Index Case: Female Fetus with a Pulmonary Mass

A 38-year-old, G_4P_0A_3, Caucasian woman undergoes a prenatal ultrasound at 23 weeks of gestation, which demonstrates a left pulmonary mass in a female fetus. The patient had two prior elective pregnancy terminations and a spontaneous abortion due to blighted ovum at 8 weeks. She is otherwise well. On ultrasound, the mass appears to be located in the left lower lobe, consists of cysts of variable sizes, and measures 22.9 × 17.3 × 10.3 mm. The ultrasound images are shown in Figure 9.1.

Q1: The perinatologist contacts you to arrange for a fetal consult. What other information would you like to obtain from the ultrasound prior to meeting the couple?

The presumptive diagnosis of a fetal cystic lung mass is congenital pulmonary airway malformation (CPAM), previously known as congenital cystic adenomatoid malformation (CCAM). It is important to quantify the size of the mass, adjusted to gestational age, through calculation of the CPAM volume ratio (CVR), calculated as (Length × Height × Width × 0.52)/head circumference. Other pertinent information to obtain from the ultrasound is the possible presence of mediastinal shift, diaphragmatic flattening or inversion, pleural effusion, hydrops, or a systemic feeding vessel. These findings, both on the initial and follow-up ultrasounds, will help determine the prognosis of the lesion, as well as indications for possible fetal interventions.

The CVR is 0.16 cm³. There is no evidence of any of the above associated findings at this time. After reporting the ultrasound results, the perinatologist inquires whether a fetal MRI should be performed.

Q2: How will you respond?

The calculation of CVR has been found to correlate quite well between fetal ultrasound and MRI. In some studies, fetal MRI was found to be highly accurate in determining the type of congenital pulmonary malformation, as confirmed by postoperative resection. However, despite being an excellent imaging modality, fetal MRI adds little to the prenatal care of most congenital lung malformations. Although no clear indications exist for fetal MRI, its best use is for lesions that do not demonstrate characteristic findings of CPAM on ultrasound or very large or symptomatic lesions in which medical or surgical fetal interventions are being considered. Nevertheless, due to its superior images, many parents strongly request fetal MRI and it is increasingly being performed routinely in fetal centers for further assessment of lung and thoracic anomalies identified on ultrasound.
A fetal MRI is performed, with images shown in the Figure 9.2. The MRI confirms a diagnosis of a congenital cystic mass in the superior portion of the left lower lobe without other abnormalities. Measurements of dimensions and CVR are in concordance with those of the ultrasound.

Q3: You describe the diagnosis in your meeting with the parents. They ask specifically about the plan for fetal follow-up, up to delivery.

The typical natural history of CPAM lesions identified during the fetal period is potential proliferation during the second trimester followed by potential stabilization or regression during the third trimester. Since the patient is close to the end of the second trimester, a weekly ultrasound would be recommended for two to three weeks, followed by less frequent ultrasounds if the lesion is stable and no new risk factors are identified. Early delivery is not recommended unless hydrops develops and persists into the third trimester, or the mother develops a mirror syndrome. Likewise, there is no indication for Cesarean section unless the therapeutic plan involves ex-utero intrapartum treatment (EXIT) to extracorporeal membrane oxygenation (ECMO) or EXIT to resection. These approaches are only used for the most severe lesions at high risk for neonatal demise after birth.

The fetus continues to progress well. The CVR increases to a maximum of 0.64 cm² during the early third trimester, but decreases subsequently with no other complications seen. A healthy baby girl is born by spontaneous vaginal delivery at 39 weeks of gestation. She has no respiratory symptoms and her vital signs and physical exam are normal. A chest x-ray is performed at 48 hours of age and is shown in Figure 9.3. It is read as normal.
Q4: Does this imply potential resolution of the lesion?

A normal or near-normal chest x-ray is a very frequent finding in an asymptomatic CPAM lesion, even relatively large ones. It does not imply disappearance or regression of the lesion. It is helpful in ruling out early expansion of the lesion after birth with mediastinal shift or other complications.

