CASE REPORT

Pleural coccidioidomycosis presenting as spontaneous pneumothorax

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SUMMARY

Coccidioides is a fungus endemic to Southwestern USA and Northern Mexico which can be asymptomatic or result in a well-defined clinical syndrome of community-acquired pneumonia. On rare occasion, coccidioidomycosis may have atypical presentations as in our patient, a 25-year-old man admitted with a 2-month history of progressive dyspnoea and cough. He was found to have a large right-sided pneumothorax with exudative pleural effusion which did not resolve following thoracentesis. Decortication was performed which revealed a dense rind of inflammatory tissue covering all lobes of his right lung. Histopathology demonstrated hyphae resembling *Aspergillus*, but culture and serology confirmed *Coccidioides immitis*. Following several months of antifungal therapy, he achieved complete clinical recovery with near-complete resolution of radiographic findings.

BACKGROUND

Coccidioidomycosis is an important cause of fungal pneumonia that is epidemiologically linked to certain geographical regions. While it has been shown to be one of the more common causes of community-acquired pneumonia in Arizona, it is usually not considered in areas of Northeast Texas where *Histoplasma* is the more commonly recognised endemic fungus. Spontaneous pneumothorax with concomitant granulomatous pleuritis and exudative pleural effusion is a rare, unexpected and uncommonly reported complication of *Coccidioides immitis* infection. While endemic mycoses are thought to have well-delineated geographical areas of activity, our case highlights the importance of taking a thorough history in patients who present with persistent, non-resolving pulmonary symptoms.

CASE PRESENTATION

A 25-year-old man with no significant medical history presented to the hospital with 2 months of gradually progressive dyspnoea on exertion and dry cough. He had been treated as an outpatient for community-acquired pneumonia with various oral antibiotics and corticosteroids without resolution of symptoms. During a particularly severe coughing spell, he noted sharp right-sided chest pain.

While most of his life was spent in Dallas, Texas, he revealed that he had worked in

Arizona 2–3 years prior to presentation. He drank alcohol sparingly and did not smoke or use drugs. He had no pertinent family history and had no allergies to medications.

On presentation, the patient was mildly tachypnoeic, but had normal vital signs otherwise. He had absent breath sounds and hyper-resonance to percussion in the right upper lobe with dullness in the right lower lobe. He did not have significant skin findings. The remainder of the physical examination was normal.

INVESTIGATIONS

Complete blood cell count and comprehensive metabolic panel were unremarkable. Fourth-generation testing for HIV was negative. A chest radiograph showed a large right pneumothorax with moderate-to-large right pleural effusion (figure 1). A chest tube was placed and a post-procedure radiograph demonstrated only mild re-expansion of the right lung with persistent moderate pneumothorax and resolution of the pleural effusion postdrainage (figure 2). Pleural fluid analysis revealed the following: pH 7.2, white cell count $0.7 \times 10^9/L$, red cell count $8 \times 10^{12}/L$, total protein 6.7 g/dL, albumin 2.8 g/dL, lactate dehydrogenase 11 145 U/L and glucose <20 mg/dL. Given our patient's failure to improve clinically, a chest CT was ordered, and it demonstrated a large right pneumothorax with a dense rind covering his collapsed right middle and lower lobes (figure 3).

DIFFERENTIAL DIAGNOSIS

A 25-year-old man presenting with both pneumothorax and concomitant exudative pleural effusion might initially be suspected of having an inciting traumatic event. As our patient denied trauma or injury preceding symptom onset, infectious, inflammatory and malignant aetiologies were entertained as possibilities.

While tuberculosis was considered and excluded, our patient did not have risk factors, epidemiology, exposures or travel that would lead us to this diagnosis. Community-acquired pneumonia could manifest with pneumothorax or a parapneumonic effusion, but treatment was rendered for this diagnosis and the time course was too lengthy. Infection with an endemic fungus, such as histoplasmosis (given his residence in North Texas) and coccidioidomycosis (given his history of travel to Arizona) were

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Figure 1 Large right pneumothorax with moderate-to-large right pleural effusion.

considered as well. Following decortication, hyphae seen in tissue raised the possibility of aspergillosis even though this clinical presentation would have been highly unusual. However, it was notable that significant construction was being undertaken in his place of work.

