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Chronic Cavitary Pulmonary Aspergillosis: An Unusual Cause of Chronic Cough, Pleuritic Chest Pain, and Hemoptysis in a 24-Year-Old Coal Mine Worker

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ABSTRACT

Pulmonary Aspergillus infections are caused by the ubiquitous fungus mold when spores found in compost, dust, and plant material are inhaled. Manifestation of the disease is represented by a delicate balance between host and pathogen interactions, making Aspergillus infection more commonly observed in immunocompromised individuals. Chronic cavitary pulmonary aspergillosis (CCPA) is a subtype of pulmonary Aspergillosis associated with a history of chronic or prior lung disease. Here, we present the case of a non-immunocompromised 24-year-old male with a history of intermittent asthma with chronic pulmonary symptoms and a finding of a lung mass on imaging. We describe the diagnostic challenge and surgical treatment of CCPA in medically refractory disease. This case is unique because our patient is relatively young and otherwise healthy, with no associated chronic lung disease.

KEYWORDS

Chronic cavitary pulmonary aspergillosis (CCPA), pulmonary aspergillosis, chronic lung disease, medically refractory lung disease, surgical treatment of chronic lung disease

INTRODUCTION

The finding of a lung mass in a young person harbors a diversely broad differential diagnosis. When combined with the patient's presenting signs and symptoms, family history, tobacco use, immunocompromised, and exposure to infectious pathogens are important clues in making the diagnosis. As the probability of malignancy rises with age, malignant etiologies in those under 35 years of age are uncommon but should be carefully investigated.[1] Infectious granuloma is the most common cause of benign lung masses, while vascular abnormalities and benign tumors represent other common etiologies.[2]

Mycobacteria, endemic fungi, and Staphylococcus aureus are the most common infectious agents.[2] Careful questioning to elucidate the risk of exposure to these pathogens is an important step in diagnosis. Immunocompromised patients should also be identified, as they are at increased risk for fungal and mycobacterial infection. Pulmonary Aspergillus infections should remain high on the differential in immunocompromised patients and those with a history of lung disease.

Aspergillus infection presents as a spectrum of pulmonary diseases, including allergic, invasive, and noninvasive aspergillosis. Allergic bronchopulmonary aspergillosis (ABPA) is almost exclusively found in immunocompetent individuals with asthma and cystic fibrosis (CF) and presents with central bronchiectasis and recurrent CF or asthma exacerbations.[3] Invasive aspergillosis is the most severe type of

pulmonary aspergillosis and commonly affects immunocompromised individuals, including those severely neutropenic, hematopoietic stem cell transplant recipients, organ transplant recipients, patients on long-term corticosteroids, and those with acquired and heredity immunodeficiency.[4] Chronic cavitary pulmonary aspergillosis (CCPA), formerly referred to as complex aspergilloma, is a subtype of chronic noninvasive aspergillosis. In contrast to other forms of pulmonary Aspergillosis infection, CCPA is not associated with immunocompromise but rather a prior or current lung disease history.[4] CCPA commonly presents with cough, shortness of breath, sputum production, chest pain, and hemoptysis.[5] Patients may have elevated inflammatory markers, and one-third of patients have sputum culture with growth of Aspergillus.[5] CCPA is associated with high morbidity and mortality due to life-threatening massive hemoptysis.[6]

Here, we describe a 24-year-old male non-immunocompromised patient with chronic symptoms of hemoptysis, cough, and pleuritic chest pain with radiographic evidence of worsening cystic lung masses and culture positive for Aspergillus, diagnosed with CCPA.

CASE PRESENTATION

Our patient is a 24-year-old male who initially presented to his primary care physician (PCP) in October 2019 with an intermittent non-productive cough which progressed to hemoptysis with white/green sputum and intermittent pleuritic chest pain over 4 months. He denied fevers, chills, weight loss, and lymphadenopathy. Our patient has a past medical history of intermittent asthma, for which he was prescribed a combination long-acting beta agonist inhaled corticosteroid (LABA-ICS) inhaler, which he seldomly used. He has no history of tuberculosis or human immunodeficiency virus (HIV). He has used one can of smokeless tobacco daily for the past 10 years and has never smoked or used illicit drugs. He has worked as a welder at a coal mine since 2017 and worked on a farm prior to this. Workup of his symptoms by his PCP included chest computed tomography (CT), which revealed a right upper lobe (RUL) lung mass suspicious for malignancy (Figure 1, C). Urine histoplasma antigen, HIV, and Interferon Gamma Release Assay (IGRA) were negative.

He was referred to thoracic surgery in January 2020 due to failed biopsy attempts at an outside facility. His symptoms remained stable, and he was started on a 2-week course of doxycycline. Chest CT showed the RUL mass contained multiple cysts with low attenuation, with the largest cystic component increasing in size from 4.3 cm to 5.3 cm since the previous study. The patient underwent navigator bronchoscopy with brushings in February 2020, and cytology revealed normal-appearing bronchial cells with no evidence of malignancy. Fungal, bacterial, and acid-fast bacilli (AFB) cultures were negative. He was referred to infectious disease due to no improvement of his symptoms. Infectious disease and thoracic surgery recommended CT-guided biopsy.

