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Long term respiratory outcomes of congenital thoracic malformations

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SUMMARY

The advent of universal antenatal ultrasonography in many countries has revealed the full spectrum of congenital thoracic malformations (CTMs) and presented clinicians with a number of practical dilemmas to do with diagnosis and management. We present a review of the most common forms of CTMs, including congenital cystic adenomatoid malformation, bronchopulmonary sequestration, and lobar and segmental emphysema.

1. Introduction

The term congenital thoracic malformation (CTM) is an umbrella phrase for developmental lesions present at birth derived from lung and its adnexal tissue, but which confers no actual histological meaning or implied derivation. Included under this umbrella are true pulmonary parenchymal lesions such as the various types of congenital cystic adenomatoid malformation (CCAM), extra- and intralobar bronchopulmonary sequestration and congenital lobar and segmental emphysemas together with less common entities such as foregut duplication and bronchogenic cysts. The characteristics of each will be outlined later.

The aim of this review is to summarise our current understanding of such lesions with a focus on what may happen outside of infancy to those who have been treated to the usual therapy – surgical resection – and those where a more conservative approach has been taken.

2. Incidence

The European Surveillance of Congenital Anomalies (EUROCAT) was established in 1979 with the aim of providing a network of population-based registers for the epidemiological surveillance of congenital anomalies. Data have been collected from 43 European registries in 20 European countries with an estimated capture of about 29% of Europe's birth population.[1] The EUROCAT database showed that in 2008, there were 222 fetuses with a CTM, which worked out as an incidence of 4.44 per 10,000 fetuses and translated to an incidence of 3.52 per 10,000 live births. During that year the estimated incidence of CCAM was 0.7 per 10,000 live births, or about one-quarter of all CTMs.

3. Common origin of congenital thoracic malformations

It is thought that lung parenchymal malformations although superficially heterogeneous in appearance, share a common embryological origin and have significant overlap. Although not an original concept, Langston re-proposed that disordered parenchymal development might be attributed to in-utero airway obstruction,[2] with the level, timing and the completeness of the obstruction producing different patterns of lung malformation. There is histological evidence for peripheral bronchial atresia/stenosis in many apparently separate entities,[3] but the mode and timing of these events is still speculative.

4. Congenital cystic adenomatoid malformation (CCAM)

The first clinical report by Ch'in and Tang of what was termed congenital adenomatoid malformation appeared in 1947.[4] In 1975, Garrett et al.[5] first reported the antenatal detection of a CCAM using greyscale ultrasound which heralded the current era in which >90% of lesions are detected in antenatal screening programmes. Although early reports in the obstetric literature[6–8] were characterised by large lesions, a marked association with other abnormalities and a poor prognosis, we now realise that the majority are relatively small lesions, which are usually asymptomatic, at least in early postnatal life.[9,10]

CCAMs appear to be derived from the proliferation of peripheral bronchiolar tissue at the expense of alveolar tissues with a single

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lobe affected in >95% of cases with no particular preference for side,[9–12] though there is a predilection for the basal lobes. Bilateral lesions are uncommon (<3%) and usually have a poor prognosis.[7]

The original Stocker classification[13] was based on postnatal histology and originally divided CCAMs into three types (1, 2 and 3). Subsequently the rarer types 0 and 4 were also proposed, expanding the classification so that type 0 was an essentially tracheobronchial defect (also known as acinar dysplasia) and characterised by firm small lungs with a bronchial airway; and type 4 an entirely alveolar defect occurring at the periphery of the lungs.[14] It is noteworthy that only types 1–3 are adenomatoid and only types 1, 2 and 4 are cystic and it is also noteworthy that Stocker himself proposed a new name for such lesions – congenital pulmonary airway malformation (CPAM) – although whether this will replace CCAM only time will tell. Type 4 CCAM is a more controversial entity as its features overlap with type 1 pleuropulmonary blastoma, the only distinguishing feature being a lack of blastema in type 4 CCAM.[15] The current characteristics of the classification are summarized in Table 1.

