Developmental Lung Lesions

13

Pablo Laje

13.1 Embryology

The development of the human lung goes through six separate stages to form a mature tracheobronchial progression of each stage highly coordinated process and guided by mesenchymal–epithelial interactions under the influence of a number of regulatory growth factors (Table 13.1).

Most lung lesions appear to develop at different time points during the **pseudoglandular stage**, with the exception of pulmonary agenesis, which occurs during the **embryonal stage**.

Table 13.1 Development of the lung

Stage	Gestational age	Description
Embryonic	26 days to 6 weeks	From formation of laryngotracheal bud arising from the anterior portion of the aerodigestive tract to division into lobar and segmental bronchi
Pseudoglandular	5–16 weeks	Development of the preacinar airways and blood vessels, growth of the bronchial tree, and development of all bronchial divisions
Canalicular	16–24 weeks	Capillary growth toward the respiratory epithelium marking the future blood–air interface
Saccular	24–36 weeks	Widening of peripheral air spaces distal to the terminal bronchioles with septa formation
Alveolar	36–term	Formation of secondary septa and budding alveoli
Microvascular	Up to 2 years post-natal	Further alveolar development and maturation

P. Laje (✉)
Division of General, Thoracic and Fetal Surgery, Children's Hospital of Philadelphia, Philadelphia, PA, USA
e-mail: LAJE@email.chop.edu

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13.2 Prenatal Diagnosis

Ultrasonography (US) is usually the first step in the prenatal evaluation of a congenital lung lesion. Serial scans are important to evaluate the prenatal behavior of the lesions, allowing planning of the pre-, peri-, and post-natal management on a case-by-case basis. We routinely perform fetal **ultrafast magnetic resonance imaging (fMRI)** on all cases of prenatally diagnosed lung lesions to define further their anatomy, to evaluate the potential effects that the lesions can exert on surrounding structures, and to search for associated anomalies. That being said, since the quality of the high-resolution U/S images improves constantly, the need for a fMRI in this context is declining.

13.3 Pulmonary Agenesis

- True pulmonary agenesis is quite rare, but varying degrees of hypoplasia are not that uncommon.
- Spectrum varies from blind-ending main bronchus with no lung tissue to malformed bronchus and poorly developed lung tissue.
- Cardiac, GI, GU, or skeletal anomalies may be present (~50%).
- Prognosis depends (1) degree of hypoplasia, (2) degree of development of contralateral lung, (3) lung volume, and (4) prognosis of their associated anomalies.
- Overall mortality ranges from 70 to 95%.

13.4 Bronchopulmonary Sequestration (BPS)

Definition
Nonfunctioning mass of lung parenchyma, isolated from the normal tracheobronchial tree, with an independent arterial blood supply arising from systemic circulation.

The venous drainage is a BPS is common to the azygous or hemizygous veins, but can also be to the pulmonary veins (Fig. 13.1). There is an exaggerated yet futile circulation through the BPS, out of proportion to the actual volume of lung tissue supplied.

BPS are subdivided into two types:

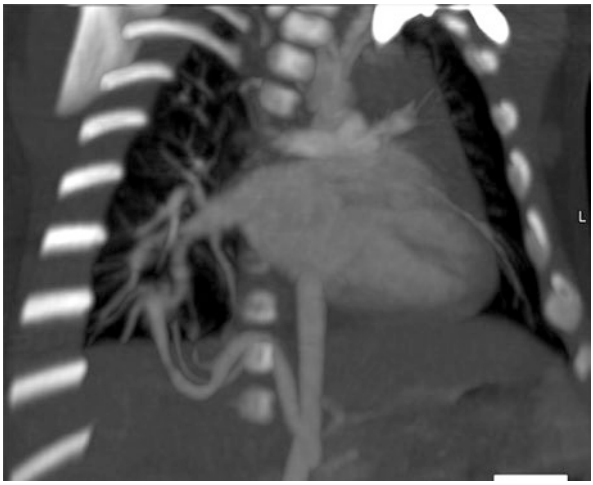

Fig. 13.1 Right lower lobe. Intralobar sequestration showing a large systemic vessel arising from the abdominal aorta, and drainage into the inferior pulmonary vein

- ***Extralobar sequestration*** (75%)—separate investment of pleura and completely isolated from other lobes.
  - Commonly located in the lower hemithorax.
  - Males >> females.
  - Occasionally are associated with diaphragmatic hernias.
  - Can be located within, or even below the diaphragm.
- ***Intralobar sequestration*** (25%)—shared pleura with the surrounding lung, and are an integral part of the lobe in which they are located.
  - May have CCAM features, in which case the lesion is called **"hybrid lesion."**

