2 Congenital Cystic Adenomatoid Malformation of the Lung

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Introduction

Congenital cystic adenomatous malformations (CCAMs) of the lung represent the most common lung defect diagnosed prenatally.

CCAMs are intrapulmonary lesions with a typical hyperechoic appearance on ultrasound (US), with or without cystic components. Both sides of the lung, both sexes, and all races are equally affected. Most fetuses with CCAM are detected prenatally and have a good outcome, but appropriate identification and ongoing surveillance are required because of the unpredictability of growth patterns for CCAM masses.

Disorder

DEFINITION

CCAM is a developmental, nonhereditary, usually mixed (solid and cystic) lung mass consisting of abnormal hamartomatous or dysplastic lung tissue and bronchoalveolar structures thought to result from abnormal branching of the immature bronchioles during early stages of lung morphogenesis.[1]

PREVALENCE AND EPIDEMIOLOGY

CCAM is the most common fetal hyperechogenic lung lesion and accounts for 50% to 75% of detected fetal lung abnormalities.[2] These lesions may display dramatic changes during pregnancy, with spontaneous regression and total resolution in more than half of cases.[3,4] Thus, postnatal studies probably underestimate the real incidence of lung lesions, with a commonly quoted incidence of 1:25,000 to 1:35,000.[5] In prenatal studies performed in nonreferred populations, an incidence of 1:4000 to 1:6000 has been reported.[6] Prenatal diagnosis has dramatically increased as a result of improvement of US equipment over time, so the precise prevalence of prenatal CCAM is still unknown and might change in the future.

ETIOLOGY AND PATHOPHYSIOLOGY

CCAM is characterized by lack of normal alveoli and originates from a dysplastic overgrowth and cystic dilatation of terminal bronchioles with various types of epithelial lining.

CCAM may have a mainly solid, mainly cystic, or mixed appearance. Stocker et al.[7] described three types of lung lesions based on cyst diameter, which probably represent differences in the origin of the dysplastic lesion in the bronchial tree levels.

- *Type I* macrocystic CCAMs are characterized by single or multiple cysts greater than 2 cm in diameter, lined by ciliated pseudostratified columnar epithelium. These represent nearly 50% of CCAM cases in postnatal series. They frequently cause mediastinal compression, are rarely associated with other anomalies, and generally have a good prognosis.
- *Type II* lesions account for up to 40% of CCAMs, are single or multiple cysts less than 2 cm in diameter, and are lined with mixed ciliary, columnar, and cuboidal epithelium, with a thin underlying fibromuscular layer.
- *Type III* lesions are microcystic, predominantly solid lesions, with small cysts (<0.5 cm). These lesions represent 10% of CCAM lesions and are histologically composed of alveoluslike structures lined by ciliated cuboidal epithelium separated by microscopic masses lined with nonciliated cuboidal epithelium.

Thus, type I represents an anomaly of the more proximal part of bronchial tree, the principal bronchioles, whereas type III represents changes in the distal most peripheral alveolar tissues. Types II and III are more frequently associated with other anomalies and have graver prognosis.

Stocker et al.[7] later expanded his classification to include another two types. Type 0, acinar dysplasia or agenesis, is very rare, involves all the lung lobes, and is incompatible with life. Type IV CCAM lesions are represented by large, thin-walled peripheral cysts caused by hamartomatous malformation of the distal acinus.

Another, more clinically appropriate classification, based on US appearance, was introduced by Adzick et al.,[8] who divided prenatally diagnosed lung lesions into two groups: *macrocystic* (type I), with cysts greater than 5 mm, which is seen on US as a cystic mass, and *microcystic* (type II) with cysts smaller than 5 mm, which appear as solid echogenic lesions on US. The presence or absence of cysts is important because this determines options for therapy in cases of fetal hydrops.