In May 2020, the patient underwent CT guided biopsy with core biopsies sent for AFB and fungal culture (Figure 1, A). On follow-up with thoracic surgery, he complained of increasing chest pain and hemoptysis. Histology at this time was negative for malignancy, while cultures grew Aspergillus with further species unable to be elucidated. At this point, the patient was lost to follow-up from thoracic surgery and the infectious disease clinic.

In January 2021, the patient returned to the thoracic surgery clinic. The patient reported that he was started on itraconazole by a provider at an outside facility and that his symptoms

had remained stable. He was again referred to infectious disease, who saw him in March 2021 when they discontinued itraconazole and started voriconazole. The patient complained of intermittent chest pain at this time, although his cough had improved. The patient continued to have good follow-up with infectious disease and tolerated voriconazole well.

In November 2021, he was seen in the ER at an outside facility for chest pain. His chest CT showed a chronic multifocal collection of pulmonary nodular lesions in the RUL, unchanged from the prior CT 11 months ago. He was seen again by thoracic surgery, where surgical management of residual disease was planned. In January 2022, he underwent right upper lobe wedge dissection with resection of residual post-disease. Interventional radiology was consulted for the CT-guided placement of a fiducial coil at the posterior margin of the RUL disease process to ensure complete removal. A 4.8 x 1.7 x 1.4 cm wedge resection with multiple cystic components was removed (Figure 2). The patient tolerated the procedure well. Fungal, bacterial, and AFB cultures were negative. Chronic granulomatous inflammation was seen on histology (Figure 2, C). The patient

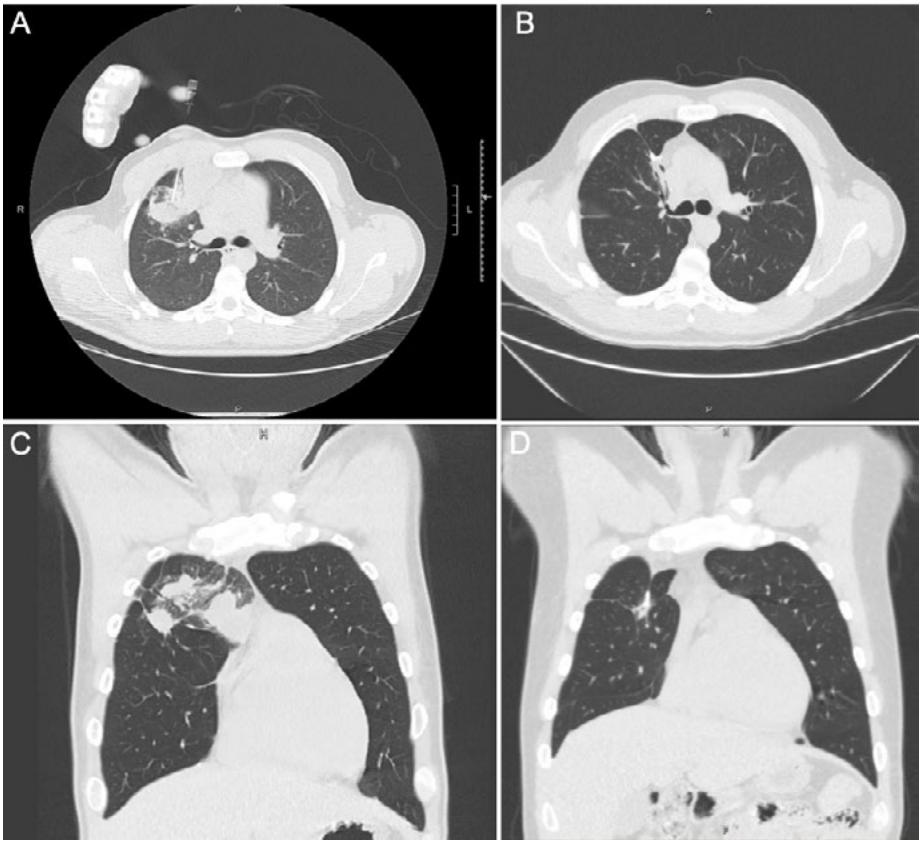

FIGURE 1. Pre- and postoperative CT images of CCPD. Non-contrast CT images in coronal and sagittal planes viewed through lung window. Postoperative images completed 4 months post wedge resection. **A**: CT guided biopsy of cystic right anterior lobe mass completed May 2020. **B**: Postoperative view of upper lobe reveals no evidence of mass or cystic components. **C**: Sagittal view of right anterior upper lobe reveals multiple cystic-appearing components with the largest seen against the mediastinum. Completed December 2019. **D**: Postoperative sagittal view reveals no evidence of lung mass.

