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Difficult to Diagnose: An Unusual Cause of Cavitary Lung Lesion

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Patient: Male, 40-year-old
Final Diagnosis: Histoplasmosis
Symptoms: Dyspnea
Medication: —
Clinical Procedure: Bronchoscopy
Specialty: Pulmonology

Objective: Unknown ethiology

Background: Cavitary lung lesions are commonly identified on thoracic imaging, but typically require further workup for definitive diagnosis.

Case Report: Here, we present the case of a 40-year-old Middle Eastern male who presented with an unusual cause of cavitary lung lesion with associated pleural mass and pleural thickening. He underwent bronchoscopic biopsy and computer tomography (CT)-guided core needle biopsy, both of which were non-diagnostic. Surgical biopsy subsequently revealed hyalinized necrotizing granulomatous tissue, consistent with histoplasmosis, and the patient was treated with itraconazole, which he responded well to.

Conclusions: This case demonstrates the importance of identifying unusual causes of cavitary lung lesions and emphasizes the role of using proper tissue sampling for diagnosis.

MeSH Keywords: Biopsy • Histoplasmosis • Lung Diseases, Fungal • Multiple Pulmonary Nodules

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Background

Cavitary lung lesions are a common abnormality seen on adult chest imaging, which come with a broad differential [1]. Diagnostic probabilities are strongly influenced by clinical context, such as immune status, chronic illnesses, and timeline of the lesion [1]. Cavitary lung lesions most often fall into 1 of 2 categories: infection and malignancy. Other less common causes are autoimmune-related diseases. History and physical examination are the essential first step in narrowing the differential diagnosis, but more advanced imaging and a biopsy are typically necessary to yield a definitive diagnosis. The combination of imaging and the duration of symptoms can help narrow the differential diagnosis using an algorithmic approach [2]. An acute process is classified as symptoms of less than 12 weeks and would be consistent with bacterial, nocardial, fungal, necrotizing pneumonias, and septic emboli. Whereas a chronic process with symptoms greater than 12 weeks would be supportive of mycobacterial, fungal, viral, malignancy, or autoimmune disorders. Radiographic imaging is not highly specific. While imaging can suggest a diagnosis, clinical context is required to form an accurate diagnosis. Common infectious causes of cavitary lesions in adults include tuberculosis, bacterial pneumonia, and mycoses [3]. In the Ohio and Mississippi River Valleys, *Histoplasma capsulatum* is a common source of mycoses-induced cavitary lung lesions in acquired immune deficiency syndrome (AIDS) patients [4,5]. However, infection is typically asymptomatic and self-limiting in immunocompetent hosts [6,7]. Here, we present an atypical cavitary lung lesion caused by histoplasmosis in an immunocompetent patient.

Case Report

A 40-year-old Middle Eastern male with a past medical history significant only for chronic, heavy cigarette smoking presented with shortness of breath on exertion and general fatigue. He had only traveled to the Middle East and United States in the past. His last visit to the Middle East was 2 years prior to his presentation. His symptoms were initially treated with albuterol and antibiotics. Chest x-Ray (CXR) revealed a peripheral left upper lobe (LUL) lesion. Computed tomography (CT) thorax without contrast then revealed a 3.0×1.4 cm pleural mass of the LUL with associated pleural thickening and ground glass (Figures 1–3), a 2.2×2.0 cm left lower lobe cavitary lesion (Figure 4), and left hilar adenopathy. Given his travel history, he was ruled out for both tuberculosis and schistosomiasis. The patient underwent CT-guided core needle biopsy of the left upper lung, which revealed necrotic debris, but was negative for malignancy, fungus, or acid-fast bacteria (AFB). A subsequent bronchoscopy with transbronchial biopsy and bronchoalveolar lavage (BAL) of the LLL, as well as

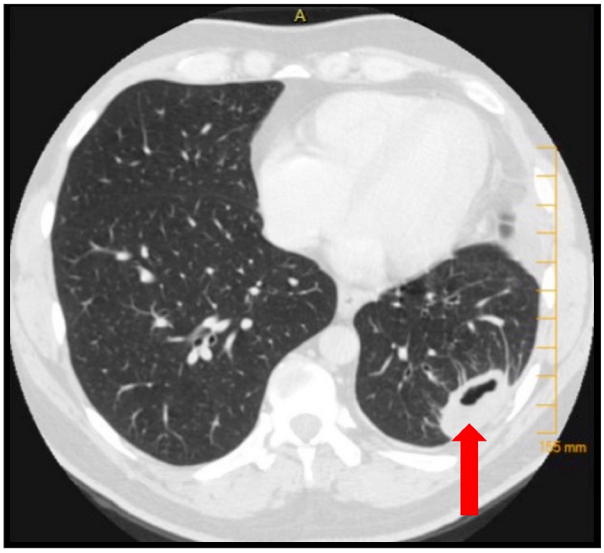

Figure 1. Left cavitary lung lesion (red arrow).

