Asymptomatic congenital lung malformations

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Congenital cystic adenomatoid malformation; Pulmonary sequestration; Bronchogenic cyst; Congenital lobar emphysema; Primary pulmonary neoplasm

Congenital lung malformations are often discovered incidentally on routine prenatal sonography or postnatal imaging. Lesions such as congenital cystic adenomatoid malformations (CCAM), sequestrations, bronchogenic cysts and congenital lobar emphysema may be asymptomatic at birth or at the time of discovery later in life. Some authors advocate simple observation because of the lack of data on the incidence of long-term complications. However, there are very few described cases where CCAM and intralobar sequestration have remained asymptomatic throughout life; complications eventually develop in virtually all patients. The most common complication is pneumonia, which may respond poorly to medical treatment. Other complications include the development of malignancies (carcinomas and pleuropulmonary blastomas), pneumothorax and hemoptysis or hemothorax. Since lung resection will be required sooner or later for CCAM, intralobal sequestration and intrapulmonary bronchogenic cysts it is best not to wait for complications to occur. For patients diagnosed prenatally, we recommend surgery at 3 to 6 months of life at the latest, so that compensatory lung growth can occur. At this age the postoperative course is usually smooth and long-term follow-up has shown normal respiratory function. Mediastinal bronchogenic cysts also tend to become symptomatic and elective resection is recommended. On the other hand, asymptomatic congenital lobar emphysema may regress spontaneously and observation is warranted. The management of small noncommunicating extralobar sequestrations is more controversial; it is known that these lesions can remain asymptomatic throughout life but complications may develop and they are sometimes difficult to differentiate from neuroblastoma.

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Congenital lung malformations include a wide spectrum of developmental abnormalities, some of which are incompatible with life or cause severe symptoms in the prenatal or neonatal period. This review focuses on malformations that may be discovered incidentally on routine prenatal sonograms or postnatal imaging. These include congenital cystic adenomatoid malformations, pulmonary sequestrations, bronchogenic cysts and congenital lobar emphysema (polyalveolar lobe and lobar overinflation).1-4

Congenital cystic adenomatoid malformation (CCAM) is considered a hamartomatous lesion of the bronchial tree by some, while others favor a localized arrest in the development of the fetal bronchial tree as the etiology.1-5 Because some types are not cystic and only one type has the adenomatoid appearance, the term “congenital pulmonary airway malformation” (CPAM) has recently been proposed.6 These lesions were initially classified into three types by Stocker,6 who more recently added two more variants (types 0 and 4).7 The pathogenesis of CCAM has been the subject of controversy.5,8-10 Langston believes that the five types may represent different malformations with varying etiologies.11

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other studies support the notion that dysregulation in the branching morphogenesis of the lung is associated with the development of abnormal lung tissue, both in CCAM and sequestration. A dysregulation of lung maturation is also suggested by the increased cell proliferation seen in CCAM. The incidence of CCAM has been estimated at 1:25,000 to 1:35,000 pregnancies in one study, while another reports a population prevalence of 9 per 100,000 total births.

**Pulmonary sequestration** is generally thought to result from an abnormal accessory tracheobronchial bud arising from the foregut. Intralobar (ILS) and extralobar (ELS) types are recognized, based on whether the visceral pleura is shared with the adjacent normal lobe or not. Typically, the lung tissue in sequestrations does not have a connection to the normal tracheobronchial tree and is supplied by an anomalous systemic artery, but many variants exist.

Most ILS are located in the lower lobes; most ELS are found postero-medially in the left lower chest but can occur within the diaphragm, below it or rarely in other locations.

**Bronchogenic cysts** result from abnormal budding of the foregut. As foregut duplication cysts, they share common features with esophageal duplication cysts but are characterized by the presence of cartilage, smooth muscle and glands in their wall. The majority are located in the mediastinum, usually adjacent to the distal trachea or proximal mainstem bronchi, but they can also be found within the parenchyma of the lung. They are usually unicocular, filled with fluid or mucus and generally do not communicate with the airway.

**Congenital lobar emphysema (CLE)** is a term used to describe a distended, hyperlucent lobe on plain radiographs, usually the left upper or the right middle lobe. Pathologically, a distinction is made between a polyalveolar lobe, in which the number of alveoli is greatly increased, and congenital lobar overinflation (CLO), in which the alveoli are markedly distended. CLO is thought to be caused by a partial bronchial obstruction creating a ball-valve effect. This obstruction may be intrinsic (bronchomalacia) or less commonly extrinsic (vascular, bronchogenic cyst), but in many instances an exact cause cannot be determined.