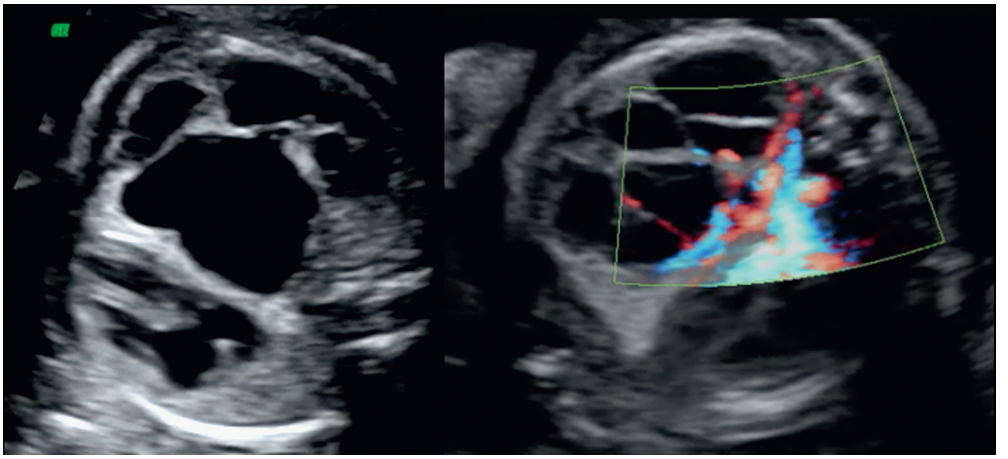

Fig. 2.1 US image of a 22-week fetus with a large macrocystic CCAM in the left lung. Significant mediastinal shift and pulmonary blood supply is note.

MANIFESTATIONS OF DISEASE

Clinical Presentation

A CCAM appears as a hyperechoic solid or cystic thoracic mass. Cysts may be single or multiple, small or occupying the entire volume of the mass. CCAM is usually unilateral and unilobar, with a slight predilection for the lower lobes of the lung. The mass is usually detected in the second trimester, commonly showing slight growth at the beginning. In half of cases, there is apparent prenatal resolution of the hyperechoic lesion, usually by around 32 weeks' gestation.[3] Large tumors are associated with mediastinal shift with displacement of the heart to the contralateral part of the thorax, flattening of the diaphragm, esophageal compression resulting in polyhydramnios, and direct cardiac compression and obstruction of venous return resulting in rare cases in hydrops fetalis.

The risk of chromosomal abnormalities is not increased significantly in isolated CCAM.[3,8] Associated anomalies are detected in 8%–12% of cases.[9,10] Commonly reported associated anomalies are renal defects, congenital diaphragmatic hernia, tracheoesophageal fistula, and congenital heart defects.[3,11,12]

The prognosis of prenatally diagnosed CCAM lesions depends on the size of the lesion and the degree of pulmonary hypoplasia, existence of associated anomalies, and development of fetal hydrops. Evaluation of the size of the lung mass by means of the *c*ystic adenomatoid malformation *v*olume *r*atio (CVR = length × height × width × 0.52 divided by the head circumference) is useful for predicting the development of hydrops.[13] A CVR greater than 1.6 presents a 75% risk to develop hydrops, whereas a CVR less than 1.5 has a 3% risk of hydrops.

Imaging Technique and Findings

Ultrasound. An echogenic cystic lung mass. The location, size, and existence of discrete lung cysts and blood supply must be evaluated using conventional spectral, color, or power Doppler US. Type I lesions are predominantly cystic masses with large cysts (Fig. 2.1), type II lesions are predominantly solid masses with small cysts (Fig. 2.2), and type III lesions are solid, homogeneous, hyperechoic masses (Fig. 2.3).

