Congenital Cystic Malformations of the lung: A 30-year Review of Cases at the Philippine Heart Center (1975-2005)

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Background --- Congenital cystic lung malformations are uncommon but potentially life-threatening anomalies of infants and children.

Methods and Results --- A 30-year retrospective review of 20 patients with congenital cystic lung malformation was done. Histopathologic examination revealed the following: congenital cystic adenomatoid malformation (n= 9) accounted for 45%, congenital lobar emphysema (n= 5) 25%, bronchogenic cyst (n=3) 15% and pulmonary sequestration (n= 3) 15%. Twelve patients were under 1 year of age 5 of whom where neonates. There was no sex preponderance in all four diseases. Most common symptoms were dyspnea, acute respiratory tract infection, fever and cyanosis while tachypnea, intercostals retractions, decreased breath sounds and tachycardia were the most common physical findings. The duration of illness ranged from 2 days to 6 years. Dyspnea was noted in 80% of patients. Lobectomy was done in 70% of patients. Immediate post-operative complication in decreasing frequency were pneumonia, atelectasis, pneumothorax, septicemia, bronchopleural fistula and bleeding were noted in 80% of patients. There was no significant correlation between survival and the number of lobes resected. Poor post-operative outcome was not associated with the types of congenital lung malformation. There was also no significant correlation between presence of post-operative complications and poor outcome. ***Phil Heart Center J 2007; 13(2):130-134.***

Key Words: Congenital Cystic Lung Malformation ■ Congenital Cystic Adenomatoid Malformation (CCAM) ■ Bronchogenic Cysts ■ Pulmonary Sequestration ■ Congenital Lobar Emphysema, Review

Congenital cystic malformations of the lung are rare but fascinating anomalies of lung develop ment that arise from an error in the embryologic development. The lung normally develops from one kind of tissue that becomes the airways arising originally from the upper digestive system, and another kind of tissue that becomes the blood vessels and connective tissue of the lung. These two kinds of tissue must "communicate" clearly with each other to form a normal lung. Errors in communication can lead to one or more of these malformations. They vary considerably in presentation and severity. Four distinct categories of congenital cystic lung malformation can be defined: cystic adenomatoid malformation, lobar emphysema, pulmonary sequestration, and bronchogenic cyst. All may present as abnormal cystic areas within the lung antenatally, in early life or later, although there are differences in clinical course and outcome.

Today, congenital cystic lung malformations are well- known diseases in infants and children because of an obvious increase in number of referrals and admissions in our institution. It is therefore the intent of this study to review patients admitted for congenital cystic lung malformation and to retrospectively evaluate our 30 years of clinical experience with 20 patients. We did a thirty-year retrospective review of medical records of patients diagnosed with congenital cystic lung malformation based on the histopathologic confirmation admitted at Philippine Heart Center between1975-2005. Age at the time of onset of symptoms, age at the time of diagnosis, age at time of treatment, clinical presentation, diagnostic methods, treatment and histopathologic findings were recorded.

Methods

The type of congenital cystic lung malformations and sex distribution are summarized in Table 1. There were nine cases of congenital cystic adenomatoid malformation (CCAM), five cases of congenital lobar emphysema (CLE), three bronchogenic cyst (BC) cases and three cases of pulmonary sequestration (PS). Three out of five cases of CLE were in females. On the other hand, two out of three cases of BC were in males, while in PS, two out of 3 cases were in females.

Results

The type of congenital cystic lung malformations and sex distribution are summarized in Table 1. There were nine cases of congenital cystic adenomatoid malformation (CCAM), five cases of congenital lobar emphysema

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(CLE), three bronchogenic cyst (BC) cases and three cases of pulmonary sequestration (PS). Three out of five cases of CLE were in females. On the other hand, two out of three cases of BC were in males, while in PS, two out of 3 cases were in females.

Table 1. Histologic Types and Sex Distribution of Patients with Congenital Cystic Lung Malformation, PHC, 1975-2005

Disease	Sex		Total
	Male	*Female*	
CCAM	5	4	9
CLE	2	3	5
BC	2	1	3
PS	1	2	3

CCAM- Congenital Cystic Adenomatoid Malformation CLE- Congenital Lobar Emphysema
BC- Bronchogenic Cyst PS- Pulmonary Sequestration

Table 2 summarized the symptoms on presentation of patients with congenital cystic lung malformations. Most common symptoms in decreasing frequency were dyspnea, acute respiratory tract infection, recurrent pneumonia and cyanosis.

