Disseminated coccidioidomycosis in an AIDS patient presented with nasal mass

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ABSTRACT

We report a case of 31-year-old man presented with low grade fever and dry cough followed by multiple skin lesions and progressive enlargement of nasal mass. Chest radiograph revealed multiple small reticulonodular infiltration in both lungs and his sputum acid fast bacilli staining was negative. Nasal mass biopsy revealed necrotizing granuloma with spherule-like material and the culture for fungus grew Coccidioides immitis. His anti-HIV antibody was positive so he was diagnosed as AIDS with disseminated coccidioidomycosis. He was treated with intravenous amphotericin B deoxycholate, complicated by shock which was suspected from inflammatory response to coccidioidomycosis or anaphylactic shock from amphotericin B deoxycholate. He was then treated with itraconazole as oral therapy. After 16 days of admission, he was improved and discharged. The nasal mass and all skin lesions were improved during follow-up. (J Infect Dis Antimicrob Agents 2011;29:75-82.)

Note: This case had been presented and discussed in the Interhospital Case Conference on Infectious Disease (ICCID), 22 December 2011, Bangkok, Thailand.

INTRODUCTION

Coccidioidomycosis is caused by the dimorphic, soil-borne, ascomycete fungi, endemic in the soil of southwestern of United States, Mexico, and parts of central and south America.1-3 Coccidioidomycosis occurs in humans and animals, commonly in dogs. Most common transmission by inhalation of arthroconidia, others by inoculated directly into skin, bone or other tissues.3 Clinical manifestations present as pulmonary coccidioidomycosis, extrapulmonary coccidioidomycosis and disseminated coccidioidomycosis.1-2 The symptoms are varies such as fever, cough, headache and skin lesions which spontaneously resolves in immunocompetent hosts.7,3 Respiratory failure or others complications may present in severe cases.2 Differential diagnosis should be considered in travelers

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who have visited endemic area. Spherule-like material revealed in tissue or culture for fungus grew Coccidioides species are important for diagnosis.2,4 Antifungals are the mainstay of treatment for coccidioidomycosis except there are indications for surgical intervention.

CASE REPORT

A 31-year-old Thai male presented with low grade fever and dry cough 8 weeks prior to admission, the symptoms lasting for only 2 weeks then subsided. He developed non-itching hyperpigmented scaling plaque at right shoulder and subsequent similar lesions appeared on both legs, right angle of lip and left pinna 2 weeks later. Finally, a big pimple-like lesion appeared on his nose 2 weeks prior this admission. The lesion progressed rapidly to be a big mass without itching, pain nor systemic symptoms. He was seen at local hospital with suspected of malignancy so he was transferred to Srinagarind Hospital.

His past medical history was unremarkable. He refused close contact to tuberculosis patient. He was a man who having sex with men, smoked 15 packs of cigarettes per year and was a social alcoholic drinker. He was a business man and owned restaurants in Los Angeles, California and Arizona. He had history of extensive traveling throughout the United States 4 months prior to his illness.

On admission at Srinagarind Hospital, the patient was a co-operative middle aged man. His vital signs were as follows: body temperature 38°C, blood pressure 130/80 mmHg, respiratory rate 20/minute, and pulse rate 80/minute. On examination revealed an ulcer with white plaque at hard palate, a large non-tender verrucous mass, fixed, firm, with yellow discharge and crusted at his nose as demonstrated in Figure 1. He had multiple cervical lymphadenopathy at both sides, about 0.5 cms in size, rubbery, not tender, and movable. One cm diameter hyperpigmented scaly papule at left pinna and lateral side of right angle of lip, and the same characteristic lesion with shallow ulcer at right shoulder, size 6 × 10 cms (as Figure 2) and similar lesions size 8 × 5 cms at both legs and back were observed. No oral thrush, oral hairy leukoplakia, nor pruritic papular eruption detected. Others examination were unremarkable.

