A 38-Year-Old Woman With Bilateral Cystic Lesions in Both Lower Lung Lobes

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Case Presentation

A 38-year-old woman visited our clinic because of intermittent nonproductive cough for several months. Her past medical history revealed no specific illness. She was a nonsmoker. On physical examination, her breath sounds were decreased on both lower lung fields. Laboratory tests revealed a leukocyte count of 8,540/µL with 74.2% neutrophils, erythrocyte sedimentation of rate 66 mm/h, and high sensitivity C-reactive protein level of 26.47 mg/L, and were otherwise normal. After reviewing the chest imaging, several diagnostic approaches were performed to define the possible causes for the cystic mass lesions, such as infections, malignancy, immunologic diseases, and embolism. There was no definitive endobronchial lesion on bronchoscopic examination, and bronchial washing was negative for malignancy. BAL cultures were negative for bacteria, Mycobacterium, virus, and fungi. Clinical assessment of the progress and response of the cystic lesions to the antibiotics revealed that there were no definitive infectious, immunologic, or malignant causes. We decided to remove the cystic lesions via surgical resection because there was no response to medical treatment, and the tissues were analyzed for diagnosis. After she received the final diagnosis pathologically, at 2-month follow-up, she had no complaints, and no evidence of the disease was found.

Radiographic examinations with chest radiograph showed multicystic masses on the posterior basal segments of both lower lobes in which multiple air-fluid levels were observed (Fig 1). In addition, chest CT scan revealed two cystic lesions located on both lower lobes, about 8 cm × 4 cm in size. They were composed of multiple lobules and fluid collections, and the walls of cysts and lobules were thin and
relatively smooth margined, showing soft tissue intensity without contrast enhancement. Interestingly, the cystic lesions on each lobe communicated with each other by a kind of canal, which was located between the heart and descending thoracic aorta (Fig 2). In addition, contrast-enhanced CT scan showed the absence of aberrant vessels leading to the cystic lesions.

![Image](https://vpn.aku.edu/das/article/body/273928117-2/jorg=journal&source=MD%20Consult%20-%20A%2038-Year-Old%20Woman%20With%20Bilateral%20Cystic%20Lesions%20in%20Bo...)

**Figure 1** A, Chest posteroanterior view shows multiple cystic lesions on both lower lung fields with air-fluid levels. B, Left lateral view shows cystic lesions on both lower lung fields with air-fluid levels.

The patient underwent left lower lobe lobectomy for the multicystic lesion. Grossly, the polycystic mass was on basal segments of the left lower lobe excised surgically. The mass size was 8.2 cm \( \times \) 3.6 cm, and the cystic mass was relatively easily dissected from surrounding tissues. The color of the inner cyst wall was gray with multiple lobules, which were filled with pus-like material. Microscopically, numerous small cysts were separated by fibrous connective tissue, and the cystic wall was lined with pseudostratified ciliated and mucinous columnar epithelium (Fig 3). About 3 months later, she underwent right lower lobe lobectomy for the remnant cystic lesions. The pathologic findings for this 8.5 cm \( \times \) 5 cm cyst from the right lower lobe were similar to those in the left lung. Using the radiologic images and the gross photograph of each specimen, we could identify the portion of the suspicious structure for the communication between two lesions. The communication was a tubular structure surrounded by walls composed of fibrous connective tissues.

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**Figure 2** Chest CT scan shows multicystic masses located in posterobasal segments of both lower lobes. A, Mediastinal window setting. B, Lung window setting. Walls of cysts and lobules are thin and relatively smooth margined, showing soft tissue intensity without contrast enhancement. The cystic lesions on each lobe are communicating through a bridge, which is located between the heart and descending thoracic aorta (arrow).

![Image](https://vpn.aku.edu/das/article/body/273928117-2/jorg=journal&source=MD%20Consult%20-%20A%2038-Year-Old%20Woman%20With%20Bilateral%20Cystic%20Lesions%20in%20Bo...)

**Figure 3** Representative hematoxylin-eosin-stained sections of the cystic masses. A, Numerous small cysts are separated by fibrous connective tissue (original magnification \( \times 20 \)). B, The cystic wall is lined by pseudostratified ciliated and mucinous columnar epithelium. Cartilage resembling a bronchial wall cartilage plate is present in the wall of this cystic area (original magnification \( \times 200 \)).