Table 2. Presenting Symptoms on Admission of Patients with Congenital Cystic Lung Malformations

Signs	CCAM N=9	CLE N=5	BC N=3	PS N=3	Total
Dyspnea	9	5	1	1	16
AURI	2	1	3	3	9
Fever	1	0	2	0	3
Cyanosis	4	2	0	0	6
Recurrent Pneumonia	0	1	3	3	7
Hemoptysis	0	0	1	1	2

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Table 3 summarized the signs noted on physical examination. The most common were tachypnea, intercostals retractions, decreased breath sounds and tachycardia.

Table 3. Presenting Signs on Admission of Patients with Congenital Cystic Lung Malformations

Signs	CCAM N=9	CLE N=5	BC N=3	PS N=3	Total
Tachypnea	9	5	1	0	15
Retractions	9	5	1	0	15
Decreased Breath Sounds	5	5	3	3	16
Tachycardia	6	5	2	1	14
Rales	1	1	1	0	3
Alar Flaring	4	3	0	0	7

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The pre-operative diagnosis of congenital cystic lung malformation on chest x-ray showed cystic lucencies in all types and mediastinal shift to opposite side both in patients with CCAM and CLE (Table 4).

Table 4. Chest Radiographic Findings of Patients with Congenital Cystic Lung Malformation

Radiographic Findings	CCAM N=9	CLE N=5	BC N=3	PS N=3	Total
Cystic Lucencies	9	5	3	3	20
Mediastinal Shift to Opposite Side	9	5	0	0	14
Presence of Infiltrates	3	0	1	1	5
Anterior herniation to the Opposite Lung	6	1	0	0	7
Emphysema of the Lobes involved	3	4	0	0	5
Atelectasis of the Adjacent Lobes	5	2	0	0	7

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The left upper lobe was commonly involved in CLE, while CCAM have multiple lobar involvements. The right lower lobe was involved in 2 out of 3 patients with BC. The left lower lobe was involved in all 3 patients with PS. (Table 5)

Table 5. Lobar Distribution of Congenital Cystic Lung Malformation

Lobe/s Involved	CCAM N=9	CLE N=5	BC N=3	PS N=3
Right Upper Lobe (RUL)	2	0	0	0
Right Middle Lobe (RML)	2	0	0	0
Right Lower Lobe (RLL)	3	0	2	0
Left Upper Lobe (LUL)	3	4	0	0
Left Lower Lobe (LLL)	1	0	1	3
RML + RLL	0	1	0	0
RUL + RLL + LLL	1	0	0	0

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Surgical resection was done in all patients consisting of lobectomy and segmentectomy, of which lobectomy was the most common (Table 6).

Table 6. Type of Surgical Resection Done on Patients with Congenital Cystic Lung Malformations

Type of Surgery	CCAM N=9	CLE N=5	BC N=3	PS N=3
Lobectomy	9	3	1	1
Segmentectomy	0	2	2	2

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Out of 20 patients who underwent surgical resection, only one died 9 days after surgery because of respiratory failure involving 2 lobes. Poor post- operative outcome was not associated with the type of congenital cystic lung malformation (Table 7).

Table 7. Post-operative Outcomes of Patients with Congenital Cystic Lung Malformations

Type of Surgery	CCAM N=9	CLE N=5	BC N=3	PS N=3
Alive	8	3	3	3
Dead	1	0	0	0

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Table 8 shows the outcomes according to the number of lobes resected.

