



Clinical characteristics and surgical treatment of congenital cystic adenomatoid malformation in adults: the largest cohort of 46 patients

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Background: Congenital cystic adenomatoid malformation (CCAM) is a rare congenital malformation of the lungs, however it lacks a summary of pathognomonic clinical and imaging features in adults. Our study aims to evaluate clinical characteristics and surgical treatment in the largest case series of adult CCAM.

Methods: The records of 46 adult patients with CCAM admitted to West China Hospital between February 2009 and March 2019 were reviewed. All patients accepted the surgery and get fully recovered. Data were collected and analyzed regarding patient demographics, medical history, preoperative investigations, intraoperative findings, and postoperative outcomes.

Results: The records of 22 men and 24 women were examined. The main systemic and respiratory symptoms included fever, productive cough, hemoptysis, and chest pain. Twenty lesions were found in the right pulmonary lobes and 26 in the left lobes. All CCAM lesions were successfully resected by surgery (35 patients had lobectomies, and the remaining 11 patients underwent wedge resections). Twenty-nine patients underwent video-assisted thoracic surgery (VATS), while 17 patients received posterolateral thoracotomy (PLT). The pathological analysis of surgical specimens revealed 26 cases of pure CCAM lesions and 20 cases of CCAM mixed with other diseases. More than 10% of patients had coexisting pre-malignant or malignant lung lesions. Four patients experienced postoperative complications. No intraoperative and postoperative deaths occurred.

Conclusions: Surgical resection remains the preferred approach for adults with CCAM and has satisfied outcomes. Clinicians should be aware of possible coexisting infections and malignancies.

Keywords: Congenital cystic adenomatoid malformation (CCAM); adult; thoracic surgery

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Introduction

Congenital cystic adenomatoid malformation (CCAM) is a rare congenital anomaly of the terminal respiratory structures (1,2), constituting up to 95% of congenital cystic lung lesions. Approximately 90% of CCAM lesions are detected during infancy. The diagnosis of CCAM in adults is extremely rare (3-5), with only 70 cases reported in English literature to date (6). The following sub-types of CCAM have been described (3): type I (75%) is characterized by the presence of one or several cysts between 2 to 10 cm; type II (10–15%) consists of numerous smaller cysts (~0.5–2 cm); type III (10%) features large cysts that are often mixed with non-cystic components. Some adult cases are asymptomatic and diagnosed by routine chest X-rays. Others may present with dyspnea, recurrent pulmonary infection, hemoptysis, hemithorax, or pneumothorax (6,7). Malignant transformation has also been reported, such as pleuropulmonary blastoma and bronchoalveolar carcinoma (2). On computed tomography (CT), CCAM lesions usually present as pulmonary cysts, but they may sometimes resemble bronchiectasis or lung tumors. The lack of specific imaging features and clinical manifestations makes diagnosis and treatment challenging for clinicians. Surgical resection, including lobectomy or wedge resection, is recommended for all patients to prevent recurrent pulmonary infections and possible malignant transformation (5,8-12).

Although CCAM in adults are always presented as case reports in the previous literature (13,14), there are few data on summary of clinical characteristics and surgical treatment in these rare lesions. Here, we report the largest case series of adult CCAM, with descriptions of patient demographics, medical history, preoperative investigations, intraoperative findings, and postoperative outcomes. We present the following article in accordance with the STROBE reporting checklist (available at <https://atm.amegroups.com/article/view/10.21037/atm-22-1747/rc>).

Methods

Patients

We collected the files of 46 CCAM patients admitted to the Department of Thoracic Surgery at West China Hospital (a 4,300-bed major medical center in Chengdu, China) between February 2009 and March 2019. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This case series study received ethical approval from the Institutional Review Board of West

China Hospital of Sichuan University, China (No. 2019-1087). Individual consent for this retrospective analysis was waived.

Assessments

We assessed patients with demographics, medical history, preoperative investigations, intraoperative findings, and postoperative outcomes. All patients received routine laboratory testing, electrocardiography (ECG), pulmonary function tests (PFTs), and chest computed tomography (CT) before surgery. Patients with a history of tuberculosis were scrutinized for possible active tuberculosis. Fiberoptic bronchoscopy was used to evaluate the lesions if they were near the hilum. Sputum culture was completed for patients with a productive cough. Anti-tuberculous or other antibacterial treatment(s) were administered preoperatively if pathogenic bacteria were identified.

Surgery was performed if the following indications were present: (I) recurrent clinical symptoms; (II) the lesion was limited to one lobe; (III) co-existing cancer was suspected; (IV) there were no contraindications for surgery. Either wedge resection or lobectomy was performed based on the size and location of the lesion, as determined by chest CT. Wedge resection was performed for peripheral lesions <3 cm, while lobectomy was used for larger or central lesions.

