Congenital Pulmonary Airways Malformation: an update

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Learning objectives

- Recognise the main theories regarding Congenital Pulmonary Adenomatoid Malformation (CPAM).

- Describe the 5 types of CPAM's under the new Stocker classification.

- Identify the post-natal imaging and management decisions.

- Understand the potential malignant implications.
Background

Congenital Pulmonary Adenomatoid Malformations (CPAMs), previously known as Congenital Cystic Adenomatoid Malformation (CCAM) encompass a range of hamartomatous anomalies thought to result from abnormal branching of bronchioles during lung development.

Patients are often young, and present with non-specific symptoms. It is important to recognise this diagnosis, as it can lead to multiple recurrent chest infections. Management is mainly supportive and preventative, although some patients may require surgery and CTs are always performed in our institution.

We aim to provide an up to date review of the CPAM classification, its implications, and the current literature regarding its treatment.
Imaging findings OR Procedure details

Background, Epidemiology and Pathogenesis

CPAM encompasses an array of hamartomatous anomalies thought to result from abnormal branching of bronchioles. The exact embryonic insult remains unclear although evidence suggest that this may occur from 5-22 weeks of gestation [1]. This results in a wide spectrum of pathologic and radiologic presentations.

CPAM is a rare condition, with documented incidence ranging from 1 in 11,000 to 1 in 35,000 live births. 85-95% of cases are unilobar [2].

Microscopic features of CPAM include polypoid projections of mucosa, presence of inflammatory cells, hypertrophy of smooth muscle and elastin within cyst walls, absence of cartilage and presence of mucous-secreting cells [3]. Genes thought to contribute to the pathogenesis of CPAMs include HOXB5 and platelet derived growth factor-B (PDGF-B) [4,5]. These genes are of clinical importance as they may lead to the development of future therapeutic strategies.

Clinical features:

Neonates present with respiratory distress syndrome and cyanosis, and as they mature there is often a history of recurrent infections over a year. Occasionally CPAMs present incidentally on imaging of asymptomatic older patients.

Prenatal imaging.

CPAMs are mostly diagnosed during antenatal ultrasound (US). The typical finding is of a solid hyperechoic or cystic lung mass within the thoracic cavity. Ultrasound in the second trimester accurately detects echogenic pulmonary lesions, assesses lung size and degree of mediastinal shift as well as the presence of polyhydramnios and hydrops. There is often poor correlation between US findings and post-natal pathology because the differential diagnosis for the sonographic appearances includes conditions such as bronchopulmonary sequestration, lobar emphysema and diaphragmatic hernia. Pre-natal MRI has been shown to be highly accurate in defining congenital lung anomalies with concordance as high as 98% in one study [6].

Postnatal imaging.

Common post natal imaging modalities include chest radiographs, ultrasound and CT. MRI and conventional angiography are also utilised occasionally. Among these
modalities, CT is the most frequently utilised modality and provides details of the intrathoracic structures which may not be apparent on plain images. There is no consensus on when to perform a CT evaluation, and many cases are already diagnosed antenatally by ultrasound. At our local institution, a 6 month initial CT and an 18 month pre-surgical CT is performed as standard protocol. Non-ionic intravenous contrast is administered at a dose of 2ml/kg, but not exceeding 125ml. A mechanical injection via a 22G or larger bore cannula is preferred.

**CPAM types and classification:**

CPAM is a heterogenous group reclassified (types 0-IV) in 2002 by Stocker et al (Fig. 1 on page 8, Fig. 2 on page 8) [7]. Three types are cystic on microscopy and the rest non-cystic. Langston subsequently described a classification system based on pathological features rather than distinct groups, due to substantial overlap among these lesions [8]. For the purposes of this review, we will follow Stocker’s classification.

**Type 0 CPAM**

Type 0 CPAM is extremely rare, and is also known as acinar dysplasia. Patients present with neonatal onset of severe respiratory failure, which is incompatible with life. Lungs are typically small and firm, with bronchial type airways and abundant mesenchyme (Fig. 3 on page 9).

**Type I CPAM**

Type I CPAM is commonest type accounting for 50-70% of cases. It arises from a distal bronchus or proximal bronchiole and is characterised by multiple cysts ranging form 2-10 cm or a single dominant cyst (Fig. 4 on page 10, Fig. 5 on page 11, Fig. 6 on page 12, Fig. 7 on page 13, Fig. 8 on page 14, Fig. 9 on page 15, Fig. 10 on page 16, Fig. 11 on page 17, Fig. 12 on page 18, Fig. 13 on page 19, Fig. 14 on page 20, Fig. 15 on page 21, Fig. 16 on page 22). It normally involves a single lobe, and has good prognosis. The cysts are typified by pseudostratified columnar epithelium, and sometimes mucous cell hyperplasia. Bronchiolar overgrowth is associated with alveolar underdevelopment. Rarely it may overlap with bronchoalveolar cell carcinoma (Fig. 17 on page 23, Fig. 18 on page 24).

