

DISSEMINATED HISTOPLASMOSIS

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Abstract

A case of disseminated histoplasmosis in a 56-year-old apparently healthy male without any history of travel to endemic zone is described. The patient presented with fever with cough, respiratory distress and disorientation. Physical findings include fever, shortness of breath, reduced level of consciousness and hypotension. Diagnosis was confirmed by presence of Histoplasma capsulatum in bone marrow aspirate. This report illustrates the importance of recognizing the possibility of histoplasmosis in Bangladesh where mimickers of histoplasmosis like pulmonary tuberculosis and visceral leishmaniasis are extremely common.

Keywords: Histoplasmosis, endemic mycoses, disseminated histoplasmosis, *Histoplasma capsulatum*, Bangladesh

Introduction

Histoplasmosis is the most common endemic mycosis in human. *Histoplasma capsulatum* is a dimorphic fungus distributed worldwide, but endemic in the Americas, Africa, and Asia.¹ It was first described by Samuel Darling in 1906 in an adult patient who presumably died of military tuberculosis.² Initial infection is through respiratory tract through which it enters the reticuloendothelial system and resides in macrophages. Most individuals with intact cellular immunity are asymptomatic or have mild pulmonary symptoms. Severe disseminated histoplasmosis develops in people with primary or secondary deficiency of cellular immunity. Immunosuppressed conditions due either to infections like AIDS or drugs raise the possibility of histoplasmosis. Approximately, 10% cases of histoplasmosis develop into progressive disseminated histoplasmosis (PDH).³ Disseminated histoplasmosis may present as acute PDH with fever, malaise, cough mimicking pulmonary tuberculosis. Chronic PDH manifests as fever, sweats, weight loss, organomegaly, lymphadenopathy.

In Bangladeshi context, reporting of histoplasmosis in medical literature is very rare. We present a case of histoplasmosis in an apparently healthy individual

who initially had pulmonary involvement and later progressed to develop disseminated histoplasmosis.

Case Report

A 56 years old previously healthy male was admitted with the complaints of fever with dry cough of 11 months duration, respiratory distress for 7 days and disorientation for 2 days. His previous medical history was unremarkable except for the fact that he was given anti-tuberculous drugs for a presumed diagnosis of pulmonary tuberculosis for 5 months before admission without any improvement. The patient denied any history of travel or sexual exposure. He was not on any drug that might have induced immunosuppression.

On general examination, the patient was febrile with a recorded temperature of 100° F(37.8° C), level of consciousness on Glasgow Coma Scale 10, tachypnic, hypotensive (blood pressure 80/60 mm Hg). Other parameters were normal. Systemic examination revealed no abnormality. The patient's laboratory investigation results showed anemia with hemoglobin 9 g/dL, ESR 60mm in 1st hour, total WBC count 9000/cm³, normal platelet count, serum creatinine 2.3 mg/dL. Sputum for Acid-fast bacillus was negative. Mantoux test was negative. HIV screening returned

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negative (Figure 1). Cerebrospinal fluid study was normal. Chest X-ray showed bilateral diffuse infiltrate. Peripheral blood smear was normal. Bone marrow aspirate showed plenty of intracellular

