Case Report

Congenital cystic adenomatoid malformation of lung: Report of three cases and review of this rare entity

Mallika Pal, Indranil Das, Rathin Hazra, Susmita Mukhopadhyay, Soumyee Bandyopadhyay

Department of Pathology, Nilratan Sircar Medical College and Hospital, Kolkata, West Bengal, India

ABSTRACT

Congenital cystic adenomatoid malformations (CCAMs) are rare congenital, developmental, nonhereditary, hamartomatous pulmonary airway malformations. Etiology is unknown. It is a rare disease with an incidence of 1 in 11,000 to 1 in 35,000. It is a disease of infancy with most of the cases diagnosed within the first 2 years of life. We report cases of three infants with CCAM (Stocker Type II and I) with brief review of literature.

Key words: Adenomatoid, ciliated, columnar, cuboidal, lung, malformation, pseudostratified

INTRODUCTION

Congenital cystic lesions of the lung are rare. The most common among them is congenital cystic adenomatoid malformation (CCAM), also known as congenital pulmonary airway malformation. It was first described as a separate entity in 1949 by Ch'in and Tang.[1] The reported incidence of CCAM ranges from 1 in 11,000 to 1 in 35,000 live births, with a higher incidence in the mid-trimester due to spontaneous resolution.[2,3] Patients usually present in the neonatal period or early childhood with respiratory distress, recurrent chest infection, hemoptysis, or failure to thrive.[4,5] Here, we present three cases of this rare lesion occurring in the 1st year of life.

CASE REPORTS

Case 1

A 1-month-old male baby presented with severe respiratory distress since birth. He had to be supplemented with oxygen round the clock. On examination, grunting and tachypnea were present. Chest X-ray showed right-sided pneumothorax. Computed tomography (CT) scan of the chest was performed, and it showed large multicystic lesion in right lower lobe with mediastinal shift. He underwent lobectomy. Intraoperative finding revealed that the lesion had a communication with tracheobronchial tree. Immediate postoperative period was uneventful. Macroscopically, it was a wedge-shaped tissue measuring 8 cm × 5 cm × 4 cm. Outer surface was smooth and congested. Cut surface was multicystic in appearance with the presence of three to four cysts, largest one measuring 4 cm in diameter. The specimen was processed for histopathological examination, and under microscope, the sections showed interconnecting cystic spaces lined by partly ciliated pseudostratified columnar epithelium partly by flattened cuboidal epithelium and they were separated by fibromuscular septa. Cartilage was not seen [Figure 1]. Hence, the diagnosis of CCAM of the lung (Stocker Type 1) was given. Further postoperative period was uneventful.

Address for correspondence: Dr. Indranil Das,
28/11 A. K. Mukherjee Road, Noapara, Baranagar, Kolkata - 700 090, West Bengal, India.
E-mail: buntyrules83@gmail.com

Access this article online

Quick Response Code:

Website: www.ccij-online.org

DOI: 10.4103/2278-0513.197868

Cite this article as: Pal M, Das I, Hazra R, Mukhopadhyay S, Bandyopadhyay S. Congenital cystic adenomatoid malformation of lung: Report of three cases and review of this rare entity. Clin Cancer Investig J 2016;5:466-9.

Case 2

A five-month-old male baby presented with respiratory distress in the emergency. He had significant history of recurrent chest infection since birth. He was then shifted to the pediatric intensive care unit and supplemented with oxygen. He underwent chest X-ray which showed cystic areas in both lung field. CT scan of the chest revealed bilateral multicystic lesions involving posterior lobe of the left lung and middle lobe of the right lung. Left-sided lobectomy was done initially as cystic lesion on that side was larger in size. Postoperatively, the patient was kept in elective ventilation for 1 day and was advised respiratory physiotherapy. Antibiotics were given and nebulization with bronchodilator was advised as and when required basis. He was put on close follow-up to see frequency of further respiratory problems and to take decision regarding the necessity and timing of opposite-sided lobectomy. Gross appearance of the resected lobe was brownish black with solid and cystic component measuring 4 cm × 3.5 cm × 3 cm. Cut surface revealed multiple small cysts, largest one measuring 1 cm in diameter. Microscopically, relatively uniform intercommunicating cysts lined by ciliated cuboidal epithelium, resembling bronchiole were seen [Figure 2]. The diagnosis of CCAM of the lung (Stocker Type 2) was confirmed.