The pathogenesis of polyalveolar lobe remains uncertain but transient bronchial obstruction in utero has been suggested.

Although the terms CCAM, sequestration, bronchogenic cyst and CLE are entrenched in clinical usage and comfortably correspond to rigid pathological definitions, there is a considerable overlap in the findings. Numerous reports describe single lesions fulfilling the criteria for CCAM and ILS or ELS, coexisting lesions in different lobes, and lesions typical of one entity on imaging but corresponding to another entity pathologically (Figures 1 and 2). Furthermore, the nomenclature and definitions have changed over time, and prominent pathologists disagree. For example, Stocker believes that intrapulmonary bronchogenic cysts and other congenital unilocular lung cysts are type 1 CCAM while others disagree. There have been attempts at revising the classification and pathogenesis of congenital lung malformations, but the new nomenclatures proposed have either led to oversimplification or have not gained wide acceptance. The emerging consensus is that imaging findings should simply be described, without attempting to make a pathological diagnosis. Adzick in 1985 first made the distinction between macrocystic and microcystic (hyperpneicchoic) lung lesions on prenatal sonograms. This is frequently interpreted as CCAM, but can be found in sequestration and other lung malformations or may represent a transient finding in normal babies.

With the increasing number of obstetrical ultrasounds performed and the improving quality of these examinations, congenital lung malformations are diagnosed more frequently before birth. These appear as hyperpneicchoic or cystic or mixed lesions within the chest (or abdomen for some sequestrations) that may displace the heart and mediastinum and occupy most of the thoracic cavity. Doppler interrogation may reveal a systemic arterial supply from the thoracic or abdominal aorta. This generally confirms a diagnosis of sequestration, although mixed lesions occur, as discussed earlier. While some congenital lung malformations may give rise to serious complications in utero, such as polyhydramnios with premature labor or hydrops with fetal demise, the majority remain stable or show evidence of regression. Some newborns will develop symptoms related to pulmonary hypoplasia, left to right shunting (in a sequestration), overinflation (within a CCAM or a CLE) or pneumothorax. However, most remain asymptomatic after birth and in many cases the chest radiograph (CXR) appears completely normal. Controversy exists as to the management of these newborns with asymptomatic congenital lung lesions discovered during routine obstetrical ultrasound examinations. The same is true for malformations discovered incidentally in infants or children, either by plain radiograph done for minor cold symptoms or by sonography, computed tomography (CT) or magnetic resonance imaging (MRI) done for unrelated reasons (Figures 3 and 4).

Based on our own experience and an extensive review of the literature, we believe that elective resection is indicated for most congenital lung malformations. We will discuss the evidence on which this recommendation is based and explain which lesions may not require intervention.

**The arguments**

Some authors recommend simple observation of patients with asymptomatic CCAM, sequestration or prenatally diagnosed “lung masses.” However, most authors favor surgical resection, at least for CCAM, intralobar sequestration and bronchogenic cysts. Finally, others recommend surgery for “significant” lesions.
but may observe smaller ones.\textsuperscript{26,38} The arguments for and against simple observation are listed in Table 1. The following paragraphs will review the evidence on which these arguments are based.

**Bronchogenic cysts and congenital lobar emphysema**

Much less controversy exists about the management of these two entities which will be briefly discussed. Bronchogenic cysts may be recognized prenatally by their unilocular nature, but many are found incidentally on postnatal CXR. The diagnosis is easily confirmed postnatally by CT scan or MRI (Figures 2 and 3). A unilocular type 1 CCAM could be confused with an intrapulmonary bronchogenic cyst. Classically, the former should be air-filled while the latter is fluid or mucus-filled. However, air in a bronchogenic cyst could be seen secondary to infection with erosion into a bronchus and conversely, an infected CCAM is often fluid-filled. The differentiation on imaging is not crucial since resection is indicated for both, as we will see below.

