Original paper

Congenital cystic adenomatoid malformation presentation of 11 cases and literature review

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The aim of the study was to present cases of congenital cystic adenomatoid malformation (CCAM) in terms of pathological features, gender and site distribution as well as to compare the results with Stocker's classification.
A retrospective review was performed on eleven cases of CCAM obtained in 4-years period (2015-2019) in University Children's Hospital in Krakow, in Poland.
The cases for this study were 7 boys and 4 girls (64% vs. 36%). Patients age at surgery ranged from 4 days to 10 months. 6 cases involved the left lung (55%) whereas the right lung was involved in 5 cases (45%). Histopathological examination showed congenital cystic adenomatoid malformation type I in 7 cases (64%), type II in 3 cases (27%) and type III in 1 case (9%). No congenital cystic adenomatoid malformation type 0 nor IV was diagnosed.
Data obtained from this study correspond to Stocker's classification, showing that the most common CCAM types are those associated with good prognosis. Histopathological features should always confirm the nature of the lesion, that is initially suspected in the imaging examination.

Key words: congenital cystic adenomatoid malformation, CCAM, lung lesion, respiratory tract disorder.

Introduction

Congenital cystic adenomatoid malformation (CCAM) is a rare respiratory tract disorder that can lead to serious clinical problems, arising in approximately 1 in 30 000 live births which manifests in a lung as a single or multiple, cystic or adenomatoid lesion of various size. It may involve a single lobe or a whole lung and it may coexist with other pulmonary defects but is often an isolated lesion. Its pathogenesis is still not clear and it may regress spontanously. It is often diagnosed accidentally during pregnancy on ultrasound examinations. It can be classified into one of five groups (0 to IV) according to Stocker's classification system (Table I), type I being the most frequent and type 0 the rarest one [1]. This study presents and compares cases of CCAM obtained from eleven patients.

Material and methods

Our eleven cases were obtained in a 4-years period (2015-2019) in University Children's Hospital in Krakow, Poland. We took into consideration data such as age at which the patient was operated, gender, location of congenital cystic adenomatoid malformation (right vs. left lung), macroscopic appearance (which sometimes may lead to initial suspicion

of the type of CCAM), clinical diagnosis (based on medical imaging techniques) and additional lesions that were present in the lungs apart from the congenital cystic adenomatoid malformation. The aim was to compare those eleven cases in terms of above-mentioned criteria and to present their histological appearance according to Stocker's classification system [1].

Results

The cases for this study concerned 11 patients (7 boys, 4 girls, 64% vs. 36%) who were hospitalized in Universal Children's Hospital in Krakow in 2015-2019. The congenital cystic adenomatoid transformation (or the suspicion of) was clinically diagnosed in 9 cases, 2 cases were clinically diagnosed as either congenital sequestration of the lung or a cystic lesion of the lung (without exact specification). Patients age at surgery ranged from 4 days to 10 months. 6 cases involved the left lung (55%) whereas the right lung was involved in 5 cases (45%). There was a slight predilection for congenital cystic adenomatoid malformation to arise in the left lung (4 cases, 57%) rather in the right lung (3 cases, 43%) in male patients. In female patients the right and left lung distribution of congenital cystic adenomatoid malformation was even (2 cases, 50% for both right and left lung).

Total resection of the lung (right one) was performed in 1 case (9%), while lobectomy was performed in 10 cases (91%). Lobectomy involved resection of the lower lobe in 7 cases (70%), the middle lobe in 1 case (10%), the upper lobe in 1 case (10%) and the upper and the middle lobe combined in 1 case (10%).

Macroscopically the changes ranged from focal cystic lesions up to 0.8 cm in diameter to single cystic lesions up to 4 cm in diameter. Additional specimens (apart from the specimen with the main lesion) that were obtained for histopathological examination in those cases included:

- a part of ligamentum pulmonale (histologically: with blood effusions),
- single lymph node (histologically: with non-specific reactive changes),
- small parts of fibrin-like material from the pleura of the middle and upper lobe (histologically: parts of fibrous connective tissue with foci of non-specific granulation tissue, mixed-cell inflammation and fibrin).

There were coexisting changes/features that were observed histopathologically in the remaining part of specimens such as: focal atelectasis in 9 cases (81%), focal emphysema in 10 cases (90%), intra-alveolar effusions in all cases (100%), focal oedema in 7 cases (64%), non-specific granulation tissue in 2 cases (18%), hemosiderin-laden macrophages in 7 cases (64%), foamy macrophages in 4 cases (36%) and foci of inflammation in 2 cases (18%). The focal inflammation observed in 2 cases presented as either dispersed catarrhal-purulent inflammation or a focal scant mixed-cell inflammation. No malignant changes were observed histologically in any of the specimens.

