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Fisher's unique variant in Stocker's type II congenital cystic adenomatoid malformation of the lung : a case report

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Abstract

An eight-week-old infant presented with dyspnoea two months after an uneventful normal vaginal delivery. Radiologically, a sharply outlined radiolucent area surrounded by atelectasis was seen in the upper lobe of the left lung. A left upper lobectomy was performed with the clinical impression of congenital pulmonary emphysema. The resected specimen displayed multiple cysts 2 to 6 mm in diameter. Microscopically,intracystic papillary mesenchymal ingrowths lined by respiratoryepithelium were present. Based on both the gross and microscopical features, a diagnosis of Fisher's variant of type II congenital cystic adenomatoid malformation (CAM) was made. The postoperative follow-up showed excellent recovery and normal development of the child.

Key words: congenital cystic adenomatoid malformation of lung, cystic lung disease, lung cysts, neonatal respiratory distress.

INTRODUCTION

Congenital cystic adenomatoid malformation (CAM) of the lung is a rare developmental malformation characterized by the formation of cysts of varying sizes and proliferationof terminal bronchiole–like structures. It accounts for 25% of cystic lung diseases.'

Although the first case of CAM was reported in 1897 by Stoerk, it was only in 1949 that CAM was recognized as a definite entity by Ch'in and Tang.[2] The morphological classification (type I, type II and type III CAM) primarily based on the size of cysts as described by Stocker *et* al[3] is widely used because of its clinical prognostic value.[4] Fisher *et* al[5](1982), reported for the first time a unique variant exhibiting striking intra-cystic mesenchymal papillary in-growths lined by respiratory epithelium, histologically, in the lung of a neonate with Stocker's type I CAM (3-10 cm diameter cysts) .

To the best of our knowledge similar intracystic papillary in-growths as described by Fisher *et al* in type I CAM has not been reported in CAM type II anomaly.,Hence, we report a case with this unique association.

CASE REPORT

An eight-week-old Malay male infant, the fourth sibling, was born on 18.12.1995 weighing 3.4 kg after a full-term normal, vaginal delivery at Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia. The maternal obstetric history was unremarkable.The neonatal course was uneventful and the baby was discharged on the second day. The infant was well until four days prior to the admission on 16.02.1996, when he developed shortness of breath, weak crying and reduced feeding. On the day of admission dyspnoea had increased. There was no history of fever, cough, running nose, vomiting or regurgitation.

On physical examination, the general condition of the baby was fair and he weighed 4.6 kg. The baby was in obvious respiratory distress with grunting and tachypnoea. The respiratory rate was 70/minute and the pulse rate was 132/minute and regular. Examination of the cardiovascular system revealed a soft systolic murmur. The respiratory system showed a pigeon chest deformity with supraclavicular and intercostal retractions on the left side. Breath sounds were decreased on the left and increased on the right side of the chest. No adventitial sounds were present. There were no signs of neck rigidity or cyanosis. Examination of other systems revealed no abnormality or congenital defects. Results of routine laboratory tests were within normal limits.

A chest roentgenogram revealed grossly hyperinflated left lung with a sharply outlined radiolucent area with herniation of the lower part

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of the upper lobe of the left lung towards the right lung medially causing mediastinal shift towards the right side. Heart and pulmonary vasculature were normal. The right lung fields were clear. A provisional clinical diagnosis of congenital lobar emphysema was made and a left upper lobe lobectomy performed. The postoperative course was uneventful and the baby was discharged on the sixth postoperative day.

Pathology

The resected specimen consisted of a roughly pear-shaped piece of lung tissue weighing *56* gms and measuring 80x70x30 mm. On palpation, it was crepitant and floated on water. Externally it was covered by a smooth and glistening pleura–like capsule. The cut surface showed multiple dilated cystic spaces ranging in size from 2 mm to 6 mm (Fig. 1). The cystic spaces occupied the major bulk of the specimen and blended with the surrounding solid lung parenchyma. Grossly, no definite bronchial structures were identified.

Histology revealed multiple small cysts surrounded by larger irregular cystic spaces in a loose myxomatous stroma. The large cysts were lined by pseudostratified cuboidal to columnar cells with few PAS positive cells in between. Foci of primitive cartilaginous plates were noted around the large cystic spaces . No bronchial structure or mucigenous cells (goblet cells) were found. No haemopoietic foci were detected. The smaller cysts showed striking ingrowths of primitive mesenchymal tissue forming papillary projections lined by respiratory epithelium (Fig. 2). Muscular blood vessels were present elsewhere in the stroma. No cellular atypia or malignant features were seen.

Special stains (PAS, alcian blue, Masson trichrome and van Gieson's) demonstrated the presence of elastic and collagenous tissues in the stroma especially around the large cysts. Immunohistochemistry showed positive staining for cytokeratin (CK) and epithelia1 membrane antigen (EMA) in the respiratory epithelium. The stromal cells were reactive with vimentin. There was no immunoactivity for desmin and S-100 protein.