Q5: What follow-up or treatment would you recommend at this point?

This baby has an asymptomatic lesion which is likely to remain so, at least early in life. While some surgeons have advocated resection prior to discharge from hospital or before 3 months of age, there is no evidence to support this practice and no clear advantages to this approach. The baby may be discharged with CT scan imaging of the thorax at 3–4 months of age to assess the lesion in detail. A discussion can then ensue with the parents regarding resection versus observation.

Figure 9.4 shows axial and coronal cuts of the CT scan performed at 4 months of age, demonstrating a large cystic malformation of the left lower lobe. The baby grows and develops well and remains asymptomatic. You recommend an elective resection after reviewing the CT scan.

Q6: How would you explain to the parents the rationale for resection in this asymptomatic child?

Controversy exists regarding observation versus resection of asymptomatic lesions. However, the majority of pediatric surgeons still favor resection for a number of reasons. Congenital cystic malformations of the lung represent abnormal epithelial-lined cysts that communicate with the bronchial tree, but do not participate in ventilation. As such, they are prone to infection, typically presenting as severe pneumonia or lung abscess in an otherwise well child. Resection can be more complicated after infection, especially if thoracoscopic techniques are planned. Although the likelihood is quite low, asymptomatic cystic malformations can both harbor malignancy (pleuropulmonary blastoma) or undergo malignant degeneration (bronchioalveolar carcinoma). Since the lung continues to form alveolar units until 4–8 years of age, compensatory lung growth likely occurs after resection of these anomalies. Finally, operative morbidity and mortality for lung resection in childhood is quite low. Thoracoscopic techniques may have further reduced the potential long-term morbidity, in the form of musculoskeletal deformities.
The parents accept the recommendation for elective left lower lobectomy and the procedure is performed thoracoscopically at 10 months of age. The patient recovers well and is discharged on the third postoperative day. The gross findings at surgery are similar to that of another patient, shown in Figure 9.5, who underwent an open lobectomy 12 years prior.

**Figure 9.5** Left lower lobe CPAM

Q7: How do pathologic findings in CPAM help explain the etiology of these lesions?

The histology of the resected left lower lobe is shown in Figure 9.6. This is Stocker type 1 (large-cyst type) CPAM. The multiple cysts measure from 0.3 to 3.0 cm in diameter, extending close to the pleura. The histology shows respiratory epithelial cystic lining overlying a smooth muscle layer without cartilage. No typical mucus-producing cells are identified. A communication is seen between the cystic lesions and lung parenchyma. There is often a glandular appearance to the lung, explaining the previous nomenclature of adenomatoid malformations. Since this is not evident in all malformations, the term CPAM is more inclusive.

**Figure 9.6** Pathology
Discussion

Congenital pulmonary airway malformations (CPAMs) were formerly referred to as congenital cystic adenomatoid malformations (CCAMs). The term CCAM reflected the adenomatoid or “endocrine” appearance of these lesions on histology, which often demonstrated bronchiolar proliferation without alveolar development. However, since not all lesions are grossly cystic and the anomaly can occur at variable levels in the tracheobronchial tree, the term CPAM has been adopted as more reflective of the entire spectrum. The classification of CPAM type, based on cyst diameter on histology, as originally defined by Stocker, has been largely replaced by the simple separation of lesions into microcystic (cysts <5 mm) and macrocystic (cysts ≥5 mm), based on prenatal and postnatal imaging. This classification has clinical utility and helps define the therapeutic options for symptomatic lesions. For example, microcystic CPAM typically appears solid on ultrasound, is more likely to become symptomatic during fetal life, and is more likely to respond to maternal steroid treatment.