In all CCAM types, blood supply is classically from pulmonary vessels, but sometimes the masses may have a systemic vascular supply, similarly to bronchopulmonary sequestration (BPS)

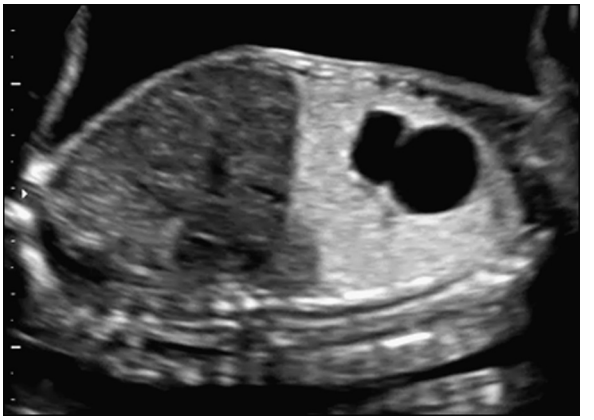

Fig. 2.2 Sagittal section of a large CCAM with a mostly solid component but two medium-sized cysts.

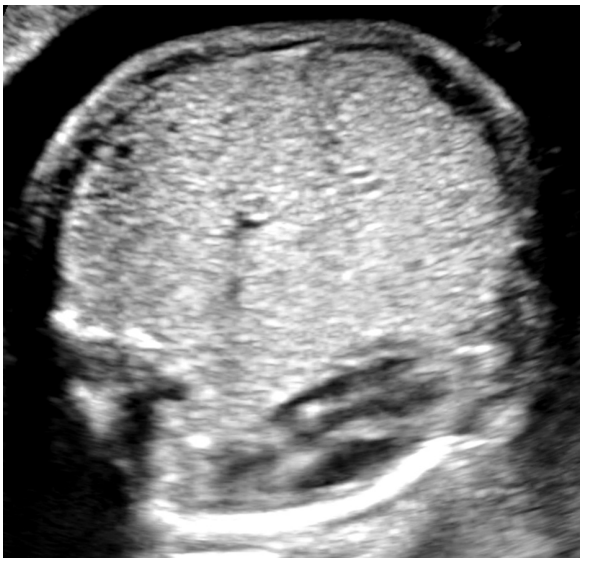

Fig. 2.3 Axial section of a large microcystic CCAM. There is a uniformly hyperechoic solid mass in the left lung, which creates a significant mediastinal shift. The right normal lung is virtually invisible behind the heart.

(Chapter 3), and these are termed *hybrid CCAM-BPS lesions* (Fig. 2.4).

The work-up should include fetal echocardiography and comprehensive sonographic evaluation to rule out associated anomalies, hydrops and early manifestations of cardiac decompensation, such as appearance of tricuspid regurgitation, Doppler abnormalities of ductus venosus flow, and polyhydramnios. Karyotyping should be seriously considered, especially in cases with associated anomalies.

Fetuses with CCAM must be followed closely. Depending on the type and size of the lung lesion, US surveillance should be scheduled biweekly or weekly.

Magnetic Resonance Imaging. Magnetic resonance imaging (MRI) has been used to evaluate fetal lung masses but has not shown a substantial advantage over US (Fig. 2.5).

CLASSIC SIGNS

Echogenic unilateral, well-defined, solid or cystic lung lesion
Involves part of the lung, with predilection to the lower lobe
Absence of feeding arterial vessels arising from the systemic circulation

Differential Diagnosis From Imaging Findings

Several lung lesions should be considered in the differential diagnosis of CCAM:

1. *Intralobar bronchopulmonary sequestration*. A BPS is usually a well-circumscribed, echogenic solid mass that receives arterial blood from the systemic circulation. This feature is pathognomonic for this condition, but not always easily found. On US, BPS is indistinguishable from microcystic CCAM. As mentioned, cystic lesions clinically and histologically apparent as CCAM may have a systemic blood supply. There is no clear histologic distinction between these two entities and mixed forms (hybrids) are common.[14,15]
2. *Congenital lobar emphysema (CLE)*. CLE is lobar overinflation without destruction of the alveoli, usually located in the upper lobe of the lung. On US, CLE is indistinguishable from microcystic CCAM, and the nature of solid lesions sometimes can only be proven pathologically.
3. *Peripheral bronchial obstruction caused by bronchial atresia or bronchogenic cyst*. This lesion also appears as a solid, echogenic mass, involving a lobe or the entire lung. Dilatation of the

