Fatal disseminated histoplasmosis in a previously healthy person

Siripen Panthuwong, M.D.,
Pisud Siripaitoon, M.D.,
Khachornsakdi Silpapojakul, M.D.

ABSTRACT

*Histoplasma capsulatum*, a dimorphic fungus that causes human disease (histoplasmosis), is endemic in eastern USA, the Caribbean, Central and South America, and in South East Asia. Patients with HIV infection, solid organ transplantation, and those who are receiving immunosuppressive agents are predisposed to disseminated histoplasmosis. Disseminated infection in immunocompetent persons is quite uncommon. We reported here, a case of fatal disseminated histoplasmosis in a presumed immunocompetent patient. (*J Infect Dis Antimicrob Agents* 2011;29:11-5.)

Note: This case had been presented and discussed in the Interhospital Case Conference on Infectious Disease (ICCID), 13 October 2011, Chonburi, Thailand.

CASE REPORT

A 40-year-old female, fertilizer vendor from Nakornsrithammarat Province, was admitted to Songkranagarind Hospital on the 23 August 2011 with a history of having prolonged fever and small neck nodes enlargement treated with herbal medicines for a year. Her clinical condition did not improve. Fever persisted with progressive jaundice for the last 2 months. Sixteen kilograms weight loss was also reported.

Initial physical examination revealed a thin pale woman with a body temperature of 38.8°C and marked icteric sclera. Enlarged, diameter range 0.5-2 cm., bilateral submandibular and cervical lymph nodes were palpated. Liver was enlarged to 4 cm below right costal margin. Splenomegaly, 2 cm below left costal margin, with moderate tenderness also detected.

Initial laboratory studies disclosed the followings: WBC 5,830 cells/mm³ (N 90%, band 4%, L 2%, M 2%, E 2%), hematocrit 20%, platelet 15,000/mm³. Liver function test showed total bilirubin 20.9 mg%, direct bilirubin 19.8 mg%, aspartate aminotransferase (AST) 148 U/L, aminotransferase (ALT) 148, alkaline phosphatase 193 U/L. Renal function test, urine examination, and

Division of Infectious Diseases, Department of Medicine, Prince of Songkla University, Songkhla 90110, Thailand.
Reprint request: Siripen Panthuwong, M.D., Division of Infectious Diseases, Department of Medicine, Prince of Songkla University, Songkhla 90110, Thailand.
Keywords: *Histoplasma capsulatum*, histoplasmosis
chest radiograph were unremarkable. Anti-HIV antibody test was negative. Computer tomography abdomen showed few mildly enlarged retroperitoneal and pelvic nodes and diffuse hepatosplenomegaly without focal lesion. Gall bladder, bile ducts, pancreas, and adrenal gland were unremarkable. Bone marrow studies revealed multiple intracellular pear-shapes, small yeast like organisms with budding morphologically compatible with *H. capsulatum* by Gomori’s Methamine Silver (GMS) stain (Figure 1). On the third day of admission, she developed scattered erythematous maculopapular rash predominately at lower extremities without neither pain nor itching. Few small budding yeast (GMS stain) morphologically compatible with *H.capsulatum* was demonstrated from skin biopsy. Finally bone marrow and skin tissue culture confirmed growth of *H. capsulatum*. Conventional 1 mg/kg/day of amphotericin B was started. Three days later, it was switched to liposomal amphotericin B due to rising of serum creatinine. However, multiorgan failure, and refractory shock developed. She died on the seventh day of treatment. Postmortem liver and spleen pathology demonstrated extensive involvement by *H. capsulatum* (Figure 2).

**DISCUSSION**

Histoplasmosis is endemic in eastern USA, the Caribbean, Central and South America, and South East Asia. The etiologic agent, *H. capsulatum*, was typically found in humid areas where soil is enriched with organic material such as bird and bat droppings. It is a dimorphic fungus, existing as mold in the environment and as yeast in human body. The common signs and symptoms of disseminated histoplasmosis are fever (100%), lung involvement (70%), weight loss (60%), hepatomegaly (60%), splenomegaly (40%), and peripheral lymphadenopathy (30%). Involvement of gastrointestinal system (eg. bleeding due to mucosal ulceration), and the central nervous system (chronic lymphocytic meningitis), have been reported. Despite frequent gastrointestinal and hepatic involvement in disseminated histoplasmosis (70-90%), histoplasmosis may uncommonly present as cholestatic jaundice as in our case.

The clinical manifestations of histoplasmosis are quite different in the immunocompetent and immunocompromised patient. Most of the immunocompetent patients are asymptomatic or have clinically insignificant infection, whereas more severe or disseminated diseases occur in immunocompromised patients. In a retrospective review of patients with disseminated histoplasmosis diagnosed at Mayo Clinic over a 15-year period between 1991 to 2005, 59% of cases occurred in immunocompromised patients. This study also indicated that immunocompromised patients with histoplasmosis were more likely to have bone marrow suppression and elevated liver enzymes than immunocompetent patients (64% vs. 43%).

This patient was a non-HIV-middle-aged woman without a history of malignancy diseases, chronic organ failure, or immunosuppressive medication usage. Thus, we presumed as an immunocompetent patient that presented with disseminated histoplasmosis. Since 20% of disseminated histoplasmosis is known to occur in otherwise healthy persons especially in those who had a heavy inoculums exposure to the fungi, we postulated that she might have contracted this deadly form of the disease from exposure to large quantities of contaminated soil during her career as a fertilizer vendor.

A large urban histoplasmosis outbreak in India demonstrated that the only risk factor for fatal disseminated infection was immunosuppression. Fatal disseminated infections occurred in 73.8% of immunosuppressed patients compared to 6.5% of...
patients without underlying immunosuppression (p<0.05). For the non-immunosuppressed patients, fatal or disseminated infections were significantly more frequently found in patients over 54 years of age.\(^2\) Center for Disease Control Cooperative Mycoses Study data, showed that adrenal gland involvement with insufficiency was found in half of patients with severe histoplasmosis and probably contributed to the mortality.\(^11\) However, our patient did not have this endocrine dysfunction because her serum cortisol level during shock was 38.4 μg/dL.

Amphotericin B is the drug of choice for treatment of severe disseminated histoplasmosis.\(^{12-16}\) Without treatment, the mortality rate is 80%\(^17\) compared to 23% amphotericin B treated patients.\(^{11,18-19}\) Even with amphotericin B treatment, this patient showed no improvement and died due to extensive involvement with histoplasma.

References

Figure 1. (A) Bone marrow aspiration showed multiple small intracellular, pear-shaped, yeast-like organisms (arrows), (B) Bone marrow biopsy (H&E, original magnifications X40), demonstrated chronic granulomatous inflammation with (C) numerous intracellular small yeast-like organisms (arrows), (D) exhibited many budding in Gomori’s Methenamine Silver stain.


Figure 2. Postmortem pathology of the liver (A) and the spleen (B) (H&E, original magnifications X40), showed extensive involvement by numerous small intracellular yeast-like organisms.


