Prenatal and postnatal imaging evaluation of Congenital Pulmonary Airway Malformation (CPAM) and Pulmonary Sequestration: what the radiologist needs to know

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Learning objectives

Congenital pulmonary airway malformation and pulmonary sequestration represent two entities of the spectrum of bronchopulmonary foregut malformation. These conditions may be detected incidentally on prenatal ultrasound examinations or postnatal chest radiograph, performed for other indications, or they may present with associated conditions and complications.

We propose to achieve these objectives:

• To identify the usual prenatal and postnatal imaging features of congenital pulmonary airway malformation and pulmonary sequestration, with a brief comparison of the radiological findings.
Background

**Bronchopulmonary foregut malformations (BPFM)** are a heterogeneous group of uncommon pulmonary developmental abnormalities, which may present at varying ages and with overlapping symptoms and radiological features. These conditions are rare but important causes of morbidity in infants, presenting with acute respiratory distress, polyhydramnios and hydrops; however, they may also remain asymptomatic until adulthood and found incidentally [1].

BPFMs result from defective budding and differentiation of the embryonic foregut and tracheobronchial tree, occurring during the first weeks of lung development; however, the type and timing of the insult is not well understood and a number of causes have been postulated, including trauma, ischaemia, infection and adhesions [1,2]. Interruption of the development of the pulmonary tree and pulmonary vessels at different times and sites will result in varying anomalies in the affected area of lung. In particular, an early interruption of this process results in continued development of the primitive systemic capillary supply to a region of lung, determining congenital pulmonary malformation, pulmonary sequestration or a mixture of the two lesions [1].

**Congenital pulmonary airway malformations (CPAMs)** are characterized by multicystic or solid lung lesions that largely result from early airway maldevelopment. The term "congenital pulmonary airway malformation" has been recommended as being preferable to the term "congenital cystic adenomatoid malformation", since the lesions are cystic in only three of the five types of these lesions and adenomatoid in only one type (type 3) [2].

Although rare, CPAMs are the most common congenital lung lesions, accounting for 30%-40% of all congenital diseases. Data from large population registries suggest an incidence of CPAM in the range of 1 per 11,000 to 35,000 live births [3, 4].

Traditionally, CPAMs have been classified at pathologic analysis by Stocker according to cyst size and histologic resemblance to segments of the developing bronchial tree and airspaces [5]. Nowadays, the newer classification scheme includes five subtypes and is an extension of the original scheme (Fig. 1) [2]:

- **Type 0** has a tracheobronchial origin, representing an acinar dysgenesis or dysplasia; it cannot be distinguished at imaging.

- **Type 1** is most common and is seen in 65% of CPAM lesions of bronchial or bronchiolar origin; it is composed of single or multiple large cysts (2-10 cm in diameter) surrounded by smaller cysts and a compressed normal parenchyma.
- **Type 2** occurs in 25% of cases and has a bronchiolar origin; it is composed of various smaller cysts (0.5-2-cm in diameter).
- **Type 3** represents 10% of the cases and has a bronchiolar-alveolar duct origin (adenomatoid type); it consists of small cystic lesions that are smaller 0.5 cm in diameter, with no discernible cystic spaces, appearing as microcystic or solid.
- **Type 4** has a distal acinar origin (the "unlined" cyst lesion); usually appears as a large cyst at imaging and is indistinguishable from type 1 CPAM on imaging [1, 2, 6].

A CPAM may communicate with the proximal airways, although this communication is abnormal. Most CPAMs derive their blood supply from the pulmonary artery and drain via the pulmonary veins [2].

CPAMs can be associated with other anomalies, like cardiac, renal and chromosomal abnormalities [1].

The natural history of and prognosis for a CPAM are variable and depend on the size of the malformation, presence of pulmonary hypoplasia, mediastinal shift and fetal hemodynamic alterations. The presence of fetal hydrops is the main indicator of a poor outcome and it is generally an indication for fetal intervention. However, in many cases of CPAM the malformation progressively decreases in size during the third trimester, such that the infant is asymptomatic at birth [6]. If not recognized antenatally, CPAMs are usually discovered between the neonatal period and 2 years of age, manifesting as respiratory difficulty or infection. Symptomatic infants who are diagnosed postnatally are treated with surgical resection, which generally consists of lobectomy or segmental resection. Surgical intervention for asymptomatic CPAMs remains controversial. Recurrent infection and a questionable small risk of malignancy have been cited as reasons for elective resection [2].

