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HIV and Pulmonary Coccidioidomycosis: Surgical and Treatment Dilemmas

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Abstract

Coccidioidomycosis is an important opportunistic pathogen among individuals with impaired cellular immunity such as HIV. Among the various clinical entities, pulmonary disease is the most common presentation.

A 48-year-old HIV-infected Caucasian male presented to an outside hospital with a history of fever, shortness of breath, purulent cough, and weight loss. Computed tomography (CT) of the chest revealed a 5-cm right upper lobe cavitary lesion. Bronchoscopy results yielded cultures initially positive for normal respiratory flora. Cytology was negative for malignancy but revealed evidence of fungal elements. The patient was treated with a course of antibiotics for presumed bacterial lung abscess. Two months later, the patient presented again to an outside facility with similar complaints which had worsened in intensity. He was placed on antifungal therapy after prior data had revealed scant fungal growth. The patient subsequently established care at the VA Hospital. Serial CT scans over the following two years showed slight enlargement of the cavitary lesion. Due to persistent clinical symptoms including intermittent hemoptysis, fatigue, and dyspnea on exertion despite the use of chronic antifungal therapy, the patient underwent surgical resection of the cavitary process. Intraoperative culture data confirmed the presence of *Coccidioides immitis.* Post surgery, chronic antifungal therapy was continued.

Pulmonary cavitary lesions caused by Coccidioidomycosis may require surgical intervention with progressive enlargement or if there are symptoms refractory to antifungal therapy. However, the optimal timing of resection for such lesions is not well defined. Similarly, treatment duration post surgical resection is lacking and requires further study.

Background

Coccidioidomycosis is a disease endemic to the southwestern United States, parts of Mexico, and Central and South America. It is caused by *Coccidioides* spp. which are soil dwelling thermal dimorphic fungi. Often called “valley fever”, coccidioidomycosis affects an estimated 150,000 persons annually.[1,2] The mode of transmission is typically as a result of inhalation of the arthroconidia. Disease presentation can be varied including pulmonary infection varying from early respiratory infection, pulmonary nodules and cavities and chronic fibrocavitary pneumonia, fungemia, and extrapulmonary dissemination. Diagnosis is made by skin testing, serological methods, culture, and identification of endosporulating spherules in body fluids or tissue.[3] Underlying medical diseases that affect T-cell function such as HIV are known to increase the risk of disease acquisition.

Case Description

A 48 year old HIV positive Caucasian male with past medical history significant for COPD, mesangial capillary glomerulonephritis, hyperlipidemia, chronic tobacco abuse, and previously treated Hepatitis C presented to the VA hospital to establish continuity of care.

Six months prior to evaluation, the patient had relocated to New York after residing in Arizona for approximately 25 years. Three months after the patient’s move, he sought care at an outside hospital with a history of intermittent fever, night sweats, fatigue, dyspnea, and foul smelling sputum. Clinical examination at that time revealed a hemodynamically stable obese male with right posterior mid lung expiratory wheezing and crackles. Absolute CD4 count was 276 with an undetectable HIV RNA viral load. Computed tomography of the chest revealed a 5cm thick walled cavity in the posterior segment of the right upper lobe with an air fluid level. Bronchoscopy was pursued. Cytology from the bronchial wash was negative for malignancy but Gomori Methenamine Silver (GMS) staining revealed fungal structures consistent with hyphae and pseudohyphae. Subsequent microbiological data returned positive for normal oral flora only and was negative for acid-fast bacilli. Of note, Coccidioides antibody and immunodiffusion testing were negative and urinary Histoplasmosis urinary antigen was negative. The patient was placed on levofloxacin and clindamycin for a presumed bacterial lung abscess and released.

The patient was seen in follow-up by an outside provider one month later. Repeat imaging revealed an enlarging abscess cavity with continued air-fluid level despite almost eight weeks of antibiotic therapy. Bronchoscopy was again performed with unrevealing microbiological data other than growth of *Candida albicans* and *Candida glabrata*. Almost one week later, the patient was admitted due to fever, progressive shortness of breath, and cough. The patient was empirically placed on broad spectrum antibiotics and seen by Infectious Diseases. Multiple serological tests were acquired including serum galactomannan, Quantiferon testing, and serum Cryptococcal antigen all returning negative. Due to the patient’s past residence in a region endemic for Coccidioidomycosis, the patient was placed on empirical antifungal therapy with itraconazole. He stabilized and eventually was discharged. It was one month later that the patient then presented to the VA for further follow-up.

