Spontaneous pneumothorax secondary to chronic cavitary pulmonary histoplasmosis

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ABSTRACT

_Histoplasma capsulatum_ is a dimorphic fungus that causes histoplasmosis. Chronic cavitary pulmonary histoplasmosis is rare, and typically manifests as apical cavitary lesions in patients with pre-existing chronic obstructive pulmonary disease. We report a case involving a 60-year-old female who presented to our facility with acute onset of dyspnea and dry cough. Chest x-ray revealed a large left-sided pneumothorax with nearly complete collapse of the left lung. A chest computed tomography scan revealed a left upper lobe cavitary lesion with a bronchopleural fistula. After thoracic surgical bleb resection, a surgical specimen sent for biopsy was positive for _Histoplasma capsulatum_. The patient’s pneumothorax was subsequently diagnosed as chronic cavitary pulmonary histoplasmosis, and itraconazole treatment was initiated. After admission, the patient underwent a thoracotomy with deortication to improve lung expansion; however, the patient’s pneumothorax persisted. After a prolonged hospital stay and serial chest x-rays that showed stable residual pneumothorax, the patient was discharged to a long-term acute care facility and itraconazole treatment was continued. Two months after discharge, a repeat chest x-ray showed resolution of her left-sided pneumothorax. This case report highlights the importance of considering pulmonary histoplasmosis (or other endemic pulmonary fungal infections) when a patient presents with apical cavitary lesions.

1. Introduction

_Histoplasma capsulatum_ is a dimorphic fungus that is classically endemic to the Midwestern and Central USA [1]. This includes the Mississippi and Ohio River Valleys in which parts of North Texas are included [2]. It typically enters hosts through the respiratory tract and only causes symptoms in a small number of patients [3]. Infection with _Histoplasma capsulatum_, termed histoplasmosis, can present in a variety of ways, including both acute and chronic forms. Symptoms are somewhat non-specific, and include chest pain, productive cough, dyspnea, fever, and fatigue [3]. Chronic cavitary pulmonary histoplasmosis is one of the rarest presentations of histoplasmosis, and typically manifests as apical cavitary lesions in patients with pre-existing chronic obstructive pulmonary disease [3]. These apical cavitary lesions are frequently mistaken for malignancy or pulmonary tuberculosis. It is important to remember that chronic pulmonary infection with _Histoplasma capsulatum_ can cause apical cavitary lung disease, it is often misdiagnosed, and lack of appropriate treatment portends a poor prognosis [4,5].

2. Case report

Our patient was a 60-year-old Hispanic female with a history of alcoholic cirrhosis and long-standing tobacco abuse who presented to our facility with complaints of a one-day history of acute onset of dyspnea and dry cough. She had never experienced these symptoms with this level of severity, and her symptoms began suddenly without any pre-existing strenuous activity. She described the pain as a sharp sensation, worse with deep inspiration, and located in the left anterior portion of her chest. She rated the pain as a 7/10 in severity, which was largely unchanged since symptom onset. She had not attempted to treat the pain with any over-the-counter medications. She denied fever, weight loss, night-sweats, lymphadenopathy, sore throat, hemoptysis, abdominal pain, rash, or joint pain.
In the emergency department, she was found to have an oxygen saturation of 79% on room air. The patient was placed on supplemental oxygen by nasal cannula with subsequent improvement in her oxygen saturation to greater than 90%. Physical exam was significant for decreased breath sounds and hyperresonance to percussion over the left lung fields. There was no tracheal deviation noted. Cardiac examination was unremarkable upon auscultation, and there was also no evidence of decompensated cirrhosis, such as ascites or hepatic encephalopathy. A chest x-ray revealed a large left-sided pneumothorax with nearly complete collapse of the left lung (Figure 1). A chest tube was placed in the emergency department with adequate placement confirmed on chest x-ray with improvement of the pneumothorax. She was then admitted to the general medical floor. The following day, a repeat chest x-ray was performed which showed only a mild decrease in size of the pneumothorax from the prior day. A computed tomography (CT) scan of the chest without contrast revealed the presence of a left upper lobe cavitary lesion measuring 0.7 × 2.7 cm with a bronchopleural fistula (Figure 2). Persistent air-leak was noted from the patient’s chest tube since admission. Cardiothoracic surgery was consulted, and video-assisted thoracic surgical bleb resection was performed due to persistent air-leak from chest tube. The surgical specimen was sent for bacterial, acid-fast bacilli, and fungal cultures. All cultures from the specimen were negative except for the fungal cultures, which were reported as growing Histoplasma capsulatum. Of note, three different sets of sputum acid-fast bacilli cultures were obtained and were negative, effectively ruling out active pulmonary tuberculosis. The infectious disease service was consulted and felt that the patient’s pneumothorax was likely due to chronic cavitary pulmonary histoplasmosis. Itraconazole was started at a dose of 100 mg by mouth daily for treatment of the infection. The patient was asked extensively about risk factors for exposure to Histoplasma capsulatum and denied recent travel, history of foreign travel, exposure to bird or bat droppings, construction sites, farmhouses, wood cutting or gathering, and cave spelunking. During admission, serial daily chest x-rays were performed to assess for re-expansion of her lung. Despite bleb resection, the lung did not fully expand, putatively because of entrapment due to an inflammatory rind. The patient then underwent a thoracotomy with decortication in hopes of improving lung expansion. During the thoracotomy, she was noted to have adhesions of both the upper and lower lobes of the left lung to the mediastinal pleura which were taken down. The patient’s pneumothorax persisted despite surgical efforts. She was discharged after a prolonged hospital stay to a long-term acute care facility after serial chest x-rays showed stable residual