**What is the diagnosis?**
Diagnosis: Bilateral congenital cystic adenomatoid malformation, type 1

Discussion
Clinical Discussion

Congenital cystic adenomatoid malformation (CCAM) is a rare pulmonary developmental disorder with replacement of normal pulmonary tissues by dilated bronchiolar-like airspaces having variable size and distribution.\[1\] According to one report, the incidence of CCAM is approximately 1.2 per 10,000 births.\[2\] It occurs sporadically, and there is no genetic predisposition or gender predilection.\[3\] The pathogenesis of CCAM remains unknown, although it is known as a failure of normal lung development.\[1\] .\[4\] .\[5\] Normal mammalian lung development begins as an outpouching of the developing foregut during the third week of embryogenesis. The outpouching proceeds to form two bronchial buds that penetrate into the associated splanchnic mesoderm at 4 weeks' gestation. Lung development is divided into several stages: pseudoglandular (embryonic period to 17th week), canalicular (17th to 24th week), terminal sac (24th week to term), and alveolar (postnatal life). Stocker classification type 3 resembles the pseudoglandular period of lung development, type 2 the canalicular period, and type 1 cannot be cataloged as one specific stage as it may arise from the pseudoglandular or canalicular period.\[4\] It has been reported that CCAM results from a failure of interaction between endoderm and mesoderm\[6\] or an imbalance between an increased cell proliferation and a decreased apoptosis within the developing lung.\[7\] In addition, CCAM is produced by a developmental failure due to a hypovascular development,\[8\] as seen in other malformations.\[9\]

CCAM is most commonly found in the neonatal period, and up to 90% of the cases are diagnosed within the first 2 years of life.\[10\] With advances in high-resolution diagnostic imaging techniques used for gestational follow-up, late-onset CCAM undoubtedly becomes rarer, and its detection requires a higher level of suspicion for its diagnosis.\[11\] Clinical features of CCAM are variable, from asymptomatic to pulmonary complications. It usually presents in infancy with respiratory distress secondary to a space-occupying lesion that compromises normal lung tissues. Recurrent respiratory tract infection is the most common complication of adult CCAM presentation.\[12\] In addition, adult presentation includes shortness of breath, lung abscess, spontaneous pneumothorax, pyopneumothorax, hemoptysis, cerebral air embolus during a long flight, and gastrointestinal bleeding with entire lung involvement.\[11\] .\[13\] .\[14\] Of all complications associated with CCAM, neoplastic transformation is the one with the worst prognosis and is usually found in older children or young adults. The incidence of CCAM-associated bronchioloalveolar carcinomas is <1%.\[15\] Large cyst-type CCAM is associated with bronchioloalveolar carcinoma, rhabdomyosarcoma, and pleuropulmonary blastoma.\[10\] In our present case, the patient had had no chronic or recurrent respiratory complications, which could make the suspicion for CCAM difficult.

As presentation with CCAM in adulthood is rare, no specific treatment guidelines exist. Surgical resection, such as segmentectomy, lobectomy, and pneumonectomy, is the treatment of choice in symptomatic cases of CCAM and cystic pulmonary lesions with uncertain radiologic findings to prevent infection and potential neoplastic transformation and to examine the uncertain lesion histologically.\[10\] Prognosis of CCAM presenting in adulthood depends on the pathologic features, infection, and potential for malignant transformation.\[1\] In cases with bilobar or bilateral lesions, prognosis is known to be poor because of pulmonary hypoplasia of the residual lung.\[16\]