**Pulmonary sequestration (PS)** is the second most common BPFM after CPAM, with an estimated incidence of 0.15%-6.4% of all congenital pulmonary malformations [7]. It is generally defined as a portion of lung that does not connect to the tracheobronchial tree and has an anomalous systemic arterial supply, which is most commonly derived from the thoracic aorta; however, the arterial supply has also been noted to arise from the abdominal aorta, coeliac trunk, intercostal artery, subclavian artery and renal artery. PS occurs almost always within the lower lobes and slightly more often in the left lung than in the right lung [1].

PS can be further classified as extralobar or intralobar, depending on the morphologic patterns of sequestration (Fig. 2).
• **Intralobar sequestration** (ILS) accounts for 75% of all PS, shares the pleural investment with the normal lung and usually drains into the pulmonary venous system.

• **Extralobar sequestration** (ELS) accounts for 25% of all PS, has its own pleural investment and a systemic venous drainage. It may be associated with other congenital systemic anomalies, such as congenital diaphragmatic hernia, cardiac abnormalities, pulmonary hypoplasia or foregut duplication cysts. It may be located below the diaphragm, mimicking a neuroblastoma or adrenal hemorrhage [2].

PS is believed to arise from a supernumerary lung bud caudal to the normal lung bud. If the lung bud arises before the development of the pleura, it is invested with adjacent lung and becomes an ILS. If the lung bud arises after pleura formation, it grows separately and acquires its own pleural covering [2].

Both types of PS may be associated with polyhydramnios and in utero hydrops fetalis, due to compression of the esophagus and thoracic venous structures by a large lesion [6]. ILS often presents in childhood or adulthood rather than in the neonatal period, with infection, cough or hemoptysis. ELS, if it does not present in the neonatal period, is usually clinically silent [1]. Symptomatic infants require prompt surgical resection. Most recognized pulmonary sequestrations are surgically resected electively, even in asymptomatic patients due to the risk of infection, hemorrhage and questionable malignancy [2].

**Hybrid conditions**, which have histologic and imaging features similar to those of both CPAM and PS, are commonly diagnosed at pathologic analysis, suggesting that these two entities have a common embryologic origin [6].

In this educational exhibit, we describe the most common radiological features of these conditions and provide a comparison on imaging.
**Fig. 1:** Congenital pulmonary airway malformation types

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<table>
<thead>
<tr>
<th>CPAM Type</th>
<th>Type 0</th>
<th>Type 1</th>
<th>Type 2</th>
<th>Type 3</th>
<th>Type 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stoker classification</td>
<td>Type I</td>
<td>Type II</td>
<td>Type III</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Developmental origin</td>
<td>tracheal/bronchial</td>
<td>bronchial/bronchiolar</td>
<td>bronchiolar</td>
<td>bronchiolar/alveolar</td>
<td>acinar</td>
</tr>
<tr>
<td>Proportion of CPAM</td>
<td>2%</td>
<td>60-65%</td>
<td>15-25%</td>
<td>5-10%</td>
<td>10%</td>
</tr>
<tr>
<td>Cyst size</td>
<td>none</td>
<td>2-10 cm</td>
<td>0.5-2 cm</td>
<td>microcystic/solid</td>
<td>large multilocular</td>
</tr>
<tr>
<td>Timing of presentation</td>
<td>birth</td>
<td>prenatal</td>
<td>postnatal</td>
<td>prenatal</td>
<td>postnatal</td>
</tr>
<tr>
<td>Clinical presentation</td>
<td>lethal pulmonary hypoplasia</td>
<td>asymptomatic, respiratory distress or infection</td>
<td>asymptomatic, respiratory distress or infection</td>
<td>prenatal (hydrops), postnatal respiratory distress</td>
<td>incidental finding</td>
</tr>
</tbody>
</table>