Table 8. Surgical Outcomes of Patients with Congenital Cystic Malformation According to Number of Lobes Resected

Number of Lobes	Alive n-19	Dead n-1
One	17	1
Two	2	0

Post-operative complications were noted in the majority of patients with pneumonia as the most common cause in all the congenital cystic lung malformations (Table 9)

Table 9. Post-operative Complications of Patients with Congenital Cystic Lung Malformation

Complications	CCAM N=9	CLE N=5	BC N=3	PS N=3	Total N=20
With complications	8	4	2	2	16
Septicemia	2	0	0	0	2
Pneumonia	5	3	1	2	11
Hypoxemia	6	2	0	0	8
Pneumothorax	4	1	1	2	8
Atelectasis	4	2	0	2	8
Bronchopleural Fistula	2	0	0	0	2
Bleeding	1	0	0	0	1

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The mean age of onset of symptoms, age of diagnosis, and age of intervention are summarized in table 10. All patients with CCAM were less than 1 year of age at the time of onset of symptoms and diagnosis. 80% of patients with CLE were less than 1 year of age at the time of onset of symptoms. However, 40% were diagnosed more than 1 year of age (7 and 14 y/o). 55% presents during the first week of life, most with respiratory distress (CCAM).

Table 10. Mean Age of Onset, Diagnosis and Treatment of Patients with Congenital Cystic Lung Malformations

Disease	Mean Age (days) ± SD		
	Onset of Symptoms	Time of Diagnosis	Time of Surgery
CCAM	35.22 ±55.65	54.33±55.38	68.8 ± 61.0
CLE	450.8±972.34	15.81±2245.91	1141.2 ± 2223.13
BC	2798.33±1281.84	2555.2±1672.64	2918.3 ± 1277.5
PS	516.66±917.08	2798.33±1381.83	2555 ± 1672.6

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Discussion

During the development of the embryo, separation of the trachea and esophagus occurs, and migration of the early lung bud takes place. The lung tissue shows further differentiation thereafter into airway epithelium and alveolar cells. In this developmental stage, numerous abnormalities can take place. Bronchopulmonary foregut malformations are combinations of these forms of disordered lung growth such as dysplasia, hypoplasia, or hyperplasia involving one or more structural component of the lung.[13] Any abnormality involving the structural component of the lung would give rise to the different types of congenital cystic lung malformation.

Congenital cystic lung malformation consists of pulmonary sequestration (PS), cystic adenomatoid malformation (CAM). Congenital lobar emphysema (CLE), and bronchogenic cyst (BC).[3,6,7,8,9,10,11,13] All may present as abnormal cystic areas within the lung antenatally , in early life or later, although there are differences in clinical course and outcome. A wide variety of symptoms can lead to the differential diagnosis of congenital cystic malformation of the lung, including respiratory distress, cough, stridor, recurrent pulmonary infections, hemoptysis, dysphagia, pneumothorax, or life-threatening event with respiratory failure. Common presenting symptoms are respiratory distress in early life as was found in CCAM and CLE. This may be due to the pressure effects caused by the lung cyst compressing the surrounding mediastinal structure. The same findings were also seen in this study. Recurrent pulmonary infections and persistent radiographic abnormalities in older children were noted in intralobar PS and BC as was found in this study. It is similar to the cases reported by Gustafson et al.[12]

CCAM may present at birth, or most commonly, in the neonatal period. Only 10% of cases present after the

first year of life. Rarely, presentation may be delayed until later childhood when episodes of recurrent infection, continued slow growth or serendipitous discovery reveal the lesion.

CCAM has no clear sexual or racial predilection. The lesion is unilateral as was found in eight out of nine patients in this study. Occasionally multilobar involvement has been reported which was found in one of the patient in this study who eventually succumb to death because of respiratory failure. Right and left sided involvements occur with equal frequency. In a review of literature, the oldest patient reported was 14 years old at the time of diagnosis. Three patients, aged 35, 24, 7 years, are reported. The 35 and 7 years old patients presented with episodes of recurrent infection while a 24 year old patient, a preoperative chest radiograph was done prior to surgical repair of a facial fracture.[3] There is a debate about the advisability of segmental resection versus lobectomy for CCAM. Segmental resection has been promoted as a lung tissue preserving surgical management of CCAM. However segmental resection has a higher complication rate and repeat surgery for lobectomy due to incomplete removal of abnormal lung tissue is not infrequently required. In this study, a right lower lobe lobectomy was done in one of the patient with involvement of three lobes for the reason that involvement of the right upper lobe and left lower lobe were just minimal. However, after nine days, patient died because of respiratory failure. Lobectomy has been shown to be a more safe and effective procedure. This was done in all patients with CCAM in this study. If necessary, resection of more than one involved lobe is possible, although compromised long-term physical activity can be expected.