13.4.1 Clinical Features

Most are detected by routine antenatal US. They rarely cause prenatal symptoms such as hydrothorax due to the presence of lymphatic congestion. Postnatally, most are asymptomatic (particularly the extralobar BPS), but a number of complications can develop:

- Infection—despite lack of bronchial connection but more common in intralobar BPS.
- High-output cardiac failure: tachypnoea, tachycardia, cardiomegaly. Occurs as a result of the high-volume shunt caused by the systemic perfusion.

13.4.2 Postnatal Investigations

- CXR—typically solid, basal lesion.
- CT (with IV contrast) scan.

13.4.3 Postnatal Management

- Symptomatic BPS needs a surgical resection, either by thoracotomy or by thoracoscopy.
- Asymptomatic BPS can be resected surgically or managed expectantly. The approach varies widely around the world, and there is no consensus on what happens in the long-term to lesions that are not resected.

13.5 Congenital Cystic Adenomatoid Malformation[1]

Definition
A multicystic mass of lung parenchyma with an overgrowth of immature bronchioles and a paucity of alveoli.

13.5.1 Classification

The original classification of Congenital Cystic Adenomatoid Malformation (CCAM) was based on histological assessment of resected lung tissue and popularized[2] by Col. JT Stocker who divided CCAMs into three types depending on their location, cystic structure, size, and epithelial lining. This was enlarged with the addition of two further categories on either side to retain the original I–III numbering system (Table 13.2).

For those where the first contact was often antenatal and in the absence of a resection a furthermore pragmatic classification emerged (Adzick[3] Classification). This is simply based on the size of the cysts as assessed at prenatal US:

(i) **Macrocystic lesions** (≈ 75% of cases) which contain a dominant cyst or multiple cysts that are ≥5 mm in diameter.
(ii) **Microcystic lesions** (≈ 25% of cases) presenting as a solid echogenic mass or multiple cysts <5 mm diameter.

We believe that this classification has a more accurate correlation with the potential clinical presentations and the potential management strategies (Figs. 13.2 and 13.3). As mentioned above, CCAMs can have aberrant systemic vasculature, and these are referred to as hybrid lesions.

[1] **Terminology:** CPAM is clearly replacing CCAM as the phrase of choice, though originally used an umbrella term for all these developmental lesions it is coming to be a synonym for CCAM.

[2] J. Thomas Stocker—pathologist at Armed Forces Institute of Pathology (to 2011), Washington DC.

[3] N. Scott Adzick—pediatric surgeon at Children's Hospital of Philadelphia.

Table 13.2 Stocker histological classification of CCAM (aka CPAM)

Type	%	Histology	Appearance	Notes
0	<2	Acinar dysplasia	Solid	Usually fatal
I	50	Pseudostratified ciliated columnar epithelium	Single/multiple >2 cm diameter	
II	45	Ciliated columnar/cuboidal epithelium	Multiple small cysts <2 cm diameter	
III	<5	Cuboidal epithelium	"Solid," multicystic V small <2 mm cysts	
IV	<2	Alveolar epithelium	Multiple thin-walled cysts	Merges into Pleuropulmonary blastoma (PPB)

