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Case report

Congenital cystic adenomatoid malformation in adults: Report of a case presenting with a recurrent pneumothorax and a literature review of 60 cases

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A B S T R A C T

Congenital cystic adenomatoid malformation (CCAM) is a congenital pulmonary cystic disease that is mostly detected and diagnosed prenatally or during the neonatal period, while rarely being observed in adults. Here, we report an adult case of CCAM that was diagnosed following surgery for a recurrent pneumothorax. We further review 60 case reports on adult CCAM that have been previously published. The patient was a 29-year-old woman with a severe left pneumothorax. Her computed tomography scan showed the presence of multiple pulmonary cysts at the base of the left lower lobe. Since she had experienced a left pneumothorax twice previously, surgery was indicated. A wedge lung resection of the pulmonary cysts was performed thoracoscopically. The postoperative pathological diagnosis was type I CCAM. From the review, 7 adult CCAM patients (11.7%) out of 61, including the patient in the present case, presented with pneumothorax, while 21 patients (35%) presented with infection. Thirty-nine foci of CCAM (65%) were located in lower lobes. Moreover, malignancies were associated in 8 cases (13.3%). We propose that if multicystic lung lesions are found in pneumothorax patients, particularly in lower lobes, CCAM should be considered during the differential diagnosis, even in adults.

1. Introduction

Congenital cystic adenomatoid malformation (CCAM) is a congenital pulmonary cystic disease in which the adenomatoid proliferation of the bronchiolar epithelium results in the formation of multiple cysts in the lung's lobes. Most CCAMs are detected and diagnosed prenatally or during the neonatal period when patients present with dyspnea and cyanosis. CCAMs are also sometimes detected in infants and school-age children following respiratory infections, but they are rarely found in adults. We report an adult case of CCAM that was diagnosed following the patient's admission for surgery for a recurrent pneumothorax, and we present a review of 60 case reports on adult CCAM that have been published in the international literature.

2. Case presentation

The patient was a 29-year-old woman who presented with anterior chest pain. She had a history of a left pneumothorax, with episodes that occurred at the ages of 18 years and 23 years, but not during menstruation. A severe recurrence of the left pneumothorax was identified on a chest radiograph (Fig. 1), and the patient was referred to our hospital for thoracic drainage.

At the initial visit, the patient's height and weight were 152 cm and 56 kg, respectively. Her blood pressure was 113/82 mmHg, her pulse was 96 bpm and regular, and her percutaneous oxygen saturation was 97%. She was not menstruating. The laboratory test results did not show any abnormalities in her whole blood cell count or blood chemistry. Chest computed tomography (CT) scanning, which was performed after the inflation of the left lung following chest tube insertion, revealed the presence of multiple pulmonary cysts at the base of the left lung that had a maximum diameter of 22 mm (Fig. 2).

As the patient's left pneumothorax had occurred three times, she underwent surgery on the fourteenth hospital day. The surgery involved making an incision to widen the wound to 25 mm for tube insertion. A 3-mm camera port was placed posterior to the wound, and surgery using the “thoracoscopic one window plus puncture method” [1] was performed. Multiple pulmonary cysts were found at the base of the left lower lobe, which was in contact with the diaphragm (Fig. 3). Pulmonary cysts were not detected in the apical portion or in the apical segment (S^6) of the left lung. None of the findings suggested the presence of endometrial tissue in the diaphragm or in any other part of the thoracic cavity. A wedge resection of the left lower lung, which

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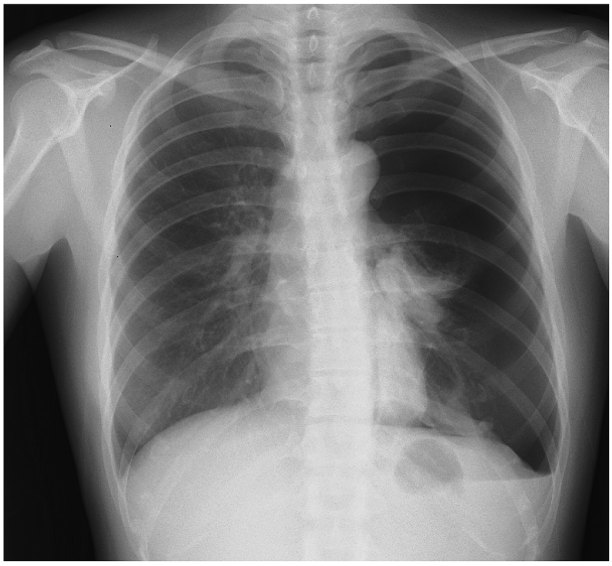

Fig. 1. A chest radiograph obtained during the initial visit. A severe left pneumothorax and slight pleural effusion are evident.

included the pulmonary cysts, was performed using an automatic suturing device. The patient's postoperative course was uneventful. The chest tube was removed one day after surgery, and the patient was discharged on the second postoperative day. The patient remained free of pneumothorax recurrences at 22 months.