Radiologic Discussion

Chest radiographs and CT scan may reveal an opacity or a lucent, cystic, fluid-filled mass resembling an abscess in the pulmonary zone affected, and high-resolution CT scanning is proposed as a reliable paraclinical investigative procedure that allows more accurate assessment for the site and extent of CCAM. Radiographic analysis may preoperatively suggest the diagnosis, especially when a multicystic pattern like our present case is evident. When the cystic lesion is single, the differential diagnosis with the congenital parenchymal cysts and other cystic lesions is not possible only on the basis of the radiologic features. In particular, in the case of wall thickness >4 mm, the differential diagnosis should include various etiologies: neoplastic origin (bronchogenic carcinoma, metastases, lymphoma), infections by bacteria (\textit{Staphylococcus aureus}, gram-negative bacteria, \textit{Mycobacterium}, actinomycosis, and nocardiosis), fungi (aspergillosis, mucormycosis, and cryptococcosis) and/or parasites, immunologic diseases (Wegener granulomatosis), pulmonary embolism, pneumoconiosis, localized bronchiectasis, CCAM, and pulmonary sequestration.\[17\] The multicystic lesion with thick walls and solid content observed in our present case is more often seen in pulmonary sequestration, in infectious causes, and in necrotic cancer. In fact, it can be easy for CCAM to be confused with lung infections on radiologic examination. Moreover, small CCAM lesions may not be visible on chest radiographs.\[1\] Therefore, using more advanced modalities, differential diagnosis has to be done from other rare cystic tumors, and the effort to find the small lesions is required.\[13\] Specifically, in light of an association with pulmonary sequestration, the contrast-enhanced CT scan or CT scan angiogram is noteworthy for the distinction between CCAM and sequestration, since the absence of aberrant vessels to the cystic lesion is a key feature of CCAM. In all the series reported, CCAM occurs with equal frequency in the right and left lung, usually confined to one lobe, and there is a predilection for occurrence in the posterior basal segments of the lower lobes.\[12\] The cases of multilobular disease are much less frequent, and thus the cases of bilateral diseases are rarer.\[1\] Interestingly, our current patient had CCAM in both lobes, the posterior basal segments of the lower lobes, with a communicating bridge. It did not communicate any tracheobronchial tree or pleural space. The radiologic feature of the bridge between the two cystic lesions was similar to fibrotic septum in the lesions themselves. Supporting this radiologic finding, histologic examination showed that the bridge was composed of fibrotic connective tissues. Therefore, we hypothesized that this communicating bridge may be formed as the result of repetitive inflammation in the cystic lesions.

Pathologic Discussion

In histopathologic examinations, CCAM lesions consist of cysts and solid airless tissues, usually with no cartilage in the wall. They may
partially or entirely affect the pulmonary lobes.\textsuperscript{[10]} CCAM can be readily distinguished from other intrapulmonary cysts and postinfectious pulmonary abscesses by the multiplicity of cysts of various sizes, by the presence of smooth muscle and absence of scar, and by the presence of respiratory lining cells and mucin-secreting cells.\textsuperscript{[10]} On the basis of clinical, gross, and histopathologic criteria, Stocker et al.\textsuperscript{[18]} have classified CCAM into three types: type 1 is the most common type of CCAM (about 60\% of cases) and is rarely associated with anomalies. This type is curable with surgical resection. Pathologic features of type 1 CCAM are single or multiple cysts with a maximum diameter of 10 cm with ciliated pseudostratified tall columnar epithelia, high content of smooth muscle cells, and elastic tissues. In some cases, cartilage is present in the wall of the cyst. Most adult patients with CCAM have Stocker type 1 features on histopathology, presumably because the severe forms are either stillborn or are operated during childhood. Type 2, accounting for 20\% to 30\% of cases, contains numerous smaller cysts, usually <1 cm in diameter, resembling ecstatic terminal bronchioles. Large alveolar-like structures are present among the cysts. In 50\% of the cases, type 2 CCAM has been found to be associated with extralobar pulmonary sequestration\textsuperscript{[19]} and carries a worse prognosis because of the association of this type with other congenital anomalies.\textsuperscript{[20]} Type 3, accounting for 10\%, forms a solid and bulky mass, composed of regularly spaced bronchiole-like structures separated by masses of alveolus-like structures lined by cuboidal epithelium. In the modified classification in 2002, according to their resemblance to normal anatomic structures from proximal to distal, types 0 and 4 were added.\textsuperscript{[21]} A type 0 lesion involves all five lobes and is incompatible with life. Type 4 CCAM is rare overall, accounting for <15\% of all CCAMs. This type is peripheral, typically solitary lesions, comprising thin-walled cystic spaces lined predominantly by pneumocytes with the intervening stroma being generally of low cellularity and showing no cytologic atypia, in which lesions are histologically similar to cystic pleuropulmonary blastomas. In fact, in a large percentage of cases of type 4 CCAM, cystic pleuropulmonary blastomas have been identified; thus, type 4 CCAM lesions should be considered malignant.

**Conclusion**

In this report, we describe a rare case of CCAM detected in adulthood, which showed bilateral presentation having a communicating bridge between each contralateral lobar lesion without any chronic or respiratory complications, with reviewing the clinical, radiologic, and pathologic features of CCAM. Histopathologically, it was defined as a CCAM type 1 as judged by the modified Stocker classification. Although the incidence is low, chest physicians should be aware that CCAM can be detected in adulthood without any chronic or recurrent respiratory complications and that it can show bilateral presentation, which in some cases can even communicate with each other. In addition, we recommend using more advanced modalities, such as chest CT scan, for differential diagnosis from other cystic diseases, because CCAM can be confused with lung infections, such as an abscess, on radiographic examination.

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