

Congenital Cystic Adenomatoid Malformation and Extralobar Pulmonary Sequestration in an Infant

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= Abstract = Although congenital cystic adenomatoid malformation (CCAM) and extralobar pulmonary sequestration (EPS) are different entities, they sometimes share common morphologic features, raising a possibility of a morphogenetic link. We report an autopsy case of a neonate who had features of both EPS and CCAM. An abnormal left lung with three separate lobes was found in the left thoracic cavity after removal of herniated abdominal viscera through the Bochdalek foramen. Two lobes without bronchial connections were directly connected with the descending aorta, and showed typical histologic features of CCAM. The lung tissue with normal bronchial connection and pulmonary artery supply showed identical features to these accessory lobes. Our case provides an evidence that CCAM and EPS can occur in a single individual and in the same side of the lung, and therefore raises a possibility that these two lesions could be different expressions of the same disease.

Key Words: *Congenital cystic adenomatoid malformation, Pulmonary sequestration, Lung, Neonate*

INTRODUCTION

Congenital cystic adenomatoid malformation (CCAM) and extralobar pulmonary sequestration (EPS) are rare congenital anomalies that can rarely be combined in one individual (Morin *et al.* 1989; Dibden *et al.* 1986; Stocker and Kagan-Hallet 1979; Demos and Teresi 1975; Halloran *et al.* 1972; Hutchin *et al.* 1971; Aslam *et al.* 1970). CCAM is usually defined as any congenital cystic lesion in the lung with adenomatous proliferation of bronchiolar structure of variable size and distribution (Morin *et al.* 1989). Meanwhile EPS is

an accessory lung tissue which has no communication with the tracheobronchial tree and receives a systemic arterial supply (Katzenstein and Askin 1990). These two seemingly different entities share common histological features, and sometimes it is difficult to separate them solely on the basis of gross and microscopic examinations. The main difference is the presence of an aberrant systemic vascular supply in EPS, which cannot be confirmed or does not exist at all clinically. Minor differences include the fact that chronic inflammation and/or fibrosis are present in EPS and also the fact that "adenomatoid" structures are composed solely of bronchiolar structures in CCAM. However, the latter feature could not be clearly differentiated in premature lung tissue. Both lesions are congenital and have been suspected to be caused by developmental insult. An autopsy case that showed features of both CCAM and EPS in the lungs prompted this report.

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CASE REPORT

This one-day-old male neonate presented with generalized cyanosis. He was born by fullterm cesarean section delivery. At birth, he weighed 2.8 kg and showed bluish skin color with no crying. The pregnancy was uneventful and it was the first pregnancy for this mother. At nursery, physical and radiologic examination revealed a left diaphragmatic hernia. An emergency patch insertion was performed. However, blood gas data did not improve after corrective surgery and he continued to show cyanosis. He died one day after surgery.

At autopsy, the body measured 33.5 cm and 55.5 cm in crown-rump and crown-heel lengths, respectively. The skin was generally pale bluish and chest circumference (32 cm) was greater than abdominal circumference (30 cm). The left chest contained herniated abdominal organs consisting of a segment of the small intestine, splenic flexure of the large bowel, spleen and left lobe of the liver. After removal of the herniated abdominal contents, three separated lobes of the left lung could be seen (Fig. 1). One was connected to the left main bronchus and pulmonary vessels. The other two lobes had no connections with the normal broncho-pulmonary trees. Part A (Fig. 1) having normal broncho-pulmonary connections weighed 8 gm and showed a triangular shape. The average diameter of the cysts was 0.1 cm, of which the largest one was not over 0.2 cm in diameter. Part B and part C (Fig. 1) having no normal broncho-pulmonary connection weighed 3.2 gm and 9.6 gm, respectively. They were connected to the descending aorta and an unidentified artery directed to the pulmonary artery. Cut sections of these three lobes revealed multiple tiny cysts in the hemorrhagic background. The right lung weighed 12.4 gm and was trilobated. It was aerated but consolidated. Cut section was hemorrhagic with no recognizable cysts.

