CONGENITAL CYSTIC DISEASES OF THE LUNG IN INFANTS AND CHILDREN: OUR EXPERIENCE WITH 64 CASES

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Abstract

Background
Congenital cystic diseases of the lung comprise a group of rare but closely related conditions with variable clinical features. This is a review of our experience with 64 cases outlining aspects of clinical features, diagnosis and management.

Patients and methods
The medical records of all infants and children with the diagnosis of congenital cystic diseases of the lung were retrospectively reviewed for age at diagnosis, sex, clinical features, diagnosis, treatment and outcome. The histology was obtained from the histopathology report.

Results
A total of 64 (39 males and 25 females) infants and children with congenital cystic diseases of the lung were treated. Their age at presentation ranged from 1 day to 15 years (mean 2.1 years). There were 23 cases of congenital lobar emphysema, 3 cases of pulmonary sequestration, 20 bronchogenic cysts and 18 cases of congenital cystic adenomatoid malformation. Twenty three (14 males and 9 females) patients had congenital lobar emphysema. Their age at presentation ranged from 1 day to 8 months (mean 3.1 months). The majority presented with variable degrees of respiratory distress symptoms and some of them were diagnosed because of repeated attacks of chest infection. Nine presented immediately after birth with respiratory distress symptoms, two of them had severe symptoms necessitating surgery within the first week after their delivery. In 19 patients the left upper lobe was affected and in the remaining 4, the right upper lobe was affected. Three patients (2 males: 1 female) had pulmonary sequestration. Two had extralobar pulmonary sequestration and the third had intralobar pulmonary sequestration. Twenty patients had bronchogenic cysts. There were 12 males and 8 females. Their age at diagnosis ranged from 2 months to 15 years (mean 4.2 years). Their clinical presentation was variable ranging from mild respiratory symptoms (2 patients), recurrent chest infection (11 patients) and respiratory distress (2 patients). In 5 patients, the cysts were discovered incidentally on routine chest x-ray. Two patients were born with large bronchogenic cysts and initially had mild respiratory distress but within two months, their symptoms increased necessitating thoracotomy and lobectomy. In 12 patients, the bronchogenic cysts were intra-lobar (right upper lobe 3, right lower lobe 4, right middle lobe 2, and left upper lobe 3). In 8, bronchogenic cysts were extra-lobar (right posterior mediastinum 4 and para-tracheal in 4). Eighteen patients had congenital cystic adenomatoid malformation. There were 11 males and 7 females. Their age at diagnosis ranged from 1 week to 12 years (mean 3.2 years). The presentation of these patients was also variable. The majority (14 patients) presented with repeated attacks of chest infection. In two patients, the diagnosis was confused with left congenital diaphragmatic hernia.

Conclusions
Congenital cystic diseases of the lung comprise a unique group of malformations with variable clinical presentation ranging from asymptomatic to those who present early with respiratory distress. Their common presentation is repeated chest infections. Awareness of this is important to obviate associated morbidity and mortality. Asymptomatic or mildly symptomatic congenital lobar emphysema can be treated conservatively, but the majority of patients with congenital cystic diseases of the lung require surgical excision.

Keywords: congenital cystic diseases of the lung, congenital cystic adenomatoid malformation, bronchogenic cyst, broncho-pulmonary sequestration, congenital lobar emphysema

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Introduction
Congenital cystic diseases of the lung compromise a group of several closely related, and rare conditions that share common clinical and embryological features but differ histologically [1]. Congenital lung malformations are relatively rare but potentially life threatening anomalies. These include congenital cystic adenomatoid malformation, pulmonary sequestration, bronchogenic cyst and congenital lobar emphysema [1,2]. Their clinical presentation is variable ranging from life threatening respiratory distress in the neonatal period to repeated chest infections while others may be asymptomatic discovered as incidental findings on chest X-ray [1-3]. This study is an analysis of our experience with 64 infants and children with congenital cystic diseases of the lung, outlining aspects of presentation, diagnosis and management.