**Fig. 2:** Pulmonary sequestration classification

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<table>
<thead>
<tr>
<th>Pulmonary sequestration</th>
<th>Intralobar sequestration</th>
<th>Extralobar sequestration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion of pulmonary sequestration</td>
<td>75%</td>
<td>25%</td>
</tr>
<tr>
<td>Pleural investment</td>
<td>shares the pleural investment with the normal lung</td>
<td>has it own pleura</td>
</tr>
<tr>
<td>Venous drainage</td>
<td>usually into the pulmonary venous system</td>
<td>systemic venous drainage</td>
</tr>
<tr>
<td>Timing of presentation</td>
<td>childhood or adulthood</td>
<td>neonatal period</td>
</tr>
<tr>
<td>Clinical presentation</td>
<td>recurrent infections, cough or hemoptysis</td>
<td>asymptomatic, respiratory distress, cyanosis or infection</td>
</tr>
<tr>
<td></td>
<td>CPAM</td>
<td>Pulmonary sequestration</td>
</tr>
<tr>
<td>----------------------</td>
<td>-----------------------</td>
<td>-------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Proportion of BPFM</strong></td>
<td>30%-40%</td>
<td>0.15%-6.4%</td>
</tr>
<tr>
<td><strong>Airway communication</strong></td>
<td>communicate with the proximal airways</td>
<td>not connected to the tracheobronchial tree</td>
</tr>
<tr>
<td><strong>Blood supply</strong></td>
<td>pulmonary artery and veins</td>
<td>systemic arterial supply (branch of the aorta) venous drainage via pulmonary veins (ILS) or systemic veins (ELS)</td>
</tr>
<tr>
<td><strong>Associated anomalies</strong></td>
<td>CV anomalies, renal hypoplasia, chromosomal abnormalities</td>
<td>cardiac anomalies, diaphragmatic hernias, gastric duplication</td>
</tr>
</tbody>
</table>

**Fig. 3:** Physiopathological comparison between congenital pulmonary airway malformation and pulmonary sequestration

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Findings and procedure details

Antenatal ultrasound

In recent years, improvements in imaging, particularly in fetal ultrasound (US), have allowed earlier detection of smaller pulmonary masses. Most of the lesions are discovered on ultrasound at around the end of the second trimester (range 16-36 weeks), although the time of discovery often depends on the date of the first antenatal scan. Ultrasound can then be used to monitor the intra-uterine course of the lesion. Furthermore, the role of ultrasound has become ever more important in deciding when intervention may be appropriate [1].

- Fetal US of CPAM demonstrates numerous variable-sized cystic lesions as anechoic spaces intermixed with echogenic soft tissue, corresponding to the non-cystic part of the lesion and compressed adjacent lung (Fig. 5).
- A microcystic CPAM type 3 may have a similar imaging appearance to PS, since both are identified as a hyperechoic apparently solid lesions. In PS, color Doppler US may identify the feeding artery originating from the descending aorta, although making an accurate diagnosis is difficult.
- Hydrops fetalis, polyhydramnios and mediastinal shift may be detected on ultrasound as ancillary sonographic features, which have been associated with a poor prognosis [1, 2].

Fetal magnetic resonance imaging

Prenatal sonography remains the primary imaging modality for evaluating the fetus, because it is safe, largely accessible and inexpensive. However, in cases of inconclusive sonographic findings, the use of fetal MRI helps to identify potentially lethal pulmonary abnormalities. The MRI sequences used to evaluate the fetal chest include fast sequences such as single-shot fast spin-echo, fast spoiled gradient echo and free induction steady-state precession sequences. T2-weighted images are the most useful to evaluate the lung anatomy [6].

- The imaging finding of CPAMs vary depending on the subtype. Type 1 and type 2 lesions usually appear as hyperintense unilocular or multilocular regions with discrete walls on T2-weighted images (Fig. 6). Type 3 lesions manifest as homogeneously hyperintense solid masses with normal adjacent parenchyma.
- MRI findings of PS usually include a solid, well-defined, uniform, hyperintense mass on T2-weighted images. To differentiate between these entities, the systemic arterial supply (present only in PS and hybrid conditions) should be identified [6].
- Compressed lung has a sufficiently distinct signal from normal lung to identify its extent. This raises the possibility of calculating the volume of
affected and unaffected lung and thus the degree of pulmonary hypoplasia, and this could be useful as a post-natal prognostic guide [1].

Postnatal imaging

After birth, radiography and CT scanning are necessary for determination of the type and extent of the lesions.