On microscopic examination three separated left lobes showed different histologic findings

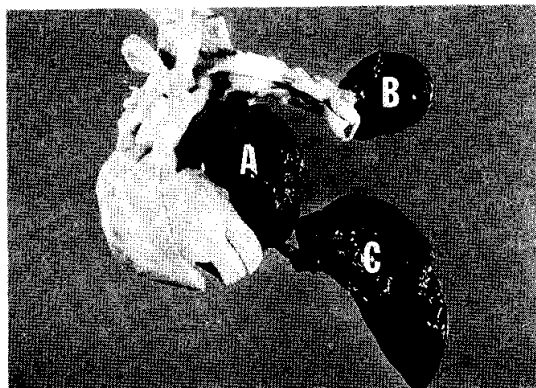


Fig. 1. The left lung consists of three abnormal lobes. Part A (A) is connected to the left main bronchus and pulmonary vessels. Part B (B) is connected to the descending thoracic aorta with no bronchial continuity. Part C (C) is connected to the unidentified artery with no bronchial continuity.

although the basic lesions were similar. All were comprised mostly of small cysts lined by stratified or simple ciliated cuboidal epithelia resembling respiratory bronchioles (Fig. 2). There was neither skeletal muscle nor cartilage. Some lining epithelial cells had clear cytoplasm. Larger cysts were separated by loose edematous connective tissue and were lined by ciliated columnar epithelia resembling terminal bronchioles (Fig. 2). The diameter of the cysts in part A measured 100 to 600 μm . There was a focal hyaline membrane formation in the cystic space in part A. Comparing the size of the cysts in part A and C, part B had the smallest cysts ranging from 50 to 500 μm in diameter. Although part C had no connection with the bronchial tree, one area showed a cyst that was surrounded by a semilunar cartilage island resembling immature bronchiolar cartilage (Fig. 3). There was no inflammation in part B and C. These gross and microscopic features are summarized in Table 1. The right lung showed acute bronchopneumonia with hyaline membrane formation. No adenomatoid malformation was noted in this lung.

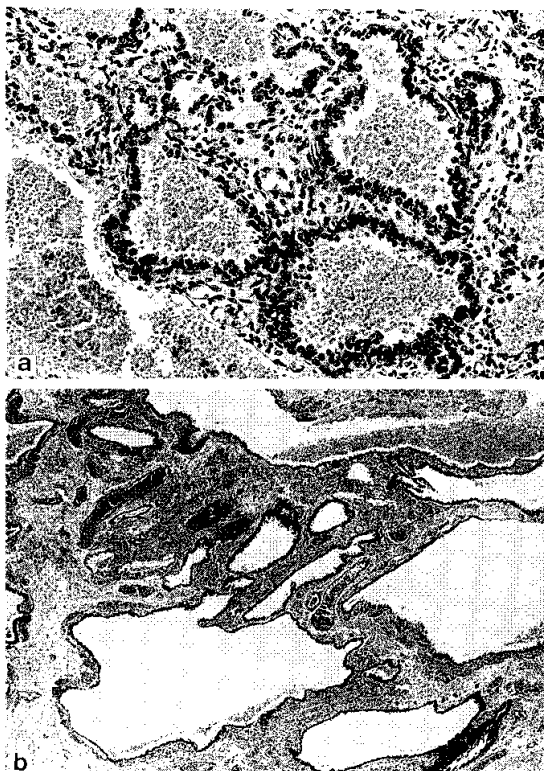


Fig. 2. (a) Medium power photomicrograph of the case exhibits multiple regular cysts lined by stratified cuboidal epithelium and filled with red blood cells. (b) Low power photomicrograph shows the irregular size and shape of cystic structures and loose intervening stroma with hemorrhage.

Other autopsy findings included atrial septal defect, petechial hemorrhage in the esophagus, stomach, appendix and mesentery, intrathyroidal thymus, thyroid cyst and an accessory spleen.