Follow-up of the patient after surgery showed no evidence of residual pulmonary disease and the child had attained normal development during the last four years and eight months.

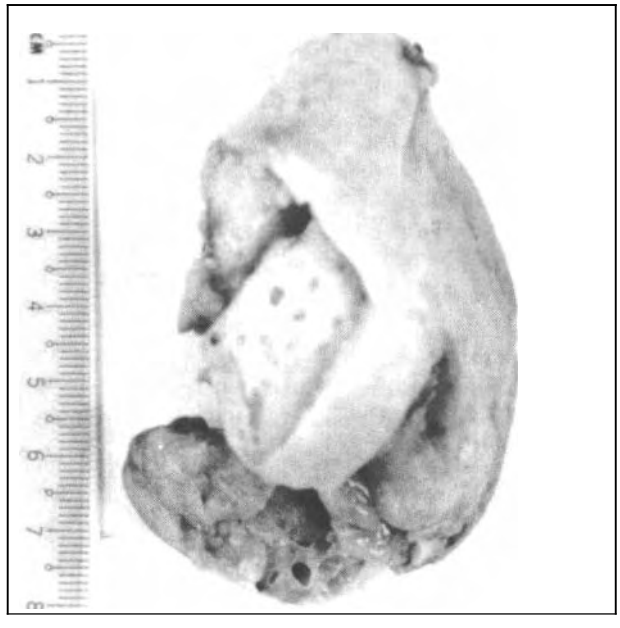

FIG. 1: Gross photograph of partially opened lung lesion showing small cystic spaces (center and lower part) measuring 2 to 6 mm in diameter. Part of the outer surface covered by a glistening capsule is also shown.

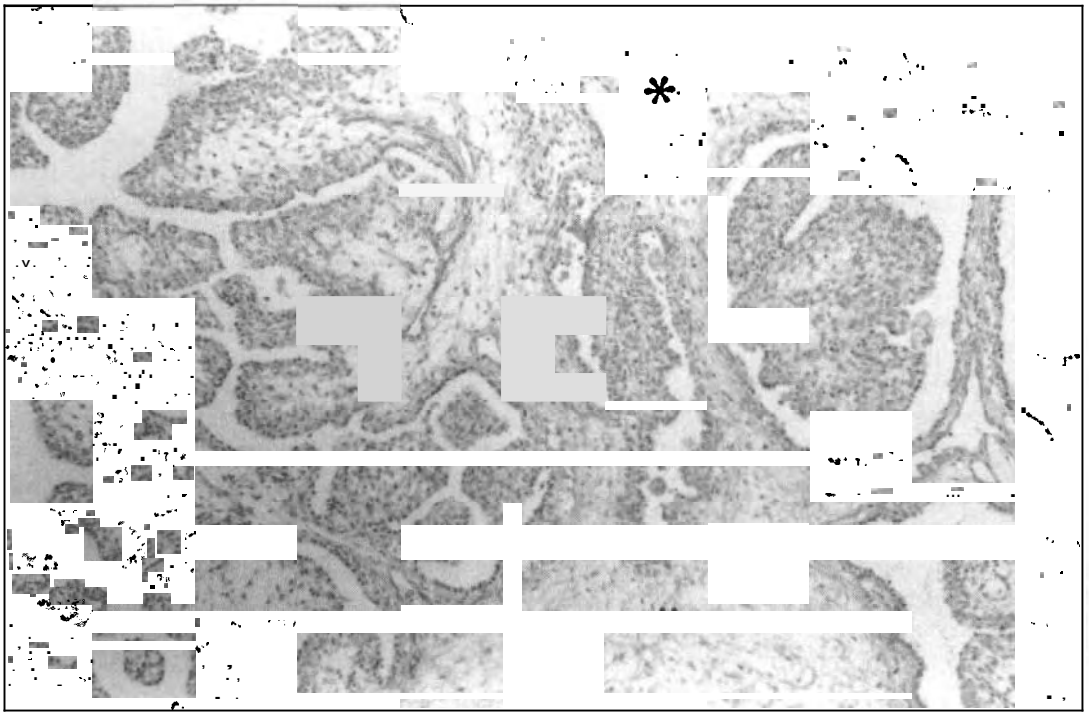

FIG. 2: Microphotograph showing smaller cysts with intraluminal papillary in-growths of mesenchymal stroma lined by proliferating respiratory epithelium. Loose myxoid stroma (*) is conspicuous outside the cysts. H&E X 100.