- In the early neonatal period, chest radiographs in type 1 and 2 CPAMs may demonstrate a round soft-tissue mass (completely or partially fluid-filled) (Fig. 7) that gradually becomes filled with air, since there is delayed clearance of fetal lung fluid from the cysts through the abnormal airway. It may be seen as a solitary well-defined air-filled cyst with thin walls or as multiple cysts of varying size (Fig. 8). Air-fluid levels may be identified. Large lesions may cause a mass effect with resultant mediastinal shift, depression and even inversion of the diaphragm. Lesions may change in size on interval imaging. CT may allow better evaluation of CPAMs, demonstrating a heterogeneous mass with well-defined air-filled cystic spaces and variable surrounding soft-tissue attenuation (Fig. 9 and 10). Type 3 CPAM appears on chest x-ray as a large homogeneous mass, similar to type 1 lesions filled with fluid. Postnatal CT may demonstrate an ill-defined area of increased attenuation [1, 2].

- Classically, on postnatal imaging, ILS will be seen as a soft-tissue mass with a cystic structure containing air-fluid levels, with a smooth or lobulated contour. The lung within the ILS can be aerated by collateral drift via the pores of Köhn. Dilated bronchi may be visualised within the lesion. CT of ILS may show a cystic structure with single or multiple cysts containing air or fluid, focal emphysema, or a hypervascular focus of lung parenchyma. ELS produces an airless mass with fluid-filled cysts often lying adjacent to the diaphragm. On chest radiograph this appears as a well-defined triangular mass with no air bronchograms. Air within ELS may indicate communication with the gastrointestinal tract. Similar to CPAM, PS can be found in any part of the lung but most commonly in the postero-basal segments on the left side. Feeding vessels may be identified when intravenous contrast is given (Fig. 11 and 12), although they cannot be demonstrated in most cases. MRI is better at identifying feeding vessels and their source [1, 2].

- Recurrent lower lobe pneumonia that does not clear with antibiotic therapy may be the clue to the diagnosis of a misunderstood CPAM or PS in adulthood (Fig. 13, 14 and 15)[1, 2].
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### IMAGING FINDINGS

<table>
<thead>
<tr>
<th></th>
<th>CPAM (Type 1 and 2)</th>
<th>CPAM (Type 3)</th>
<th>Intralobar sequestration</th>
<th>Extralobar sequestration</th>
<th>Collateral findings</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fetal US</strong></td>
<td>numerous variable-sized anechoic/cystic lesions intermixed with compressed adjacent lung</td>
<td>hyperechoic apparently solid lesions</td>
<td>hyperechoic solid lesions; color Doppler US may identify the feeding artery</td>
<td>hyperechoic solid lesions; color Doppler US may identify the feeding artery</td>
<td>hydrops fetalis, polyhydramnios and mediastinal shift (poor prognosis)</td>
</tr>
<tr>
<td><strong>Fetal MRI</strong> (T2-weighted images)</td>
<td>hyperintense unilocular or multilocular regions with discrete walls</td>
<td>homogeneously hyperintense solid masses with normal adjacent parenchyma</td>
<td>solid, well-defined, uniform, hyperintense mass systemic arterial supply should be identified</td>
<td>solid, well-defined, uniform, hyperintense mass systemic arterial supply should be identified</td>
<td>possibility of calculating the volume of affected and unaffected lung and the degree of pulmonary hypoplasia</td>
</tr>
<tr>
<td><strong>Chest radiograph</strong></td>
<td>round soft-tissue mass (completely or partially fluid-filled), air-filled cyst with thin walls or multiple cysts of varying size</td>
<td>large homogeneous mass</td>
<td>soft-tissue mass with a cystic structure containing air–fluid levels, with a smooth or lobulated contour</td>
<td>triangular mass with no air bronchograms, often lying adjacent to the diaphragm</td>
<td>mediastinal shift, depression and inversion of the diaphragm</td>
</tr>
<tr>
<td><strong>Chest CT</strong></td>
<td>heterogeneous mass with well-defined air-filled cystic spaces and surrounding soft-tissue attenuation</td>
<td>ill-defined area of increased attenuation</td>
<td>soft-tissue mass with a cystic spaces, focal area of emphysema, or a hypervascular focus of lung parenchyma</td>
<td>airless mass with fluid-filled cysts</td>
<td><em>Feeding vessels</em> may be identified on pulmonary sequestration when intravenous contrast is given</td>
</tr>
</tbody>
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**Fig. 4:** Comparison between congenital pulmonary airway malformation and pulmonary sequestration on imaging

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**Fig. 5:** CPAM type 2 in a fetus at 35 weeks gestation. Longitudinal sonograms show multiple small anechoic cysts in the left hemithorax (maximum diameter 1.4 cm). No feeding vessel was noted on color Doppler.