Case 3

An eight-month-old female baby presented with intermittent fever and respiratory distress. She had moderate growth failure. On examination, tachypnea was present and breath sound was diminished in left lower lung field. She underwent chest X-ray which showed left-sided pneumothorax. CT scan of the chest revealed irregular cystic lesions involving lateral segment of the lower lobe of left lung. Left-sided lobectomy was done. Postoperative period was uneventful and the patient was discharged after 5 days of postoperative hospital stay. Gross appearance of the resected lobe was irregular grayish-black measuring 7 cm × 5.5 cm × 3 cm. Cut surface shows 4-5 large cysts, largest one measuring 4 cm in maximum dimension. Microscopically, variable-sized intercommunicating cysts lined by partly cuboidal epithelium and partly ciliated pseudostratified columnar epithelium partly by flattened cuboidal epithelium were seen [Figure 3]. The diagnosis of CCAM of the lung (Stocker Type 1) was confirmed.

DISCUSSION

CCAM is an uncommon congenital malformation of the lung which presents usually in early childhood. The exact cause of CCAM is unknown. With advances in ultrasonography, this abnormality may be diagnosed in fetal life. A common association is the presence of polyhydramnios in mother within 23rd week of gestation.

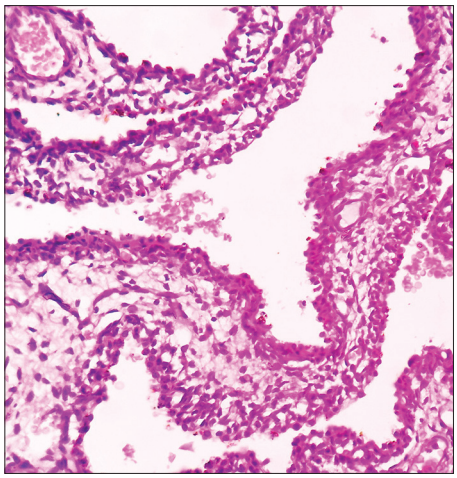

Figure 1: Histopathological examination in the first case revealed cystic spaces lined by partly ciliated pseudostratified columnar epithelium partly by flattened cuboidal epithelium (H and E, ×400)

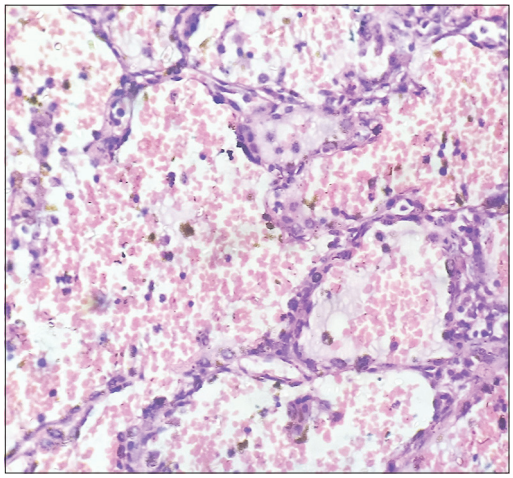

Figure 2: Histopathological examination in the second case revealed that cysts were lined by ciliated cuboidal epithelium, resembling bronchiole (H and E, ×400)

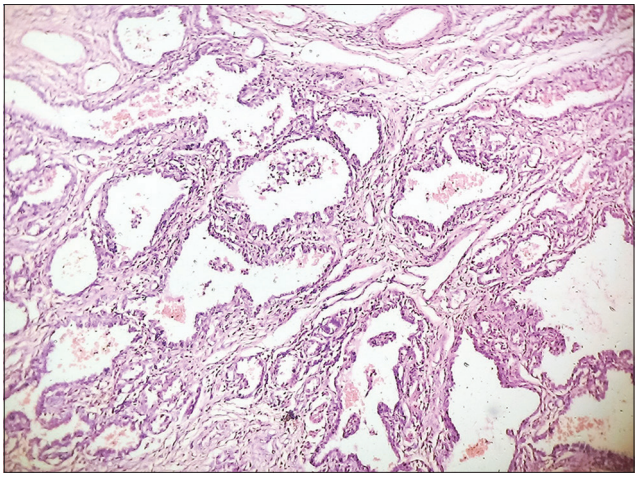

Figure 3: Histopathological examination in the third case revealed that the cysts were lined by ciliated pseudostratified columnar epithelium (H and E, ×400)