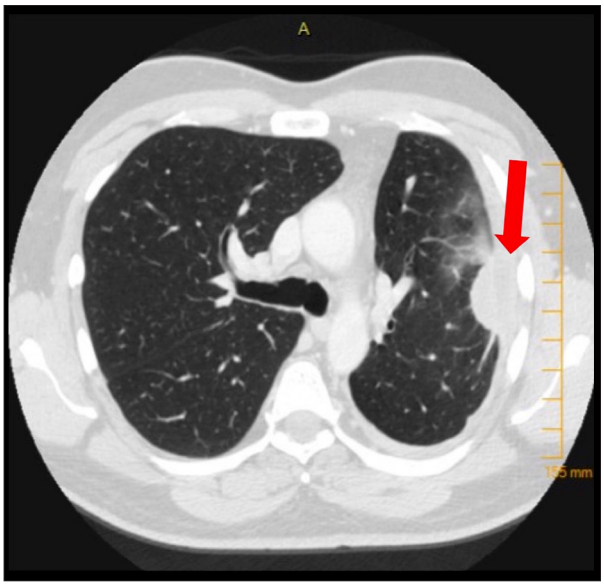

Figure 2. Left pleural-based mass (red arrow) with pleural thickening and ground glass.

endobronchial ultrasound/transbronchial needle aspiration of station 10L (>2 cm) was also negative for malignancy, fungus, or granuloma. Follow up CT thorax revealed that the lesions had increased to 4.0×1.9 cm in the LUL, 2.9×1.3 cm in the LLL, and 2.0×3.2 cm on the left hilar node. Six months later, the lesions had further increased to 4.5×2.5 cm in the LUL and 5.1×2.5×4.3 cm in the LLL on non-contrast CT. Two repeated attempts at CT-guided biopsy were followed by a video assisted thoracoscopic surgery (VATS), which were again negative for malignancy, fungus, or granuloma. Six months follow-up non-contrast CT again revealed interval increase to 5.6×4.1×4.2 cm in the LUL and 6.2×3.1×3.3 cm in the LLL, and hilar lymphadenopathy. Cardiothoracic Surgery unit was then consulted, and

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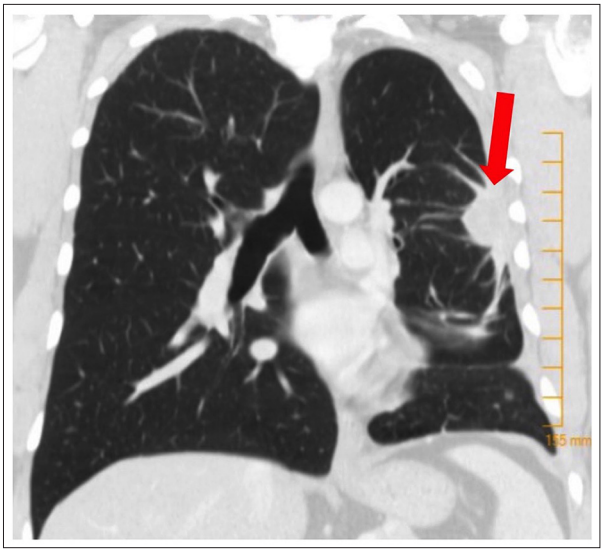

Figure 3. Coronal images of the superior pleural-based lung lesion indicated by red arrow.

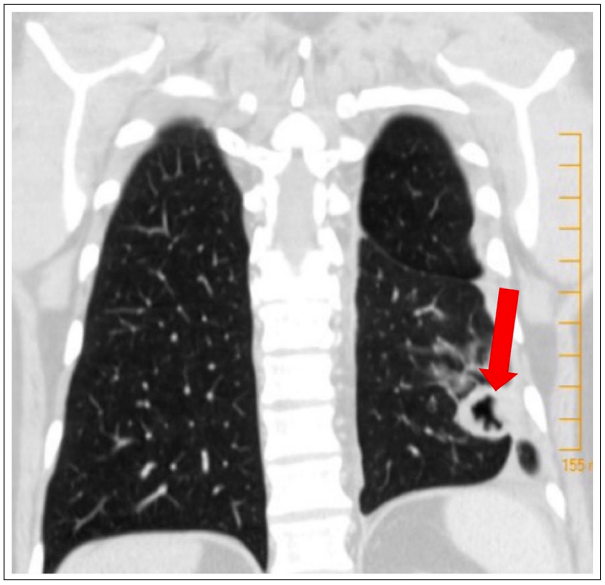

Figure 4. Coronal view of the inferior cavitary lung lesion (red arrow).

a 1.7×2.2 cm VATS biopsy of the LLL lesion yielded a hyalinized, necrotizing granuloma consistent with histoplasmosis. The patient was started on itraconazole at that time, which he responded to well.