Macroscopically, the patient had multiple cystic lesions (Fig. 4). The histopathological examination revealed multiple cystic lesions that exhibited adenomatous changes, and some of the cysts were lined with a cuboidal or pseudostratified, short columnar epithelium. Some of the cyst walls were lined with a ciliated epithelium. The stroma around the cysts was infiltrated by cells (mostly lymphocytes), and its capillary blood vessels were dilated, suggesting the presence of chronic inflammation. The cyst walls did not contain cartilage, and there was no disruption or destruction of the bronchi. These findings led to a diagnosis of a Stocker type I CCAM/congenital pulmonary airway malformation (CPAM). There was no evidence of malignancy (Figs. 5 and 6).

3. Discussion

CCAM was first described in 1897, when Stoerk et al. [2] described cystic lesions in a newborn's lung. In 1949, Ch'in et al. [3] established that this condition was a disease. Subsequently, Kwittken et al. [4] reported that CCAM is a congenital disease in which adenomatous

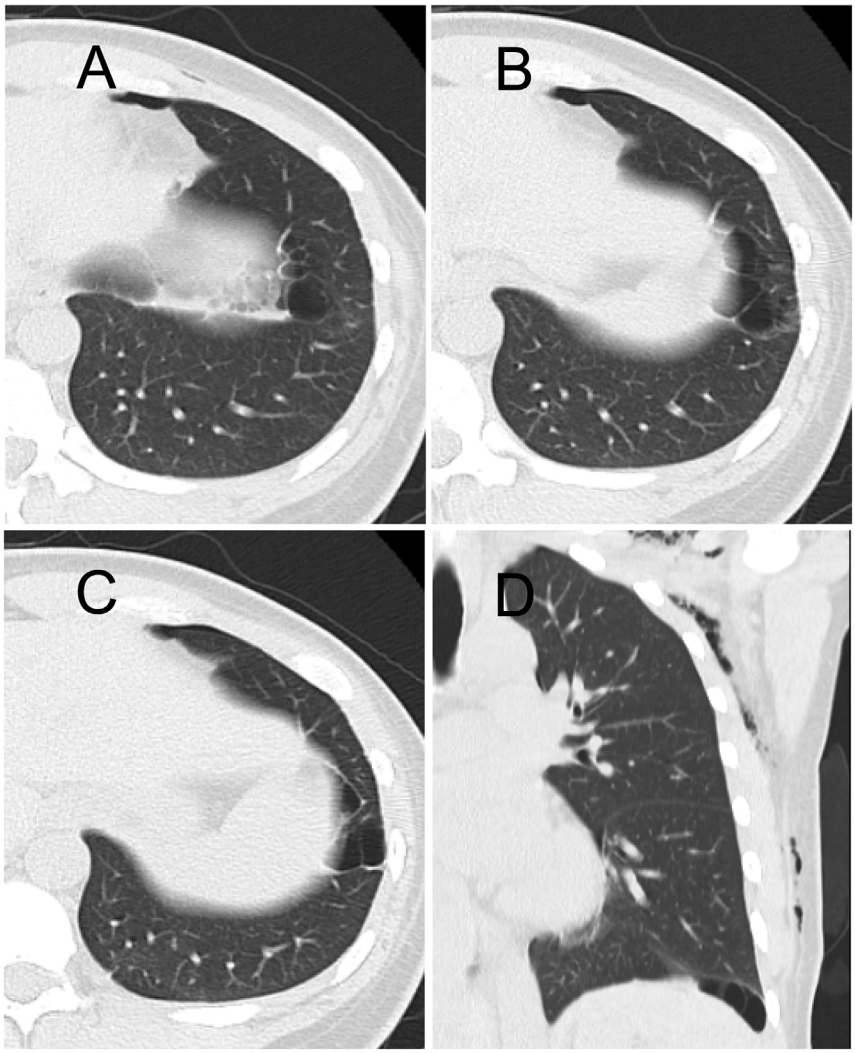

Fig. 2. Chest computed tomography scans. The axial views (**a, b, c**) and a coronal view (**d**) revealed the presence of multiple pulmonary cysts with a maximum diameter of 22 mm at the base of the left lung.