Patients and methods
From January 1992 to December 2012, a total of 64 infants and children with congenital cystic diseases of the lung were treated. Their medical charts were retrospectively reviewed for age at presentation, sex, clinical features, radiological investigations, management, histological features and outcome. Although, the diagnosis was based on the clinical, radiological and operative findings, the final diagnosis was based on histological features.

Results
A total of 64 infants and children with congenital cystic diseases of the lung were treated. There were 39 males and 25 females. Their age at presentation ranged from 1 day to 15 years (mean 2.1 years). There were 23 cases of congenital lobar emphysema, 3 cases of pulmonary sequestration, 20 bronchogenic cysts and 18 cases of congenital cystic adenomatoid malformation.

Congenital lobar emphysema (CLE)
Twenty three patients had congenital lobar emphysema. There were 14 males and 9 females. Their age at presentation ranged from 1 day to 8 months (mean 3.1 months). The majority presented with variable degrees of respiratory distress symptoms and some of them were diagnosed because of repeated attacks of chest infection. Nine of them presented immediately after birth with respiratory distress symptoms, two of them had severe symptoms necessitating surgery within the first week after their delivery. The symptoms of the remaining seven improved and were discharged home to be readmitted subsequently at the age of 2 months, 2 ½ months, 3 months, 4 months, 4 months, 4 ½ months and 5 months respectively with severe respiratory distress necessitating surgery. One patient presented at the age of 3 months with pneumonia and mild respiratory distress and found to have congenital lobar emphysema. She was treated conservatively and improved significantly. On follow up, she remained asymptomatic and the affected lobe decreased markedly in size. The remaining 13 patients presented with repeated attacks of chest infection and were diagnosed to have congenital lobar emphysema. Some of them had more than one attack of pneumonia prior to diagnosis. One patient presented at the age of 1 month with chest infection and was diagnosed to have congenital lobar emphysema, but the parents refused surgery. This patient suffered recurrent attacks of chest infection and finally had surgery at the age of 6 months. The oldest patients was 8 months old who had three attacks of chest infection prior to diagnosis. In 19 patients the left upper lobe was affected and in the remaining 4, the right upper lobe was affected. The diagnosis in all of them was made by chest radiograph (Fig. 1) which showed distension and dilatation of the affected lobe as well as shift of the mediastinum and herniation of the emphysematous lobe to the opposite side. Fifteen of our patients had CT-scan of the chest which showed hyperinflation of the left upper lobe of the lung with right mediastinal shift and herniation of the emphysematous lobe to the opposite side behind the sternum pushing the trachea to the other side (Fig. 2). None of our patients had associated anomalies. All our patients were operated on except one who improved conservatively. They underwent left thoracotomy and left upper lobectomy in 18 and right thoracotomy and right upper lobectomy in 4. Classically, there is protrusion of the distended lobe outside the thoracic cavity once the chest is opened (Fig. 3). Histological examination showed large, markedly over distended alveolar spaces without tissue distraction consistent with CLE. One patient had in addition interstitial alveolar lymphocytic infiltrate, alveolar edema, congestion, focal increase in interstitial fibrous tissue and a striking number of desquamative mononuclear cells with prominent cytomegalovirus inclusions. Post-operatively all the patients did well except one who developed a broncho-pleural fistula. This was treated conservatively but did not close and required operative closure. In spite of this the air leak persisted postoperatively for about 10 days before it finally stopped spontaneously. There was no mortality and on follow-up ranging from 18 months to 9 years all patients are asymptomatic and well.

Pulmonary sequestration
Three patients (2 males: 1 female) had pulmonary sequestration. Two had extralobar pulmonary sequestration and the third had intralobar pulmonary sequestration. One of
them was a newborn with left congenital diaphragmatic hernia who was found to have extralobar pulmonary sequestration discovered intra-operatively. This was excised at the time of hernia repair but the patient died on the 5th postoperative day because of hypoxemia secondary to pulmonary hypoplasia. The second patient presented at the age of 4 years with a large paraesophageal hernia. He had CT-scan preoperatively which showed an associated pulmonary sequestration with a separate feeding vessel from the abdominal aorta (Fig. 4). He was operated on trans-abdominally and found to have a large paraesophageal hernia containing stomach and intestines and an associated extralobar pulmonary sequestration with a separate feeding vessel from the abdominal aorta (Fig. 5). The pulmonary sequestration was excised and the paraesophageal hernia was repaired. Postoperatively, he did well and was discharged home in a good general condition. The third patient presented at the age of 3 years with recurrent attacks of chest infection. She had a CT-scan which showed an intra-lobar pulmonary sequestration involving the left lower lobe with a separate feeding vessel from the abdominal aorta. She underwent left lower lobectomy and post-operatively she did well and was discharged in a good general condition.

