Case Report

Systemic Mycosis Caused By Cryptococcus neoformans, Penicillium marneffei, and Histoplasma capsulatum in a Patient with Acquired Immunodeficiency Syndrome

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Abstract

A patient with human immunodeficiency virus infection presented with prolonged fever, diarrhea, nonproductive cough, and molluscum contagiosum-like papulonecrotic lesions. Presumptive diagnosis of disseminated histoplasmosis was made by microscopic examination of Wright's-stained touch smear of skin specimen obtained by biopsy. Histoplasma capsulatum, Cryptococcus neoformans, and Penicillium marneffei were isolated from cultures of skin and bone marrow. Treatment with parenteral amphotericin B was started several days before culture results were reported. The patient responded well to treatment.

INTRODUCTION

Pneumocystis carinii is the most important pathogen causing morbidity and mortality in patients with acquired immunodeficiency syndrome (AIDS) in the United States and Europe. In the developing countries, opportunistic infections caused by other microorganisms are more frequently observed. In Thailand, although tuberculosis is still the major indicator disease for diagnosis of AIDS, the problem of systemic mycosis is growing. Apart from Candida species which usually cause superficial infection in most patients with AIDS, disseminated infections caused by Cryptococcus neoformans, Penicillium marneffei, and Histoplasma capsulatum are common. In this communication, a

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case of AIDS presented with an episode of disseminated infection caused by three fungi and *Salmonella enteritidis* bacteremia is reported.

**CASE REPORT**

A 30-year-old man was admitted to the Department of Medicine, Chiang Mai University Hospital on January 18, 1992 because of fever, diarrhea, and non-productive cough for six weeks. The patient denied the history of any underlying illness, intravenous drug abuse, homosexual behavior, or having received blood transfusion. He had frequent heterosexual contact with female prostitutes for many years without the use of condom.

Physical examination revealed the body temperature of 40.5 °C, mild jaundice, oral thrush, and generalized lymphadenopathy. Heart and lungs were normal. Liver and spleen were moderately enlarged. Discrete erythematous papules with central umbilication were seen at the patient's chest, back, and abdominal wall. The size of each papule was approximately 0.3 cm in diameter. The initial laboratory findings included a hemoglobin of 9.4 g/dL; white blood cell count of 10400 /mm³, with differential count of 76 per cent neutrophils and 24 per cent lymphocytes; and platelet count of 110,000 /mm³. The analysis of cerebrospinal fluid (CSF) obtained from lumbar puncture yielded a protein level of 170 mg/dL and glucose of 60 mg/dL. There was no white blood cell, bacteria, or fungus. The test for detection of cryptococcal antigen in the CSF was not available. The HIV antibody was repeatedly positive by ELISA (Vironostika® HIV MXT, organon Teknika B.V., Boxtel, Holland). Enumeration of T lymphocyte subsets was not routinely available at our hospital. The chest roentgenography was normal. Cultures of three specimens of blood grew *Salmonella enteritidis* and the patient was treated with oral cotrimoxazole. Microscopic examination of Wright's-stained touch smear of skin specimen obtained by biopsy and bone marrow aspirate revealed abundant intracellular and extracellular spherical, and oval yeast cells of 3-5 µm in diameter. There were many budding yeast cells. A presumptive diagnosis of disseminated histoplasmosis was made and treatment with amphotericin B was started.

*Histoplasma capsulatum* and *Cryptococcus neoformans* were isolated from fungal culture of the skin biopsy specimen. Culture of bone marrow grew *Histoplasma capsulatum, Cryptococcus neoformans* and *Penicillium marneffei.* *Cryptococcus neoformans* was also isolated from the culture of the CSF. Resolution of fever and skin lesions was evident after two weeks of treatment and the patient was planned to receive amphotericin B for a total course of 8 weeks.

**DISCUSSION**

The incidence of opportunistic fungal infections in AIDS patients is very high throughout the world including Thailand. In the first 174 AIDS patients admitted to Chiang Mai University Hospital during the 5-year period between 1987 and 1991, 61 were treated for tuberculosis. 35 patients were infected with *P. marneffei.* *Cryptococcal* meningitis was diagnosed in 40 patients and disseminated histoplasmosis in 3 patients.

In this paper, we report a very rare AIDS patient who presented with a single episode of mixed systemic mycoses caused by three kinds of fungi, i.e., *H. capsulatum, C. neoformans,* and *P. marneffei.* The main objective of this communication is to emphasize that Thailand is one of the areas of endemicity for these three fungi. The symptoms and signs in our case are not specific for diagnosis of disseminated fungal infection or central nervous system infection. The most important clue for making early diagnosis is the appearance of the cutaneous lesions. The popular lesions with central umbilication resembling the skin lesions of molluscum contagiosum had been described in AIDS patients with disseminated cryptococcosis, histoplasmosis, and *P. marneffei* infection. The microscopic examination of Wright's-stained touch smear of skin specimen obtained by biopsy and bone marrow aspirate revealed budding yeast cells characteristic of *H. capsulatum.* A presumptive diagnosis of disseminated histoplasmosis was made and amphotericin B therapy was started without waiting for the microbiological and histopathologic results. The unexpected finding is that, in addition to the isolation of *H. capsulatum, C. neoformans* and *P. marneffei* were also isolated from skin and bone marrow cultures. However, all these three fungi are known to be sensitive to the given treatment, i.e., amphotericin B.

The most important problem in management of fungal infection is the difficulty of making early diagnosis. In general, diagnosis of systemic mycosis depends on the isolation of causative fungus from clinical specimens and the histopathological findings in tissue sections. Waiting for the results of these procedures, which usually take about one to three weeks, the patients may get worse and die without therapy. With the bedside microscopic examination of the Wright's-stained touch smears of biopsy specimens, the presumptive diagnosis of systemic mycosis can be made. Then antifungal therapy can be empirically started before the laboratory results are available.
REFERENCES