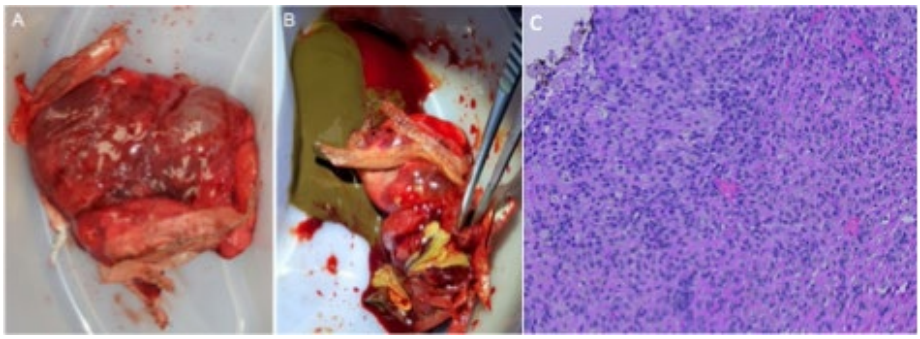

FIGURE 2. Intraoperative specimen. Residual pulmonary aspergillosis was resected by right upper lobe wedge dissection. **A**: Gross specimen shows a 4.8 x 1.7 x 1.4 cm wedge of the right upper lobe. Multiple cystic-appearing components contained in the wedge. Staple line can be seen. **B**: Multiple cystic pockets expressed opaque material when incised. **C**: Right upper lobe wedge resection showing lung parenchyma with focal chronic inflammation and granulomatous inflammation. No fungal organisms identified.

returned to thoracic surgery and the infectious disease clinic for follow-up and denied chest pain, cough, hemoptysis, and dyspnea. A 6-month course of voriconazole was started postoperatively. CT chest 4 months post-op showed no residual disease (Figure 1, B & D).

DISCUSSION

Diagnosis and control of disease in CCPA is a challenging task. Diagnosis of CCPA requires symptoms and radiologic features to be present for at least three months, no or minimal immunosuppression, and microbiologic (Aspergillus growth in culture or sputum polymerase chain reaction (PCR)) or immunologic (elevated Aspergillus IgG antibody) evidence of Aspergillus infection.[4] Various radiographic findings are found on CT imaging, including cavitations in the upper lung lobes that may contain fungal balls, bronchiectasis, pleural thickening, and effusions, making early CCPA diagnosis challenging.[7]

Our patient lacks traditional risk factors for Aspergillus infection, including prior tuberculosis infection, malignancy, AIDS, and immunocompromised state. Our patient has a five-year history of working in a coal mine, prior work on a farm, a 10-year history of smokeless tobacco use, and a history of asthma with non-compliant combination LABA-ICS inhaler use. "Farmer's lung" has classically been described as inoculation with A. fumigatus in non-immunocompromised hosts in highly-colonized environments such as farms.[8] A small number of reports have described associations between Aspergillus infection and work in coal mines, including the increased presence of A. fumigatus in the sputum of coal miners with coal workers' pneumoconiosis.[9] This combination of subtle immunodeficiency with tobacco use and asthma, combined with our patient's history of work in potentially highly-colonized environments, may have led to the development of CCPA.

CCPA is often treated pharmacologically, while surgical intervention is typically reserved for patients with persistent symptomatic local disease refractory to medical management and those with hemoptysis unresponsive to treatment. Patients with symptomatic CCPA require a minimum of six months of treatment with oral itraconazole or voriconazole.[4] Our patient with CCPA had symptomatic disease refractory to approximately one year of itraconazole and 6 months of voriconazole treatment. Benign-appearing surrounding

lung parenchyma and normal pulmonary function testing indicated that he was a candidate for surgical resection. Symptomatic patients with a single aspergilloma or CCPA with localized disease may undergo surgical resection for disease control. Better outcomes have been described in the resection of single aspergillomas when compared to CCPA, including decreased recurrence rate and reduced post-op complications such as bleeding, air leak, and pneumothorax.[10] In localized disease, wedge resection is the recommended surgical approach to preserve lung tissue.[11] Local resection is associated with better outcomes, including reduced length of postoperative antibiotics.[6,11] Our patient tolerated local wedge resection well, with no complications postoperatively, and has been compliant with 5 months of post-operative voriconazole to date.

CONCLUSION

Pulmonary aspergillosis is a rare fungal infection that should always be included in the differential diagnosis of patients with chronic cough, hemoptysis, and pleuritic chest pain with radiographic findings of a lung mass. This case is unusual because our patient is relatively young and otherwise healthy, with no associated chronic lung disease. CCPA unresponsive to oral first-line antifungal therapy should consider surgical resection of disease in the setting of good overall pulmonary function and localized disease with a 6-month course of oral antifungal postoperatively.

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