Pyo-mediastinitis: A complication of pulmonary coccidioidomycosis

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A rare fatal case of pulmonary coccidioidomycosis complicated by mediastinal and visceral abscesses treated with antifungal medications is described. The case report discusses the potential need for early surgical intervention to drain mediastinal and visceral abscesses as a primary mode of therapy in disseminated coccidioidomycosis for a successful control of infection and clinical outcome.

Key Words: Abscess; Coccidioidomycosis; Pyo-mediastinitis; Surgical drainage

Médiastinite purulente: complication d'une coccidioïdomycose pulmonaire

Voici un cas rare de coccidioïdomycose pulmonaire mortelle, compliquée d'abcès viscéraux et médiastinaux, qui a été traité aux antifongiques. Il sera question, dans le présent exposé de cas, de la pertinence de l'intervention chirurgicale précoce pour drainer les abcès viscéraux et médiastinaux, et ce comme principale forme de traitement dans les cas de coccidioïdomycose disséminée, afin de juguler l'infection et d'obtenir de bons résultats cliniques.

Coccidioidomycosis is an infection caused by the soil-inhabiting fungus *Coccidioides immitis*. The fungus is endemic in the Southwest desert including Arizona (1). Coccidioidomycosis is normally a self-limited infection in healthy hosts presenting as a mild flu-like illness in approximately 40% of infected persons and progressing to severe pulmonary or disseminated disease in 1% to 10% of symptomatic cases (2). The early diagnosis of coccidioidomycosis infection relies on clinical suspicion and serological testing because direct tissue culture or histopathology may be delayed or difficult. We describe a rare fatal case of pulmonary coccidioidomycosis complicated by multiple mediastinal and visceral abscesses.

CASE PRESENTATION

A 78-year-old white woman was admitted to the intensive care unit with acute respiratory distress syndrome secondary to community acquired pneumonia for mechanical ventilation. Patient was an active smoker of 50-pack-year history and has lived in Arizona for the past four years. The patient was receiving hydroxyurea 500 mg twice daily for Philadelphia chromosome negative chronic myelogenous leukemia diagnosed on bone marrow biopsy four months previously and was discontinued on admission to the intensive care unit. The patient had received radioactive iodine, I-131, for Grave's hyperthyroidism one year before. There was no history of diabetes mellitus, liver disease or prior treatment with corticosteroids. Mediastinal lymphadenopathy was noted on a surveillance computerized

tomography of the thorax six months earlier (Figure 1A). A repeat thoracic and abdominal computerized tomography on admission to the intensive care unit showed right middle lobe pulmonary cavity lesion (Figure 1B, left) and multiple enlarged mediastinal lymph nodes with central necrosis and abscess formation (Figure 1B, right), and smaller military abscesses in both the liver and spleen. After initiation of mechanical ventilation bronchoscopic bronchoalveolar lavage was performed, which indicated on staining the presence of rare Gram-negative bacillus bacteria without additional speciation. Broad antibiotic coverage for Gram-negative bacteria was started on admission to intensive care unit. Antifungal treatment with intravenous fluconazole at 400 mg daily was initiated on day one after admission to the intensive care unit, when coccidioidomycosis diagnosis was confirmed serologically. *C immitis* serology confirmed the presence of both Immunoglobulin (Ig) G and IgM antibodies to the fungal species indicating a primary pulmonary coccidioidomycosis infection. On day 5, bronchoalveolar lavage fluid grew only *C immitis*. On the same day, the patient developed septic shock and concurrent blood cultures grew only *C immitis*. At that time, fluconazole therapy was converted to a continuous intravenous infusion of amphotericin B (at 1 mg/kg every 24 h) in addition to broad antibiotic coverage for Gram-negative bacteria. Surgical consultation was requested for operative drainage of mediastinal and abdominal abscesses. The family declined surgical intervention, and the patient subsequently died from multiple organs

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Figure 1) Computerized tomography of the thorax: **A** (left and right) Small mediastinal lymphadenopathy six months earlier; **B** (left and right) Right middle lobe cavity nodule, bilateral diffuse interstitial nodularity (left) and mediastinal lymphadenopathy with central liquefaction necrosis (right) associated with pulmonary coccidioidomycosis on admission to intensive care unit

dysfunction syndrome while receiving antifungal therapy on day 17 of her intensive care unit stay. Autopsy confirmed multiple enlarged mediastinal lymph nodes with central necrosis and liquefied pus (Figure 2a). Histopathological examination of the abscesses confirmed the presence of spherules of *C immitis* (Figure 2b). Pus and tissue cultures obtained at autopsy from abscesses found in the spleen and liver grew only *C immitis*. An autopsy examination of the central nervous system was not performed.