Histopathological examination showed congenital cystic adenomatoid malformation type I in 7 cases (64%), type II in 3 cases (27%) and type III in 1 case (9%). No congenital cystic adenomatoid malformation type 0 and IV was diagnosed.

Microscopically lesions diagnosed as CCAM type I revealed large cysts lined with ciliated pseudostratified epithelium with foci of mucus cells and cartilage, CCAM type II showed numerous small cysts lined with columnar and partially cuboidal epithelium, and CCAM type III revealed numerous small cysts lined with "plump" cuboidal epithelium.

In our studies congenital cystic adenomatoid malformation type I involved the right lung in 3 cases (42%) and left lung in 4 cases (58%) and could be found in 1 case in the specimen obtained in total resection of the lung (14%), in the specimens from lower lobe lobectomy in 4 cases (58%), in the specimen from middle lobe lobectomy in 1 case (14%) and in the specimen from the upper lobe lobectomy in 1 case (14%). Congenital cystic adenomatoid malformation type II involved the right lung in 1 case (33%) and left lung in 2 cases (67%), and it could be found in 3 cases of lower lobe lobectomy (100%).

Table I. Macro- and microscopic features of CCAM types

Type 0	Small, firm lungs, microscopically with bronchus-like structures, numerous cartilage plates, prognosis: lethal condition
Type I	Large cysts up to 10 cm in diameter (one may be dominant), microscopically lined with ciliated pseudostratified cells, mucus cells and cartilage may be present, prognosis: good
Type II	Small cysts up to 2 cm in diameter, lined with cuboidal or columnar ciliated epithelium, may have solid areas, prognosis: poor
Type III	Solid gross appearance, small air spaces lined with cuboidal epithelium, prognosis: poor (depends on the extent of the lesion)
Type IV	Large cysts up to 10 cm in diameter, lined with flattened epithelium, prognosis: good (differential diagnosis should always involve pleuropulmonary blastoma)

