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CONGENITAL CYSTIC ADENOMATOID MALFORMATION*

Report of Two Cases and Review of the Literature

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Congenital cystic adenomatoid malformation (CCAM) of the lung is a rare pulmonary lesion, characterized by an excessive overgrowth of the terminal respiratory bronchioles. The lesion is almost always unilateral and may occur in any lobe. We present two children with CCAM. The first case was a one-day-old female infant admitted with respiratory distress and cyanosis. The second case was a 19-month-old girl with a nine-month history of recurrent respiratory infections. Preoperative diagnosis of both cases was intrapulmonary mass. The histopathological examinations revealed CCAM.
Key words: congenital cystic adenomatoid malformation, pulmonary malformation, lung.

The congenital cystic adenomatoid malformation (CCAM) is an unusual lesion combining the features of dysplastic overgrowth, hamartoma and/or even neoplasia. CCAM is caused by an overgrowth of terminal bronchioles at the expense of saccular spaces, resulting in an adenomatoid proliferation of bronchiolar elements and cystic formations. CCAM is primarily found in newborns or very young children, although cases have been described in adults. Generalized edema, respiratory distress, cyanosis and inspiratory retraction are present in most instances, and these complications may be severe enough to cause death. No racial or genetic predisposition has been noted[1]. CCAM is seen more commonly in males. Antenatal diagnosis has been reported[2-4]. CCAM was first described as a separate entity by Ch'in and Tang[5]. In this study, we present the histopathologic findings in two cases of CCAM (type 3 and type 1) of the lungs in newborn infants.

Case Reports

Case 1

The case was a one-day-old female, the product of a full-term pregnancy, born to a 23-year-old mother. In her pregnancy, polyhydramnios had developed without evidence of hydrops. The patient was admitted to the University of Akdeniz Teaching Hospital shortly after birth because of severe respiratory distress and cyanosis. The baby was noted as normal at birth and no sign of

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respiratory distress was present. Her Apgar score was nine. On examination, symmetrical chest wall movement was noted. Breath sounds were decreased over the superior segment of the left lower lobe. Fine rales were noted over the basal segment of the left lower lobe. Peripheric cyanosis was present. The remainder of the physical examination was normal. At the time of hospital admission, the white blood cell count was 29,200/mm^3, sedimentation rate was 18 mm/h. Hemoglobin was 17.8 g/dl; a hematocrit of 53 percent and a platelet count of 127,000/mm^3 were measured. Arterial blood gas on room air was not known. Her body temperature was 36.5 °C. The patient's diagnosis was thought to be a diaphragmatic hernia. Chest radiograph was taken for differential diagnosis. It showed a dense consolidation, round in shape, in the left lower lobe, with compression of heart and surrounding normal lung. The patient was sent to the pediatric surgery department for operation.

During thoracotomy a large mass (8 x 6 cm) was found over the superior segment of the left lower lobe and this was dissected form the normal lung tissue.

Grossly, the round mass was covered by a smooth-to-finely-wrinkled grayish-pink pleura. It weighed 110 g and measured 6 x 5 x 3.5 cm. The cross-section showed gray-pink spongy homogeneous tissue. The solid lesion was composed of multiple, curved, branched structures that resembled immature or dysplastic bronchioles (Fig. 1).

Fig. 1: Case 1, cut surface of the mass showing spongy homogeneous appearance with multiple cleft-like structures.

Microscopically, the tissue consisted of numerous bronchiolar-like cysts, less than 0.3 cm in diameter, with the exception of scattered, larger, bronchiolar-like structures. Irregular, satellite-shaped, bronchiolar-like structures, lined by cuboidal or low-columnar epithelium, were surrounded by alveolar ductules and saccules lined by cuboidal epithelium (Fig. 2). The thin walls contained loose connective tissue with few smooth muscle and elastic fibers, confirmed by Elastica van Gieson's stain.