**Type II CPAM**

Type II CPAM accounts for 15-30% of cases and arises from terminal bronchioles. Type II CPAMs comprise of smaller (0.5-2cm) cysts as well as more solid areas (Fig. 19 on page 25, Fig. 20 on page 26, Fig. 21 on page 27 and Fig. 22 on page 28). There are associations with renal agensis, cardiovascular defects, diaphragmatic hernia
and syrngomyelia. Histologically it involves overgrowth of the bronchiolar epithelium, separated by alveolar tissue which is underdeveloped.

**Type III CPAM**

Type III CPAM is the solid type on imaging (Fig. 23 on page 29), but is in fact microcystic on histology. Micscoscopically, there is an excess of bronchiolar structures separated by air spaces that resemble late foetal lung. There is virtual absence of small, medium and large pulmonary arteries within the lesion.

**Type IV CPAM**

Type IV CPAM are peripheral thin walled cysts that are often multiloculated (Fig. 24 on page 30, Fig. 25 on page 31, Fig. 26 on page 32). They are lined by type I or II alveolar type cells with the intervening stroma being thin and comprising loose mesenchymal tissue (Fig. 27 on page 33, Fig. 28 on page 34). There is concern that a spectrum of disease may exist between these lesions and pleuropulmonary blastomas (PPBs). PPB is the most frequent malignancy associated with paediatric lung cysts (Fig. 29 on page 35, Fig. 30 on page 36). Imaging alone cannot differentiate benign lung cysts from PPBs, and even on histology it is not always possible to distinguish type IV CPAM from PPB. PPB is associated with cystic nephroma in 9.2% of patients [9].

**Associations/Complications**

CPAMs are occasionally associated with cardiac defects, facial clefts, neural tube defects, renal dysplasia and agenesis and omphalocele. CPAMs are also associated with recurrent pneumothoraces. As mentioned above, there remains a concern of possible malignant transformation despite its rarity (e.g. bronchioloalveolar carcinoma, rhabdomyosarcoma, pulmonary blastoma, and mucinous adenocarcinoma). However, for most CPAM types there is no increased risk [11].

**Prognosis**

Antenatal indicators of poor prognosis include large lesions, bilateral lung involvement and hydrops fetalis. Pulmonary hypoplasia seen with larger lesions is a common cause of neonatal death.

**Postnatal treatment decisions**

Treatment decisions depend on the patient's presentation. Symptomatic patients with large CPAMs exerting mass effect and recurrent infections will be referred for consideration of surgery. However, the decision making is less clear in asymptomatic
patients. Currently there is little consensus in the literature regarding recommendations for timing of surgery in asymptomatic CPAM patients. There are advocates for both surgical intervention and conservative watchful waiting. Asymptomatic patients may eventually become symptomatic, and there is a school of thought that surgery could prevent non-malignant complications and possible malignant transformation. Surgeons may opt to delay surgery to allow for optimal lung development in infants and children. A recent metaanalysis has concluded that nearly 50% of patients may remain symptomatic, and of these 3% will develop symptoms as infants while under active nonintervention. Elective surgery has a better outcome than emergency surgery, and should be taken into consideration. Surgery is generally undertaken before 10 months of age [10]. Surgical decisions remain difficult, and complete removal does not prevent neogenesis [11,12]. It is still unclear whether lung cancers cause cysts, or if congenital cysts eventually develop into lung cancer.
Fig. 1: Mindmap approach to CPAM

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### Revised classification of Stocker (2002) CPAMs

<table>
<thead>
<tr>
<th>Inc.</th>
<th>Gross Appearance</th>
<th>Microscopy</th>
<th>Other features</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>1-3%</td>
<td>Solid. The lungs are small and firm throughout.</td>
<td>Bronchial airways with cartilage, smooth muscle and glands separated by abundant mesenchymal tissue</td>
</tr>
<tr>
<td>1</td>
<td>60-70%</td>
<td>Large cysts (up to 10cm)</td>
<td>The cysts are lined by pseudostratified ciliated cells that are often interspersed with rows of mucous cells</td>
</tr>
<tr>
<td>2</td>
<td>10-15%</td>
<td>Sponge-like multiple small cysts (&lt;2cm) and <strong>solid</strong> pale tumour-like tissue</td>
<td>The cysts resemble dilated bronchioles separated by normal alveoli Striated muscle in 5%</td>
</tr>
<tr>
<td>3</td>
<td>5%</td>
<td>Solid</td>
<td>Excess of <strong>bronchiolar structures</strong> separated by small air spaces with cuboidal lining (fetal lung)</td>
</tr>
<tr>
<td>4</td>
<td>15%</td>
<td>Large cysts (up to 10cm)</td>
<td>The cysts are lined by a flattened epithelium resting upon loose mesenchymal tissue</td>
</tr>
</tbody>
</table>

**Fig. 2:** Revised Stocker classification of CPAM from 2002

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Fig. 3: Type 0 CPAM - Bronchial type airways and abundant mesenchyme

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Fig. 4: 11 year old child in whom CPAM was diagnosed antenatally. Patient had been well, until he presented with drowsiness and reduced appetite. Interestingly the typical clinical findings of fever or cough was absent.