4.1. Clinical features

As befits the complexity and variation in pathology, the nature of clinical features also varies considerably. In fetal life, large space-occupying lesions (of whatever histology) may cause mediastinal shift, impairment of venous return and hydrops leading to fetal demise typically in the third trimester.[6,7] A proportion (<20%) will cause early respiratory distress within the first month after birth requiring early surgical excision.[8–10,16] The remainder are asymptomatic but are prone to develop infection (pneumonia, lung abscess, empyema, etc.) and occasionally cyst rupture leading to pneumothorax. A recent systematic literature review has suggested that the median age of symptom development in this group was about 10 months.[17] The malignant potential of such lesions will be addressed in detail later.

5. Bronchopulmonary sequestrations

Bronchopulmonary sequestrations were first termed 'accessory pulmonary lobes' by Rokitansky in 1861, but later renamed 'pulmonary sequestration' by Pryce in 1946.[18,19] These lesions are composed predominantly of solid lung tissue with no bronchial communication and the arterial blood supply is derived from systemic rather than pulmonary blood vessels (e.g. the aorta). There is a long-standing classification of sequestrations into intralobar and extralobar types dependent on appearance.

- Intralobar sequestration (ILS): often embedded in normal parenchyma and covered by visceral pleura in continuity with the normal lung. The venous drainage is usually into the pulmonary vein.
- Extralobar sequestration (ELS): invariably solid with its own separate pleural covering, separate from the normal lung.

Most sequestrations are medio-basal in location (left > right) and about 10% are actually located below the diaphragm.[20] ELS may be found in association with diaphragmatic hernias, but other anomalies are less common (e.g. chest wall anomalies, vertebral deformities, hindgut duplications and congenital heart disease).

Very large sequestrations can act as space-occupying lesions and diminish respiratory reserve but most appear silent. A peculiar complication, not seen with CCAM, is high output cardiac failure associated with the sequestration's redundant circulation and occasionally massive left-to-left shunt. Some of these will present during the antenatal period[21] with hydrothorax and pleural effusion, requiring in-utero drainage. A novel approach to some obvious echogenic lesions (usually thought to be sequestrations) has been in-utero laser ablation.[22]

6. Hybrid lesions

This term refers to the overlap between CCAM and sequestration.[23] Several surgical series have shown that some lesions do not fit neatly into the above two categories and are usually labelled hybrids.[9] Features might include:

- Anatomical ELS but with histological appearance more compatible with CCAM;
- ELS and CCAM occurring in the same patient;
- Obvious CCAM lesions in a lobe but with an accessory systemic blood supply.

7. Lobar and segmental emphysema

Congenital lobar emphysema (CLE) is characterised by hyperinflation of one lobe (rarely more), secondary to bronchial obstruction (perhaps due to a cartilage defect) with a resulting ball-valve effect.[24,25] It usually affects the left and right upper lobes and tends to present early with respiratory distress, tracheal and mediastinal displacement. CLE also seems to appear relatively infrequently in the larger series of antenatally detected CTMs, suggesting that their prenatal ultrasound appearance is relatively innocuous.[9]

Table 1
Congenital pulmonary airway malformation: current classification.[14]

Type	Incidence	Cyst size and character	Histology	Notes
0	Rare		Complete failure of development beyond pseudoglandular stage.	Congenital acinar dysplasia (lethal)
1	Common	Large (>2 cm), can be multiple.	Pseudostratified ciliated columnar epithelium, interspersed with rows of mucous cells.	
2	Common	Multiple small cysts, 'sponge-like'	Dilated bronchiole-like structures interspersed by simplified alveolar parenchyma. Occasional striated muscle.	
3	Rare	Solid	Bronchiolar structures are separated by small air spaces with cuboidal lining resembling late fetal lung.	
4	Rare	Large cysts	Peripheral and lined by alveolar or bronchiolar epithelial cells resting upon loose mesenchymal tissue.	Related to regressed and grade 1 PPB

PPB, pleuropulmonary blastoma.