Disseminated Histoplasmosis in an immuno- competent Individual

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Abstract

Disseminated histoplasmosis in an immunocompetent individual is a rare phenomenon. The microconidia of this dimorphic fungus are transmitted through inhalational route and undergo dissemination. Cytopenias in the background of immunocompetence is an extremely rare finding in disseminated histoplasmosis. Here, we report a case of disseminated histoplasmosis in an immunocompetent patient presenting with fever, hepatosplenomegaly and bicytopenia.

Keywords: **Disseminated histoplasmosis, dimorphic fungus, microconidia, immunocompetence, cytopenias.**

Introduction

Histoplasmosis is a systemic mycosis caused by the dimorphic fungus called histoplasma capsulatum. Also known as Darling's disease, it is endemic in Americas and tropics, Africa and parts of eastern India.[1-3] Though commonly found in immunocompromised individuals, disseminated histoplasmosis in immunocompetent individuals is extremely rare. The spores (microconidia) of this fungus are found in soil and bird droppings and it is transmitted by inhalational route. Progressive disseminated histoplasmosis presents with fever, malaise, hepatosplenomegaly and lymphadenopathy. Other features of the disease include renal failure, disseminated intravascular coagulation, gastrointestinal manifestations in the form of nausea and vomiting, cytopenias, skin lesions, adrenal insufficiency and neurological manifestation like encephalopathy.[4,5] Here, we describe a patient of disseminated histoplasmosis from eastern India.

Case Report

40 year old non- diabetic and non- hypertensive male farmer presented with moderate grade fever for past two months associated with fatigue and anorexia. There was no associated history of cough with hemoptysis, jaundice, bleeding manifestations, arthralgia, dysuria, night sweats or upper gastrointestinal bleeding. He was a known smoker but there was no history of alcoholism or unprotected sexual intercourse.

On examination, he was found hyposthenic, normotensive and anemic with hepatosplenomegaly but no lymphadenopathy. Liver was palpable 2 cm beyond right costal margin and was firm in consistency. Spleen was felt 4cm beyond left costal margin. Rest of examination findings were within normal limits. On investigation, his peripheral blood picture showed hemoglobin 8.3g/dl, TLC-1300, DC-N70%, L20%, M3%, E6% B1%, Platelet-1.95 lac/cu.mm, reticulocyte count of 1.3%, ESR-36mm, DCT-negative. LFT showed bilirubin-0.6 mg/dl, SGOT-75, SGPT-65, ALP-559U/L, TP-7.10, ALB-3.4, GLOB-3.7. P time was 14.7sec, control-11.2 sec, INR-1.3. Lactate dehydrogenase, Serum ferritin, Renal Function Test, urine routine examination were normal, and blood and urine cultures showed no growth. Malaria parasite and antigen test were negative. Antibody to RK 39, HIV1 and 2, HBsAg and anti HCV were negative. Chest X ray was normal. Ultrasonography of whole abdomen showed enlarged spleen size 17 cm and enlarged liver. To investigate the cause of bicytopenia, bone marrow aspiration was done

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which showed presence of large number of histiocytes. Few histiocytes showed presence of round boat shaped inclusion body with refractile halo around it (fig.1).

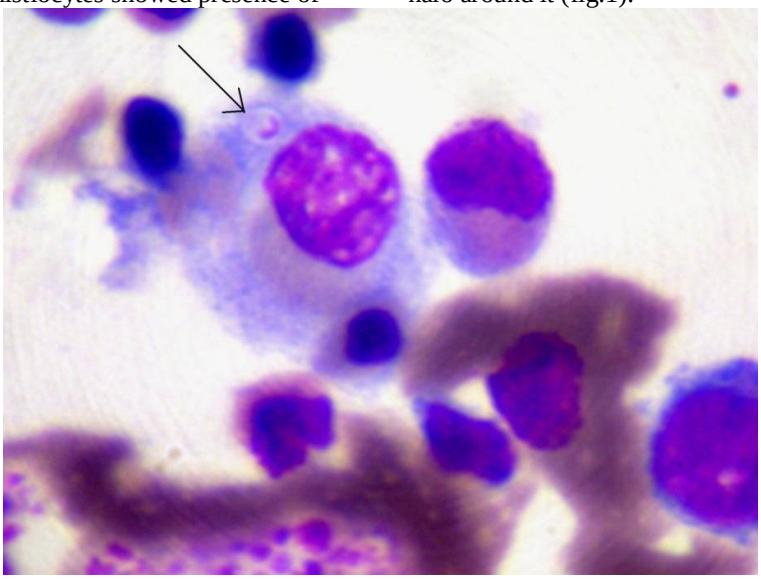

Figure 1.Bone marrow aspirate showing a histiocyte with round boat shaped inclusion body having surrounding refractile halo (marked by arrow), suggestive of histoplasma