A chest tube was inserted for every patient after surgery and was removed when daily drainage was <200 mL without identifiable air leakage. A chest X-ray was taken to confirm adequate lung expansion. All patients received intra- and postoperative prophylaxis with ceftriaxone. For patients with an anaphylactic response to β -lactams, clindamycin was administered instead. Patients were discharged from the hospital when fully recovered.

Statistical analysis

Statistical Product and Service Solutions (SPSS) software version 22.0 (SPSS, Inc., Chicago, IL, USA) was used to analyze the data. Descriptive statistics were used to analyze the categorical and continuous variables.

Results

Patient demographics are summarized in *Table 1*. A total of 46 patients (22 males and 24 females) were included. The median age at diagnosis was 42.9 years (15–70 years). CCAM lesions did not show any anatomical preferences

Table 1 Clinical characteristics of all patients with CCAM

Characteristics	Value (N=46)
Age (years), median [range]	42.9 [15–70]
Gender, n (%)	
Male	22 (47.8)
Female	24 (52.2)
Smoking, n (%)	
Yes	12 (26.1)
No	34 (73.9)
Location of lesions, n (%)	
RUL	8 (17.4)
RLL	12 (26.1)
LUL	11 (23.9)
LLL	15 (32.6)
Clinical symptoms, n (%)	
None	17 (37.0)
Cough + sputum production	17 (37.0)
Cough + hemoptysis	6 (13.0)
Chest pain	6 (13.0)
Preoperative diagnosis, n (%)	
Bronchiectasis	7 (15.2)
Pulmonary cyst	6 (13.0)
Pulmonary tuberculosis	2 (4.3)
Pulmonary sequestration	3 (6.5)
Lung tumor	28 (60.9)
Surgical therapy, n (%)	
Lobectomy	35 (76.1)
Wedge resection	11 (23.9)
Surgical procedure, n (%)	
VATS	29 (63.0)
PLT	17 (37.0)
Pleural adhesions, n (%)	
No	14 (30.4)
Yes (LPA: SPA)	32 (69.6)
Postoperative type, n (%)	
I	11 (23.9)
II	7 (15.2)
III	28 (60.9)

Table 1 (continued)**Table 1** (continued)

Characteristics	Value (N=46)
Postoperative pathology, n (%)	
CCAM	26 (56.5)
CCAM + PS	6 (13.0)
CCAM + PM	6 (13.0)
CCAM + EEC	1 (2.2)
CCAM + PT	1 (2.2)
CCAM + PLAM	1 (2.2)
CCAM + LC	5 (10.9)
Complications, n (%)	
Pneumothorax	2 (4.3)
Pneumonia	1 (2.2)
Deep venous thrombosis	1 (2.2)
Mortality	0

CCAM, congenital cystic adenomatoid malformation; RUL, right upper lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe; VATS, video-assisted thoracic surgery; PLT, posterolateral thoracotomy; LPA, local pleural adhesion; SPA, severe pleural adhesion; PS, pulmonary sequestration; PM, pulmonary mycosis; EEC, ectopic esophageal cyst; PT, pulmonary tuberculosis; LC, lung cancer; PLAM, pulmonary lymphangioliomyomatosis.

in our cohort. While 17 out of 46 patients (37.0%) were asymptomatic, 29 patients (63.0%) presented with systemic and respiratory symptoms, including fever, productive cough, hemoptysis, and chest pain. On chest CT, CCAM lesions manifested with diverse features, including solid mass, cyst, cavitary lesion, bronchiectasis, pulmonary sequestration with aberrant artery, or pneumonic lesions (*Figure 1*). Some lesions had a mixture of different imaging features. All CCAM lesions were fully resected (35 cases underwent lobectomy, and 11 underwent wedge resection). Thirty-three patients (71.7%) presented with various degrees of pleural adhesions, which were separated during the surgery. Twelve patients with severe pleural adhesions underwent prolonged surgery. Twenty-nine patients (63.0%) had video-assisted thoracic surgery (VATS) while 17 patients (37.0%) received posterolateral thoracotomy (PLT). One patient who commenced VATS was switched to thoracotomy due to severe pleural adhesions. Histological examinations of the resected specimens revealed 26 cases