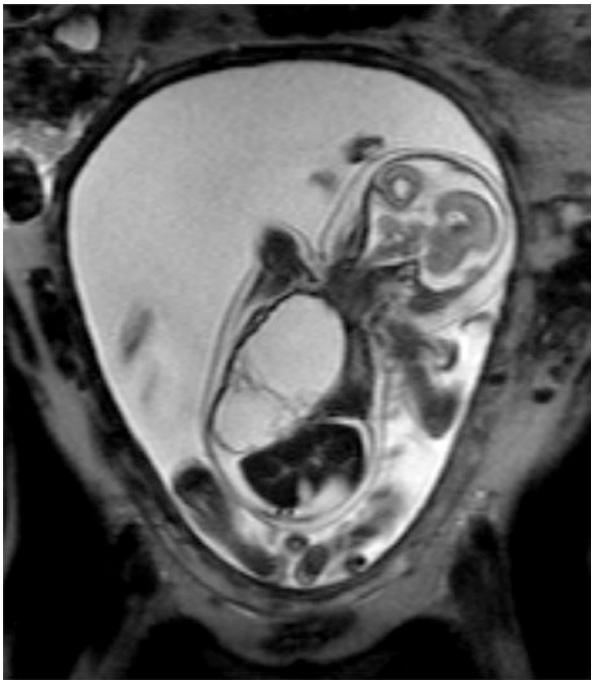

Fig. 13.2 Macrocystic CCAM on the right side, causing hydrops fetalis

Diagnosis: Most CCAMs are nowadays detected on prenatal US. Fetal ultrafast magnetic resonance imaging (fMRI) can be used to further define the anatomy, to evaluate the potential effects on surrounding structures, and to search for associated anomalies. Close US surveillance throughout the pregnancy is important to detect early those lesions that can cause fetal distress, allowing a proper perinatal management.

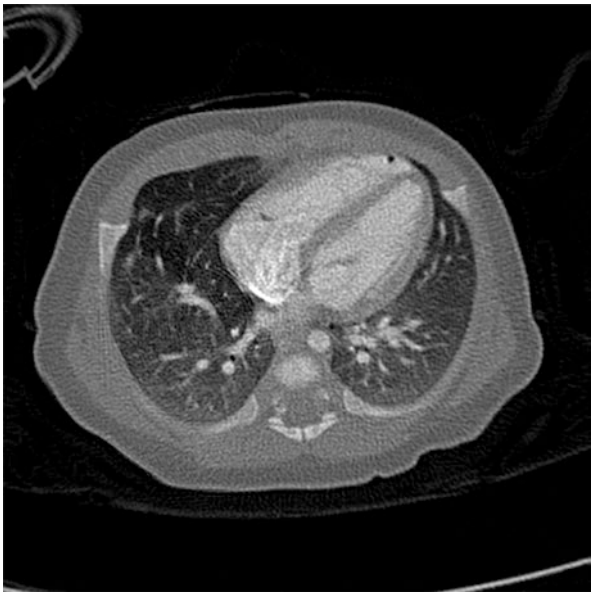

Fig. 13.3 Microcystic CCAM on the right upper lobe, on a postnatal CT scan

13.5.2 Clinical Presentation

- Most CCAMs are asymptomatic during the prenatal life.
- CCAMs that have rapid growth can cause mediastinal shift, hydrops fetalis, and death.
- Postnatally, large lesions can cause severe respiratory distress, requiring immediate postnatal resection. More commonly, CCAMs remain asymptomatic.
- Potential complications that can occur over time are: pneumothorax, infections, rapid expansion with respiratory distress, and malignant transformation.

13.5.3 Management

- The prenatal and perinatal behavior of a CCAM can be somewhat predicted by correlating its size to the size of the fetus' head (c.f. congenital diaphragmatic hernia).
  - Formula of the volume of an ellipsoid, and the size of the head is calculated by measuring its maximum circumference. These two measures generate the **"CCAM volume / head circumference ratio," or CVR.** The higher the CVR, the worse the prognosis.
  - Lesions with a CVR > 1.6 are likely to cause hydrops, and need to be evaluated frequently by ultrasound (i.e., 2–3 times per week).
  - Lesions with a CVR < 1.2 can be evaluated once every 2 weeks.

- Hydrops fetalis respond well to the maternal systemic corticosteroids. If there is a dominant large cyst, a percutaneously-placed "thoraco-amniotic" shunt can reverse the hydrops. Fetal resection is an option in very selected cases, but is almost anecdotal nowadays, with the discovery of the remarkable response to steroids.
- Postnatally, any symptomatic CCAM should be resected without delay, either by thoracotomy or by thoracoscopy. The best technique is the one with which the surgeon feels more comfortable with.
- The management of asymptomatic CCAMs is somewhat **controversial** (understatement!). Many centers around the world recommend resecting all lesions within the first 3 months of life, to eliminate all risks, and to provide maximum time for compensatory lung growth. Others advocate for resection around 12 months of age. Finally, many centers recommend observation alone, under the assumption that many cases will never develop symptoms. In our view, the presence of systemic vessels in CCAMs/hybrid lesions is an indication for a resection, since there is no justification to perpetuate the redundant work-load of the heart.
- CCAMs can develop a variety of unusual malignancies, including bronchioalveolar carcinoma, and pleuropulmonary blastoma (DICER 1 +ve) (Table 13.3).