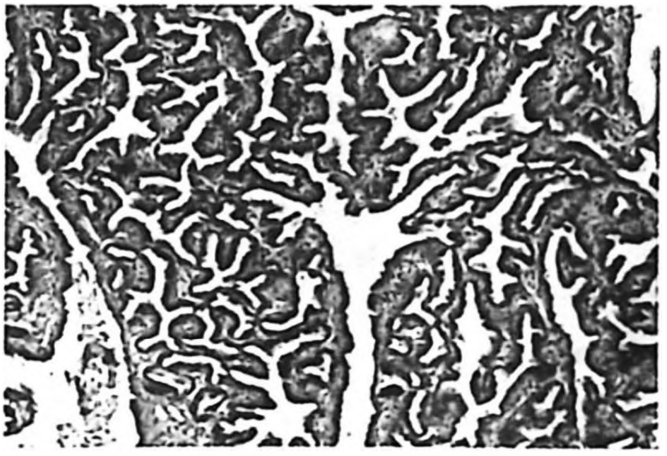

Fig. 2: Microphotograph from the same case showing irregular satellite-shaped, bronchiolar-like structures (hematoxylin and eosin; X10).

Case 2

Search of the files of our department revealed one other case of CCAM.

A 19-month-old girl was admitted to the University of Akdeniz Teaching Hospital with pneumonia. She had a nine-month history of recurrent respiratory infections. A chest x-ray showed a heterogeneous consolidation in the inferior segment of the left lung, with multiple tubular and linear lucencies and early pneumatocele formation. A thoracic computed tomography (CT) scan showed a multicystic lesion in the left lobe with compression of surrounding areas of the lung. Macrocystic lesions were composed of single or multiple cysts. The largest cyst measured 41 x 21 mm. During thoracotomy, an overinflated left lower lobe containing multiple cysts was found. A left lower lobectomy was performed.

Macroscopically, the mass was covered by a gray-to-pink pleura and measured 7.5 x 6 x 2 cm. Cross-sections showed larger cysts (1-3 cm in diameter) with smaller surrounding cysts. Microscopically, the larger cysts were lined with ciliated, pseudostratified columnar epithelium, and the smaller ones by cuboidal-to-columnar epithelium (Fig. 3). Mucus-

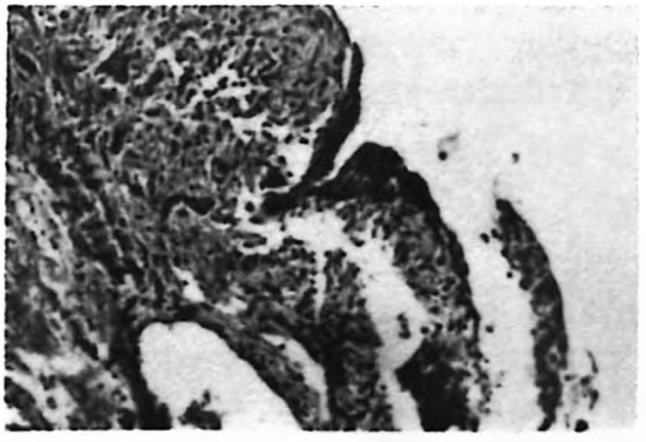

Fig. 3: Microphotograph from Case 2. The larger cyst is lined by pesudostratified columnar epithelium. It is surrounded by smaller cysts (hemotoxylin and eosin; X10)

producing cells were present in the epithelial lining of the larger cysts and in the bronchioles alveolar ductlike structures adjacent to the larger cysts. The walls of the cysts contained prominent smooth muscle, fibrous and elastic tissue.

Discussion

In 1993, Cloutier et al.[6] reviewed the literature and found 153 cases. Our updated search revealed an additional 42 cases of CCAM, excluding our two cases.

