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An Incidental Finding and Unusual Presentation of Atypical Coccidioidomycosis in a 72-Year-Old Man: A Case Report

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Abstract

This case report presents an unusual and challenging diagnostic scenario involving a 72-year-old man who recently returned from a trip to Maui, Hawaii. While in Maui, the patient presented with a fever and fatigue that resolved spontaneously. However, he had an observable rash on his head and was given a steroid injection to resolve the rash. Later on his trip, the patient experienced a dry, nonproductive cough which resolved with a five-day course of prednisone. While visiting Michigan, the patient began to experience neck pain and visited Troy Beaumont Hospital for further treatment. Meningitis tests were negative. Vancomycin was given due to the detection of gram positive coccidioidomycosis in the culture, but this was later proven to be a contaminant. Coccidiomycosis does not initially have specific symptoms. Despite negative coccidioidomycosis antigen tests, the patient exhibited features more consistent with blastomycosis and cryptococcus, highlighting the complexities of diagnosing fungal infections with atypical presentations. The case emphasizes the importance of considering alternative fungal pathogens native to endemic regions and pursuing comprehensive diagnostic measures to establish an accurate diagnosis. Lastly, the discussion about recommendations for antifungal therapy and preventative measures for individuals at risk of respiratory fungal infections is critically important for the advancement of early detection of fungal infections.

Keywords

Coccidioidomycosis, Blastomycosis, Cryptococcus, Fungal Infections, Diagnostic Challenges, Atypical Presentation

1. Introduction

Fungal infections, particularly coccidioidomycosis, can pose significant diagnostic challenges when they present atypically. This case was brought to the attention of Beaumont Hospital in Troy, Michigan due to its irregularity and unique presentation. This prompted the need for further investigation. To ensure a comprehensive evaluation, a team of highly specialized physicians was assembled to investigate the negative test results despite the patient's clinical symptoms and suspected etiology. The research conducted an in-depth understanding of fungal infections, their various presentations, and the appropriate antibiotic management for bacterial infiltrates. Due to the negative coccidioidomycosis antigen tests, the patient's clinical features pushed the physicians to also test for other fungal infections such as blastomycosis and cryptococcus. This case report aims to address the complexities associated with diagnosing fungal infections, emphasizing the importance of considering alternative pathogens native to endemic regions, as well as recognizing the continued relevance of traditional methods such as cultures and thorough patient history.

2. Case Presentation

We present the case of a 72-year-old man who sought medical attention due to an unusual presentation to the emergency department in Troy, Michigan with neck pain following a recent trip to Maui. The patient's medical history is unremarkable for any chronic infections, immunocompromised, cardiovascular, respiratory, or other organ system dysfunctions. During his time in Maui, the patient initially experienced a transient episode of fever and fatigue lasting approximately six hours, which resolved spontaneously. The following morning, he observed a rash on his head that is similar to rashes that he has developed in the past from an allergic reaction to NSAIDs. With a reported white blood cell count (WBC) of 13,000, the patient received a steroid injection. Later on his trip, he developed a nonproductive, dry cough that showed improvement with a five-day course of prednisone. However, he was later diagnosed with an allergic reaction due to the steroids at a follow-up appointment in Maui.

On a later visit to Michigan, the patient began experiencing neck pain and sought medical attention at Troy Beaumont Hospital. Patient's labs were remarkable for elevated C Reactive Protein (CRP) at 51.9 and Erythrocyte Sedimentation Rate (ESR) at 22. Imaging studies of the neck incidentally revealed multiple masses in the upper lobes of both lungs. Laboratory investigations, including blood cultures, initially indicated the presence of gram-positive cocci, which were later identified as contaminants. The patient was given vancomycin which led to an improvement in the cough and neck pain. Physical examination did not reveal erythema nodosum. The patient's coccidioidomycosis blood antigen test was negative. A bronchoscopy-guided biopsy confirmed the presence of necrotizing pneumonia with granulomatous features, which are non-specific findings but prompted further testing. This led to additional serum antigen tests for blas-

tomycosis and cryptococcus, however they yielded negative results. This prompted a comprehensive exploration of alternative causes. Finally, a fungal culture recovered Coccidioides immitis, establishing it as the causative agent in this case.

3. Discussion

Coccidioidomycosis is becoming a significant public health concern due to its increasing occurrence, many undiagnosed cases, and a higher virulence compared to other fungal infections endemic to North America [1] [2]. It is estimated that there are around 150,000 coccidioidal infections annually, with hospital admission paired and subsequent anti-fungal treatment observed in approximately one-third of cases [1]. Over time, the proportion of severe coccidioidomycosis cases are expected to rise due to increased exposure to the pathogen caused by soil disruption and easier access to both national and international travel [1].