**Bronchogenic cysts**

Twenty patients had bronchogenic cysts. There were 12 males and 8 females. Their age at diagnosis ranged from 2 months to 15 years (mean 4.2 years). The clinical presentation was variable ranging from mild respiratory symptoms (2 patients), recurrent chest infection (11 patients) and respiratory distress (2 patients). In 5 patients, the cysts was discovered incidentally on routine chest X-ray. Two patients were born with large bronchogenic cysts and initially had mild respiratory distress but within two months, their symptoms increased necessitating thoracotomy and lobectomy (Fig. 6). In 12 patients, the bronchogenic cysts were intra-lobar (right upper lobe 3, right lower lobe 4, right middle lobe 2, and left upper lobe 3). In 8, bronchogenic cysts were extra-lobar (right posterior mediastinum 4 and para-tracheal 4). In all, the diagnosis was made by chest x-ray and thoracic CT-scan (Fig. 7). All were operated on via either a right or left thoracotomy depending on the site of the cyst and all those with intra-lobar bronchogenic cysts had lobectomy while those with extra-lobar bronchogenic cysts had excision of the cysts only. In all, the diagnosis was confirmed histologically. The size of the cysts was variable but all cysts were lined by respiratory columnar epithelium. The wall of the cysts were fibro muscular and contain islands of cartilage (Fig. 8). In the intra-lobar bronchogenic cysts, the surrounding lung tissue showed hemorrhage, congestion and compressed or dilated alveoli. Post-operatively, all did well and were discharged home in good general conditions.

**Congenital cystic adenomatoid malformation**

Eighteen patients had congenital cystic adenomatoid malformation. There were 11 males and 7 females. Their age at diagnosis ranged from 1 week to 12 years (mean 3.2 years). The presentation of these patients was variable. The majority (14 patients) presented with repeated attacks of chest infections. In two patients, the diagnosis was confused with left congenital diaphragmatic hernia. One of them was a newborn who was diagnosed and operated on as a case of congenital diaphragmatic hernia but
intra-operatively, there was no evidence of a diaphragmatic hernia. He was then referred to our hospital. The second patient was a 2.5 years old girl was being investigated for left congenital diaphragmatic hernia including CT-scan and contrast study. She was found to have congenital cystic adenomatoid malformation involving the left lower lobe. In the remaining two patients, congenital cystic adenomatoid malformation was asymptomatic and found on routine chest x-ray. In all the diagnosis was made by chest-ray and CT-scan (Fig. 9 and 10). All our patients had type I congenital cystic adenomatoid malformation except one who had type III. All our patients were operated on and underwent lobectomy of the affected lobe. One of patients who was operated on in another hospital as congenital diaphragmatic hernia died prior to excision of congenital cystic adenomatoid malformation. In the majority of our patients (12 patients), congenital cystic adenomatoid malformation affected the left lower lobe, and in 3 the right upper lobe was involved. In the remaining 3, the right lower lobe, the left upper lobe and right upper and middle lobes were affected respectively. Histopathology of the resected lobe showed large areas of fibrosis with cystic formations of varying sizes filled with mucus and macrophages, lined by cuboidal or columnar epithelium and rarely metaplastic squamous epithelium. There was chronic inflammatory cell infiltrate in some areas with formation of lymphoid follicles, but no epitheliod or giant cell granulomas.