**Bronchogenic cysts** and other foregut duplications are not known to spontaneously disappear. They may become symptomatic by a mass effect on the trachea or bronchus and are one of the causes of CLO. They can also cause dysphagia, become infected or bleed, leading to hemoptysis or hemothorax.\textsuperscript{21,22,61,70-72} Up to one third of foregut duplications contain gastric mucosa.\textsuperscript{61} Rare cases of malignancy have also been described, although in some reports the differentiation between intrapulmonary bronchogenic cyst and type 1 CCAM could be questioned.\textsuperscript{66,71} The general consensus is that bronchogenic cysts should be resected even if asymptomatic.\textsuperscript{73} This can safely be performed by thoracoscopy for isolated mediastinal cysts.\textsuperscript{61,74,75}

**Congenital lobar emphysema** is rarely detected prenatally.\textsuperscript{23} It appears as an echogenic homogenous lung mass which may regress before birth.\textsuperscript{23} The typical postnatal imaging is well known, although some overlap exists as we have seen (Figure 1). When CLE is discovered in an asymptomatic patient, treatment is usually conservative because the lesion may regress. When the emphysematous lobe causes mediastinal shift and progressively increasing symp-
toms, then lobectomy is indicated. This usually requires a thoracotomy because the involved lobe does not collapse, making a thoracoscopic approach difficult and even dangerous. Most cases of lobar emphysema discovered beyond the neonatal period are acquired, often after bronchiolitis, and tend to resolve spontaneously.76

Disappearing fetal lung lesion versus regression of a congenital lung malformation confirmed postnata l

Several authors have observed a complete regression of echogenic lung lesions by fetal ultrasound.15,16,20,26,29,31,35,36,42-44,55,77-80 Too often, authors conclude that a CCAM has vanished.38 One should abstain from making a histological diagnosis based on prenatal imaging, let alone try to classify the presumed CCAM according to Stocker's types and establish prognosis based on this!15 The differential diagnosis of such lesions includes CCAM, sequestration, diaphragmatic hernia, tracheal or bronchial atresia, neuroblastoma and transient bronchial plugging.15,35,36,42 While the sonographic examination may become completely normal before birth, adequate postnatal imaging is required before the findings can be said to have disappeared. All large series have documented several patients in whom a lung lesion became undetectable by fetal ultrasound toward the end of gestation, who had a normal two-view CXR but a clearly visible lesion on CT scan.15,20,29,31,38,41,50,80,81 The proportion of such patients

Figure 2   This patient was diagnosed with a mixed cystic/echogenic lung lesion on prenatal U/S; this appeared to resolve before birth. (A) Postnatally she was asymptomatic but CXR showed opacification of the right upper chest. (B) The initial CT scan was most compatible with a fluid-filled lobar emphysema. On subsequent CXR the mass slowly decreased in size, remaining otherwise unchanged and appearing more like thymus. The radiological impression of thymus was reinforced by an U/S examination. (C, D) Finally, at 19 months of age the CT scan was repeated, revealing a prominent thymus, a subcarinal bronchogenic cyst (*) and areas of lucency in the right upper and middle lobes (arrows). Microscopic examination confirmed a bronchogenic cyst, which surprisingly communicated with the upper lobe bronchus, and CCAM type 2 in the right middle lobe. Both upper and middle lobes contained areas of atelectasis alternating with overinflated areas.
with a detectable malformation on CT scan varies from less than 50% to nearly 100%, depending on the series.26,31

In asymptomatic patients with a normal CXR, we usually perform the CT scan electively on an outpatient basis after a few weeks of age. Some do it in the first month31,37 while others wait until 6 weeks38 or even 6 months if the neonatal CXR is normal.82 If the scan is technically adequate and no lesion is visible, then we can comfortably observe the patient and recommend repeat studies only if symptoms develop. In such patients, the explanation for the prenatal images cannot be ascertained. Unfortunately, many authors consider this as a CCAM that has disappeared.38,82 In older patients CCAM can be confused with postpneumonia pneumatoceles (Figure 5).76 In the absence of a previous CXR, a follow-up period of weeks to months may be necessary; a lack of resolution or a suspicious appearance on CT scan are indications for resection. The types of CCAM associated with asymptomatic patients are most often types 1, 2 and 4. On CT scanning, these appear as cystic lesions of various sizes (types 1 and 4), as multiple smaller cysts of uniform size, or a hyperinflated area (type 2) (Figures 6 and 7). They may also appear as solid lesions, especially in the first few days of life because of fluid retention within the CCAM (Figures 1 and 2).3,4,20 Type 3 lesions usually present as solid masses and are rarely asymptomatic, while the rare type 0 lesions are uniformly fatal.