Our patient had not lost weight, had preserved appetite and did not have constitutional symptoms suggesting underlying malignancy or disseminated disease. In addition, chest CT should have demonstrated lymphadenopathy or mass lesions.

Since our patient appeared to have isolated pleural disease, with no extrapulmonary manifestations, a systemic

Figure 2 Mild re-expansion of the right lung with persistent moderate pneumothorax and resolution of the pleural effusion postdrainage.

Figure 3 Large right pneumothorax with a dense rind covering the collapsed right middle and lower lobes.

inflammatory or autoimmune condition also seemed unlikely.

TREATMENT

Due to the failure of lung expansion after chest tube placement along with CT findings, the cardiothoracic surgery team performed a diagnostic video-assisted thoracoscopy and right thoracotomy with total lung decortication. Intraoperatively, the patient was found to have a 3–5 mm thick inflammatory rind covering all lobes of the right lung without abnormality noted in the underlying lung parenchyma.

Histopathology showed numerous branching fungal hyphae (figure 4), suggestive of *Aspergillus*. Liposomal amphotericin B was initiated pending results of tissue culture and serologies. (1,3) beta-D-glucan was positive at 328 pg/mL (normal <90 pg/mL). *Aspergillus* galactomannan antigen enzyme-linked immunoassay (EIA) was found to be negative. The patient was positive for *Coccidioides* IgG antibody by EIA. *Coccidioides* antibody was also detected by immunodiffusion. Fungal culture grew *C. immitis* and no other organisms.

Figure 4 Numerous branching fungal hyphae.

Figure 5 Near-complete radiographic resolution of the right pneumothorax.

OUTCOME AND FOLLOW-UP

The patient was transitioned to oral fluconazole and completed a 4-month course of therapy with complete resolution of symptoms and near-complete radiographic resolution of his right pneumothorax (figure 5).

DISCUSSION

Coccidioidomycosis is an important cause of fungal pneumonia that is epidemiologically linked to Southwestern USA and Northern Mexico. While it has been shown to be one of the more common causes of community-acquired pneumonia in Arizona, it is usually not considered in the areas of Northeast Texas where *Histoplasma* is the more commonly recognised endemic fungus. As was the case with our patient, the present-day high volume of occupation-related travel has led to various endemic fungal infections manifesting in unexpected areas.¹

Coccidioidomycosis is usually associated with mild disease in immunocompetent patients and often does not necessitate antifungal therapy.² However, our patient's spontaneous pneumothorax with concomitant primary granulomatous pleuritis and exudative pleural effusion was a rare, unexpected and uncommonly reported complication of underlying *C. immitis* infection. While immunocompromised patients have been shown to be at risk for severe pulmonary disease when infected with *C. immitis*, it is difficult to explain how our seemingly immunocompetent and healthy young patient would present with such severe pulmonary manifestations due to this organism.³ Others have hypothesised that immunocompetent patients are able to mount a more robust immune response to pulmonary coccidioidomycosis, thus leading to increased pleural vascular permeability resulting in pleural effusion formation.⁴

While pleural effusions have been shown to be common in hospitalised patients with coccidioidomycosis, coexistent pneumothorax is a rarely described entity. A review of 146 patients admitted with coccidioidomycosis to a large tertiary care hospital in the San Joaquin Valley region of California revealed that 22 patients (15%) presented with a pleural effusion. Among those 22 patients, 5 (22.7%) were found to have an empyema (one of whom had a concomitant

pneumothorax). A large review of the literature showed that pneumothorax occurred in six of the nine cases of complicated pleural coccidioidomycosis described.⁵