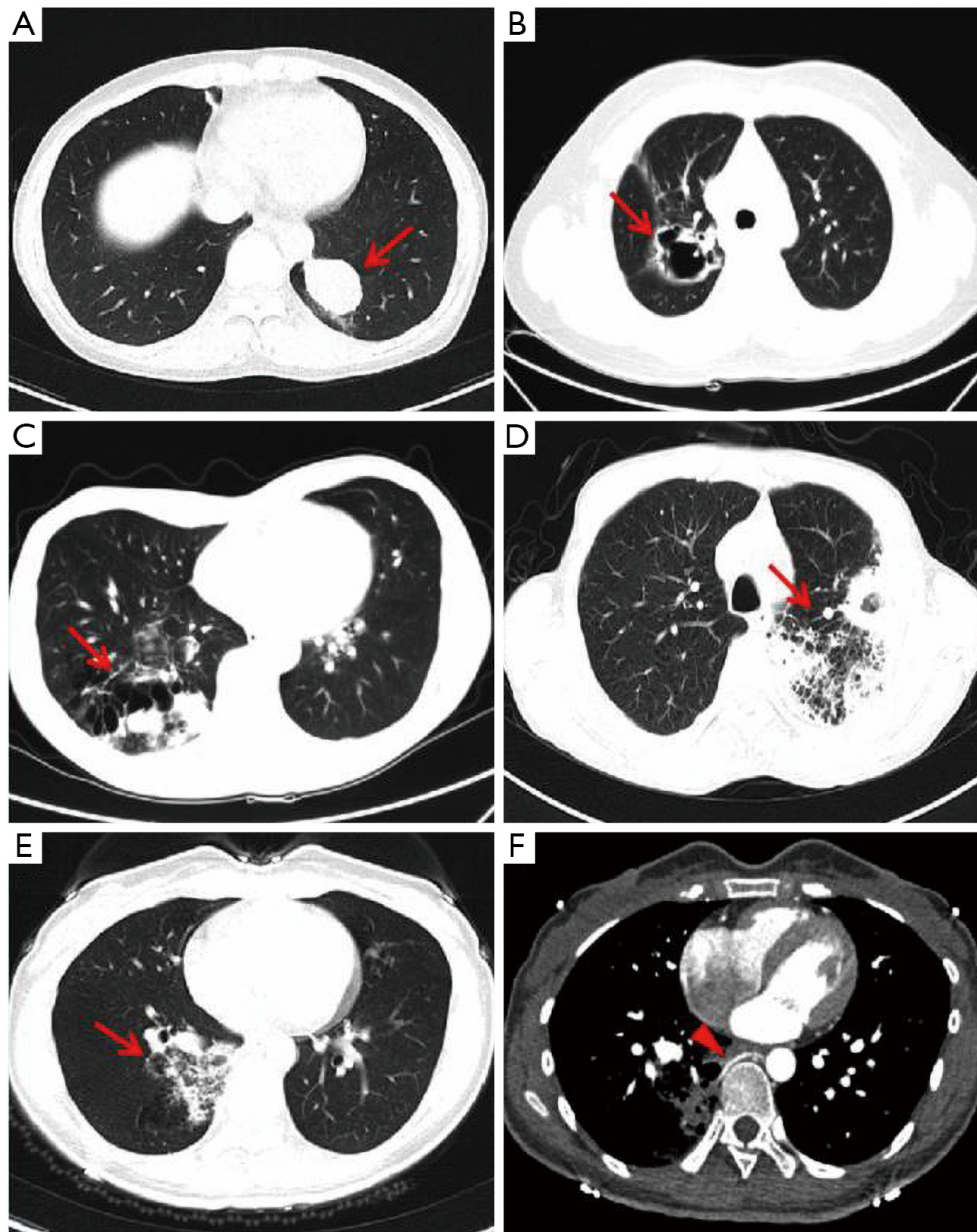


Figure 1 The chest CT images of different patients. (A) Case 1: chest CT shows a 6 cm × 5 cm mass in the left lower lobe (red arrow); (B) Case 2: chest CT shows a 6 cm × 5 cm cavity in the right upper lobe (red arrow); (C) Case 3: chest CT shows multiple cysts in the left lower lobe (red arrow); (D) Case 4: chest CT shows an extensive inflammatory lesion in the left upper lobe (red arrow); (E,F) Case 5: chest CT scan shows a localized inflammatory lesion (red arrow) with an aberrant artery from the aorta (red arrowhead) in the right lower lobe. CT, computed tomography.

of pure CCAM lesions and 20 cases of mixed CCAM with other diseases (six cases of pulmonary sequestration, six cases of pulmonary mycosis, five cases of pre-malignant or malignant lung lesions, one case of ectopic esophageal cyst, one case of tuberculosis, and one case of pulmonary

lymphangi leiomyomatosis). Postoperative complications occurred in 4 patients (8.7%): 2 patients developed pneumothorax, 1 patient acquired pneumonia, and the fourth patient developed deep venous thrombosis (DVT). No intraoperative or postoperative deaths occurred.