Sequestrations typically appear solid but may be cystic or aerated. In extralobar sequestrations (ELS) the presence of air usually signifies an esophageal connection, while intralobar sequestrations (ILS) can become aerated through the pores of Kohn or secondary to infection.2,3,56,80 The aberrant systemic artery or arteries may be demonstrated on the CT scan with I-V contrast infusion, by Doppler ultrasound or by magnetic resonance imaging (MRI),3,80 but they can also be missed.20

Until recently, there had never been documentation of a postnatal regression of a presumed CCAM proven by CT scan after birth.31,41 Most of the so-called complete regressions or disappearing lesions are based on prenatal ultrasound findings combined with postnatal clinical follow-up alone or with simple CXR.16,42,44,49,82,83 In some of the true, complete prenatal regressions the fetal images may have been secondary to transient bronchial plugging.15,36,42,78,82,84,85 Fetal neuroblastomas are also known
to involute spontaneously. In other patients, the lesion may still be present at birth but not detectable by physical examination or CXR. A large series from Toronto reported 35 infants with asymptomatic CCAM, 17 of whom had not undergone resection and had been observed between 5 months and 9 years (median 3 years). The authors did not report any postnatal disappearance of confirmed lesions. The only 2 cases of postnatal regression of presumed CCAM were recently reported from Paris. The abstract mentions 6 cases of vanished CCAM, but the CT scan after birth was normal in 4 of these. In the other 2 patients, the CCAM is said to have vanished “during the first months of life” in one and “during the first years of life” in the other. No images are provided and a precise description of the initial findings is lacking.

In contrast, sequestrations with a proven systemic arterial supply have been shown to completely and spontaneously involute both prenatally and postnatally in several publications. Another report documents the occlusion of the aberrant artery from spasm caused by the angiogram catheter (without embolization), followed by involution.

Table 1 Arguments for and against simple observation of patients with asymptomatic congenital lung malformations

<table>
<thead>
<tr>
<th>Arguments for observation:</th>
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<tr>
<td>- Asymptomatic patient, incidental finding</td>
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<tr>
<td>- Unknown natural history</td>
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<td>- Possible regression</td>
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<td>- Risks of thoracotomy and lung resection</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Arguments against prolonged observation:</th>
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<tbody>
<tr>
<td>- High risk of infection, which may render the subsequent surgery more difficult</td>
</tr>
<tr>
<td>- Reported cases of malignancy occurring in such lesions (or indistinguishable from them on imaging)</td>
</tr>
<tr>
<td>- Risk of pneumothorax or sudden cyst enlargement with respiratory compromise</td>
</tr>
<tr>
<td>- Not a “normal variant” and unlikely to remain asymptomatic</td>
</tr>
<tr>
<td>- Faster post-operative recovery in a young asymptomatic child</td>
</tr>
<tr>
<td>- Resection in infancy allows compensatory lung growth</td>
</tr>
</tbody>
</table>

Figure 4 A 3-year-old boy was diagnosed with pneumonia five months before referral. (A) A CXR done because of persistent cough showed a nonaerated mass at the left base and possibility of a localized eventration. An ultrasound examination was done, revealing an aberrant blood supply to the mass. (B) The aberrant venous drainage is easily appreciated on CT scan. (C) This reconstructed image from the CT scan allows an appreciation for the location and systemic arterial supply of this extralobar sequestration (arrows).
Several of these reports consist of subdiaphragmatic ELS, but others deal with intrathoracic ELS\textsuperscript{88} or ILS.\textsuperscript{89}

**Infection**

Most older reviews, textbook chapters and clinical series reveal that beyond the neonatal period, infection is undoubtedly the most common presenting symptom for both CCAM and ILS.\textsuperscript{1-4,6,7,45,54,56,59,69,93,94} This is also true in our experience.\textsuperscript{17,40} Patients may present with a history of cough, fever or recurrent pneumonia. In such patients the differential diagnosis includes pneumatocele complicating bacterial pneumonia. A previous CXR showing a lung anomaly or repeated CXR showing a lack of resolution of “pneumatoceles” confirm the congenital nature of the underlying lesion (Figure 5). In one series, one third of the infections disclosing the CCAM occurred in the first year of life.\textsuperscript{94} Older patients may present with bronchiectasis or hemoptysis.\textsuperscript{1-4,6,7,51,52,95} Air may be present in ILS despite the lack of connection with a normal bronchus.\textsuperscript{3,56,96} The communication with the contiguous normal lobe via the pores of Kohn probably explains the frequency of infection in ILS.\textsuperscript{17} Such is not the case with ELS, which is most often discovered incidentally on CXR or during investigation or treatment of an associated diaphragmatic malformation, namely eventration or congenital diaphragmatic hernia.\textsuperscript{3,52,97,98} One report cites a 91\% versus 14\% incidence of infection with ILS versus ELS in a review of 28 pediatric and adult patients.\textsuperscript{51} The only ELS patient (1/7 = 14\%) with infection had an esophageal bronchus. There are also numerous case reports of unusual infections in ILS, such as Aspergillus, Mycobacteria and Nocardia.\textsuperscript{99-102}