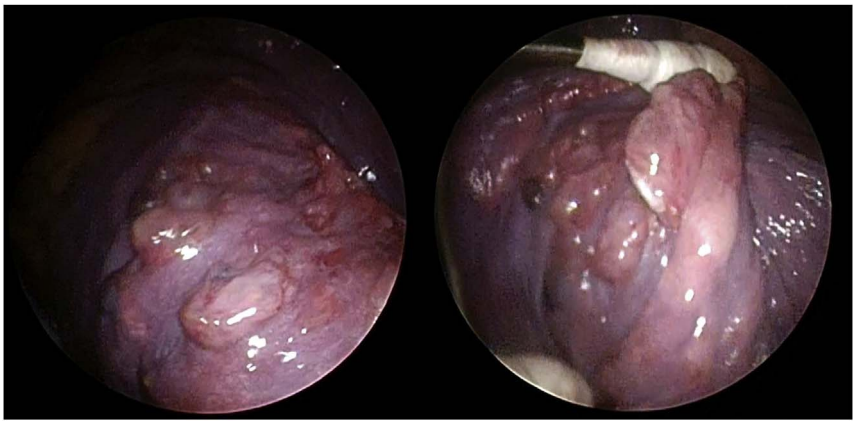

Fig. 3. An intraoperative photograph. Multiple pulmonary cysts were present at the base of the left lower lobe that were in contact with the diaphragm.

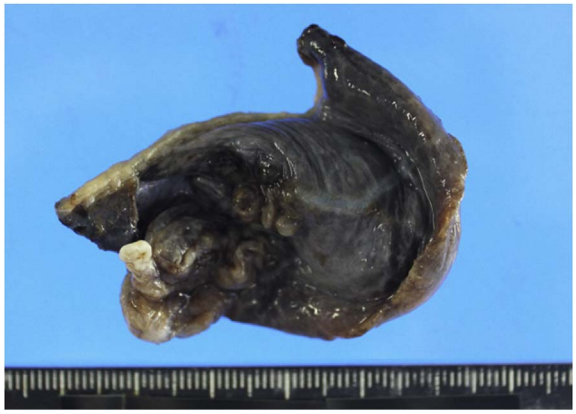

Fig. 4. A macroscopic view of the resected lung specimen showing multiple cystic lesions.

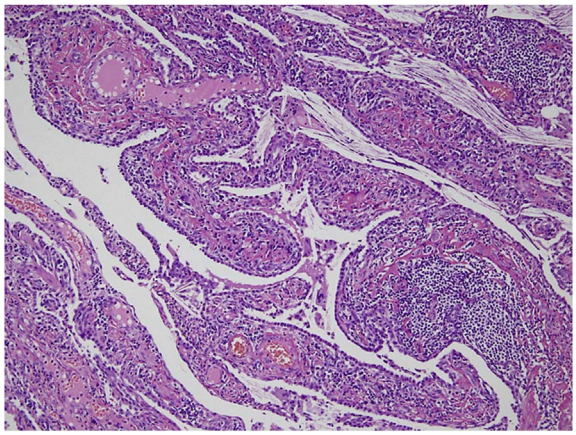

Fig. 5. Low magnification microscopy of the resected lung specimen. The stroma around the cyst was infiltrated by cells, mainly lymphocytes, and its capillary blood vessels were dilated, suggesting the presence of a chronic inflammation (hematoxylin and eosin, × 100).

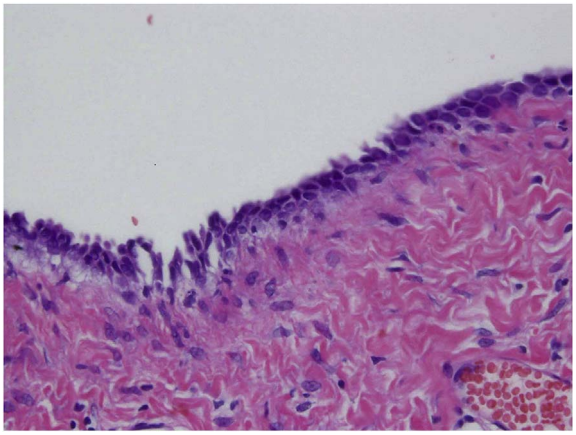

Fig. 6. High magnification microscopy of the resected lung specimen. Some of the cysts were covered by a cuboidal or pseudostratified epithelium, and some of the cysts' walls were lined with ciliated epithelium (hematoxylin and eosin, × 250).