DISCUSSION

Congenital cystic adenomatoid malformation (CAM) of the lung is a rare hamartomatous pulmonary lesion occumng in premature or stillborn infants with anasarca.[2] It encompasses all congenital cystic lung lesions characterized by the presence of abnormal bronchiolar structures of varying sizes and distribution.[1,6]

The current classification of CAM is based on the size of the cysts [2,3,4] at the time of clinical or pathological examination of the surgical or autopsy specimen. Type I CAM contains few cysts measuring 3 to 10 cm in diameter, Type II CAM have focal cysts 0.5 to 2.5 cm in diameter and Type III show diffuse cysts <0.5cm in diameter. The common histological diagnostic feature of all types of CAM is the presence of multiple, irregular, variably sized, bronchiolar–like cystic structures lined by cuboidal to ciliated pseudostratified columnar epithelium. The cyst walls have excessive elastic tissue and smooth muscle but no cartilage or bronchial structures are usually found. The presence of inflammation and fibrosis preclude the diagnosis of CAM. The clinical prognosis of the patient depends on the type of CAM with type I CAM having the best , type III the worst and Type II an intermediate outcome.'

Fisher *et al*[5] described a cystic lesion of the left upper lobe of the lung in an eleven-week old infant resembling type I CAM with cysts lined by respiratory epithelium and containing numerous large intraluminal papillary projections with cores of loose mesenchyme. In contrast to type I CAM, the cysts in our case were less than two centimeter in diameter (2 to 6 mm) which places the condition as type II CAM. The cysts were scattered and blended with the surrounding pulmonary parenchyma. Such a combination of type II CAM with intracystic papillary proliferation has not been reported in the literature before. Although a few primitive cartilaginous plates were present near the large bronchiole–like cystic spaces in our case there was no wide spread proliferation of chondroid or other mesenchymal tissue as reported by Benning[6] and Heller.[7]

As in our patient, the usual clinical presentation in the neonatal period is that of acute respiratory distress. Hence, the differential diagnoses include bronchogenic cyst, extralobar seqestration, congental lobar emphysema, pulmonary lymphangiectasis and diaphragmatic hernia. A bronchogenic cyst is histologically a discrete mass and does not communicate with tracheobronchial tree. Pulmonary sequestration

is a mass of nonfunctioning lung tissue supplied by anomalous arteries and lacks communication with the tracheobronchial air route. In lobar emphysema the overdistended alveoli are normal histologically with loss of cartilage plates in the bronchi. A barium contrast study is recommended if a diaphragmatic hernia is suspected.[4]

CAM is an acute surgical emergency and if resection is delayed, expansion of the cysts may lead to increasing atelectasis of the lung impeding venous return and resulting in cardiac failure. The clinical diagnosis is generally made by physical examination and radiology which shows an irregular, sharply outlined radiolucent area surrounded by atelectasis. The mediastinum and lung may be shifted with or without herniation towards the opposite lung.' In adult life, its presentation varies from chronic, asymptomatic to progessive enlargement of the cysts causing obstructive features and infection.[8,9] Recently, three cases of bronchioloalveolar carcinoma arising in CAM have been reported in adults.[10,11] The tumour cells were positive for carcinoembryonic (CEA) antigen. This adds another important dimension to this rare and benign entity.

With the increase in diagnostic facilities, such as high resolution computerised tomography and ultrasound, the emphasis has been on the early prenatal/perinatal diagnosis of CAM, so that proper pre and perinatal counselling and management can be done.[12,13] Aspiration in utero for foetal hydrops as a result of CAM[14] and even foetal lung biopsy for the diagnosis of CAM in utero have been tried on a few occasions.[15]

An important development in CAM has been the production of a sheep model of CAM by Rice et *al*[16] which helped in understanding the pathophysiology of hydrops in CAM. The authors implanted inflatable tissue expander intrathoracically in six foetal sheep at 120 days (17 weeks) of gestation and inflated it daily with 25 to 50 ml of saline. Based on this model they concluded that the hydrops that developed in CAM is due to compression of the inferior vena cava leading to obstruction of the cardiac venous return and central venous hypertension. This pathophysiological change was reversed by deflation of the expander. This deflation technique was applied by Brown et *al*[14] successfully in the management of hydrops in CAM by multiple serial aspirations of the cysts in the foetus.

Reported anomalies associated with CAM are hydrops, Seckel's syndrome, linear nevus sebaceous, intraabdominal sequestration, bilateral renal agenesis, hypoplasia of the left heart etc. Fortunately, none of these abnormalities were found in our case.

The exact aetiopathogenesis of CAM is still unclear. The nature of embryological insults resulting in developmental abnormality is yet unknown. However, the embryologic timing of the malformation appears to be after the embryonic phase in the seventh to twentieth weeks when smooth muscle and cartilage are differentiated from the surrounding mesenchyme.

In conclusion, it could be said that CAM is a very rare, usually neonatal congenital cystic lung disease which presents as a surgical emergency. If recognized early and resection is performed the prognosis is generally good although the long term outcome depends on the type of CAM. All cases of CAM in adults need follow up since malignancy has been documented in CAM in adults. This case illustrates the rare combination of Stocker's type II CAM with Fisher's unique variant of intracystic papillary in-growths of immature mesenchymal tissue in an infant and the excellent outcome after surgery.

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