Other than the rare cases with communication to the esophagus or stomach, the risk of infection in ELS appears very low, although foci of chronic inflammatory cells were present in 35\% of cases in a recent review.\textsuperscript{98}

**Malignancy**

There are more than forty reported cases of malignancy associated with CCAM or “congenital lung cysts.” Most cases were reported in the last 15 years; these neoplasms consist mainly of pleuropulmonary blastomas (PPB) in infants and young children, and bronchioloalveolar carcinoma (BAC) in older children and adults (Tables 2 and 3).\textsuperscript{63,65,67,71,103-126}

The association between CCAM and malignancy is now more than anecdotal. A large review of childhood lung
neoplasms revealed that 8.6% of malignant tumors were associated with previously documented cystic malformations. There is a clear link between CCAM type 1 and BAC. First, mucinous cells present in type 1 CCAM were found to produce gastric mucins, similar to those found in bronchioloalveolar carcinoma. These authors point out that ectopic gastric mucosa or metaplasia is an important source of carcinogenesis in other organs such as the esophagus, pancreas and ovary. Another report compares the glandular component of CCAM to the mucous cells in hyperplastic polyps of the colon, supporting the potential for malignant transformation of CCAM and other congenital cystic changes of the lung. De Perrot demonstrated increased proliferative activity consistent with atypical adenomatous hyperplasia in some areas of a bronchogenic cyst (which could be considered as type 1 CCAM by some pathologists) that also contained an incidental BAC. Stacher and colleagues showed that some type 1 CCAM were associated with atypical goblet cell hyperplasia and chromosomal aberrations, supporting their preneoplastic status.

The link between PPB and CCAM is not as clear. PPB is a neoplasm that includes tumors previously reported as rhabdomyosarcomas or other sarcomas. It is subclassified into three types. Unlike BAC which is seen in older children and adults, PPB is a disease of young children, the average for type I being 10 months. Presentation in neonates and early infancy has been described. The etiology of these tumors is debated. Type 2 CCAM occasionally exhibits skeletal muscle differentiation, as can be found in

Figure 6  A fetus was diagnosed with a large mixed solid/cystic lung lesion filling 80% of the thoracic cavity at 19 weeks gestation. Despite severe mediastinal shift and inversion of the diaphragm, hydrops did not develop and the lesion gradually regressed after 24 weeks gestation. The baby was asymptomatic at birth. (A) Chest radiograph at birth showed multiple luencies in the right lung with mediastinal shift. (B) Six days later the image was much less impressive. (C) Given the initial size of the lesion, CT scan was performed earlier than usual, at 3 weeks of age. Multiple cysts are seen in the right lower lobe. (D) This reconstructed CT image demonstrates the cysts involving most of the lower lobe, reaching up to the apex of the thorax. Although the baby remained asymptomatic, the fear of sudden enlargement with respiratory distress led to an early elective lobectomy at 5 weeks of age. She was discharged 4 days after surgery. Microscopic examination revealed a type 2 CCAM.
PPB and rhabdomyosarcomas. However, type I or purely cystic PPB is usually associated with larger cysts, more typical of type 4 CCAM. Controversy exists as to whether the tumor develops within a CCAM or whether the cystic lesion represents PPB from the onset. In a report of 50 cases from the PPB registry, the authors propose that CCAM could be a precursor to PPB just as nephrogenic rests and nephroblastomatosis are to Wilms tumor. They also cite cases where CCAM occurred in a sibling of a PPB patient or where bilateral cystic lung changes were associated with unilateral PPB. Another report describes a child who developed PPB in the right mid-thorax after having undergone resection of a right apical pleural cyst and left upper lobe bronchogenic cyst in the neonatal period. There is strong circumstantial evidence that type I (purely cystic) PPB may evolve to type II (mixed) or type III (solid) PPB over time, with a much worsened prognosis. Therefore, even if some cases were cystic PPB rather than CCAM from the onset, the fact remains that these two entities cannot be differentiated on radiological grounds, hence the need for resection.