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Fig. 5: The same 11 year old child had a CT after symptoms had subsided. It demonstrated a large cystic component compatible with type I CPAM.

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Fig. 6: CT of the same 11 year old child. In addition to the large cystic component (shown in Fig 6), the inferior slices demonstrated areas of hyper trans-radiancy, which contained a brochocele.

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**Fig. 7:** MIP images of the same 11 year old child with type I CPAM and a bronchocele.

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Fig. 8: This infant had no previous medical history, but became unwell with respiratory tract infections at 8 months. The initial chest radiograph showed a well defined centrally lucent lesion which was initially presumed to be an abscess.
Fig. 9: Axial CT of the same 8 month old infant, showing a large cystic lesion containing an air fluid level.

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Fig. 10: Sagittal reconstructions of the same 8 month old child, again demonstrating an air fluid level. Note the low attenuation adjacent to the lesion which is occasionally found in CPAM. They are due to tiny areas of cysts with thin-walled bronchiolar structures that blended with lung parenchyma.

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Fig. 11: 18 year old female who was a keen diver with a background of asthma. She presented with recurrent pneumothoraces, in this instance on the left.

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Fig. 12: Same 18 year old female. Left sided chest drain was inserted.

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Fig. 13: CT of the 18 year old diver. Left lower lobe cystic lesion with an area of adjacent low attenuation lung parenchyma. Histology showed a large cyst filled with inspissated mucus, with local inflammatory reaction where mucus has extravasated locally. The surrounding lung contains irregular cystic spaces lined by bronchial epithelium with intervening alveolar tissue showing marked secondary inflammation. Histology features best fit those of type I CPAM.

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Fig. 14: Same 18 year old patient with coronal reconstructions.

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Fig. 15: Pathology specimen of a type I CCAM demonstrating a large cystic lesion (>2cm).

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Fig. 16: A different patient with type 1 CPAM, who developed a complication of pneumothorax. Note left sided chest drain.

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Fig. 17: There is a risk of malignant transformation of type I CPAM into an adenocarcinoma. This is a CT of a patient with type I CPAM changes in 1991.

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**Fig. 18:** This is the same patient in 2001. Multiple right sided pulmonary lesions proven to be adenocarcinoma. Note that the left CPAM cystic changes have become more fluid filled and confluent.

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Fig. 19: 3 year old female child who had been diagnosed with CPAM at 22 weeks during an antenatal ultrasound scan. She was monitored and did not require any hospital admissions. Note the relatively innocent chest radiograph.

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**Fig. 20:** CT of the same 3 year old patient after a period of watchful waiting. The post-operative diagnosis is a type II CPAM.

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Fig. 21: Chest radiograph of a different patient eventually diagnosed with type II CPAM. Note the right lower zone consolidation and increased lucency.

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Fig. 22: CT of the same patient with right lower zone changes, histologically diagnosed as type II CPAM. The cysts are smaller. Again note the lowered lung attenuation in the right lower lobe.

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**Fig. 23:** CT of a Type III CPAM with solid appearances.

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Fig. 24: Radiograph of a type IV CPAM in a young child. There is increased radiolucency of the right hemithorax and volume expansion.

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Fig. 25: CT of the same patient with type IV CPAM, demonstrating thin walled multiloculated cysts.

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Fig. 26: Bubbly macroscopic appearance of type IV CPAM.

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**Fig. 27:** Type IV CPAM demonstrating "bland cyst walls".

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Fig. 28: Type IV CPAM shows multiple large thin walled cysts lined by flattened alveolar epithelium. The underlying stroma shows loose mesenchymal tissue with no hypercellular areas.

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Fig. 29: CT of a patient demonstrating bilateral cystic lesions, and was diagnosed with "congenital cysts".

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**Fig. 30:** CT of the same patient 2 years later, which showed a large soft tissue mass in the right hemithorax. Macroscopic appearances as shown, which had a histological diagnosis of PPB.

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**Fig. 31:** Macroscopic sample from a different patient - PPB cystic type.

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Conclusion

CPAMs are detected more frequently in the era of prenatal US. Chest radiographs and CTs are the common postnatal imaging modalities. Radiologists should be aware of the imaging features and potential implications. Currently there is no unified strategy for investigation and surgery, and management decisions vary among institutions.
References