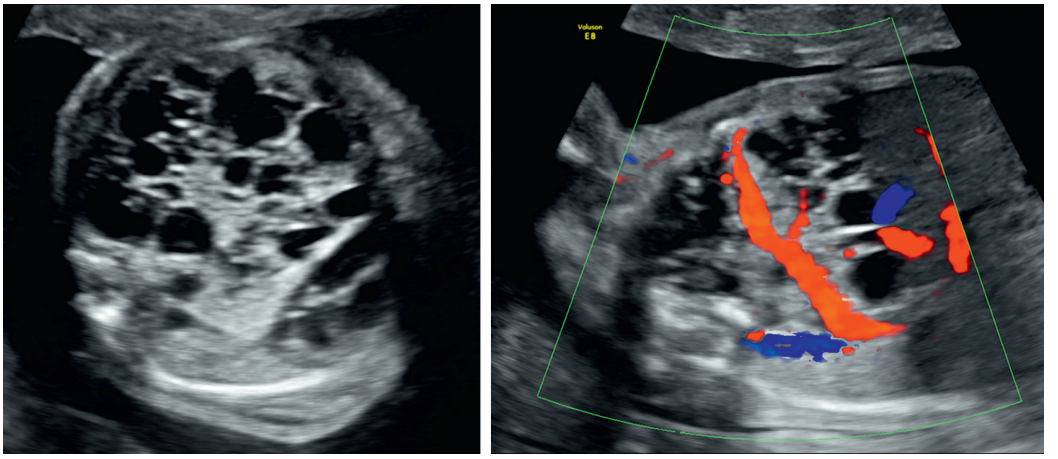

Fig. 2.4 Solid cystic mass in the left lung. Use of color Doppler allows visualization of an arterial supply vessel, which originates directly from the aorta leading to a diagnosis of CCAM-BPS hybrid.

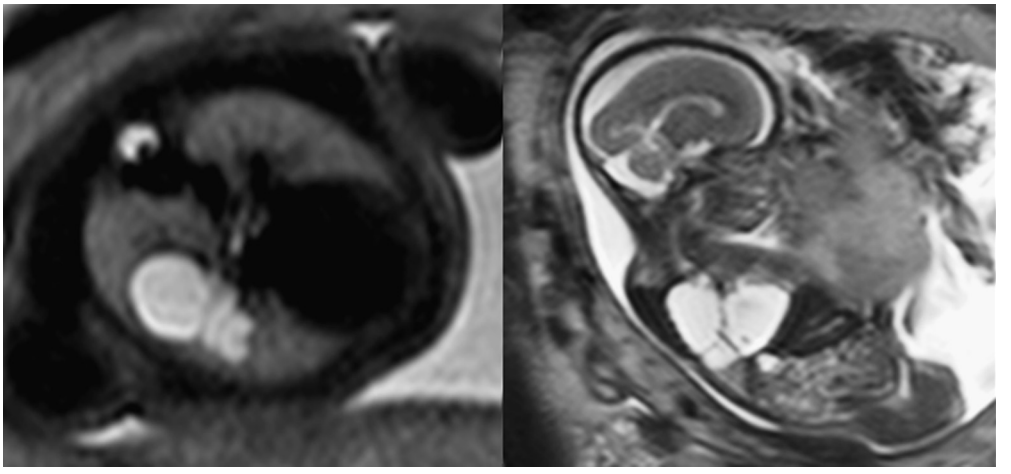

Fig. 2.5 MRI of a 29-week fetus with macrocystic CCAM. The transverse and sagittal views of the fetal thorax show hyperintensive cystic lesions in the right lung.