Among the five cases with coexisting pre-cancerous lesions or neoplasms, one patient was found to have atypical adenomatous hyperplasia (AAH), two had highly differentiated mucinous adenocarcinoma, one had highly differentiated adenocarcinoma, and one had pulmonary carcinoid tumor. The immunohistochemistry (IHC) of the pulmonary carcinoid tumor revealed moderate levels of phosphoenolpyruvate carboxykinase 1 (PCK1) but high expressions of neuroendocrine markers, such as chromogranin A (CgA), CD56, and synaptophysin. After discharge, all five patients were followed up regularly by medical oncologists at outpatient clinics, where they received periodic CT.

Discussion

CCAM is a rare congenital pulmonary disease. Most patients are diagnosed during infancy, and only a small proportion are diagnosed during adulthood. Adult patients with CCAM are often diagnosed during regular physical examination or due to recurrent pulmonary infection. In our study, 63.0% of the adult patients were diagnosed due to respiratory symptoms, such as cough, sputum, and hemoptysis. In contrast, almost all pediatric patients present with cough and dyspnea (15). In our study, the CT scans often showed the adult CCAM lesions as a solid mass or cyst, similar to imaging manifestations seen in pediatric cohorts (4,16). Other coexisting congenital anomalies, including pulmonary sequestration, heterotopic esophageal cyst, and arteriovenous malformation (AVM), have been reported (7,17-19). However, no patients had coexisting arteriovenous malformations in our cohort, which may reflect the possible difference between pediatric and adult cohorts.

Chest CT provides detailed information about the size and location of the lesions, which helps determine the surgical choice between wedge resection or lobectomy (20). Moreover, contrast CT may reveal aberrant vessels in patients with pulmonary sequestration. In our study, contrast CT identified that all six CCAM patients with pulmonary sequestration had abnormal arteries. These torturous abnormal arteries should be carefully handled during surgery to avoid excessive bleeding. Fiberoptic bronchoscopy was used to biopsy the lesions close to the bronchus and to determine if the bronchus was invaded by pathogens.

CCAM may increase the risk of infection by pathogenic microorganisms, including tuberculosis and other

bacterial, fungal, hydatid, and viral infections. Although the risk is lower than pediatric cohorts, we suggest routine screening to prevent any severe infections superimposed by hospitalization and the stress of surgery (15).

Previous studies have reported several types of coexisting malignancies or transformations, such as pleuropulmonary blastoma, bronchoalveolar carcinoma, malignant mesenchymoma, and rhabdomyosarcoma (2,21,22). In our cohort, >10% of patients had coexisting pre-malignancies or malignancies. Additionally, our study is the first to report the coexistence of small pulmonary carcinoid tumor, a rare pathology, with adult CCAM. Thus, all CCAM specimens should be scrutinized extensively for underlying coexisting cancer. Currently, there are no guidelines on the follow-up for patients with comorbid CCAM and cancer. Thus, we recommend all adult CCAM patients be followed up in outpatient oncology clinics periodically to ensure no recurrence of CCAM or any associated neoplastic lesions.

A previous study of pediatric populations has suggested that type I CCAM is the most frequent (75%), whereas type III is the rarest (3). However, type III accounted for the majority of patients in our study (28 patients, 60.9%), which reflects a significant difference in pediatric and adult cohorts. While most type I and II lesions resemble non-specific inflammation, many type III CCAM lesions resemble tumors on CT. Future studies are needed to determine if type III CCAM lesions are more commonly associated with lung malignancies in adults.

Due to recurrent pulmonary infections and the increased risk of neoplastic transformation, surgical resection is the definitive treatment for CCAM (6,9,23). Both PLT and VATS are the mainstream surgical techniques. The choice between PLT and VATS is usually made based on the surgeon's experience and the complexity of the specific case. During surgery, severe pleural and hilar adhesions may be found in some patients, possibly due to repeated infections. Adhesions may lead to incomplete resection of CCAM lesions, significant blood loss, and prolonged surgery. Extended procedures may thus increase the risk of postoperative complications, such as infections, sepsis, and respiratory distress.

Although CCAM appears to be a benign lesion with an excellent prognosis in our adult cohort, our small sample size made it difficult to determine if coexisting CCAM and lung malignancy represent a worse prognosis. Careful screening for underlying infections is also critical to ensure optimal patient outcomes, as shown in our cohort where no patient suffered from severe infectious complications or

death. Future studies are needed to refine the guidelines for adult CCAM.

Conclusions

In summary, surgical resection is recommended for CCAM in adults and demonstrates an overall excellent prognosis. However, clinicians should be aware of possible coexisting infections and malignancies.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <https://atm.amegroups.com/article/view/10.21037/atm-22-1747/rc>

Data Sharing Statement: Available at <https://atm.amegroups.com/article/view/10.21037/atm-22-1747/dss>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://atm.amegroups.com/article/view/10.21037/atm-22-1747/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board of West China Hospital of Sichuan University, China (No. 2019-1087) and individual consent for this retrospective analysis was waived.

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