Up to one-third of antenatally diagnosed cystic lesion resolves before birth.[6-9] Stocker published a classification

of CCAM which later revised by Stocker in 2002 and this is currently the most acceptable classification used for diagnosis and treatment planning [Table 1].[10] CCAM is caused by consequence of embryogenic insults before the 35th day of gestation and abnormal development occurs in terminal bronchiolar structure. Bronchography studies and serial microscopic examination showed that bronchial atresia is the primary defect leading to the development of CCAM. The morphology of the lesion, i.e., the type of malformation, is determined by the extent of dysplastic lung growth beyond the atretic segment. Modern pathological studies have suggested that CCAM may arise from failed interaction between mesenchyme and epithelium during development and a lack of maturation. This observation was confirmed by immunohistological studies. Thus, the discordance between vascularity and proliferation in CCAM may represent an arrest in vascular development and a loss of synchrony between stroma and epithelium. It was suggested that in the developing lung, the interaction between epithelial cells and interstitial cells is crucial to normal lung development. The imbalance between cell proliferation and programmed cell death or apoptosis has been demonstrated in CCAM. Investigation of other factors that downregulate apoptosis or upregulate proliferation in CCAM may further illuminate the pathogenesis of this entity.[11,12] Clinical presentations of CCAM are in the neonatal period respiratory distress (80%) secondary to mass effect and pulmonary compression or hypoplasia and in severe case due to air trapping. Beyond neonatal period, CCAM presents with recurrent or persistent pneumonia, pneumothorax, and rarely hemopneumothorax.[13,14] Diagnosis of CCAM is accomplished by imaging studies, but only histopathology is confirmatory. Chest X-ray may show a mass containing air-filled cysts. Sometimes, a large cyst in a small baby may be misdiagnosed pneumothorax. CT scan provides a more detailed anatomy. The typical appearance is of multilocular cystic lesions with thin walls surrounded by normal lung parenchyma. The presence of superimposed infection with the lesion may complicate the appearance. Chest radiographs can suggest a localized patchy density, namely a cystic mass; however, multi-dimension CT best demonstrates the cystic and solid components while ruling out bronchiectasis or a major bronchial obstruction.[15,16] Differentiating Type 3 CCAM from intrathoracic bronchopulmonary sequestration (BPS) may be challenging. Both Type 3 CCAM and BPS are solid-appearing echogenic masses with well-defined borders. They are primarily distinguished through their blood supply, with BPS having direct systemic vascularization off the aorta. However, differentiation may be difficult, especially if the vascular connections cannot be visualized. Other diagnoses such as congenital diaphragmatic hernia (CDH), congenital lobar emphysema, and bronchogenic cyst should be considered. In CDH, the lung mass is intestine, which may appear cystic and thus mimic CCAM and/or BPS. The presence of peristalsis suggests CDH. The stomach may also be intrathoracic, in which case it may fill and empty. The absence of an intra-abdominal stomach bubble also suggests CDH. Depending on the size of the CDH, the herniated organs may move from intrathoracic to intra-abdominal. CDH and both CCAM and BPS have also been reported in the same patient, further complicating the diagnosis.[17] Mediastinal masses such as cystic hygroma and teratoma must be considered in the differential. Teratoma tends to be more vascular and may create more ultrasound shadowing. A bronchogenic cyst is usually isolated and originates from the upper airway, with which a direct connection can sometimes be visualized. However, if the cyst is more removed from the airway, differentiating it from a macrocystic CCAM may be difficult. Extralobar sequestration (ELS) and intralobular sequestration cannot usually be distinguished, but a pleural effusion would suggest the former. Intra-abdominal ELS are usually located on the left and must be distinguished from adrenal and renal lesions such as neuroblastoma and mesoblastic nephroma. Another diagnosis to consider is enteric duplication cysts, which are also more common but have a more cystic appearance. Magnetic resonance imaging may be useful in distinguishing these lesions; however, the technique has not been studied extensively.[18]

Surgical management of CCAM and BPS involves lobectomy or nonanatomical segmentectomy. Timing of surgery is important. Early surgery may be associated with adequate growth and expansion of the remaining lung to restore the total lung volume and satisfactory pulmonary function test. Most of the studies opined in favor of surgery in between 6 and 12 months of age.[19] Calvert and Lakhoo

Table 1: Stocker's classification of congenital cystic adenomatoid malformation of lung

Stocker type	Incidence (%)	Origin	Features
I	50-70	Bronchi/bronchiole	Single or multiple large cysts (3-10 cm), confined to one lobe and filled with air or fluid. Associated congenital anomalies up to 11%
II	10-15	Bronchiole	Consist of multiple evenly distributed, medium-sized cysts (0.5-2.0 cm) that resemble terminal bronchioles. Associated with a higher incidence (50%) of other congenital anomalies
III	5-10	Bronchiolar/alveolar	Large bulky lesions with evenly distributed small cysts. May be limited to one lobe or entire lung
0	1-3	Tracheobronchial	Solid appearance with small and firm lungs
IV	2-8	Distal acinar	Large cysts up to 10 cm

suggested resection between 3 and 6 months of age of all CCAMs diagnosed prenatally to avoid infection risk which is much more common if resected after 6 months.[20]

