Broncholithiasis From Histoplasmosis in a Pediatric Patient: Case Report and Review of Literature

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Broncholithiasis is a calcification in the airway. Though broncholiths are not common, it is even more unusual in a pediatric patient. We present a 15-year-old immunocompetent pediatric patient who had a broncholith that was found and removed by bronchoscopy.

Broncholiths are calcified structures or hard concretions that have eroded, at least in part, into the tracheobronchial tree. Broncholithiasis is defined as bronchial inflammation or obstruction resulting from broncholiths, which usually arise from adjacent calcified mediastinal lymph nodes [1]. Broncholiths have been associated with pulmonary tuberculosis since 1885. Histoplasmosis has been recognized as another main cause in adults during the past half century [2]. Broncholithiasis is rare in childhood and has not been associated with histoplasmosis. We present such a case in an immunocompetent pediatric patient who presented with hemoptysis.

CASE REPORT

The patient was a previously healthy, 15-year-old white female who was referred for pulmonary evaluation after an episode of hemoptysis, described as approximately 1 teaspoon of blood. She had a dry cough and chest pain for 2 months before this episode. Early in the course, a chest radiograph was normal, and she was treated for presumed Mycoplasma pneumoniae infection and asthma exacerbation with azithromycin, systemic oral steroids, and inhaled albuterol. On evaluation after the hemoptysis, she had no tachypnea, abnormal breath sounds to auscultation, or other abnormal findings on physical examination. Growth and development were normal for age. Initial studies included a normal complete blood count and complete metabolic panel. She had an elevated erythrocyte sedimentation rate of 32 mm/hour and a C-reactive protein level of 15.5 mg/L. The tuberculin skin test was nonreactive. Pulmonary function tests were normal. Computed tomography (CT) of the chest showed extensive calcified mediastinal adenopathy and calcified granulomatous changes within both hila and lower lobes.

Flexible bronchoscopy revealed a rounded mass in the medial right mainstem bronchial wall approximately 1 centimeter from the carina. It had a broad, flesh-colored base with a white top and minimal vascularity (Figure 1). The mass broke apart during biopsy, and all of the material was removed easily with forceps. The fragments were placed in a container with a glutaraldehyde and water mixture, and the specimen disintegrated during transport to the pathology laboratory to the degree that further evaluation was not possible. Bronchoalveolar lavage (BAL) fluid showed benign bronchial and squamous epithelial cells, alveolar macrophages, and small numbers of acute and chronic inflammatory cells. Cultures from the BAL were negative for bacteria, mycobacteria, and fungi. The patient had an elevated serum antibody titer of 1:64 to Histoplasma capsulatum yeast phase by complement fixation (CF). She was seronegative for complement fixing antibody to the mycelial antigen. H and M bands were not detected in immunodiffusion (ID) assay. CF and ID assays were negative for Blastomyces dermatitidis, Coccidioides immitis, and Aspergillus fumigatus.
Based on clinical, radiological, serological, and histopathological data, the patient was diagnosed with broncholithiasis secondary to histoplasmosis. This diagnosis had not been suspected until the lesion was seen during bronchoscopy. She was treated with 200 mg of oral itraconazole solution daily. Upon reevaluation 8 weeks later, she was asymptomatic and therapy was discontinued. Repeat bronchoscopy at that time showed a nonerythematous indentation of the right mainstem bronchus in the area of the previous broncholith (Figure 2). She remained asymptomatic after 18 months of follow-up.

**DISCUSSION**

We report the first case of broncholithiasis associated with *H capsulatum* infection in a child. Broncholiths most often develop when infected peribronchial or hilar lymph nodes calcify and erode into the adjacent tree. Erosion is prompted by the repetitive visceral motions of respiration, circulation, and deglutition [2–4]. *Mycobacterium tuberculosis* is the most common cause of broncholithiasis worldwide, but in the United States, especially the Ohio River basin, *H capsulatum* is the most common cause in adults [5].

Broncholithiasis due to any cause is extremely rare in children. To the best of our knowledge, only 3 other cases of broncholithiasis in children <18 years old have been reported: a 14-year-old with *Mycobacterium kansasii* infection [6], a 14-year-old with ciliary dyskinesia without known infectious etiology [7], and a 17-year-old listed in a case series of broncholithiasis without mention of etiology [4].

In adults, broncholiths occur equally in both genders, with median age of 50 years at presentation. Most broncholiths arise in the right lung, especially the proximal right middle lobe bronchus and origin of the anterior segmental bronchus of the upper lobe, secondary to airway anatomy and lymph node distribution. Other infectious causes of broncholithiasis include *M kansasii*, *B dermatitidis*, *C immitis*, *Cryptococcus neoformans*, *Actinomyces israelii*, and *Nocardia asteroides* [8, 9]. Noninfectious causes include pulmonary silicosis, aspiration of bone tissue in food or in situ calcification of aspirated foreign material, erosion by and extrusion of calcified or ossified bronchial cartilage plates, and calcified material from distant sites (such as the kidneys) that migrated to a bronchus [9].