Discussion

We described a rare case of histoplasmosis in an endemic area presenting in a patient with no immunosuppression. He presented with vague pulmonary symptoms, such as fatigue and shortness of breath. Imaging revealed hilar lymphadenopathy and cavitary lung lesions, which prompted further workup and biopsies. However, consecutive biopsies were negative for malignancy, fungus, and bacteria. A needle core biopsy and bronchoscopy only revealed necrotic tissue. Inconclusive imaging and biopsies delayed the diagnosis of histoplasmosis 6 months in this patient, who continued to suffer symptoms and experience decreased quality of life. The diagnosis was able to be confirmed after surgical biopsy of the left lower lobe (LLL) cavity in which histopathology was consistent with histoplasmosis.

Histoplasmosis is classically considered an endemic illness associated with the Ohio and Mississippi River Valley areas in America, in which Memphis is located, and parts of Asia and Africa. Increasingly cases are being recognized outside of this class geographic distribution. Other areas, such as Brazil, Argentina, India, and South Africa, are at risk as well [8]. A case was reported of an immunocompetent patient from Greece, a non-endemic area, who developed chronic pulmonary histoplasmosis and the only risk factor in developing histoplasmosis was his visit to America many years ago [9]. Physicians working within the classic endemic areas are usually familiar with the presentation and approach to diagnosis of histoplasmosis, but the importance for all physicians to become familiar with recognizing this disease is being demonstrated with these new cases. With rising numbers of cases in non-endemic areas, histoplasmosis, it is important to recognize the clinical manifestations, diagnostic approach, and treatment strategies of this disease [10].

Histoplasma capsulatum is a fungus transmitted by inhalation of spores [11]. Clinical manifestations are characterized into 3 categories: acute, chronic, or disseminated fungal disease [12]. The severity and progression of disease depends on host cellular immunity [13]. After pathogen inhalation, the immune system activates macrophages, epithelial cells, and lymphocytes [14]. The cellular immune system usually limits disease progression, and most infected people are asymptomatic [15]. Chronic and disseminated histoplasmosis are considered opportunistic infections seen in immunocompromised individuals, including HIV/AIDS patients and organ transplant recipients [16,17].

The diagnosis of histoplasmosis is multifactorial. Clinical presentation, radiologic manifestations, and patient history can indicate histoplasmosis; however, a definitive diagnosis requires culture, fungal stains, serologic test, and/or microscopic visualization [18]. Isolation of the organism in culture remains the gold standard for the diagnosis of histoplasmosis, but the incubation can range from days to weeks. This can result in a significant delay in diagnosis and treatment, which can even be fatal in severe cases. Fungal staining allows for more rapid results than culture, but it has a lower sensitivity [19]. Antigen detection is another laboratory method that provides rapid

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results, with high sensitivity when both urine and serum are tested [20]. However, in regions where histoplasmosis is endemic in the population, positive antigen tests are of limited utility as many individuals are asymptomatic carriers. Recently, polymerase chain reaction (PCR) methods have shown rapid and reliable detection of histoplasmosis, as well as differentiation from other mycoses. A study showed the sensitivity and specificity of PCR assay for histoplasmosis was 73% and 100%, respectively [21]. Compared to culture methods, PCR methods are easier and safer for laboratory personnel. Delay of diagnosis can lead to progression of disease, as can inappropriate treatment. If inflammatory causes are incorrectly suspected, corticosteroid use would likely lead to progression of histoplasmosis [22].

Conclusions

In conclusion, our case demonstrates the importance of sensitive and specific clinical tests in establishing histoplasmosis diagnosis. It is also important to consider histoplasmosis in immunocompetent patients whose presentation is compatible with the diagnosis. Further research on histoplasmosis has demonstrated how non-endemic areas can also be affected by this disease, leading us to reconsider the bias toward classic epidemiologic distribution of histoplasmosis. Diagnosis of histoplasmosis requires dynamic physician knowledge of clinical symptoms, patient history, geographic distribution, and radiological presentation. Our patient did not fall into the typical patient population and biopsies initially failed to rule in a diagnosis which delayed treatment in our patient. Despite aggressive sampling, his diagnosis remained elusive until adequate tissue was surgically sampled. Studies have demonstrated PCR assay utility in diagnosis by accurately reaching a diagnosis in a shorter amount of time [23]. In the future, advances in diagnostic testing may preclude the need for surgical biopsy for patients, such as was required in this case.

Conflict of interest

None.

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