Discussion

Congenital cystic diseases of the lung comprises a spectrum of developmental abnormalities. These are however rare but clinically significant abnormalities and physicians caring for these patients should be aware of this as early diagnosis is important to avoid morbidity and mortality. These abnormalities include congenital lobar emphysema, congenital pulmonary cystic adenomatoid malformations, bronchopulmonary sequestrations, and bronchogenic cysts [1-4]. These cysts can present early and acutely with respiratory distress but more commonly, they are prone to long-term complications namely recurrent pulmonary infection and rarely malignant transformation [5-7]. This calls for early diagnosis and elective resection even in those with asymptomatic, incidentally discovered lesions. The only exception is those with congenital lobar emphysema who can be managed conservatively if the patients are stable, asymptomatic and can be followed-up closely [8-11]. Congenital lobar emphysema (CLE) is characterized by massive distension of the affected lobe of the lung, usually the left upper lobe or the right middle lobe. Involvement of the lower lobes is rare, occurring in less than 5% of patients. In 19 (82.6%) of our patients, the left upper lobe was affected and in the remaining 4, it was the right upper lobe. Over distension and expansion of the affected lobe as a result of air trapping leads to compression of the surrounding lung tissue as well as the contralateral lung. This may cause life-threatening respiratory distress, which if not recognized and treated, may be fatal. It is also important to evaluate these patients cardiologically including an echocardiogram as congenital cardiac anomalies may be present in as many as 10% of these patients [12, 13].

CLE is a comparatively rare condition. Nuchtern and Harberg [14] during a 10 year period treated only 6 (0.6%) patients with CLE out of 1051 thoracic surgical operations performed during the same period. Wesley et al. [15] over a 10 year period reviewed 22 patients with congenital lung cysts, 3 of them were CLE. In a collective series of 57 cases of congenital

![Figure 3: A clinical photograph showing herniation of the distended lobe outside the chest in a patient with congenital lobar emphysema.](image1)

![Figure 4: CT-scan showing a large paraeosophageal hernia with associated pulmonary sequestration.](image2)
lungs reported from Riyadh, Saudi Arabia, there were 37 cases of CLE [16]. Over a 21 year period, we treated 23 children with CLE.

The exact etiology of CLE is not known. Several factors have been proposed, but congenital deficient cartilaginous support (bronchomalacia) of the involved bronchus is present in 50% to 60% of the cases. Hislop and Reid described the findings of a polyalveolar lobe in some of these patients where there is a three to five fold increase in the number of alveoli [17]. Other rare causes include extraluminal obstruction and compression of the affected bronchus by abnormal blood vessel or congenital lung cyst, congenital bronchial stenosis and redundant bronchial mucosal flaps. All of these factors lead to a ball-valve effect that permit inflation of the affected lobe during periods of negative intra-thoracic pressure, but collapses and obstruct the affected bronchus during expiration. This leads to air trapping and over expansion of the affected lobe of the lung. In all our patients there was no identifiable extrinsic cause for CLE but one of our patients was found on pathological examination to have an associated cytomegalovirus interstitial pneumonia. The significance of this from an etiological point of view is not exactly known but interestingly, only this patient developed persistent post-operative air leak.

Congenital lobar emphysema typically affects young infants less than 6 months of age and it is more common in males than females. All our patients presented before 6 months of age except one who presented at the age of 8 months and there were 14 males and 9 females. Although the majority of patients with congenital lobar emphysema present early as an acute neonatal respiratory distress, a small group of them may be asymptomatic or present at a later age with recurrent chest infection. We found chest radiograph to be diagnostic of CLE, but sometimes if the affected lobe is grossly distended it is not uncommon for this to be confused with tension pneumothorax. This is specially so in an infant with acute respiratory distress. A chest tube drainage should be avoided in these patients and close and careful inspection of the chest radiograph can differentiate between the two by the presence of lung markings in CLE. CT-scan of the chest may be valuable in identifying and locating extrinsic etiological factors such as bronchogenic cyst, which must be considered whenever CLE is diagnosed. The early age onset of congenital lobar emphysema preclude the possibility of aspiration a foreign body as an etiological factor. In addition, aspiration usually affects the lower lobe and if bronchoscopy is considered necessary, it should be performed in the operating room as there is a possibility of air trapping and progressive respiratory distress which may lead to cardiorespiratory arrest and preparations should be made for emergency thoracotomy if necessary. The treatment of CLE is total lobectomy which must be performed early to overcome the potentially life threatening acute respiratory distress and reduce the possibility of subsequent infection. A conservative management of CLE can be adopted for patients who are stable, asymptomatic and can be followed-up closely [16, 18]. Some of these patients will improve with time and undergo spontaneous resolution most likely as a result of maturation of the cartilaginous bronchial rings. Only one of our patients was treated conservatively with subsequent resolution of CLE. The importance of careful anesthetic induction cannot be over

