Findings that shed new light on the possible pathogenesis of a disease or an adverse effect

Antenatal management of pulmonary hyperplasia (congenital cystic adenomatoid malformation)

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Summary

A 26-year-old lady was seen in antenatal clinic. Her anomaly scan at 20 weeks showed significant fetal abdominal ascites and an enlarged echo bright right lung with cardiac displacement. These findings were consistent with recognised type III congenital cystic adenomatoid malformation (CCAM). An induction of labour was undertaken at 32 weeks' gestation due to increasing maternal morbidity. Labour was complicated by abdominal dystocia and a fetal paracentesis was performed, draining 800 ml. A bradycardia developed and the baby was ultimately stillborn. Post mortem examination the right lower lobe bronchus was atretic. The features were typical of those traditionally described as type III CCAM, but in the context of bronchial atresia, are better described as pulmonary hyperplasia.

BACKGROUND

Previously, cases of congenital cystic adenomatoid malformation (CCAM) had been categorised using the classification by Stocker *et al*¹ based on cyst diameter and cyst type. However, some cases of CCAM can be explained by airway atresia or obstruction. It may be that many cases of previously described CCAM are in fact unrecognised bronchial atresia.

CASE PRESENTATION

A 26-year-old lady in her first pregnancy was seen in Antenatal clinic. Her initial booking scan at 8 weeks appeared

normal, however her anomaly scan at 20 weeks showed significant fetal abdominal ascites and an enlarged echo bright right lung with left cardiac displacement. Repeat scans at 21 and 22 weeks showed evidence of nuchal oedema, mediastinal shift and findings consistent with recognised type III CCAM (see figures 1 and 2). Karyotyping was also undertaken, which was normal.

There was no significant medical or social history.

OUTCOME AND FOLLOW-UP

The baby was stillborn. Post mortem examination showed evidence of bronchial atresia of the right lower

Figure 1 Ultrasound image at 21 weeks gestation, longitudinal view. Illustrated appearance of CCAM and liver.

Figure 2 Ultrasound image at 22 weeks gestation, transverse section. Illustrated appearance of the CCAM, fetal heart and spine.

Figure 3 Posterior view showing probe in patent RUL bronchus. LL = left lung, RUL = right upper lung, CCAM.

lobe. In addition the right middle and lower lobes were markedly enlarged. Internally, the intestines and kidneys showed haemorrhagic venous infarction, attributed to impaired venous return due to CCAM (figures 3–5). The

features were typical of those traditionally described as type III CCAM. The mother was fully debriefed following events and required close surveillance for future pregnancies.

Figure 4 Anterior view of removed lungs attached to trachea.

DISCUSSION

CCAM is a hamartomatous abnormality in the development of fetal terminal bronchioles. The estimated incidence is 1:25,000 to 1:35,000.² Stocker *et al*¹ developed a pathological classification for CCAM in 1977, based on cyst diameter and predominant cell types. This classification was subsequently revised to include five groups based on site of origin of the malformation as shown in table 1.³

Although Stocker's classification is useful to some extent for pathological classification, it is now understood that some cases of CCAM can be explained by airway atresia or obstruction.⁴ In bronchial atresia, histological examination of enlarged pulmonary lobes reveals microcystic maldevelopment.⁴ It is likely many cases previously diagnosed as CCAM were actually due to unrecognised bronchial atresia. Histological changes similar to those described in type III CCAM are also seen in laryngeal atresia. It is now recognised that some cystic lesions previously diagnosed as CCAM are in fact forms of cystic pleuropulmonary blastoma.⁵ There are many associated abnormalities with cystic lung malformations, described in table 2.^{6,7}

A recent retrospective case note analysis by Davenport *et al*⁸ in 2004 identified that, out of 67 fetuses with congenital cystic lung disease, 25 had histological diagnoses of CCAM, 6 of pulmonary sequestration but 11 had hybrid features. Many features of the associated cystic lung disease correlated with antenatal ultrasound features (size of cyst [$p=0.03$], in-utero behavior [$p=0.06$], mediastinal shift [$p=0.05$]) and the need for surgery but not with the final histological diagnosis. This highlights the importance of a histological diagnosis within the spectrum of cystic lung disease.

Management of CCAM can be classified as primary or secondary following airway atresia or obstruction, as in this case. Antenatally, such congenital cystic malformations can be complicated by hydrops and mediastinal shift. Depending on the degree of malformation, for example with bronchial atresia, the prognosis can be extremely variable. Mann *et al*⁹ proposed that in fetuses whom develop hydrops by 32 weeks, steroid treatment, delivery and urgent surgical resection of affected lobes improves long-term survival.

Figure 5 Histological RML marked increase in alveolar and bronchiolar spaces.

Table 1 Stocker’s classification of CCAM

Stocker classification	Histological differentiation	Prevalence ()
0	Involved all lung lobes	<2
I	Single or multiple cysts >2 cm in size	60–70
II	Single or multiple evenly distributed cysts <2 cm in size	15–20
III	Solid lesions <0.5 cm size	5-10
IV	Large air filled cysts	<10

Table 2 Associated adnormalities with CCAM

Associated abnormalities
Lung associations
Bronchopulmonary sequestrations
Lobar emphysema
Non lung associations
Renal dysgenesis
Renal agenesis
Intestinal atresia
Oesophageal duplications cysts
Congenital cardiac disease

The role of steroid treatment is itself intriguing. Tsao *et al*¹⁰ found that by administering betamethasone antenatally to fetuses with CCAM and non immune hydrops there was complete resolution of hydrops. Indeed it was reported that all three infants were delivered at term with no respiratory compromise, however this area needs further research owing to the small data sample.

There have been reported fetal interventions in cases of CCAM secondary to airway obstruction such as amnioreduction and thoracoamniotic shunt placement. However, such interventions carry a risk of premature labour and further research is necessary.¹¹

The prognosis of CCAM-like lesions such as bronchial atresia remains controversial. Thorpe-Beeston and Nicolaides¹² highlighted that prognosis was related to associated lung abnormalities and hydrops, which ultimately lead to fetal demise. However, Adzick *et al*¹¹ found that overall prognosis was dependent on the relative size of CCAM rather than the histological lesion type. Notwithstanding, large lesions still can regress in size and therefore cannot unequivocally be predictive of a poor prognosis. Laberge *et al*¹ undertook a series of 48 cases over five centres to highlight the natural history of CCAM-like lesions. It was found that 56% of lesions regressed spontaneously even though they showed initial progression.

Postnatally, Lakhoo *et al*¹³ report that a conservative approach in asymptomatic infants is contentious. However, surgical resections of affected tissue may further prevent long-term complications, especially with cases of airway atresia.

In summary, early identification and ultrasound surveillance are essential to monitor pulmonary abnormalities. However, understanding of CCAM-like lesions has progressed since Stocker’s original classification, with some lesions now understood to be secondary to airway obstruction, rather than being primary lesions. Consequently, a collaborative approach in deciding continued surveillance and involvement of the multidisciplinary team is ideal when managing such pulmonary abnormalities.

Learning points

- ▶ The understanding of CCAM-like lesions has progressed since the original classification in 1977 by Stocker *et al.*²
- ▶ The management of CCAM-like lesions is complex and requires multidisciplinary collaboration.

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Patient consent Obtained.

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