CCAM accounts for approximately 95 percent of congenital cystic lung diseases, and represents 25 percent of the congenital lung malformations[4,6]. This malformation is a cystic hamartomatous anomaly that may involve all or part of a lung. It consists of abnormal bronchiolar structures of varying size and distribution.

Embryologically, the origin of the conducting airways derived from endoderm, whereas the respiratory component stems from mesenchyme that concentrates around the tips of the bronchi[3].

Three major histological types of CCAM are described by Stocker et al.[7]. Histological criteria for its diagnosis include: Type 1 lesion is a large cystic or predominant cystic type. It accounts for nearly 65 percent of cases[1]. Single or multiple large cysts (3-10 cm in diameter) lined by ciliated pseudostratified columnar epithelium with numerous polypoid projections are surrounded by smaller cysts. The cysts' walls contain prominent smooth muscle, fibrous and elastic tissue and, occasionally, cartilage plates[1,6-9].

Type 2 lesion is a medium cystic type. It accounts for about 25 percent of cases[9]. Multiple distributed cysts (0.5-3 cm in diameter) are lined by cuboidal and columnar epithelium. The cysts are separated by thin, fibromuscular walls, elastic fibers, cartilage plates, and striated muscle fibers, but no mucogenic cells are expected[1,6-9].

Type 3 lesion is a small cystic or solid type, and occurs in 10 percent of cases[9]. Cysts are rarely over 0.2 cm in diameter, with the exception of scattered larger bronchiolar-like structures. They are composed of curved channels or cysts, lined by cuboidal epithelium. Their thin walls contain loose connective tissue with smooth muscle and elastic fibers[1,6-9].

Histological findings of our cases are consistent with type 3 CCAM and type 1 CCAM, respectively.

Prenatally, polyhydramnios is common. The etiology of polyhydramnios may be due to loss of protein from the lesion into the amniotic fluid[10]. Our first case manifested polyhydramnios. However, polyhydramnios is not a prognostic indicator[6], Fetal hydrops was caused by the malformation resulting in vena caval obstruction and cardiac compression. In our first case, the chest radiograph showed cardiac compression, which has been accepted as a prognostic indicator.

Clinically, CCAM is usually seen before the age of two years. CCAM occurs either in children less than six months of age with respiratory distress, including cyanosis and inspiratory retraction, or in older children with histories of chronic infectious respiratory distress. Our second case had recurrent lower repiratory infections. CCAM can occasionally be discovered by incidental chest radiograph[9]. If a CCAM is a huge lesion, it results in fetal cardiac compression, as in our first case who was admitted to hospital with respiratory distress and cardiac compression or fetal death.

Right and left lung are nearly equally involved and the lower lobes are affected in about 60 percent of the cases[9].

The diagnosis is often made from clinical and radiologic features. The definitive diagnosis is usually made by surgical resection of the mass and histological examination.

Clinically, differential diagnosis must be made extralobar sequestration, bronchogenic and enteric cysts, pulmonary abscesses, and mediastinal cystic teratoma[6,9]. However, these conditions do not cause acute problems in the newborn. Extralobar sequestration is discovered incidentally, or becomes a result of recurrent infections, especially in older patients. Presence of a CCAM or a sequestration is an indication for resection.

Type 1 lesion has a good prognosis, whereas type 2 lesion has a poorer outcome due to its more frequent association with other anomalies, which have been reported as predominately renal agenesis and cardiac anomalies. Anomalies are noted in 15 to 20 percent of all cases with CCAM[1,9]. Our cases had no other anomalies. Type 3 lesion has a high mortality due to its large size and association with maternal polyhydramnios and fetal anasarca. Our first patient's clinical condition was reported to be good after resection.

We think that the first case is interesting because CCAM does not usually present with respiratory distress in a one-day-old infant. In summary, CCAM is an uncommon congenital malformation. If infants less than six months of age present with respiratory distress, CCAM should be considered in differential diagnosis. In the differential diagnosis of recurrent respiratory infection, CCAM must be also considered.

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