In the environment, coccidioidomycosis species grow as mycelia and produce arthroconidia and when inhaled by mammals they transform into spherules [3]. Even a single or a small number of arthroconidia exposures can lead to disease [3]. The primary infection is characterized by early respiratory symptoms such as cough, chest pain, the shortness of breath, fever, and fatigue [4]. While most cases resolve on their own, approximately 5% - 10% of individuals develop complications or chronic pulmonary disease [3]. Dissemination, primarily through the bloodstream, may occur after pulmonary infection, but extrapulmonary disease is observed in only about 0.5% of coccidioidal infections [2]. Although most individuals with extrapulmonary spread do not have identified immunodeficiency, those who are immunocompromised are particularly vulnerable [5]. It has been historically recognized that African or Filipino ancestry is associated with a higher risk of dissemination, although the exact magnitude of this risk is unclear [6]. Other factors that increase the risk of dissemination include decreased cell-mediated immunity, infection during pregnancy, and male gender [6]. While complications of dissemination can manifest within weeks to months, nearly all cases emerge within two years [7]. Disseminated disease can be divided into meningeal, which is the most severe form, and non-meningeal, which commonly affects the skin, joints, and bones. Clinical suspicion is crucial in diagnosing coccidioidomycosis, especially when there is exposure to the endemic region. Patients often receive multiple courses of oral antibiotics before a definitive diagnosis is made. Laboratory tests may show mild increases in white blood cell count and inflammatory markers. More than half of patients with early respiratory infection exhibit abnormal findings on chest radiographs. Diagnosis is typically established by detecting specific antibodies against coccidioidomycosis, identifying spherules in histopathology, or isolating coccidioidomycosis species in fungal cultures [7]. Although antibody titers of 1:16 or higher using complement fixation tests have been associated with extrapulmonary dissemination, a definitive diagnosis of dissemination requires the identification of coccidioidomycosis species through culture, histopathology, and/or ribosomal ribonucleic acid sequencing from at least one site other than the lungs [8] [9].

The initial symptoms of rash and subsequent development of a nonproductive cough and neck pain raised concerns for fungal infections common in the endemic region of Arizona and Southwestern United States [6]. However, the negative results of coccidioidomycosis antigen tests and subsequent negative results for blastomycosis and cryptococcus necessitated further investigation. The patient's lack of response to vancomycin, combined with the pathologist's indication of necrotizing pneumonia with granulomatous features, was suggestive for fungal elements more consistent with blastomycosis and cryptococcus. However, the typical clinical presentation of cryptococcus includes symptoms such as headaches, pneumonia, and fever [9]. These symptoms were not observed in this case. Blastomycosis also typically presents with a nonspecific flu-like illness with fever, chills, myalgia, headache, chest pain, and a nonproductive cough [10]. The patient's rash was inconsistent with these expected findings. Due to the deviations that were seen, it is crucial to consider alternative fungal infections and pursue additional diagnostic measures to establish an accurate diagnosis.

The incubation period of coccidioidomycosis is seven to twenty-one days [11]. A negative serological test is found in individuals that have been tested prior to allowing the host to produce antibodies. This can also be true if an individual is immunocompromised [11]. The patient was seen in Michigan after one week of his initial presentation of symptoms. This may not have been enough time for the patient's immune system to fully develop antibodies against the antigen, contributing to the false negative. It is also advised that a patient has multiple serological antigen and antibody tests if there is suspicion for a fungal infection to avoid the possibility of false negatives [11].

4. Conclusion

This case emphasizes the complexity of diagnosing fungal infections in atypical presentations. The 72-year-old man's symptoms and travel history initially prompted physicians to run tests for coccidioidomycosis, but when these tests came back negative, it led them to explore alternatives such as blastomycosis and cryptococcus. The negative antigen tests for the suspected fungi highlight the need for comprehensive evaluation, including imaging, bronchoscopy-guided biopsy, and culture analysis, to establish an accurate diagnosis. Awareness of the various fungal pathogens and their regional distribution is vital in managing patients with respiratory symptoms, especially in individuals who have traveled to endemic regions. Despite the prevalence of PCR and molecular testing, it was the traditional culture method that ultimately provided us with the correct diagnosis in this case report. We recommend antifungal therapy with fluconazole (Diflucan) or itraconazole (Sporanox, Tolsura) for three months with follow-up after completing antifungal therapy [12]. It is also advised to check the complete blood count (CBC) monthly. Patients who have recovered from coccidioidomycosis infection are at risk for long-term lung infections, such as recurrent pneumonia [12]. For patients who are immunocompromised, we highly recommend preven-

tative measures such as: avoiding areas with a lot of dust such as construction or excavation sites, staying inside during dust storms, avoiding activities that involve close contact with dirt or dust, and using air filtration measures indoors [7].

Disclosures

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