CLE is mainly a disease of infancy and always involves one lobe, with rates of occurrence as follows: LUL- 41%, RML- 34%, and RUL- 21%. The left upper lobe distribution in our cases was similar to those in the literature and previous studies.[1, 2] However patient can show multilobar involvement but is rare as was found in one patient in this study. Rarely, CLE may be discovered as an incidental finding in an asymptomatic older child or an adult. The traditional treatment of CLE is lobectomy of the involved lobe or lobes. This was done in three patients with CLE in this study. Segmentectomy was done in two patients. A few patients with exhibited mild symptoms were reported as treated conservatively with medical treatment.

PS is an uncommon congenital anomaly consisting of a mass of dysplastic lung tissue that has no normal connection with the tracheobronchial tree and the pulmonary arteries. The anomalous arterial blood supply usually comes from the abdominal and thoracic aorta with equal frequency. Sequestration are found in two forms: (1) intralobar sequestration, in which the sequestered part of lung lies within normal pulmonary visceral pleura; and (2) extralobar sequestration, in which the abnormal segment of lung is completely separate and enclosed in its own pleural investment. In our cases, intralobar sequestration was found. The usual radiographic appearance is that of a solid or cystic mass in the base of one lung. Almost invariably, symptoms are related to the presence of an airway communication, as demonstrated in 23 out of 32 patients from the review of files of three Army Medical Centers, the largest single series in the literature.[4] No patient with an aerated sequestrum was without marked symptoms. Conversely, few patients with a non-aerated sequestrum exhibited noticeable symptoms. Recurrent fever, chills, and purulent sputum were far the most commons. Less common, but related to chronic infection, are hemoptysis and massive intrapleural hemorrhage. Any indolent process seen on chest roentgenogram should raise suspicion of sequestration, especially if the posterior basilar region is involved. The findings of posterior basilar involvement were also similar in this study. Aortography may be helpful, especially in the patient with an asymptomatic mass noted on routine chest roentgenogram. If the sequestrum is non-aerated and aortography is pathognomonic, then consideration can be given to a non-operative approach. If at any time the patient becomes symptomatic, resection can be done as was done in this study. Simple excision is always adequate for extralobar sequestration. Lobectomy is usually necessary for intralobar sequestration which was done in one of the patient in this study. Occasionally, however, basilar segmentectomy can be performed. Two patients underwent segmentectomy in this study.

BC develop from an abnormal budding of the ventral foregut between the 26th and 40th week of gestation. As such, they are often more appropriately termed foregut duplication cysts. The frequency of BC is unknown presumably because most patients are asymptomatic. Though usually an incidental finding, morbidity from BC has been reported from the cyst becoming secondarily infected or from post-obstructive pneumonia. Dysphagia and dyspnea have resulted from compression of a large cyst on the esophagus and airways. Cases have been reported of cyst rupture and hemorrhage within the cyst. The frequency in different races is unknown. Frequency in each sex is also unknown. In this study, male: female ratio was 2:1. Large cysts may present in the pediatric population because of compression of the esophagus or trachea or because of infection as was seen in this study manifested as pleural effusion and pneumonia. In adults, the cysts typically present as an incidental mass in either the mediastinum or the lung. BC is located most commonly in the mediastinum (85%). Common locations include precarinal, paratracheal, and retrocardiac sites. Intrapulmonary BC is less common (15%) however this was found in this study. Chest radiograph is usually adequate

is usually adequate for detecting larger mediastinal or lung masses; however, it is limited in differentiating solid from fluid. This typically shows a sharply demarcated spherical mass of variable size, most commonly located in the middle mediastinum around the carina. When the cysts is infected or contains secretions, it may appear as a solid tumor or may demonstrate an air fluid level as found in this series. CT findings are characteristic when the lesion demonstrates water density. If the lesion demonstrates soft tissue density, differentiating the cysts from lymph nodes or other solid lesions is difficult. MRI findings are usually diagnostic for mediastinal cysts. In this study, a chest radiograph was done to support preoperative diagnosis and was confirmed by histologic findings.