While the evidence linking CCAM with PPB and BAC is growing, we could only find a handful of reports linking sequestration with malignancy. A recent case report describes a lymphoepithelioma-like carcinoma within an ILS in an adult, and the authors could only find one previous case of squamous cell carcinoma (SCC) in an ILS, two cases of SCC in ELS and one mesothelioma in an ILS. The report from the PPB registry suggested that in four of their cases an exclusively extrapulmonary tumor may have arisen within an ELS or a bronchogenic cyst; the authors also refer to another report of PPB within an ELS. Our literature search did not yield any other report associating sequestration with malignancy since 1995, but there are reports of a carcinoid tumor arising in an ILS and a benign sclerosing hemangioma within an ILS. One adult patient with ILS presented with elevated tumor markers (both CA 125 and CA 19-9), which returned to normal after resection; the ciliated cylindrical epithelium within the sequestration stained positively for the tumor markers.

**Pneumothorax, sudden cyst enlargement and other complications**

We previously reported a 15-year-old boy who presented with recurrent pneumothorax and was found to have a small ELS in the major fissure and a CCAM of the lower lobe (Figure 8). Others have described pneumothorax from CCAM in patients ranging from the newborn period to adulthood. In a recent review, Lejeune and coworkers found six previous cases, two of these being in adults, with one death from bilateral spontaneous pneumothoraces. Another review of CCAM in adults quoted two more reports of spontaneous pneumothorax and one of dyspnea. Acute presentations with cyanosis, chest pain and shortness of breath in infants or older children have also been reported. More recent reports include pneumothorax from CCAM in a preterm infant, a pyopneumotho-
Table 2: Mesenchymal malignancy associated with cystic lung malformations

<table>
<thead>
<tr>
<th>First author (ref.)</th>
<th>Year of publication</th>
<th>Type of lung cyst</th>
<th>Type of malignancy</th>
<th>Age at Dx of malignancy (months)</th>
<th>Comments</th>
</tr>
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<tbody>
<tr>
<td>Stephanopoulos (167)</td>
<td>1963</td>
<td>“Cystic hamartoma”</td>
<td>Myxosarcoma</td>
<td>18</td>
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<td>Ueda (168)</td>
<td>1977</td>
<td>CCAM</td>
<td>RMS</td>
<td>18</td>
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<td>Martinez (124)</td>
<td>1978</td>
<td>“Polycystic disease”</td>
<td>Pulmonary blastoma</td>
<td>24</td>
<td></td>
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<td>Valderrama (169)</td>
<td>1978</td>
<td>Extrapulmonary sequestration</td>
<td>Pulmonary blastoma</td>
<td>48</td>
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<td>Sumner (170)</td>
<td>1980</td>
<td>Congenital lung cyst</td>
<td>Mixed Mesenchymal sarcoma</td>
<td>108</td>
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<td>Krous (171)</td>
<td>1981</td>
<td>Bronchogenic cyst (intrapulmonary)</td>
<td>Embryonal RMS</td>
<td>30</td>
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<td>Weinblatt (122)</td>
<td>1982</td>
<td>“Cystic lung disease”</td>
<td>Pulmonary blastoma</td>
<td>30</td>
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<td>Holland-Moritz (172)</td>
<td>1984</td>
<td>“Pneumatocele”</td>
<td>PPB</td>
<td>48</td>
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<td>Morales (173)</td>
<td>1986</td>
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<td>Pulmonary blastoma</td>
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<td>Williams (174)</td>
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<td>CCAM</td>
<td>Embryonal RMS</td>
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<td>Allan (175)</td>
<td>1987</td>
<td>“Congenital origin of cysts not confirmed”</td>
<td>RMS</td>
<td>21, 30</td>
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<td>Shariff (125)</td>
<td>1988</td>
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<td>RMS</td>
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<td>18, 22</td>
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<td>1991</td>
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<td>Calabria (114)</td>
<td>1993</td>
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<td>Paupe (113)</td>
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<td>Pulmonary blastoma</td>
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<td>Seballos (123)</td>
<td>1994</td>
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<td>Pulmonary blastoma</td>
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<td>Tagge (110)</td>
<td>1996</td>
<td>Bilateral pneumatoce</td>
<td>PPB</td>
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<td>Adirim (106)</td>
<td>1997</td>
<td>CCAM type 1</td>
<td>Pulmonary blastoma</td>
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<td>D’Agostino (108)</td>
<td>1997</td>
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<td>Embryonal RMS</td>
<td>22</td>
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<tr>
<td>Federici (63)</td>
<td>2001</td>
<td>CCAM type 1</td>
<td>PPB</td>
<td>36</td>
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<tr>
<td>Ozcan (103)</td>
<td>2001</td>
<td>CCAM type 4</td>
<td>Embryonal RMS</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Papagiannopoulos {134} (+ MacSweeney (121))</td>
<td>2001</td>
<td>CCAM</td>
<td>PPB grade 3</td>
<td>30</td>
<td></td>
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<tr>
<td>Stocker (181)</td>
<td>2002</td>
<td>CPAM type 4</td>
<td>PPB</td>
<td>48</td>
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</table>