Figure 1. Chest x-ray showing large left-sided pneumothorax on initial presentation.
pneumothorax. Itraconazole was continued, with plans to continue for a total of 1 year of antibiotic therapy. Two months following discharge, a repeat chest x-ray showed resolution of her left-sided pneumothorax (Figure 3).

3. Discussion

*Histoplasma capsulatum* is a dimorphic fungus which is classically endemic to the Ohio and Mississippi River valleys. However, its presence has been noted on nearly every continent, and more than half the world’s population potentially lives in areas of endemicity [1]. *Histoplasma* nearly always infects hosts via the respiratory tract, and in rare cases may enter hosts through organ transplantation from infected donors [6]. After inoculating the host, the infection can have a variety of manifestations depending on the age or comorbidities of the host. The majority of patients infected with *Histoplasma capsulatum* are asymptomatic [3]. However, those who are symptomatic can have a broad range of clinical presentations, ranging from mild to lethal. We will limit our discussion to the pulmonary forms of the disease.

Acute pulmonary histoplasmosis is a syndrome typically characterized by relatively non-specific symptoms including fever, malaise, headache, and weakness, accompanied by a non-productive cough [3]. Substernal chest discomfort is occasionally a complaint as well. This presentation is common in individuals, particularly children, who are exposed to the organism for the first time. Hilar and mediastinal lymphadenopathy are often present, along with a patchy pneumonia on chest x-ray. A minority of patients present with erythema multiforme or erythema nodosum [3]. A more severe form of acute pulmonary histoplasmosis occurs in patients that are exposed to a large inoculum of the organism, or in those who are immunosuppressed. Patients with severe disease often develop respiratory failure and acute respiratory distress syndrome. While acute pneumonia due to *Histoplasma* is often mild and self-limiting, the severe form may require treatment with anti-fungal agents.

Chronic cavitary pulmonary histoplasmosis is an indolent form of *Histoplasma* infection. All patients with this form of disease have previously been exposed to and inoculated with *Histoplasma*, whether or not they developed an acute pulmonary syndrome. Almost all patients with this syndrome have chronic obstructive pulmonary disease, particularly emphysema, and tend to be elderly [3]. On biopsy, inflammation is typically seen adjacent to emphysematous bullae. The bullae become thickened and necrotic, eventually leading to fibrosis and the formation of cavitary lesions. These are most commonly seen in
the apical and posterior segments of the lungs. The cavities may enlarge over time, and in some cases may lead to development of a bronchopleural fistula, as in our patient. In addition to respiratory complaints, other symptoms may include fever, weight loss, and night sweats. Treatment is prolonged and involves anti-fungal therapy, typically oral itraconazole. Amphotericin B may also be used, although its side-effect profile is significantly less favorable.