Financial support and sponsorship

The study was supported by the Department of Pathology, Nilratan Sircar Medical College and Hospital, Kolkata.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Ch'in KY, Tang MY. Congenital adenomatoid malformation of one lobe of a lung with general anasarca. Arch Pathol (Chic) 1949;48:221-9.
2. Laberge JM, Flageole H, Pugash D, Khalife S, Blair G, Filiatrault D, *et al*. Outcome of the prenatally diagnosed congenital cystic adenomatoid malformation: A Canadian experience. Fetal Diagn Ther 2001;16:178-86.
3. Gornall AS, Budd JL, Draper ES, Konje JC, Kurinczuk JJ. Congenital cystic adenomatoid malformation: Accuracy of prenatal diagnosis, prevalence and outcome in a general population. Prenat Diagn 2003;23:997-1002.
4. Parikh D, Samuel M. Congenital cystic lung lesions: Is surgical resection essential? Pediatr Pulmonol 2005;40:533-7.
5. Kumar B, Agrawal LD, Sharma SB. Congenital bronchopulmonary malformations: A single-center experience and a review of literature. Ann Thorac Med 2008;3:135-9.
6. Davenport M, Warne SA, Cacciaguerra S, Patel S, Greenough A, Nicolaides K. Current outcome of antenally diagnosed cystic lung disease. J Pediatr Surg 2004;39:549-56.
7. Mashiach R, Hod M, Friedman S, Schoenfeld A, Ovadia J, Merlob P. Antenatal ultrasound diagnosis of congenital cystic adenomatoid malformation of the lung: Spontaneous resolution in utero. J Clin Ultrasound 1993;21:453-7.
8. Graham D, Winn K, Dex W, Sanders RC. Prenatal diagnosis of cystic adenomatoid malformation of the lung. J Ultrasound Med 1982;1:9-12.
9. Akrivis CH, Varras M, Demou A, Bellou A, Stefanaki S, Antoniou N. Prenatal diagnosis of congenital cystic adenomatoid lung malformation: Case report and review of the literature. Clin Exp Obstet Gynecol 2003;30:259-62.
10. Stocker JT. Congenital pulmonary airway malformation: A new name and an expanded classification of congenital cystic adenomatoid malformations of the lung. Histopathology 2002;41:424-31.
11. Moerman P, Fryns JP, Vandenberghe K, Devlieger H, Lauweryns JM. Pathogenesis of congenital cystic adenomatoid malformation of the lung. Histopathology 1992;21:315-21.
12. Cangiarella J, Greco MA, Askin F, Perlman E, Goswami S, Jagirdar J. Congenital cystic adenomatoid malformation of the lung: Insights into the pathogenesis utilizing quantitative analysis of vascular marker CD34 (QBEND-10) and cell proliferation marker MIB-1. Mod Pathol 1995;8:913-8.
13. Lee SC, Cheng YL, Yu CP. Haemopneumothorax from congenital cystic adenomatoid malformation in a cryptorchidism patient. Eur Respir J 2000;15:430-2.
14. Irving IM. Malformations and acquired lesions of lungs, pleura and mediastinum. In: Lister J, Irving IM, editors. Neonatal Surgery. London: Butterworth and Co. Ltd.; 1990. p. 265-71.
15. Sahu S, Muthuvel S, Naware SS, Dhavala SS. Congenital cystic adenomatoid malformation of lung. Med J Armed Forces India 2008;64:268-9.
16. Discioscio V, Feraco P, Bazzocchi A, Femia R, Romeo C, Fasano L, *et al.* Congenital cystic adenomatoid malformation of the lung associated with bronchial atresia involving a different lobe in an adult patient: A case report. J Med Case Rep 2010;4:164.
17. Ryan CA, Finer NN, Etches PC, Tierney AJ, Peliowski A. Congenital diaphragmatic hernia: Associated malformations – Cystic adenomatoid malformation, extralobular sequestration, and laryngotracheoesophageal cleft: Two case reports. J Pediatr Surg 1995;30:883-5.
18. Hubbard AM, Adzick NS, Crombleholme TM, Coleman BG, Howell LJ, Haselgrove JC, *et al.* Congenital chest lesions: Diagnosis and characterization with prenatal MR imaging. Radiology 1999;212:43-8.
19. Keidar S, Ben-Sira L, Weinberg M, Jaffa AJ, Silbiger A, Vinograd I. The postnatal management of congenital cystic adenomatoid malformation. Isr Med Assoc J 2001;3:258-61.
20. Calvert JK, Lakhoo K. Antenatally suspected congenital cystic adenomatoid malformation of the lung: Postnatal investigation and timing of surgery. J Pediatr Surg 2007;42:411-4.