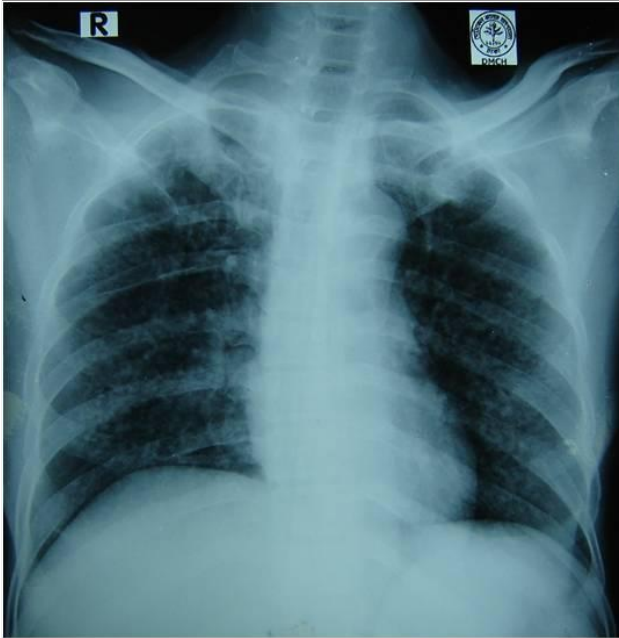


Fig.-1: Chest X-ray showing bilateral diffuse pulmonary infiltrate

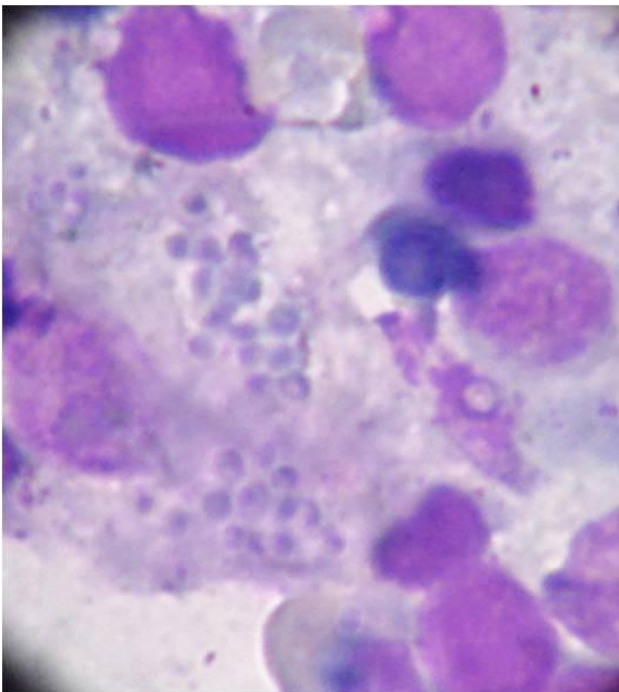


Fig.-2: Bone marrow aspirate showing numerous *Histoplasma Capsulatum* (Leishman stain)

rounded to oval parasites with eccentric crescent shaped nucleus suggestive of *Histoplasma Capsulatum* (Figure 2).

The patient was started on intravenous amphotericin B. His condition improved initially with temperature returning to baseline. Unfortunately, the patient developed aspiration pneumonia on 5th post admission day and expired.

Discussion

Histoplasmosis is endemic in parts of North and South America, Asia and Africa. It is the most common endemic mycoses in the United States. The causative agent *H. capsulatum* grows in soil laden with excreta of chickens, pigeons, starlings, blackbirds, and bats.⁴ Exposure occurs through contact with chicken houses, soil containing large amount of bird or bat guano and old houses or caves known to be bat roosts.⁴

Incidence of histoplasmosis in non-endemic areas is far fewer than endemic areas. Commonly, histoplasmosis occurs in non-endemic areas due to travel or residence in endemic areas. Additionally, it may be found outside endemic areas where microfoci of *Histoplasma* are the source of infection.⁵ Incidence figures of histoplasmosis in Bangladesh are unavailable. Sporadic cases have been reported in different literature. A review of literature revealed only 3 cases of histoplasmosis from Bangladesh including one patient who had a renal transplant and was on immunosuppressive agents.^{2,4,6}

The severity of clinical manifestation depends on size of the inoculum, underlying health of the patient and immune status to *Histoplasma*.¹ Majority of patients with AIDS present with disseminated infection while immunocompetent individuals demonstrate clinical features ranging from asymptomatic infection to rapidly fatal pulmonary infection. In between, patients may develop a variety of clinical manifestations including acute or subacute pulmonary disease, progressive disseminated disease, pericarditis, arthritis or, less commonly, fibrosing mediastinitis.¹

Disseminated histoplasmosis may present either as self-limited disease or progressive disseminated histoplasmosis.⁵ The self-limited condition is found in acute histoplasmosis. It occurs during the first few weeks of illness when hematogenous dissemination leads to development of various

clinical features. Hepatomegaly, splenomegaly, bone marrow suppression, elevated hepatic enzymes are some of the features. Calcified granuloma in the spleen is a common finding in people living in the endemic zone. Blood culture is rarely positive in acute stage. Specific cell-mediated immunity plays an important role in controlling the infection in lung and extrapulmonary tissues.