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**Fig. 6:** CPAM type 2 in a fetus at 23 weeks gestation. Sagittal (a) and coronal (b) T2-weighted MR images show a large multilocular mass (diameters 47x30x43 mm) with small cysts inside (maximum size 8 mm) and high signal intensity, occupying almost all the posterior portions of the right lung (arrow). Polyhydramnios is also noted (curved arrow).

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**Fig. 7:** Chest radiograph of a 1-day-old newborn shows multiple small air-filled cysts in the right apical zone (arrow) and a large oval-shaped opacity (maximum diameter 46 mm) in the right mid and lower zones (curved arrow), causing leftward mediastinal shift. A CT scan was later performed for a better evaluation, confirming the diagnostic hypothesis of type 1 CPAM.

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Fig. 8: Chest radiograph of a newborn shows multiple small air-filled cysts in the left lower zone (arrow). A CT scan was later performed for a better evaluation, confirming the diagnostic hypothesis of type 2 CPAM.

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**Fig. 9:** Chest CT scan of a 11-week-old newborn with type 1 CPAM. a) Coronal reformatted image (lung window) shows multiple large air-filled cysts in the right lower lobe (arrow), with maximum diameter of 26 mm. b) MinIP reconstruction of the same patient depicts the large cystic lesion (arrow).

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**Fig. 10:** Axial CT scan, on soft tissue window (a) and lung window (b), of a 1-week-old newborn with CPAM type 1, shows a large, round cyst, completely fluid-filled, in the apical segment of the right upper lobe (arrow), with maximum diameter of 25 mm. b) 3D Volume Rendering better depicts the regions of affected and unaffected lung.
**Fig. 11:** Sagittal oblique reformatted MIP image CT angiography of a 63-year-old woman shows a homogeneous mass in the anteromedial segment of the left lower lobe (arrow). A feeding artery is seen arising from the thoracic aorta (curved arrow). Features are consistent with pulmonary sequestration.
**Fig. 12:** Incidental finding of a pulmonary sequestration during a CT scan in a 50-year-old man with retroperitoneal sarcoma (star). Coronal reformatted image on arterial phase shows a homogeneous mass in the anteromedial segment of the left lower lobe (arrowhead). A feeding artery (curved arrow) is seen arising from the abdominal aorta, a finding that is diagnostic for sequestration.

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Fig. 13: CT scan of a 22-year-old man suffering from recurrent pneumonias since childhood. Coronal MIP (a) and MinIP (b) reconstructions show a large, well-defined area of low attenuation in the left upper lobe (arrow), without mass effect to the adjacent tissue. No systemic arteries or anomalous arterial supply was identified within the lesion. Presuming a radiological diagnosis of congenital lobar emphysema or a bronchogenic cyst, a segmental resection was performed after 3 months of observation. On histological examination, it was made a diagnosis of type 4 CPAM lesion.

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**Fig. 14:** Incidental finding of a CPAM type 1 in a 36-year-old man with medical history of hemoptysis. Chest CT (lung window) shows a large cystic lesion with internal septa in the anteromedial segment of the left inferior lobe (arrow).

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**Fig. 15:** CPAM type 1 in a 73-year-old man with medical history of recurrent pneumonia. 
a) Chest radiograph shows multiple cysts of varying size on the right lung (arrow). b) Coronal MinIP reconstruction of the same patient depicts the large cystic lesions (arrow).

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Conclusion

CPAM and pulmonary sequestration are commonly detected at routine prenatal ultrasound or in the immediate neonatal period. However, silent forms of these disorders may not become apparent until the child is older, and some people are not diagnosed until adulthood. Familiarity with the various imaging features of these abnormalities is crucial for prenatal counselling and appropriate peri- and postnatal management.
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