In summary, we presented 20 cases of congenital cystic lung malformation and compared to the literature and previous studies. Findings in 20 cases showed CCAM as the most common, followed by CLE, BC and PS. In patients with CCAM and CLE, cystic lesions were discovered by respiratory distress. Signs of infection was a core clinical feature in patients with BC and PS. As to the diagnostic modality, diagnosis of congenital cystic lung malformation was based initially on chest x-ray which serves as a starting point for diagnostic evaluation in this study. Two patients with CCAM, one with BC and one with CLE were diagnosed by CT scan. In all of the cases, pulmonary resection is indicated as soon as the diagnosis is made.

References

1. Celia T. Sy, M.D., Alexander O. Tuazon, M.D., Elena G. Chua-Lobo, M.D., Jose C. Gonzales, M.D. and Cristan Q. Cabanilla, M.D. Congenital Cystic Diseases of the Lung: A 12 year review of cases at the Philippine Children's Medical Center ('82-93)
2. Shin-ichi Takeda, Shinichiro Miyoshi, Masayoshi Inoue, Kenichi Omori, Meinoshin Okumura, Hyung-Eun Yoon, Masato Minami, Hikura Matsuda. Clinical Spectrum of Congenital Cystic Disease of the Lung in Children. *Eur J Cardio thorac Surg 1999; 15: 11-17*
3. George L. Zumbra, Lt Col, Robert L, Treasure, Col Girard Seitter, Lt Col, Tracy E. Strevey, Col, Walter Brott, Col, and David C. Green, Col, all MC, USA- Pulmonary Sequestration. *Ann Thorac Surg 1975;20:2.*
4. Donald H. Hulnide, M.D., David P. Naidich, M.D, Dorothy I. Mc-Cauley, M.D. Helen D. Feiner, M.D., Ann M. Avitabile, M.D., M. Alba Greca, M.D., Nancy B. Genieser, M.D. Late Presentation of Congenital Cystic Adenomatoid Malformation of the Lung. Diagnostic Radiology 1984; 151: 569-573
5. A.G. Coran and R. Drongowski. Congenital Cystic Disease of the Tracheobronchial Tree in Infants and Children. Experience with 44 consecutive cases. Archive of Surgery.
6. Adel K. Ayed and Abdulla Owayed. Pulmonary Resection in Infants for Congenital Pulmonary Malformation. Chest 2003; 124; 98-101.
7. PV Bailey, T. Tracy Jr. RH Connars, D de Mello, JE Lewis and TR Weber. Congenital bronchopulmonary Malformations. Diagnostic and Therapeutic Considerations. The Journal of Thoracic and Cardiovascular Surgery, Vol 99, 597-602.
8. Marshall Z. Schwartz and Priya Ramachandran. Congenital Malformations of the Lung and Mediastinum- A Quarter Century of Experience From a Single Institution- Journal of Pediatric Surgery, Vol 32, No 1, 1997: pp 44-47.
9. Elisabeth Horak, Johannes Bedner, Ingmar Gassner, Thomas Schmid. Congenital Cystic Lung Disease: Diagnostic and Therapeutic Considerations. Clinical Pediatrics Apr 2003 Vol. 42, Iss. 3; pg.251,11 pgs.
10. Evrard V, Ceulemans J, Coosemans W, De Baere T, De Leyn P, Deneffe G. Devlieger H, De Boeck C, Van Raemdonck D, Lerut T. Congenital Parenchymatous Malformations of the Lung. World J Surg. 1999 Nov;23 (11): 1123-32.
11. Ugur Ozcelik, M.D., Ayhan Gocmen, M.D., Nural Kiper, M.D., Deniz Dogru, M.D., Embiya Dilber, M.D. and Gunes Yalcin, M.D. Congenital Lobar Emphysema: Evaluation and Long-Term Follow-Up of Thirty cases at a Single Center
12. Robert A. Gustafson, M.D., Gordon F. Murray, M.D., Herbert E. Warden, M.D., Ronald C. Hill, M.D. and G. Edward Rosar, M.D. Intralobar Sequestration. A Missed Diagnosis
13. Shin-ichi Takeda, Shinichiro Miyoshi, Masayoshi Inoue, Kenichi Omori, Meinoshin Okumura, Hyung-Eun Yoon, Masato Minami, Hikaru Matsuda. Clinical Spectrum of Congenital Cystic Disease of the Lung in Children