BPD, bronchopulmonary dysplasia; CCAM, congenital cystic adenomatoid malformation; CPAM, congenital pulmonary airway malformation (synonym to CCAM); PPB, pleuropulmonary blastoma; RMS, rhabdomyosarcoma; RLL, right lower lobe; RUL, right upper lobe.
rax in an 18 year old, and other pneumothoraces and expanding cysts causing severe respiratory distress which are mentioned as the presenting sign in several series. Since they lack a normal communication with the airway, sequestrations rarely give rise to large cysts or to spontaneous pneumothorax but this can happen in ILS secondary to infection. Other complications such as hemothysis, hemothorax and infarction have been described. ELS can also undergo torsion.

Conclusion

Indications for surgery

Asymptomatic congenital lobar emphysema may resolve and should be observed once underlying lesions are excluded. Bronchogenic cysts require resection. For sequestrations, it is clear that ELS may remain asymptomatic throughout life and may be found because of associated anomalies. They may also regress spontaneously. The risk of malignancy appears low despite its frequent association with type 2 CCAM. The risk of infection is small in the absence of cysts or communication with the foregut and the risk of other complications is dependent on the presence of a systemic arterial supply. Some authors advocate resection in all cases, while others are willing to observe if the lesion is not visible on CXR, is small, or does not have a significant systemic arterial blood supply. A period of observation appears warranted for these lesions, particularly subdiaphragmatic ELS. Alternatives to resection have been proposed, including simple ligation of the artery and embolization. Curros and colleagues recommend to wait until one year of age to decrease the risk of complications. This could also allow for a period of observation to assess for involution. Resection by thoracoscopy is another alternative. Curros and colleagues recommend to wait until one year of age to decrease the risk of complications. This could also allow for a period of observation to assess for involution. Resection by thoracoscopy is another alternative. In cases of subdiaphragmatic ELS or when a systemic arterial blood supply cannot be demonstrated, operation may be advocated because the lesion may represent a neuroblastoma. However, recent trends would favor the observation of regressing neuroblastoma and an ongoing Children’s Oncology Group study is examining the safety of this approach for small adrenal lesions. Others have used percutaneous needle biopsy to differentiate ELS from neuroblastoma but this may not be necessary since both lesions could simply be observed.

While there is an ongoing debate about the congenital or acquired nature of ILS1-4,11,30,32,95 a lesion diagnosed before or soon after birth is obviously congenital. In ei-
ther case, the lesion communicates with the airway and is prone to recurrent infection and other complications. Resection is advocated in all intralobar sequestration cases.1-4,51-56,77,95,136,154

All congenital lung lesions with large cysts confirmed by postnatal CXR or CT scan should be resected even in asymptomatic children.1-4,6,7,28,29,31,36,40,50-56,58,60,62,69,77-80,82-84,103-120,127,131,134,136,141-143,155 CCAM is definitely not a variant of normal; at the time of Hellmuth’s review in 1998, only 24 cases had been described in adults including his own.143 Most had recurrent infections, pneumothorax, hemoptysis, while some asymptomatic patients had BAC. The same is true for the few adults described since then.59,64,121,146 There is also much overlap between CCAM and ILS,17,28,29 therefore both lesions should be approached in a similar fashion.