![Figure 5: Intraoperative photographs showing extralobar pulmonary sequestration with a large blood supply coming from the abdominal aorta in a patient with large paraesophageal hernia.](image1)

![Figure 6: Intraoperative photograph showing a large bronchogenic cyst causing respiratory distress in an infant.](image2)
emphasized as these patients may not tolerate positive pressure ventilation which can lead to air trapping with rapid and massive enlargement of the affected lobe, mediastinal shift and cardiac arrest [19]. With improved safety of pediatric anesthesia, we found surgical resection to be both safe and effective in the management of CLE [19]. Total lobectomy is tolerated well in infants and children as growth and expansion of the remaining lung tissue is known to occur in children up to the age of 5 years with subsequent total lung volume and function ultimately returning to normal. Bronchogenic cysts arise from an abnormal budding of the ventral foregut. They are relatively rare but considered the most common cystic lesion of the mediastinum. In 2008, Shanti and Klein reported a series of 236 patients who had pulmonary resection for cystic lung lesions, 47 (20%) of them had bronchogenic cysts [20]. We treated 20 infants and children with bronchogenic cysts over a period of 21 years. Approximately 85% of bronchogenic cysts are mediastinal, and 15% are intrapulmonary but in our series 12 (60%) were intra-lobar and 8 (40%) were extra-pulmonary. Bronchogenic cysts have also been described in more remote locations, including the interatrial septum, neck, abdomen, and retroperitoneal space. Bronchogenic cysts do not usually communicate with the bronchial tree, and are therefore typically filled with secretions and not air filled. The presentation of bronchogenic cysts are also variable and mainly depend on the location of the cyst rather than the size of the cyst. Limaiem et al. [21] reported 33 cases of bronchogenic cysts and identified 4 categories of presentation: asymptomatic (6%); general symptoms including anorexia, weight loss, and fever; respiratory symptoms including chest pain, hemoptysis, cough, and dyspnea; and other symptoms including dysphagia and back pain. The main presentation of our patients was recurrent chest infection but two of our patients presented early with respiratory distress because of the large size of the cysts. In 5 of our patients, the cysts were asymptomatic, discovered incidentally. We found CT-scan valuable in defining the exact site and size of the cyst and should form part of the evaluation of these patients. We like others advocate surgical resection of all bronchogenic cysts even if asymptomatic. This is to avoid the known associated morbidity and although rare but also the potential malignant transformation. The recent advances in minimal invasive surgery made thoracoscopic resection of bronchogenic cysts more advantageous than the open technique [22]. Histologically, bronchogenic cysts are lined by ciliated cuboidal or columnar epithelial and occasionally, the cysts may contain gastric mucosa or bronchial cartilage. The wall is made up of tissues similar to that of the normal bronchial tree, including cartilage, elastic tissues, mucus glands and smooth muscle. Congenital cystic adenomatoid malformation (CCAM) results from an abnormal development of the terminal bronchioles. They account for about 25% of all congenital lung malformations. Three clinical and histologic categories of cystic adenomatoid malformation are described: (1) macrocystic (13%), which has the best prognosis and in which one or more large (>5 mm on prenatal ultrasound) cysts are lined with normal pseudostratified ciliated epithelium; (2) microcystic (73%), which has small cysts lined with ciliated columnar or cuboidal epithelium; and (3) solid cystic adenomatoid malformation (13%), which has the worst prognosis and is an airless tissue mass composed of cuboidal epithelium-lined bronchioles [23-26]. The difference in prognosis may be because the solid and microcystic lesions involve a relatively large amount of lung tissue. Macrocytic