Progressively disseminated histoplasmosis usually occurs either in patients at extremes of age or in patients with an underlying immune deficiency state due to AIDS, leukemia, lymphoma, systemic lupus erythematosus, systemic corticosteroids, solid organ transplantation, anti-tumor necrosis factor agents. Not all patients harbor an immunodeficient status.⁵ Unidentified mechanism leading to immune deficiency is thought to be behind these cases. Ongoing research has identified defects in interferon- α /interleukin-12 pathway as a possible explanation in otherwise healthy individuals who develop progressive disseminated histoplasmosis.¹ The clinical features include fever, weight loss, fatigue, respiratory complaints like cough and shortness of breath. Hepatomegaly, splenomegaly, lymphadenopathy, bone marrow involvement are found in less than 50% of cases. Less common manifestations include oropharyngeal ulcers, gastrointestinal hemorrhage, adrenal insufficiency, subacute to chronic meningitis and endocarditis. Few patients may present with acute shock-like episodes with hypotension and coagulopathy. In significant number of cases, the only findings are fever and progressive weight loss.⁵

Laboratory diagnosis of histoplasmosis can be made by growth of histoplasma in culture. Bone marrow aspirate, peripheral blood smear, lymph node biopsy, bronchoalveolar lavage fluid, tranbrochial biopsy specimen and biopsy from cutaneous lesions can be used for diagnosis.⁴ Among all these, bone marrow examination has the highest diagnostic yield.⁷ Other laboratory abnormalities include anemia, leukopenia, pancytopenia, elevated liver enzymes, increased ferritin and serum lactate dehydrogenase. Antigen detection in urine and serum by radioimmunoassay is highly sensitive in disseminated infection. It can also be used for monitoring response to treatment especially in AIDS patient. The most common finding on chest imaging is diffuse interstitial or reticulonodular infiltrates

and military infiltrates.⁵ Chest X-ray in chronic pulmonary histoplasmosis may also show upper lobe involvement with cavitation leading to a misdiagnosis of pulmonary tuberculosis.

The recommended treatment regimen for disseminated histoplasmosis is liposomal Amphotericin B for 1-2 weeks followed by oral itraconazole for at least 12 months.⁸ Suppressive therapy with itraconazole may be required in immunocompromised patients like AIDS or organ transplant patient.⁷ Liposomal Amphotericin B is better than conventional Amphotericin B in terms of toxicity and therapeutic efficacy.

Our patient presented with chronic respiratory complaints of cough with fever followed by respiratory distress and disorientation. Before admission, his initial symptoms and imaging findings led to the diagnosis of pulmonary tuberculosis which is widely prevalent in Bangladesh. Indeed, histoplasmosis is under-reported from Bangladesh due to low index of suspicion and lack of diagnostic facility. Another possible explanation of under-diagnosis is that disseminated histoplasmosis resembles visceral leishmaniasis in many aspects with features of fever, weight loss, hepatosplenomegaly. Moreover, both of these are responsive to Amphotericin B. Our patient did not have organomegaly which is found in only one-third of patients. Bone marrow involvement is suggested by anemia and raised ESR. These findings along with thrombocytopenia are the most common hematological abnormalities.

Literature review revealed only 3 cases of histoplasmosis from Bangladesh—a 69-year-old male with oral ulcer, hepatosplenomegaly, anemia and leucopenia.⁶ Another patient was diagnosed in a neighboring country and the third patient, a renal transplant receiver on immunosuppressive therapy, was diagnosed and treated in the United States (US) where he returned from Bangladesh after a visit. This patient did not travel to or was living in histoplasmosis endemic zone of US, namely Ohio and Mississippi River Valleys. The authors concluded that the temporal relationship of his visit to Bangladesh and onset of symptoms suggested that he was infected after he came in contact with chicken houses in Bangladesh.⁴ Reports from India suggest

the presence of endemic focus in abandoned houses containing bat guano and in forest soil.^{9,10}

In conclusion, our case illustrates the importance of high index of suspicion for diagnosing histoplasmosis in a patient presenting with features suggestive of pulmonary tuberculosis but failing to respond to anti-TB after a reasonable period of time. Increasing prevalence of AIDS, organ transplantation and expanding international travel is likely to heighten the possibility of histoplasmosis in Bangladesh. Physicians need to alert themselves to this under-diagnosed infectious disease which is ultimately fatal if left untreated.

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