Over the course of the next two years, the patient was maintained on chronic antifungal therapy. He continued to complain of fatigue, dyspnea, and intermittent hemoptysis. Serial imaging had revealed a persistent cavitary lesion (Figure 1). Antifungal therapy was changed to fluconazole, however, over time, mild enlargement in the cavity was seen. Due to persistent clinical symptoms and radiographic findings, the patient was referred to thoracic surgery. He underwent a right thoracotomy with lobectomy complicated by persistent air leak. Postoperatively, the patient was given a short course of amphotericin followed by voriconazole. Tissue culture and pathology (Figures 2 and 3) confirmed the presence of *Coccidioides immitis.* He eventually stabilized and was discharged home.

Due to the patient’s somewhat complicated course, antifungal therapy was continued for six months post surgical resection. Close follow-up as an outpatient has revealed no relapse of infection to date.

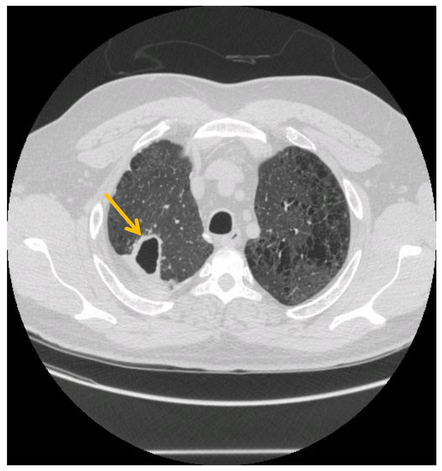

Figure 1: CT of the lung showing a right upper lobe cavitary mass

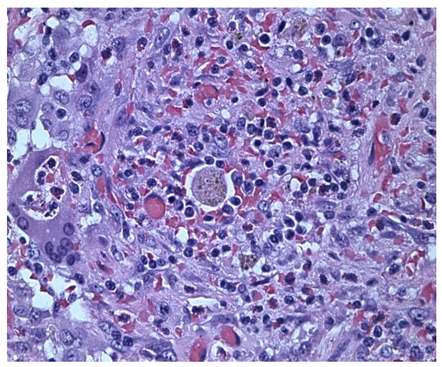

Figure 2: Hematoxylin and Eosin staining of lung tissue showing thick-walled spherule containing numerous endospores in the center

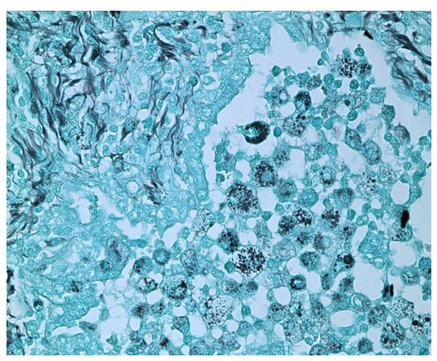

Figure 3: Gomori Methenamine Silver staining of lung tissue showing a mix of intact and ruptured spherules that are releasing endospores

Discussion

- Coccidioidomycosis is often a self-limited or subclinical infection. In immunocompromised individuals such as HIV, presentation may be more severe and extrathoracic dissemination is common.
- Cavitary disease is a prominent feature of chronic pulmonary coccidioidomycosis but interestingly is not a common presentation in those with HIV infection. Most HIV patients have diffuse reticulonodualr opacities or focal opacities, particularly in those individuals with CD4 counts less than 200.
- Disease severity primarily dictates therapeutic strategies. In pulmonary cavitary lesions, many stable asymptomatic cavities do not require surgical intervention.
- In persistent refractory coccidioidomycosis, patients should undergo surgical resection if they experience continued symptoms, lack of resolution, or growth of the cavitary disease despite adequate antifungal treatment. The proper timing of referral to a thoracic surgeon is unknown.[1]
- Initial treatment regimens typically utilize oral azole antifungal agents. Newer agents such as voriconazole, posaconazole, or caspofungin have shown promise in refractory cases.
- There is a paucity of data for treatment regimens post resection for pulmonary cavitary lesions with reports ranging from 3 to 6 months. Additional studies are needed for guidance in determining the optimal length of therapy.

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