Table 13.3 Malignancies associated with developmental lung pathology

Malignancy	Histology	Stocker type	Notes
Pleuropulmonary blastoma *Former terms—rhabdomyosarcoma, embryonal sarcoma*	*DICER1* mutations on Ch14q32.13 *Arises from mesenchymal supporting tissues*	Histological overlap with Type IV CCAM	< 4 years age I—multicysts Ir (regressed) II—cystic +solid III—solid only
Mucinous (mBAC)* *[invasive mucinous adenocarcinoma]*	*KRAS* mutations on Ch12.21–25 Arises from bronchiolar cells	Type I CCAM	Predominantly adult onset, though neonates have been reported
Non-mucinous (nmBAC) *[lepidic-predominant adenocarcinoma]*	Arises from Clara pneumocytes		Adult onset
Mucoepidermoid carcinoma		Type I CCAM	V. rare
Squamous cell carcinoma		Bronchogenic cyst	V. rare
BAC			V. rare
Leiomyosarcoma			V. rare

*Current terminology is confusing and prone to change. Historic terms are given together with current (after 2011 IASLC) nomenclature, e.g., [lepidic-predominant adenocarcinoma]
BAC—Bronchoalveolar (or Bronchioloalveolar) carcinoma

13.6 Congenital Lobar Emphysema

Definition
Overexpanded lobe (or segment) caused by a valve-like mechanism, either at the level of the bronchioles (due to bronchomalacia), or at the level of larger bronchi (due to intraluminal lesions or external compression).
Congenital or acquired.

13.6.1 Clinical Features

- LU lobe > RM lobe > RU lobe (classically).
- M:F 2:1.
- Presents during infancy with tachypnoea, especially during feeding, wheezing. Cyanosis may be seen. Signs include ipsilateral ↓ breath sounds, tracheal and mediastinal displacement. The clinical picture varies widely, from asymptomatic, to severe respiratory distress.
- CXR—hyperlucent with faint bronchovascular markings. Sometimes, there is lung herniation into the mediastinum.
- CT—The involved lobe appears hypodense in comparison with the normal lung.

13.6.2 Management

- **Lobectomy**—This is distinctly easier using an open thoracotomy and probably the thoracoscopic option is contraindicated.
- In cases that asymptomatic or mildly symptomatic, Congenital Lobar Emphysema (CLE) can be observed for some time, and operated on an elective basis. Symptomatic cases need, however, prompt resolution.

There is also a newly described variant affecting the distal segmental bronchi—here termed ***congenital segmental emphysema***. All cases have been detected prenatally with a variety of features and some exhibited postnatal expansion, often after several years. There is often a central mucus-filled cavity termed a bronchocele, which is the result of the accumulation of mucus within an atretic bronchus. Treatment is surgical excision.

13.7 Bronchogenic Cyst

Definition
Bronchogenic cysts are solitary lesions filled with mucous that result from abnormal budding of the foregut primordium.

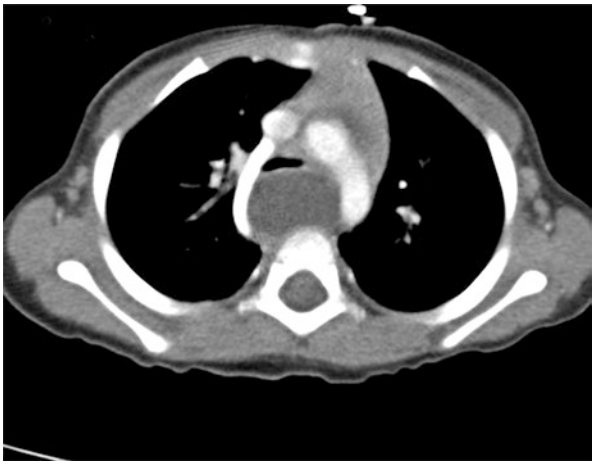

Fig. 13.4 Bronchogenic cyst located behind the carina

13.7.1 Clinical Features

- M = F.
- Usually there is no communication with the lumen of the normal airway.
- Most are located in the mediastinum, adjacent to a major airway (85%).
- Some are located within the lung parenchyma (15%) (Fig. 13.4).
- Small bronchogenic cysts are not visible by CXR. Large ones may present as a radio-opaque shadow. CT and MRI are excellent studies to delineated the exact anatomy.

Clinically, most bronchogenic cysts remain silent for a long time. In the current era, most are detected incidentally before birth.

Potential complications are: infection, compression of adjacent organs such as the airway or the esophagus), internal bleeding (rare), and malignant transformation (rare).

13.7.2 Management

- The treatment is always a surgical resection, via thoracotomy or via thoracoscopy.

Further Reading

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