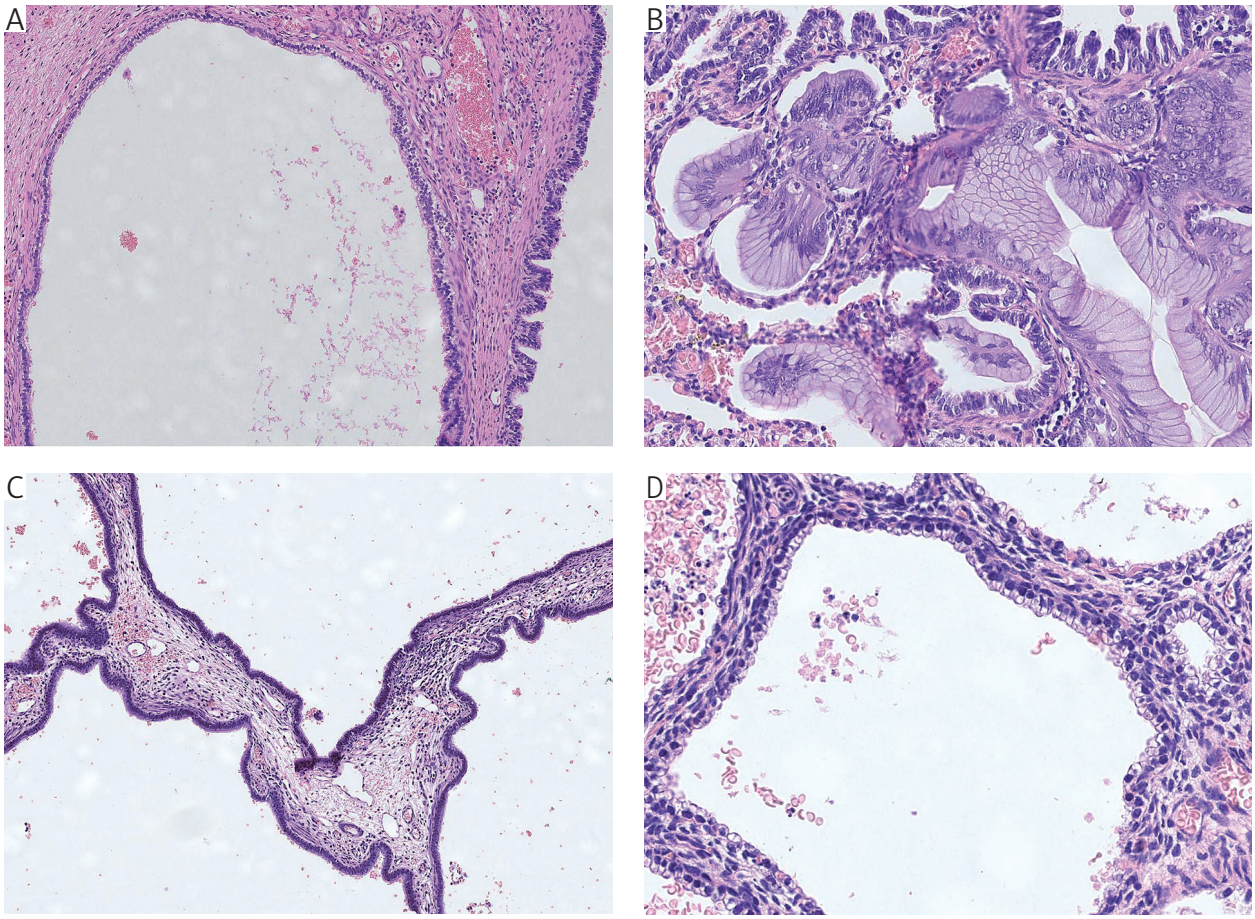

Fig. 1. A) CCAM type I, fragment of a large cyst wall lined with a ciliated columnar epithelium partially with "ruffled" appearance (HE, magnification 30×). B) CCAM type I, mucogenic cells in the wall of the cyst (HE, magnification 20×). C) CCAM type II, cyst walls with scant amount of connective tissue lined with cuboid and columnar epithelium (HE, magnification 20×). D) CCAM type III, small air spaces separated by thin walls lined with cuboidal "plump" epithelium, no mucogenic cells or cartilage (HE, magnification 40×)

Congenital cystic adenomatoid malformation type III involved the right lung in 1 case (100%) and was found in the specimen from upper and middle lobe lobectomy.

Gender-wise congenital cystic adenomatoid malformation type I was present in male patients in 5 cases (72%), type II in 1 case (14%), and type III in 1 case (14%) whereas in female patients type I was present in 2 cases (50%) and type II also in 2 cases (50%) (Fig. 1).

Discussion

Congenital cystic adenomatoid malformation was first described in 1949 by Ch'In and Tang. This entity is a developmental anomaly localized in lungs (one or both). The incidence is 1 in 30 000 live births but its frequency is believed to be rising [2]. The pathogenesis is not fully understood nor totally clearly explained but molecular studies show a group of different genes expressed in those anomalies [3]. Congenital cystic adenomatoid malformation may be a life-threatening condition [4] or it may undergo regression. Although CCAMs are congenital they can be asymptomatic [5, 6] and be detected later in life [7, 8]. Malignant transformation within CCAM is not frequent but may occur at any age [9]. Congenital cystic adenomatoid malformation is a part of a spectrum of congenital pulmonary lesions that also include pulmonary sequestrations, bronchogenic cysts, and congenital lobar emphysema [10, 11, 12]. The vast majority of congenital cystic adenomatoid malformations are diagnosed by fetal ultrasonography with additional MRI and CT postnatally and the surgery is the fundamental treatment of symptomatic CCAMs [13].

The cases in our studies concerned 11 patients aged from 4 days to 10 months. The histological presentation of the lesions was rather typical. Histologically CCAM is divided into five types; the origin of those types is also widely distributed in the anatomical structures in the lungs. Type 0 is of tracheal or bronchial, type I of bronchial or bronchiolar, type II of bronchiolar, type III of bronchiolar-alveolar

and type IV of distal acinar origin. Among all types CCAM type I is by far the most frequent, comprising about 60% to 70% of the cases, followed by type II (10-15%), type IV (15%), type III (5%) and type 0 (1-3%). Our study reflects those proportions in cases of CCAM type I, II and III. No type 0 or IV was diagnosed which is probably due to the relatively low count of cases.

In conclusion, congenital cystic adenomatoid malformation is a disorder in the genesis of the respiratory tract that manifests itself as a one of five different types with distinct macroscopical and histological features. They can be associated with good or poor prognosis and one of the types (type 0, the rarest one) is associated with a fatal outcome. The most common, type I, has a good prognosis and in our studies it appeared statistically most often. Although postnatal CT is the most reliable examination method for confirming the presence of CCAM, one should remember that the histopathological findings are essential for making the final diagnosis.

The authors declare no conflict of interest.

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