DISCUSSION

The underlying immune suppression from hematological malignancy and cytotoxic chemotherapy, as well as heavy smoking history, were undoubtedly risk factors for systemic dissemination of *C immitis* in this case report (3). Patients considered at high risk for systemic dissemination and increased mortality from *C immitis* have advanced age, congestive heart failure, cancer, diabetes mellitus, heavy smoking history, chronic corticosteroids use, Afro-American race and pregnancy (4,5).

Systemic coccidioidomycosis can present as acute sepsis, particularly in an immunocompromised host or in high risk patients residing in an endemic area (6,7). Medical treatment of systemic coccidioidomycosis focuses on early initiation of parenteral antifungal medications with either azole agents (eg fluconazole, itraconazole, or ketoconazole) or amphotericin B, as well as hemodynamic and organ support of the critically ill (8-10). In this case, clinical deterioration to septic shock and multiple organ dysfunction ensued in spite of medical treatment generally recommended for systemic coccidioidomycosis

Figure 2) Autopsy pictures: **A** Open thorax with purulent discharge from mediastinal lymph nodes and pyo-mediastinitis associated with pulmonary coccidioidomycosis. **B** A histopathological microscopic examination of one of the abscesses showing the presence of two spherules of *Coccidioides immitis* (Original magnification x 200)

(5,9,10). Large mediastinal abscesses formed within necrotic lymph nodes were refractory to antifungal medications as confirmed by repeated growth of *C immitis* from blood and tissue cultures. There are no reported cases or studies in the literature on either the incidence of mediastinal abscesses or the optimal surgical intervention necessary to treat such a complication when associated with pulmonary coccidioidomycosis. Operative intervention has been selectively reserved for visceral coccidioidomycosis resistant to antifungal therapy (11-14). Percutaneous drainage of hepatic abscesses, cholecystectomy or splenectomy has been described for the involvement of these organs. Mediastinal surgical drainage is frequently performed to relieve pericardial or airway compression in chronic granulomatous infections. However, the extent of surgical intervention required for purulent necrotic mediastinal nodes associated with coccidioidomycosis has not been described. Early timing of adjunct surgical intervention can improve the treatment response to antifungal agents for extrapulmonary coccidioidomycosis infection (12-14). Others have recommended an initial trial of medical treatment with intravenous and/or enteral antifungal agents for a period of time before surgical intervention (3,11,15). The latter recommendation will delay

surgical treatment of visceral coccidioidomycosis and inevitably worsened clinical outcome in high risk patients as illustrated by this case report (5,6,13). It may also be argued that surgical intervention in this particular case may not have altered the final outcome because of advanced presentation with mediastinal abscesses and concurrent visceral involvement. However, early diagnosis and timing of surgical intervention with effective medical therapy is the key to successful treatment of coccidioidomycosis.

Prevention of severe pulmonary disease and systemic dissemination has been proposed in high risk patients residing in endemic areas (4,5). Early treatment with oral antifungal azole agents and perhaps vaccination against *C immitis* promise to decrease future incidence of severe complications associated with extrapulmonary coccidioidomycosis (16).

CONCLUSIONS

This fatal case of pulmonary coccidioidomycosis is unique because of early and rapid development of mediastinal and visceral coccidioidomycosis abscesses. Early detection of mediastinal and visceral coccidioidomycosis abscesses should prompt early surgical intervention for drainage as a primary mode of therapy in addition to effective antifungal therapy. Delay of surgical intervention is likely to result in multiple organ involvement and translates into poor prognosis.

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