Calcification of lymph nodes in pulmonary mediastinal histoplasmosis develops as acute granulomatous inflammation that progresses to fibrosis. This may occur within several months to several years and is more rapid in children than in adults [10, 11]. The time course between calcification of nodes and formation of broncholiths is not well characterized. An adult lung transplant patient who developed a broncholith secondary to histoplasmosis in the donor lungs developed a calcified left hilar lymph node 1 year after transplant, which led to broncholithiasis with 70 percent obstruction of the airway 21 months later [12]. In addition, the previously mentioned pediatric case report of the 14-year-old male with *M kansasii* developed his broncholith in only 8 months [6].

The most common symptom of broncholithiasis is nonspecific chronic cough, but hemoptysis (30–85 percent of patients), lithoptysis (less than 20 percent of patients), chest pain, wheezing, and fever also occur. Our patient had prolonged cough and chest
pain followed by a single episode of limited hemoptysis. Complications from broncholithiasis include recurrent pneumonia, bronchiectasis, and esophageal fistulae. Massive hemoptysis can occur if there is erosion into the aorta or pulmonary artery [13].

Diagnosis of broncholithiasis, regardless of etiology, can be made when calcifications are evident in the large airways on radiographic studies. Chest CT may demonstrate lesions not evident on plain chest radiographs. Thin collimation increases the sensitivity of chest CT. In 1 study, CT identified calcified lymph nodes in all cases. Other findings seen were due to bronchial obstruction or injury and included atelectasis, infiltrates, bronchiectasis, and air trapping [14]. The disappearance of a previously identified calcified nodule or change in its position on serial radiographs could also indicate broncholithiasis [9].

Laboratory confirmation of *H capsulatum* infection can be difficult in patients who have localized pulmonary disease or who are in convalescent phase of infection. Biopsy of necrotic lymph nodes in patients with granulomatous mediastinitis may reveal a few yeast-like organisms. Fibrotic tissue from later stages of infection typically reveals no organisms. Fungal cultures of such lesions are usually negative. Enzyme immunoassay (EIA) for antigen detection is most useful in the immunocompromised host with disseminated infection, in whom urine and serum EIA have sensitivities of 95 and 86 percent, respectively. However, in patients with mild acute pulmonary histoplasmosis, only 10 to 20 percent will have detectable antigenuria, and those with granulomatous mediastinitis or mediastinal fibrosis usually do not have detectable antigen in urine or serum [15].

Serologic tests are the most reliable means of laboratory confirmation for patients with acute pulmonary histoplasmosis or who are later in the course of infection, such as our patient. CF and ID assays remain the standard tests. The CF assay detects antibodies against yeast and mycelial phase antigens. A single titer of 1:32 to either antigen is suggestive of infection. These antibodies may persist for years after infection, so a single titer may indicate past exposure to *H capsulatum*. A 4-fold increase in antibody titer during the first weeks to months after acute infection is diagnostic [15]. CF assays can have cross-reactivity with other fungal infections. Titters may not be detectable for 2 to 6 weeks after infection and may be negative in immunocompromised hosts [16]. In our patient, the single 1:64 CF yeast phase titer is consistent with acute infection within a few months to a few years past.

ID assays test for the presence of H and M precipitin bands and have approximately 80 percent sensitivity in acute infection. M bands can be detected early in infection and may persist for months to years after resolution. H bands are less commonly detected and are seen primarily in chronic or severe infections [15]. Seroreversion to negative results within 1 to several years is common with ID assays, and the negative ID results would not be unexpected in a patient (such as ours) with a late complication of histoplasmosis.

Bronchoscopy can be both diagnostic and therapeutic for broncholithiasis. In adults, 25 to 50 percent of broncholiths may be visualized during fiberoptic bronchoscopy. Management of patients with broncholiths consists of physically removing the stone. Flexible or rigid bronchoscopic extraction of broncholiths that are free or partly eroded into the tracheobronchial tree is considered safe and is usually effective. Laser ablation may be used for stone removal or for control of bleeding or stone ablation. Risks of bronchoscopic removal include possible loss of fragments into distal airways, or hemorrhage during manipulation of an adherent or embedded broncholith. Airway trauma during removal can lead to fistula formation [1, 4, 17].

Thoracotomy may be required when bronchoscopy is unsuccessful, bronchial fistulas to other mediastinal structures are present, hemoptysis is severe, or airway obstruction or bronchiectasis has led to recurrent pulmonary infections [4, 17]. Bronchotomy with sleeve resection may suffice and preserve lung function when airway impact is localized without distal suppuration or bronchiectasis [18]. Sometimes lobectomy may be required (eg, bronchiectasis with recurrent infections) [16, 17].

Antimicrobial therapy may also be warranted, depending on the underlying etiology. Antifungal treatment is not indicated routinely when broncholithiasis is the only manifestation of histoplasmosis, because calcification of mediastinal lymph nodes occurs late in the course and generally after host control of the infection [19]. In retrospect, administration of itraconazole was not necessary for our patient, and this was discontinued after further consideration at follow-up.

**CONCLUSION**

Chronic cough and hemoptysis in a child in the setting of calcifications on chest radiograph or CT should alert clinicians to the possibility of broncholithiasis. Histoplasmosis is the most common cause of
broncholithiasis in the United States, especially in highly endemic areas. Removal is often accomplished by bronchoscopy, although surgery may be required. The need for antimicrobial therapy varies by etiology and stage of infection.

References