The initial hemoglobin concentration was 9.7 g/dL and white blood cell counts was 15,000 cell/mm³, 72% neutrophils, 9% lymphocytes, 5% monocytes, and 14% eosinophils. The platelet count was 330,000/mm³, MCV 76 fl, RDW 16%, normochromic normocytic blood picture. The renal function revealed normal (blood urea nitrogen 7.7 mg/dL and creatinine 0.7 mg/dL) and normal electrolytes. The liver function test revealed mild elevation of transaminase (100 mg/dL of SGPT, 61 mg/dL of SGOT). Anti HIV antibody test was positive, absolute CD4 count 513 cells/mm³, 20.5%. His serum cryptococcal antigen, VDRL, HBSAg, and anti-HCV were negative. Chest radiograph revealed multiple small reticulonodular infiltration both lungs (as Figure 3). Sputum smear for acid fast bacilli (AFB), modified AFB, and Wright stains were negative finding. After knowing his HIV status, the differential diagnosis of his entire problems would be disseminated opportunistic infections especially fungal infections. However, the clinical manifestation of the huge mass is not common presentation of cryptococcosis, histoplasmosis or penicilliosis. In addition with several negative results of mass lesion and the oral ulcer scraping for Wright, gram, AFB and modified AFB staining make these fungal infections less likely. The nasal mass lesion was progress causing upper airway obstruction while waiting for the mass lesion biopsy result. Along with history of residing and traveling in the United States and the severe symptoms, we decided to initiate empirical amphotericin B to cover both coccidioidomycosis and blastomycosis. The initial nasal mass lesion biopsy
Figure 1. Verrucous mass with minimal yellow discharge with crust at nose, about 6 cms in diameter, firm, not tender, fix.

Figure 2. Hyperpigmented plaque with shallow ulcer with scale at right shoulder, about 6x10 cms.

Figure 3. Chest radiograph showing multiple small reticulonodular infiltration prominent at both lower lungs.
pathology revealed only inflammation, no organism was found. The mass lesion responded to amphotericin B. It decreased in size and patient could discontinue oxygen mask. We communicated with ENT man that we need a second adequate tissue biopsy. In the meantime, we continued treatment with amphotericin B. His clinical course was complicated with shock after 11 days of amphotericin B treatment. Shock developed five minutes after administration of amphotericin B. We suspected the cause from amphotericin B that lead the patient to anaphylaxis. However, the inflammatory response to spherules degranulation could not be ruled out. So we decided to change antifungal to oral itraconazole 400 mg/day (without loading dose) to cover both coccidioidomycosis and blastomycosis. All the lesions were gradually improved and he was discharged home after 16 days of admission. The repeated nasal mass biopsy revealed necrotizing granuloma with foreign body giant cell and spherule-like material (as Figure 4). The tissue culture for fungus grew *Coccidioides immitis* (as Figure 5). All the mycobacterial cultures were negative. The results were back after patient discharged home.

His nasal mass size was significantly decreased and his skin lesions were improved to be hyper-pigmented skin during follow-up. However he refused to commit on antiretroviral treatment but agreed to continue itraconazole for life.

**DISCUSSION**

Generally, the differential diagnosis of nasal mass was including inflammatory lesions, infection, post-traumatic deformities, benign or malignant neoplasms, vascular mass and congenital midline lesion. In HIV-positive patient, the differential diagnosis should be narrow down to opportunistic infections or lymphoma, so the definite diagnosis must be by biopsy of the mass lesion. The rapid enlargement of the mass makes malignancy less likely. History of previous residing and traveling in the United States, lead us to differential coccidioidomycosis and blastomycosis. We should realize that these two diseases have similar route of infection and clinical manifestations except for endemic area. Blastomycosis founds in North America, includes the southeastern and south central state. *Coccidioides immitis* seems to be restricted to California, but might exist in some adjacent area of Mexico and Arizona, while *Coccidioides posadasii* is found in other regions. The patient’s nasal tissue pathology revealed spherules (double-walled structures) containing endospore is the key to confirm diagnosis of coccidioidomycosis while blastomycosis reveal broad-based budding yeasts. Culture for fungus from affected body fluids or tissue specimens present mold colonies and microscopy that compatible with coccidioidomycosis as shown in Figure 5.