Diagnosis of pulmonary histoplasmosis can be accomplished by a variety of modalities. The organism can be cultured on Saubourad’s agar from various tissue samples, but takes several weeks to grow [3]. The mycelial form of the fungus is then identified under microscopy. Histopathology may also yield the diagnosis, but in vitro the fungus will manifest as a yeast form due to its dimorphic nature. Biopsies may be taken from clinically apparent sites of disease (skin, lung, etc.) or bone marrow. A variety of antibody and antigen detection assays have been developed to assist with diagnosis. The most common antigen assay used is the urine enzyme immunoassay (EIA), which is more sensitive than the similar serum assay. The antigen of interest (a polysaccharide from the cell wall) is most commonly detected in disseminated histoplasmosis and acute pulmonary histoplasmosis in which the patient has been exposed to a large inoculum of organism. Only 10% to 20% of patients with chronic cavitary pulmonary histoplasmosis or a less severe form of acute pulmonary histoplasmosis will have a positive urine antigen EIA [3]. In the case of our patient, this test was negative. Antibody tests are most useful in the setting of chronic infection, as it may take several weeks for a patient to mount a sufficient number of detectable antibodies. Both immunodiffusion and complement fixation are tests that can indirectly detect antibodies of interest, and can be used in the diagnosis of histoplasmosis. In our patient, both the complement fixation assay and immunoassay were positive for Histoplasma capsulatum.

Spontaneous pneumothorax is a rare presentation of chronic cavitary pulmonary histoplasmosis. There are only two other similar case reports upon literature search, making this a relatively unique case [7,8]. The first case report, published in 1956 from Vanderbilt University Hospital, was a 31-year-old female who initially developed constitutional symptoms and was found to have nodular infiltrations in the left lung apex [7]. Pulmonary tuberculosis was suspected and was to be further evaluated, but patient was lost to follow-up. She presented again 2 years later while pregnant. After the birth of her first child, which was uncomplicated, she developed worsening respiratory and constitutional symptoms, including increased productive cough and unintentional weight loss. Her condition progressively worsened over subsequent years without treatment, and she developed.

Figure 3. Outpatient chest x-ray two months following discharge from initial hospital stay.
sudden onset left-sided chest pain with worsened dyspnea. Evaluation with chest x-ray showed a left-sided pneumothorax with adhesions to the parietal pleura, as well as emphysema of the lungs. She experienced another spontaneous right-sided pneumothorax roughly 1 year later. This case shows some similarities with our patient, including the adhesions noted to the parietal pleura, as well as emphysema of the lungs. Whereas the patient in this case had years of worsening respiratory symptoms, constitutional symptoms, and histoplasmosis diagnosis prior to onset of her pneumothoraces, our patient did not have any constitutional symptoms or respiratory complaints prior to the development of her pneumothorax.

The second case report primarily highlighted the use of endobronchial valves in managing persistent bronchopleural fistulas [8]. The patient was a 60-year-old Caucasian female with a history of rheumatoid arthritis who presented to the hospital with acute diverticulitis. She had been taking prednisone for her rheumatoid arthritis, and thus was immunosuppressed. She was found to have significant apical cavity disease and a right-sided pneumothorax. Unlike our patient, this patient had a positive urine EIA, and also underwent bronchoscopy with bronchoalveolar lavage which was positive for Histoplasma. The chest tube that was placed for this patient required persistent continuous wall suction, and thus the patient was referred for endobronchial valve placement. Placement of the endobronchial valve in the segments involving the bronchopleural fistula resulted in successful placement of the chest tube to water seal and eventual removal of the chest tube. This patient is similar to our patient in that she is an elderly female, but there are not enough details available in this case to make further comparisons or contrasts.

Histoplasma is not the only endemic fungus that has been reported to cause spontaneous pneumothorax. There are case reports of spontaneous pneumothorax being caused by Aspergillus, Paracoccidioides, and Coccidioides species as well [9–12]. Interestingly, most of these case reports involve patients who had pre-existing emphysema or otherwise bullos deformities of the lungs.

4. Conclusion

Spontaneous pneumothorax is a rare presentation of chronic cavitory pulmonary histoplasmosis, and is a result of bronchopleural fistula formation contiguous with a cavity lesion. An important point to glean from this case is that chronic cavitory pulmonary histoplasmosis is frequently mistaken for pulmonary tuberculosis. Both diseases tend to present in the lung apices, cause cavitory lesions, and cause similar systemic symptoms such as fever, weight loss, and night sweats. It is important to maintain pulmonary histoplasmosis (or other endemic pulmonary fungal infections) in the differential diagnosis when a patient presents with apical cavity lesions, as delayed diagnosis leads to delayed treatment and portends a worse prognosis.

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