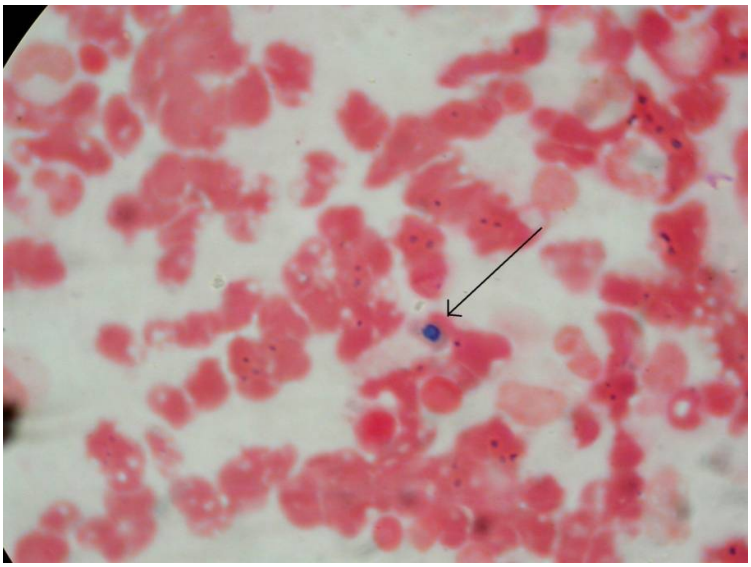

Figure 2.Pearl stain positive inclusion body within a histiocyte in the bone marrow aspirate, highly suggestive of histoplasma (marked by arrow)

Inclusion bodies were pearl stain positive, likely to be histoplasma (fig. 2). Bone marrow trephine biopsy showed a tiny granuloma, reactive megakaryocytic hyperplasia and dyserythropoiesis. Bone marrow BACTEC culture for Mycobacterium tuberculosis was negative. Fungal culture of bone marrow aspirate in Saboraud's dextrose agar with chloramphenicol and cycloheximide was positive. Liver biopsy was also done which showed occasional foci of spotty necrosis. Next, we performed serum antibody test against histoplasma showing absence of H precipitin and M precipitin which is suggestive of disseminated histoplasmosis.

The patient was started on injection liposomal amphotericin B at a dose of 3 mg/kg/day. Fever subsided from 3rd day of starting amphotericin B injection. Amphotericin B was continued for 14 days followed by oral itraconazole tablet 200mg twice daily with a plan to continue for 1 year. Patient's bicytopenia improved substantially

during discharge.

Discussion

The first case of histoplasmosis was reported in the year 1954 in India.[6] Subsequently, many cases were reported from India.[4,5] Though most of the cases occurred in the background of some form of immunodeficiency, our patient did not have any identifiable cause of immune suppression. Following inhalation of the histoplasma microconidia, the organism replicates locally in the lungs. Symptomatic hosts with primary pulmonary histoplasmosis often present with nonspecific symptoms of fever, chest pain and cough that are self limited. Immunocompetent hosts are able to control and limit infections of histoplasma; however, hosts with defective cell-mediated immunity, including patients with hematolymphoid malignancies, solid- organ transplants, and those exposed to chemotherapeutic and immunosuppressive agents, are at risk of developing progressive disseminated histoplasmosis involving the reticuloendothelial system, including the liver, spleen, kidney, lymph nodes, bone marrow and mucocutaneous tissues. It is also recognized as an AIDS- defining illness.[7]

Bicytopenia is reported in histoplasmosis whenever there is bone marrow involvement. Hood et al. reported two patients with disseminated histoplasmosis and predominant thrombocytopenia. One of them was diagnosed with histoplasmosis from autopsy.[8] Disseminated histoplasmosis should always be considered in the differential diagnosis of fever with cytopenia, irrespective of the immune status of the patient and endemicity of the disease in the region. Disseminated histoplasmosis with oral involvement in an immunocompetent patient has also been reported.[9]

For the management of disseminated histoplasmosis, liposomal amphotericin B at a dose of 3mg/kg/day is given for 1-2 weeks followed by itraconazole 200mg thrice daily for 3 days, then 200mg twice daily for a period of 12 months.[10,11]

Due to lack of awareness about histoplasmosis and prevalence of tuberculosis in our country, it may occur that many cases of histoplasmosis are being misdiagnosed as tuberculosis. Another close differential diagnosis of histoplasmosis is visceral leishmaniasis. Recognition of varied clinical manifestations of histoplasmosis, improved laboratory facilities and extensive population based studies to know the endemicity of histoplasmosis in various regions is essential for early diagnosis and effective treatment.

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