hyperplasia of the bronchiolar epithelium leads to the development of multiple cysts. In 1977, Stoker et al. [5] classified CCAM lesions into types I–III, which was mainly based on the sizes of the cysts and, in 1994, Stocker [6] defined CCAM as a hamartomatous disease that can arise in any part of the tracheobronchial tree, expanded its classification to encompass types 0–IV, and proposed the term “CPAM.” Improvements in prenatal diagnostic techniques have led to an increase in the number of patients who undergo early resections, which has made it possible to examine resected specimens that do not exhibit inflammatory changes. Thus, it has become increasingly clear that some patients who had been diagnosed with CCAM/CPAM had pulmonary sequestration or bronchial atresia. In addition, it has been suggested that the different types of CCAM/CPAM may have different etiologies. Therefore, further validation studies are needed to define the different types of CCAM/CPAM more clearly and to establish their diagnostic criteria.

Approximately 80% of CCAMs are detected and diagnosed prenatally or during the neonatal period, when patients present with respiratory failure and cyanosis initially. CCAM is often associated with other organ anomalies and aplasia, and these patients have poor prognoses. Most CCAMs that are not identified during the neonatal period are detected in infants and school-age children, and these diagnoses are triggered by infections, for example, pneumonia, and they are associated with relatively good prognoses. CCAMs are rarely found in adults. We undertook a literature search and found detailed clinical descriptions of 61 patients (Supplementary Table 1), which includes the current case; Table 1 summarizes these details. The ages of the patients ranged from 21 years to 80 years, their mean age was 38 years, and their median age was 33.5 years. Of these patients, 29 were men, 29 were women, and the sex of the remaining patients was not described. Right-sided CCAMs (n = 34) occurred slightly more frequently than left-sided CCAMs (n = 23), and bilateral CCAM occurred in three patients. The CCAMs were located in one pulmonary lobe in up to 55 patients, and particularly in the lower lobes of the lungs in 39 patients. Type I and type II CCAMs were detected in these patients, 41 of whom had type I CCAMs. The CCAMs were often discovered in the context of an infection or common respiratory symptoms, which included the presence of a cough, sputum, or respiratory distress. Of the 21 adult

Table 1
Summary of the 61 adult cases of congenital cystic adenomatoid malformation reported in the literature, including the present case.

	n (%) or median (range)
Age, years	33.5 (21–80)
Sex	
Male	29 (48.3)
Female	29 (48.3)
Unspecified	2 (3.3)
Symptoms or clinical presentation, including pleural symptoms	
Pulmonary infection	21 (35.0)
Hemoptysis	13 (21.7)
Dyspnea	13 (21.7)
Chest pain	12 (20.0)
Productive cough	10 (16.7)
Pneumothorax	7 (11.7)
Fever	6 (10.0)
Non-productive cough	4 (6.7)
Asthma	2 (3.3)
Copious sputum	1 (1.7)
Asymptomatic	8 (13.3)
Side	
Right	34 (56.7)
Left	23 (38.3)
Bilateral	3 (5.0)
Lobe location	
Lower	39 (65.0)
Upper	12 (20.0)
Middle	4 (6.7)
Pleural	5 (8.3)
Surgical procedure	
Lobectomy	34 (56.7)
Bilobectomy	4 (6.7)
Wedge resection	3 (5.0)
Segmentectomy	2 (3.3)
Pneumonectomy	1 (1.7)
Detail of resection unclear	6 (10.0)
Biopsy	2 (3.3)
Stocker classification	
I	41 (68.3)
II	16 (26.7)
Not described	3 (5.0)
Associated malignancy	8 (13.3)
Papillary adenocarcinoma	3 (5.0)
Mucinous adenocarcinoma	2 (3.3)
Acinar adenocarcinoma	1 (1.7)
Adenocarcinoma in situ	2 (3.3)

CCAM patients who had infections that included pneumonia and lung abscesses, pulmonary tuberculosis was present in two patients, aspergillosis was present in one patient, tuberculosis and aspergillosis were present in one patient, and a *Mycobacterium celatum* infection was present in one patient. CCAMs were detected in eight asymptomatic adults, which differs from the presentation of CCAMs in children. In addition, 13 patients had bloody sputum, which is a common symptom. The CCAMs were detected in the context of a pneumothorax or a history of pneumothorax in seven patients, which includes the current patient [7–12]; therefore, a CCAM should be considered in the differential diagnosis of a pneumothorax. Pulmonary cysts associated with a primary spontaneous pneumothorax have a predilection for the apex of the lung and S^6; thus, the preoperative location of the pulmonary cysts in the current case suggested a disease that differed from a primary spontaneous pneumothorax. In the present patient, the pulmonary cysts were in the lower lobe, which supported a diagnosis of CCAM.