lesions are comprised of large, air filled, non-functioning spaces involving smaller areas of the lungs. Polyhydramnios may be present if the cystic adenomatoid malformation presses on the esophagus [27-33]. Pressure on the heart and large vessels may lead to hydrops fetalis. This is seen more in type 3. All our patients had type 1 CCAM except one. The reason for this not known. In approximately 60% of patients, cystic adenomatoid malformation manifests soon in the neonatal period because of respiratory distress. It also results in recurrent chest infections because the mucociliary clearance is poor in these patients. It is not uncommon for these patients to be confused with congenital diaphragmatic hernia specially those involving the lower lobes. This was the case in two of our patients, one was operated in another hospital as congenital diaphragmatic hernia but intraoperatively, there was no evidence of congenital diaphragmatic hernia. The other patient was being investigated for congenital diaphragmatic hernia including CT-scan and contrast studies. Malignant transformation although rare but it has been reported in those with cystic adenomatoid malformation (pulmonary blastoma, rhabdomyosarcoma and bronchoalveolar carcinoma) [5-7]. This as well as the potential risk of recurrent chest infection calls for early diagnosis and surgical excision. Pulmonary sequestration accounts for 6% of all congenital lung malformations and mostly occurs in the lower lobes. A sequestration is a bronchopulmonary mass without a normal bronchial communication and with normal or more commonly an anomalous vascular supply [34]. The involved lung segments can be classified on the basis of their pleural coverage into intrapulmonary (intralobar) or extrapulmonary (extralobar) types. Extralobar sequestrations can also be seen intraabdominally. Variants of pulmonary sequestration are described as disconnected or abnormally communicative bronchopulmonary masses with normal or anomalous vascular supply [35, 36]. These lesions may have some sort of communication with the gut. Children with bronchopulmonary sequestration commonly present with recurrent respiratory infections in the same anatomic location and physicians caring for these patients should be aware of this. Associated anomalies include diaphragmatic hernia and eventration. The extrathoracic variety can be associated with hydrops fetalis or increased lymphatic transudate in the thorax. About 50% of pulmonary sequestration cases are intrapulmonic, and 60% of intrapulmonic cases occur in the left lower lobe with equal sex distributions. Patients with intrapulmonary sequestration usually present late. They may present with chronic cough, recurrent pneumonias, or poor exercise performance. Systemic arterial flow may produce a murmur, and shunts may lead to congestive cardiac failure. Squamous cell carcinoma, adenocarcinoma, and rhabdomyosarcoma may arise in the sequestration. Approximately 95% of extrapulmonary cases are left sided. Most extrapulmonary cases are detected in infancy, with boys affected 4 times more than girls. Infants usually present with a chronic cough and recurrent chest infections. In one of our patients, the sequestration was discovered at the time of congenital diaphragmatic hernia repair. This was an extrapulmonary sequestration that was excised at the same time. The other patient was found to have extrapulmonary sequestration at the time of investigation for a large paraesophageal hernia. Radiographs may reveal signs of consolidation and pneumonia. If communication with the gut is present, children may present with vomiting, failure to thrive due to poor oral intake, and abdominal

Figure 9: CT-scan showing congenital cystic adenomatoid malformation. Note the different sizes of the cysts.

Figure 10: CT-scan showing multiple cysts in a patient with congenital cystic adenomatoid malformation.
pain. CT-angiography or Magnetic Resonance Angiography is the best investigation not only to diagnose sequestration but also to demonstrate the vascular supply [36, 37]. This is of great importance at the time of surgical excision. Failure to recognize an anomalous blood supply and its ligation prior to excision may lead to catastrophic hemorrhage. To obviate this, it is important to refer these patients to a specialized center with experienced pediatric surgeons who can investigate them further and manage them accordingly.

This is specially so in the era of minimal invasive surgery where sequestrations can be resected thoracoscopically [38].

**Conclusions**

Congenital cystic diseases of the lung comprise a unique group of malformations with variable clinical presentation ranging from asymptomatic to those who present early with respiratory distress. Their common presentation is repeated chest infections. Awareness of this is important to obviate associated morbidity and mortality. Asymptomatic or mildly symptomatic congenital lobar emphysema can be treated conservatively, but the majority of patients with congenital cystic diseases of the lung require surgical excision.

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