The increasing use of ultrasound in prenatal screening and diagnosis has dramatically changed the understanding of the natural history and outcome of prenatally diagnosed CPAM. It is now clear that the large majority of prenatally identified lesions will remain asymptomatic during the fetal and neonatal period, and can be approached electively. Fetal ultrasound allows three important roles in the management of CPAM: It identifies the lesion and offers at least a presumptive diagnosis of its type. It allows for serial monitoring of the lesion and identification of any associated complications, such as mediastinal shift or hydrops. It assesses response to fetal treatment, when indicated, and helps guide plans for delivery and postnatal management. Measurement of CVR on ultrasound has been a great advance in prognosticating these lesions. A cutoff of 1.6–2.0 m2/cm3 has been used to differentiate smaller lesions, which are likely to remain asymptomatic, from larger lesions, which are likely to result in complications. The addition of fetal MRI has become routine in some fetal treatment centers, but frequently does not add significantly to the treatment plan. A fetal echocardiogram is also routinely done to screen for cardiac anomalies and exclude any hemodynamic effects of the CPAM. It is most often found to be normal.

Unlike congenital diaphragmatic hernia, lung hypoplasia is uncommon in the presence of CPAM. When symptoms occur during the fetal period, they are typically due to the space-occupying effect of large lesions. This can result in mediastinal shift, cardiac compression, polyhydramnios, and hydrops. In select centers, fetal resection was previously advocated for these complicated lesions. However, this intervention has become extremely rare due to two less-invasive fetal treatments, which have shown reproducible excellent outcomes. Microcystic CPAM has been shown to regress with one or more courses of maternal steroids, with frequent resolution of hydrops and other complications. Macroscopic CPAM lesions have responded well to thoracoamniotic shunting to decompress the cyst and decrease the space-occupying effect. The few patients who fail these maneuvers are candidates for EXIT procedures at 32 weeks of gestation and immediate support with ECMO or resection on placental circulation.

If a patient born with an asymptomatic CPAM develops subsequent symptoms, they will most likely be due to infection. Symptoms may include fever, respiratory distress, chest pain, cough, or hemoptysis. Previously healthy patients who develop a lung abscess should be suspected of harboring a previously silent malformation and imaged appropriately. Resection is not recommended during the acute infection, which almost always improves with antibiotics alone. In fact, in addition to resolution of the clinical infection, the chest x-ray may look almost normal. The clinician should therefore have a low threshold for the diagnosis of a congenital anomaly in order to prevent recurrent infection. The cases below demonstrate the presentation and management of symptomatic CPAM lesions.

Figure 9.7 demonstrates the case of a 3-year-old girl who presented with cough, fever, and moderate respiratory distress. Her chest x-ray showed a right lower lobe air-fluid level and subsequent CT scan demonstrated a lung abscess. Interestingly, she had been treated for right lower lobe pneumonia with intravenous antibiotics 1 year previously. However, she did not have adequate follow-up, and there was no documentation of resolution of the abnormal chest x-ray findings. She responded well to a course of intravenous, followed by oral, antibiotics. An attempt at thoracoscopic lobectomy 4 weeks after presentation was converted to thoracotomy due to severe persistent inflammation and obliteration of the dissection plane. Figure 9.8 demonstrates the pathology, which was a Stocker type 2 (small-cyst type). There are small cysts (0.2–1.5 cm) which appear as bronchiole-like structures scattered and blended throughout the intervening alveolar parenchyma, with post-infectious changes consisting of organizing pneumonia with interstitial granulation tissue and fibrosis.
**Figure 9.7** CPAM presenting with lung abscess

**Figure 9.8** Pathology of infected CPAM
Figures 9.9 and 9.10 demonstrate another CPAM presentation in a 12-year-old, previously healthy boy who presented with fever, cough, left-sided pleuritic chest pain, and intermittent hemoptysis. A chest x-ray and CT scan demonstrated an infected cystic cavity in the left upper lobe with surrounding pneumonia. He responded well to intravenous, followed by oral, antibiotics. Due to near normalization of his chest x-ray 4 weeks after the initial presentation, the consulting pulmonologist questioned the existence of an underlying anomaly. A repeat CT again demonstrated resolution of the pneumonia, but persistence of the cyst. At thoracoscopy, the cyst could be clearly seen, along with adhesions from the previous infection. Pathology was consistent with bronchial atresia. Figure 9.11 demonstrates an infected CPAM in the right upper lobe of a 16-month-old girl. Again, the process resolved clinically with antibiotics, with significant improvement in the chest x-ray. On thoracoscopy, six weeks after presentation, a CPAM was identified and right upper lobectomy performed. A video the thoracoscopic upper lobe resections in these patients is shown in Video 9.1.

