patient was referred for SPECT MPI using Tc-99m sestamibi. The scan showed moderate to severely reduced tracer uptake in the apical to basal inferior and inferolateral segments which did not improve on the resting scan done on a separate date. Prominent extracardiac tracer activity adjacent to the inferior and septal walls was noted in both instances. The right ventricle was also visualized, denoting right ventricular prominence.

The Quantitative Perfusion SPECT (QPS) shows a polar map of the left ventricle based on the short axis views. This quantifies the perfusion defect previously mentioned in the splash images based on the distribution of the coronary arteries.

DISCUSSION

The arterial switch operation (ASO) has been the treatment of choice for the congenital heart disease transposition of the great arteries (TGA). This is due to the favorable early, intermediate

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and long term outcome seen in the subjects who underwent this procedure. Compared with other other treatment plan or modality, the arterial switch operation has the advantage of restoring the left ventricle as a systemic pump.[1] However, complications such pulmonary stenosis, aortic insufficiency or coronary obstruction are still observed post-operatively.[2] After the operation, coronary complications are not rare, occurring during the early postoperative phase and is an important cause of death among patients.[3]

During arterial switch operation, the transfer of the coronary arteries is a difficult and complicated maneuver. Re-implantation of the coronary vessels that ensures optimal coronary perfusion is often difficult and causes problems like inadequate function and patency. Because ECG or echocardiography is inadequate to assess coronary dysfunction, SPECT MPI can be a reproducible method in determining myocardial perfusion after reimplantation.[4] Our patient, tolerated the ASO procedure, however he developed ST elevation on the 6th hospital day. This ST elevation may be due inadequate function or compromised patency of the coronary vessels, which may have been kinked or failed during reimplantation in the neoaorta. Several studies have used MPI to evaluate perfusion defect in children after ASO.[4] Hence this referral was made so further management can be guided by the test result.

Tc-99m labeled radiopharmaceuticals are the tracer of choice for pediatric patients due to their short half-life, improved image quality and dosimetry but can still emit enough photon energy that is ideal for gamma camera imaging. A key disadvantage of Tc-99m is the slow liver clearance leading to increased hepatic tracer accumulation which may increase attenuation on the myocardial scan.[5]

Children can undergo the same type of pharmacological stress as adults, using dipyridamole, adenosine or dobutamine. Exercise stress test has limited use in pediatric patients. In our institution, an intravenous infusion of dipyridamole, 0.56 mg/kg over four minutes is the available pharmacological stress method. Though cardiac rate significantly increase during this infusion the induced hy otension seen in adults are seldom chest pain) are difficult to assess specially in infants and very young children. Some centers routinely give 3-5 mg/kg of aminophylline over 1 minute infusion to reverse the side effects of dipyridamole.

Pharmacological or exercise MPI can detect angiographically proven stenosis with 70-90% sensitivity.[5]

Our patient was given an infusion of 1.5 mg of dipyridamole which is 0.5 mg/kg dose for this patient. This dose is lower by 0.6 mg/kg from the recommended 0.56 mg/kg, though there was an increase in heart rate after the infusion.

In our scan there was increased extracardiac activity coming from the liver. It was recommended to have an elapse time of 60 - 90 minutes in before rest or stress image are taken after injection of radiopharmaceutical, to reduce hepatic activity.[5]

In our patient, the perfusion defect was seen in the apical to basal inferior and inferolateral segments, which is in between the area supplied by the RCA or the LCx. This is contrary to the results of Weindling et al.[6] which demonstrated the most common site of the lesion in the distal territory of the left anterior descending artery most often the apical lateral segment of the left ventricle. According to Weindling et al.[6] these defects are usually reversible which means the lesion is ischemic. In our patient a non-reversible defect was seen and was signed out as mainly scared myocardium.

CONCLUSION

Myocardial perfusion imaging in the pediatric patient is a safe and well tolerated procedure. After an arterial switch operation assessment of post-operative complications is vital for early management of TGA patients. MPI is a useful and non-invasive tool in assessing left ventricular perfusion defects.

Further improvement on the protocol can be recommended to further enhance the MPI image pediatric patients:

1. Full sedation of the patient prior to procedure to decrease motion attenuation.
2. Use of standard I5-lead ECG for pediatric.
3. Standardized dipyridamole dose to 0.56 mg/kg.
4. Increase elapse time between radiopharmaceutical injection and imaging to 60-90 mins to decrease hepatic attenuation.

REFERENCES

1. Pasquali SK Hasselblad V, Jennifer Li JS, Kong DF, Sanders SP. Coronary artery pattern and outcome of arterial switch operation for transposition of the great rteries: a meta-analysis. Circulation. 2002; 106:2575-2580.
2. Touchot LJ, Serraf A, Litvinova A, Lambert V, Piot F, Lacour-Gayet A. Late outcome after arterial switch operation for transposition of the great arteries. Circulation. 2001; 104:1-121-I-126.
3. Losay J, Touchot-Kone A, Serraf A, Belli E, Piot ID. Coronary events after arterial switch operation for transposition of the great arteries. Circulation. 2003; 108:II-186-II-190
4. Hauser M, Bengel FM, Ktihn A, Sauer U, Braun SL. Myocardial blood flow and flow reserve after coronary reimplantation in patients after arterial switch and Ross operation Circulation. 2001;103:1875-1880.
5. Kondo Chisato. Myocardial perfusion imigaing in pediatric cardiology. Ann of Nucl Med. 2004; 18(7): 551-561.
6. Weindling SN, Wernovsky G, Colan SD, Parker JA, Boutin C, Mone SM, et al. Myocardial perfusion, function and exercise tolerance after the arterial switch operation. J Am Coll CArdiol 1994;80: 322-326.

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a. For Journal References: Surname and initial of author(s), title of article, name of journal, volume number, first page or inclusive pages. If there are more than three authors, list the first three authors and add et al.

Braunwald E and Rutherford JD. Reversible ischemic left ventricular dysfunction: evidence for the "hibernating myocardium." J Am Coll Cardiol 1986;8:1467-1470.

Dilsizian V, Rocco TP, Freedman NM et al. Enchanted detection of ischemic but viable myocardium by the reinjection of thallium after stress -redistribution imaging. N Engl J Med 1990;323:141-146.

b. For Books: Surname and initial of author(s), title and subtitle, editor, city, publishing house page, year as specific reference.

Dillman WH. The Cardiovascular System in Thyrotoxicosis. In Braverman LE and Utiger RD, eds. The Thyroid - A fundamental and Clinical Text. 6th ed. Philadelphia: JB Lippincott Co; 1991,759-770.

Figures

Illustrations should complement the text. The illustrations should be sharp and professionally rendered. Letters, numbers and symbols must be clear and of sufficient size to retain legibility after reduction. Glossy photographs of the original artwork, between 3-1/2 x 5 in. and 8 x 10 in. in size, should be submitted. Each illustration should be numbered and cited consecutively using Arabic numerals. Colored photographs will be considered for publication.

Legends

Caption for the figures must be typed, double-spaced, and must not appear in the figure. For photomicrographs, the legend should include the original magnification and the stain used.

Tables

Tables should be self-explanatory and should supplement, not duplicate the text. They should be numbered consecutively using Roman numerals.

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