There are rare reports of coccidioidomycosis manifesting with pneumothorax described in the literature. A 28-year-old man in Arizona was found to have a right hydro-pneumothorax on a chest radiograph after presenting with low-grade fever, night sweats, fatigue and sudden onset of dyspnoea and chest pain.⁶ A chest CT showed a thin-walled cavity that was associated with a mural nodule within the right lung. Following a wedge resection and decortication, he was started on ketoconazole which was discontinued after 1 week because of adverse reactions (the patient presented prior to the approval of fluconazole in the USA). The patient was deemed healthy with no evidence of residual disease 1 year postoperatively, despite his very brief course of antifungal therapy. Another case report described a 22-year-old man who had recently travelled to Mexico and Arizona and presented to a New York City hospital with dyspnoea and chest pain in the absence of systemic symptoms.⁷ He was found to have a near-complete right-sided pneumothorax, extensive right-sided pulmonary infiltrates, an 8 cm mass-like density in his right lower lobe with central cavitation and anterior mediastinal lymphadenopathy. He underwent a wedge resection and decortication with pathology demonstrating necrotising granulomas and spherules consistent with *Coccidioides*. In addition, serology was positive for this organism. The patient received 6 weeks of antifungal therapy (liposomal amphotericin B followed by fluconazole) resulting in clinical improvement. A third case described a 40-year-old man with a history of HIV/AIDS who presented with acute onset of dyspnoea in addition to a 2-month history of dry cough, fever and weight loss.³ Imaging revealed a moderate right pneumothorax, and he was started on antibiotics. When he failed to improve clinically, a bronchoalveolar lavage (BAL) was performed. BAL cultures grew *Coccidioides* spp and transbronchial biopsies revealed spherules consistent with *Coccidioides*. He was treated with amphotericin B followed by fluconazole and improved without surgery. He later revealed he had travelled to El Paso, Texas, an area endemic for coccidioidomycosis. Although these three cases describe patients with concomitant parenchymal disease manifesting with pneumothorax as a sequela of coccidioidomycosis, it should be noted that our patient presented with pleuritis alone in the absence of parenchymal disease which makes him even more unusual.

The initial morphology of *C. immitis* in our patient (ie, branching fungal hyphae) was in contrast to the multinucleated spherules typically seen in tissue infected by this fungal pathogen.⁴ Although exceedingly rare, there has been at least one other case where the initial histological examination of fluid sampled from a hydropneumothorax showed hyphae, but the underlying infection was found to be caused by *C. immitis*.⁸ The presence of hyphae and the absence of spherules were thought to be related to the low PaO₂ of CO₂ which has been shown to maintain the arthroconidial form of *C. immitis* that is common at this site of infection.⁹ The particularly aggressive pulmonary manifestations seen in this reported case were severe, but the patient had an extensive smoking history, as well as exposures to asbestos and silicosis.

Our patient's case shows that while the initial histological examination of a suspected fungal infection can be helpful, it can be inconsistent with the final culture diagnosis.

Patient's perspective

I fell ill around the beginning of February 2017 with what I thought was a common cold or the influenza. After my symptoms didn't improve within a week, I decided to go to my doctor for a diagnosis and medication. My doctor said that she felt I had symptoms of pneumonia and so she started me on a round of treatment according to that diagnosis.

During this time I took a 2-week round of medication. I continued on with daily activities and even went on a business trip to Alabama. One morning I woke up and felt a sharp pain in my side as I rolled over to turn off my alarm. When the pain didn't persist, I didn't question it and never followed up on it. For about a month I walked around and lifted weights in the gym with a collapsed lung without my knowledge. When I would perform routine daily tasks such as walking, sitting, standing and mild jogging, I felt no pain. I became aware that I had some sort of issue during two activities. The first was when I would climb the four flights of stairs to my apartment. The second was when I would perform barbell squats and presses in the gym. I noticed that I would get incredibly winded and out of breath at the top of the stairs. Lifting weights in the gym made my lungs feel like they were burning.

I returned to the doctor's office and received a similar initial diagnosis to the first. It is notable that I was seeing a different doctor than the first, as it was a non-scheduled visit and my usual doctor wasn't available that day. After I explained the situation with the stairs and the gym to the second doctor, he sent me for a chest scan. It was revealed in the scan that I had a collapsed lung and that I immediately needed to visit the emergency room.

After spending 2 days in the ER and having two different chest tubes fail to reinflate my lung, doctors with the hospital determined I would need surgery to correct the problem. After the successful surgery, I was informed that the surgeon had found a substance on the lining of my lung and that it was being sent for testing. The test showed that the substance was cocci.

Learning points

- Identify aetiologies of granulomatous pleuritis and resultant spontaneous pneumothorax.
- Recognise the rare occurrence of *Coccidioides immitis* presenting with tissue hyphae.
- Understand the importance of a thorough travel history when elucidating the aetiology of non-resolving pulmonary infections.

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