Another argument that supports resection of asymptomatic lesions is the coexistence of malignancy in a CPAM or malignant degeneration of a CPAM lesion. The exact incidence of lung cancer associated with CPAM is not known, but some studies showed that up to 5% of CPAM lesions may contain malignant elements. A lesion that may be difficult to differentiate from CPAM is pleuropulmonary blastoma (PPB), as shown in the case depicted in Figures 9.12 through 9.14. This patient was a baby girl who had a small, wedge-shaped, fluid-filled mass identified on 21-week fetal ultrasound. At 31 weeks, it appeared bi-lobed, but had not increased much in size, as shown in Figure 9.12. The

Figure 9.11  Infected right upper lobe CPAM. (From Emil S, Su W. J Laparoendosc Adv Surg Tech 2008;18:174–178, as Figures 1–6. With permission.)
Figure 9.12 Pleuropulmonary blastoma: Fetal and neonatal imaging. (Courtesy of Dr. Melinda Hall, Department of Obstetrics and Gynecology, St. Mary Hospital Center.)

Figure 9.13 Pleuropulmonary blastoma: CT scan and operative findings
The patient had no symptoms at birth or after. The chest x-ray at 2 days of age showed nonspecific haziness in the left upper lobe but, at 2 weeks, demonstrated an impressive air-filled cyst with mediastinal shift. A CT scan demonstrated large, dominant, peripheral cysts, a finding typical of PPB on imaging. The patient underwent early left upper lobectomy, with the findings noted on Figure 9.13. A type I PPB was confirmed on pathology, as shown in Figure 9.14. The large cystic areas were lined by alveolar and respiratory epithelium overlying a loose to dense fibrous stroma, containing primitive small cells in a cambium-like layer beneath the epithelium. Of note, many pathologists now consider all Stocker type 4 CPAMs to be PPB, until proved otherwise. The patient was followed closely and has done well, with no further lesions identified on 7-year follow-up. The patient also underwent screening of her kidney and spleen for synchronous lesions, as well as genetic consultation and testing for DICER-1 mutation, all of which were negative. This is the most favorable presentation of PPB. Patients who present later with type II (cystic and solid) and type III (solid) PPB typically require adjuvant chemotherapy and have less favorable prognoses. There is strong evidence that type I PPB will progress over time to types II or III.

Hybrid lesions that have features of CPAM and pulmonary sequestration are becoming increasingly recognized. These lesions show typical features of CPAM on imaging and pathology, but have a systemic arterial blood supply. They are typically found almost exclusively in the upper lobes.

Thoracoscopic lobectomy is certainly a more challenging procedure than thoracoscopic excision of extralobar sequestrations or mediastinal cysts. However, there has been steadily increasing experience with this procedure. Recovery is typically faster, and the cosmetic result is superior to open thoracotomy. The most important advantage is the decreased likelihood of scoliosis or chest wall deformities secondary to thoracotomy, although this has yet to be conclusively demonstrated. Open lobectomy should be considered within the standard of care and should be performed by surgeons who are not comfortable with advanced minimally invasive procedures in the chest. Segmentectomy has been described but not widely adopted due to potentially leaving residual disease behind and the possibility of increased incidence of prolonged air leak, which is the most frequent complication after pediatric lung resections. Video 9.2 shows a thoracoscopic left lower lobectomy in a 9-month-old boy with a hybrid lesion in the left lower lobe. Early control and division of the systemic arterial supply is essential in these cases.

**Video 9.2** ([https://youtu.be/z_Nn7w6rBJw](https://youtu.be/z_Nn7w6rBJw))

Thoracoscopic left lower lobectomy for congenital pulmonary airway malformation.
Suggested Readings