Timing for surgery

Since most patients will become symptomatic sooner or later and because of the small risk of malignancy, resection should be done in infancy. Waiting for infection to occur will only complicate the surgery and prolong the time spent in hospital as shown in a recent study,156 even though the difference was not significant in another report.45 Furthermore, a prolonged period of observation with repeated imaging studies invariably results in patients being lost to follow-up,41,49 not to mention the long-term risks of radiation.157 Some of these patients may then present with life-threatening infections26,58 or progression of a tumor.65,126 Some authors prefer to investigate and operate in the neonatal period,29,158 however this led to postoperative mechanical ventilation for an average of 2.3 days in one report.158 More recently, Adzick revised previous advice and now proposes to wait until after 4 weeks of age to decrease anesthetic risks.57 Others postpone the CT scan until 6 months of age82 or wait to operate until that age, with a 20% incidence of infection in the first 4 months.53 We usually perform the CT scan within two months of age and operate between the 3rd and 6th month, unless there is a significant mediastinal shift or any concern about malignancy. We have been able to achieve immediate extubation and a total length of stay similar to the 4.2 days reported by Marshall.156 Only once a patient developed infection during this elective waiting period; another child whose parents had initially refused surgery developed severe pneumonia at 4 years of age, requiring a prolonged course of intravenous antibiotics followed by a resection made difficult by the presence of inflammatory adhesions. Other authors use similar guidelines26,31,38,58,94 with one exception, presumably from a general thoracic surgery service, where the authors prefer to wait until 2 years of age.62

A few groups choose to operate electively on patients who remain asymptomatic only if they demonstrate “significant disease.” This was defined by one group as “evidence of mediastinal shift, diagnostic doubt, and involvement of a
significant part of the lung (>25% ipsilateral lung, as assessed on CT scan)," while for another it means "voluminous (>3 cm) or liquid-filled CCAM (according to the infectious risk)." From our experience and our literature review, we strongly favor elective surgery for any child with one or more large cyst (visible on CT scan). In other children with segmental areas of hyperlucency, the risks are not as clear (Figures 7 and 9), unless a concomitant lesion makes the operative decision easier (Figure 2). Certainly, in cases with minimal disease a repeat CT scan at 6 to 8 months of age would appear indicated before recommending surgery. We have to await the results of long-term studies on simple observation with repeat imaging before we can draw conclusions about the safety of this approach and the potential regression of congenital lung lesions confirmed after birth. Our general recommendations are summarized in Table 4.

### Table 4: Management guidelines for congenital lung malformations

<table>
<thead>
<tr>
<th>Operate</th>
<th>Observe</th>
<th>Unclear</th>
</tr>
</thead>
<tbody>
<tr>
<td>All bronchogenic cysts</td>
<td>Asymptomatic CLE</td>
<td>Segmental hyperlucency</td>
</tr>
<tr>
<td>All aerated sequestrations</td>
<td>ELS without significant shunting</td>
<td></td>
</tr>
<tr>
<td>All lesions with visible cysts on CT scan</td>
<td></td>
<td></td>
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</tbody>
</table>

**Type of resection**

Some authors have advocated segmental resection for CCAM and ILS, but this often results in incomplete resection, persistent pneumothorax and the need for completion lobectomy. Many surgeons and pathologists agree that lobectomy is safer, in part because the limit between CCAM and normal parenchyma is impossible to determine grossly. We have to await the results of long-term studies on simple observation with repeat imaging before we can draw conclusions about the safety of this approach and the potential regression of congenital lung lesions confirmed after birth. Our general recommendations are summarized in Table 4.

![Figure 9](image_url)

**Figure 9** Another child had a prenatal diagnosis of an echogenic lung lesion which regressed. The child was asymptomatic and CXR at birth was normal. (A) The CT scan at 7 months shows a right lower lobe lucency compatible with CCAM; the findings were unchanged from an earlier CT done at 6 weeks of age. (B) The lobectomy specimen demonstrated changes compatible with a polyalveolar lobe (or segment, in this case). Notice the numerous small alveoli on the far left and bottom half of the picture in comparison with the normal alveoli above (original ×20). The radial alveolar count in the abnormal area was 10 to 13 instead of the normal 6 to 7 (courtesy of Dr. Moy Fong Chen).
adequate imaging has shown this to be a rare event once the lesion is proven after birth. Complications, sometimes fatal, are expected in the majority of patients except those with asymptomatic CLE and small ELS without a major arterial supply. After presenting the evidence to families, operation can be recommended as the safer choice for most patients with ILS, CCAM and bronchogenic cysts. Simple observation should be considered experimental and should require proper informed consent and a commitment to long-term follow-up. Patients with a properly documented disappearance of a lung malformation, postnatally diagnosed as CCAM on CT scan, should be reported.

References

10. Imai Y, Mark JE: Cystic adenomatoid change is common to various forms of cystic lung diseases of children: A clinicopathologic analysis of 10 cases with emphasis on tracing the bronchial tree. Arch Pathol Lab Med 126:934-940, 2002