Pathologically, the cysts associated with CCAM are lined with a pseudostratified ciliated epithelium, they display a serrated or papillary proliferation of the bronchial epithelium, and the mucosa is characterized by the absence of bronchial cartilage and glands. Histologically, adenomatoid proliferations of the terminal bronchioles are present, the different-sized cysts are lined with a pseudostratified ciliated or simple cuboidal epithelium, papillary hyperplasia of the cyst wall mucosa is evident along with an increase in the quantity of elastic fibers present in the cyst walls, there is a lack of cartilage in the cyst parenchyma, and alveoli lined with mucus-producing cells are present. Although the absence of inflammatory changes was previously considered to be a characteristic of CCAM, it has recently been reported that CCAM is often accompanied by inflammatory changes in patients who present after puberty [13].

The differential diagnosis of CCAM includes pulmonary sequestration, bronchiectasis, bronchogenic cysts, and bronchial atresia. Pulmonary sequestration can be distinguished by the presence of abnormal blood vessels, bronchiectasis and bronchogenic cysts can be differentiated by the presence of the inflammatory destruction of cartilage and bronchi, and bronchial atresia can be distinguished by the obliteration of a bronchus. Two reports describe CCAMs that coexisted with intralobar pulmonary sequestration or bronchial atresia [11,14].

The present patient's CCAM was not detected until adulthood, despite it being congenital, which suggests that the cysts were small initially and grew as the patient grew, or that the check-valve mechanism caused them to expand and rupture. Type I CCAM lesions consist of one to several large cysts that are ≥ 2 cm and are surrounded by smaller cysts, which concurs with those found in the current case. The current patient underwent surgery for a recurrent pneumothorax. However, asymptomatic cysts can become infected or rupture, and type I CCAMs may undergo malignant transformation [11,15–18]; therefore, surgical resection is recommended for adults with suspected CCAMs. The findings from previous studies have shown that, compared with children, concomitant malignant tumors, including alveolar cell carcinomas and adenocarcinomas, are more frequently detected in patients who have undergone surgery for CCAMs [15,16]. We found case reports that described eight patients, many of whom had type I CCAMs, during our literature search [16–23].

Given that the lesions often involve most of a lung's lobe, the possibility that the residual cysts may become infected, and the potential for concomitant malignancy, many patients undergo lobectomies. On the other hand, there are reports that describe patients with benign localized lesions who did not undergo lobectomies and did not experience recurrences [9,21,24–26]. We consider a wedge resection or segmentectomy to be sufficient for the initial surgery, but only if the CT scans do not reveal any solid elements, cyst-wall thickening, or evidence of a suspected malignancy, and if the cyst is sufficiently localized to enable a complete resection. Indeed, there are no reports of patients who did not have concurrent lung cancer when a CCAM was completely resected, which would have placed them at a higher risk of developing lung cancer in the same lobe. Hence, further validation studies involving more patients are needed.

The present patient underwent a wedge resection for a primary spontaneous pneumothorax, partly because the CCAM had not been diagnosed when she was hospitalized. Since the cysts were confined to a small portion of the peripheral lower lobe of the lung, we were able to perform a wedge resection with sufficient surgical margins. The resected specimen did not contain any malignant tumors or residual cysts, and no postoperative infections occurred. The patient is scheduled for regular follow-up visits.

4. Conclusions

We have described the successful treatment of an adult case of CCAM that was detected following her hospitalization for a pneumothorax, and we have summarized the findings from 60 case reports on CCAMs in adults that are described in the literature. To the best of our knowledge, this review contains the largest number of adult CCAM cases. We propose that if multicystic lung lesions are found in pneumothorax patients, especially in lower lobes, CCAM should be considered in the differential diagnosis, even in adults, and a surgeon should seek to perform total resection of the lesion.

Consent for publication

The patient was properly informed and gave consent for her clinical information to be included in the publication of this case report and the accompanying images.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

RH described and designed the article. RH, HY, and RM were involved in treating the patient. RM, MK, and MI participated in editing the manuscript critically. All authors declare that they contributed to this article and that they have read and approved the final manuscript.

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None.

Abbreviations

CCAM	Congenital cystic adenomatoid malformation
CPAM	Congenital pulmonary airway malformation
CT	Computed tomography
S6	apical segment

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.rmcr.2018.02.002.

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