*Coccidioides species* are propagated by 2 asexual reproductive structures (arthroconidia and endospore). Arthroconidia are infectious for human and animals. Incubation period of 1-3 weeks are for primary or cutaneous coccidioidomycosis, but months to years in disseminated coccidioidomycosis. Incubation period and clinical manifestations are similar in both immunocompetent and immunocompromised hosts. Pulmonary coccidioidomycosis is the most common presentation in HIV-infected patients. And extrapulmonary or disseminated coccidioidomycosis are AIDS-defining illness which indicate antiretroviral therapy to control infection.

Pulmonary coccidioidomycosis in both immunocompetent and immunocompromised hosts may reveal nodular, cavitary lesion with or without fibrosis, reticulonodular infiltration and lung mass in chest radiograph. Diffuse reticulonodular infiltration is the most common finding in HIV-infected patients which mimic pulmonary histoplasmosis, pulmonary
Figure 4A,C,D. Histopathological sections of excised nasal mass showing spherules (double-walled structures) containing endospores.

Figure 4B. Spherule was engulfed by foreign-body giant cell macrophage.
blastomycosis and lung cancer. In acute pulmonary coccidioidomycosis may demonstrate multiple basal lung nodules, interlobular thickening and consolidations in computed tomography of chest.\textsuperscript{10}

Generally, principle treatments of coccidioidomycosis in both immunocompetent and immunocompromised hosts are depending on manifestations and response to antifungal agents. Amphotericin B deoxycholate (0.5-1.5 mg/kg per day), at least for the first several weeks until improve clinical is indicate then follow by antifungal orally at least 1 year.\textsuperscript{3,11-12} In HIV-infected patients who initially present with pulmonary coccidioidomycosis and CD4 count > 250 cells/mm\textsuperscript{3} at the time of diagnosis should continue oral antifungal treatment for at least 1 year while HIV-infected patients who have disseminated coccidioidomycosis should be prolonged or life-long oral antifungal therapy.\textsuperscript{5} Ketoconazole (400 mg/day orally) has been used in the past with significant adverse effects and no longer prefer drug.\textsuperscript{3} Several clinical trials have indicated that fluconazole (400-800 mg/day) and itraconazole (200 mg twice daily or 3 times per day orally) are efficacious.\textsuperscript{3,12} Voriconazole and posaconazole have been successfully used as salvage therapy in case of medical intolerance of prior antifungal treatment or refractory coccidioidomycosis.\textsuperscript{13-17} No comparative data exist on the use of these drugs for salvage treatment of coccidioidomycosis.\textsuperscript{17} Caspofungin has been effective in experimental murine coccidioidomycosis, but in vitro susceptibility is vary.\textsuperscript{12} Caspofungin has been successfully treated coccidioidomycosis in few case reports.\textsuperscript{18-19} There were some reports of disseminated coccidioidomycosis which successfully responded to adjunctive interferon-\textgamma therapy.\textsuperscript{20-21} In fact, medication is not only the treatment in coccidioidomycosis but also surgical treatment in some cases. Patients with ruptured or progressive enlargement of pulmonary cavity, abscess at any area, pericardial effusion, instability of spine or hydrocephalus, need additional surgical intervention.\textsuperscript{12} In HIV-infected patients, a potent antiretroviral treatment has markedly decreased in both incidence and the severity of coccidioidomycosis.\textsuperscript{22}

In summary, we reported case of 31-year-old

\textbf{Figure 5.} From culture for fungus, microscopy showing arthroconidia of \textit{C. immitis}, typical single-celled, hyaline, rectangular to barrel-shaped, separated from each other by a disjunctor cell.
man presented with low grade fever and dry cough followed by multiple skin lesions and nasal mass. Chest radiograph revealed multiple small reticulonodular infiltration both lungs. Nasal mass biopsy revealed necrotizing granuloma with spherule-like material. Nasal mass tissue culture for fungus grew *C. immitis* subsequently diagnosed as AIDS with disseminated coccidioidomycosis. Thailand is not an endemic area of coccidioidomycosis, however, differential diagnosis of the disease should be included in patients who present with compatible clinical manifestations and had history of traveling to endemic area. Appropriate investigations should be obtained and empirical treatment may be needed in severe cases.

References