DISCUSSION

Our case shows two unusual features in comparison with conventional CCAM and EPS. The first one is concomitant pathologic features of CCAM and/or EPS in three lobes. Although the association of CCAM and EPS is not rare



Fig. 3. A focus of hyaline cartilage island around the cyst is shown in part C. No bronchial connection is identified in this part.

in one lobe of lung, the combination like our case cannot be found in the literature. The second unusual feature is the size difference of cysts among the three lobes. The big lobe had large cysts and the small one had small cysts. It was claimed that different histologic features of three types of CCAM, especially in the aspect of cyst size, gave some clues as to the time of their embryonic origin (Stocker *et al.* 1988). Type I lesion (largest cyst) would occur somewhat later (7-10 weeks of gestation) than type II (before 31 days of gestation) and type III (3-4 weeks of gestation). All the three lobes in our case are classified into Stocker's type III. However, we believe that the size difference among the three lobes would provide another clue for the pathogenesis of CCAM and EPS.

Considering the fact that the basic problem is an abnormality in the process of lung development, the pathogenesis of congenital lung cysts should be similar. EPS is caused by an additional tracheobronchial bud from the embryonic foregut at the level distal to the normal lung bud formation. Since the end of 1960s, there has been a trend in the literature trying to unify various congenital lung cysts or malformations into one spectrum. In this context several investigators suggested that (1) congenital bronchial cystic disease, seques-

Table 1. Summary of the pathologic findings seen in the left lung of this case

Left lung	Part A	Part B	Part C
Lung weight (gm)	8	3.2	9.6
Cyst size (μm)	100 - 600	50 - 500	200 - 800
Bronchial connection	Normal	Absent	Absent
Vascular supply	Pulmonary artery	Descending aorta	Unidentified
Histologic diagnosis	1. CCAM 2. Focal hyaline membrane formation	CCAM	CCAM

CCAM : Congenital cystic adenomatoid malformation

tration and congenital cystic bronchiectasis were variants of a single primary complex of bronchovascular anomalies (Culiner 1968), and (2) lobar emphysema, cystic adenomatoid malformation, pulmonary sequestration, and bronchogenic cysts in children were under a single clinical group (Buntain *et al.* 1974). As regard to terminology, some investigators introduced the term, "sequestration spectrum" (Sade *et al.*, 1974; Thilenius *et al.* 1983). Other investigators introduced another name representing all of the congenital pulmonary malformations, "malinosculation" (Clements and Warner 1987). In humans bronchial branching is completed by 16 weeks of gestational age, and pulmonary artery development follows slightly later than bronchial branching. Alveolar development is completed after 26 weeks of gestational age. In the early embryonal stage, the tips of the dividing bronchial buds are supplied by a systemic capillary plexus derived from the primitive aorta. This plexus regresses as the growing lung advances, and the developing pulmonary artery takes over (Reid 1984). Clement postulated 5 possibilities involving maldevelopment based on this embryogenesis of the lung. Both the time and the site of insult appear critical in each disease. The first possibility is a total arrest of bronchial development and pulmonary arterial supply and leads to the pulmonary agenesis. A second possibility is a minor insult resulting in a localized abnormality of proximal bronchial tree and leads to the bronchial stenosis or bronchogenic cyst. A third possibility is

an arrest of pulmonary arterial growth with continued development of bronchial tree and leads to the pulmonary sequestration. A fourth possibility is a severe insult resulting in the disruption of both airway and pulmonary arterial development that leads to the combined bronchoarterial pulmonary malinosculation. The last possibility is a complete disruption of the tracheobronchial connection with continuous pulmonary arterial development that leads to the pulmonary sequestration with normal pulmonary artery, CCAM and congenital lobar emphysema. In our case, part A is categorized into the fifth possibility and part B and C is categorized into the fourth possibility. This different categorization of the each lobe in the same side of the lung in an infant means that all those congenital cystic lung disease could be developed in a patient, thus leads to a suggestion that all those congenital cystic lung diseases share a common pathogenesis and are included in one spectrum of disease complex. In this aspect, our case is a good example demonstrating different phenotypes of congenital cystic lung diseases. The third factor to be considered is a potentiality of the abnormal lung tissue. This factor is closely associated with the time of insult. The earlier the lung tissue is affected in the developmental period, the greater the chance that it becomes an abnormal lung.

Our case allows speculation on the pathogenesis and definition of congenital lung cysts, although there are enough exceptions to separate these two diseases. Accumulation of more

such cases and careful gross and microscopic examination based on developmental anatomy and histology are needed to provide a more logical explanation.

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