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CASE REPORT

Disseminated Histoplasmosis Presenting as Prolonged Fever and Pancytopenia in a HIV Patient

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ABSTRACT

Histoplasmosis is an opportunistic fungal infection commonly affecting immuno compromised hosts. In HIV patients it usually present as a disseminated form. We hereby report a case of Progressive Disseminated Histoplasmosis in a patient with advanced HIV infection, who presented with prolonged fever and pancytopenia. Bone marrow examination showed yeast forms of *Histoplasma capsulatum*. Prompt initiation of antifungal therapy and anti-retroviral therapy lead to improvement in her clinical condition. Progressive Disseminated Histoplasmosis is thus an important differential diagnosis to be considered in any HIV patient presenting with prolonged fever and pancytopenia.

INTRODUCTION

Histoplasmosis is an important opportunistic infection in HIV patients. In advanced HIV infection Histoplasmosis present as a progressive disseminated disease (1). We hereby report a case of Progressive Disseminated Histoplasmosis in a patient with Acquired Immune deficiency Syndrome who presented with prolonged fever and pancytopenia.

Case report

A 27 year old female, resident of Uttarakhand, India presented with complaints of fever of 5 months duration and generalised fatigue. Fever was low grade and intermittent without rigors and chills. She also had significant unintentional weight loss. She did not give any history of cough, diarrhoea, headache, vomiting or dysuria. Six month prior to the current presentation she was tested positive for HIV-1, after her husband was diagnosed of the same. Her baseline CD4 count was 159 cells/μL and she was started on anti-retroviral therapy with Tenofovir Disoproxil Fumarate, Lamivudine and Efavirenz. However the patient was poorly adherent to therapy.

On Examination patient was conscious, cooperative and comfortable at rest. Her blood pressure was 110/70 mmHg, pulse rate was 88/minute and respiratory rate 16/minute. Oxygen saturation was 96% in room air. Pallor was present and there was no icterus, clubbing, cyanosis, lymphadenopathy or edema. Examination of the abdomen revealed an enlarged liver 5cm below the costal margin. Tip of the spleen was also palpable.

On evaluation she was found to have pancytopenia (Hemoglobin-6.5 gm/dl, Total leukocyte count - 1500 cells/μL; Polymorphs -76%, Lymphocyte -8%, Eosinophil -1.4%, Monocyte -12.8% and Platelets 90,000 cells/ μL). Liver function tests showed a normal Bilirubin, ALT and AST levels but her Alkaline Phosphatase (5000 IU/L) and Gamma-glutamyl transferase (960IU/L) were raised. Blood Urea nitrogen and Serum Creatinine levels were normal.

Serum levels of Ferritin, Folate and Vitamin B12 were normal. Her peripheral smear showed pancytopenia. For further evaluation a bone marrow study was done. Bone marrow aspirate showed intracellular yeast forms suggestive of *Histoplasma capsulatum* (Fig. 1). Serology for Histoplasma antibodies by immunodiffusion and test for Histoplasma urinary antigen was positive.

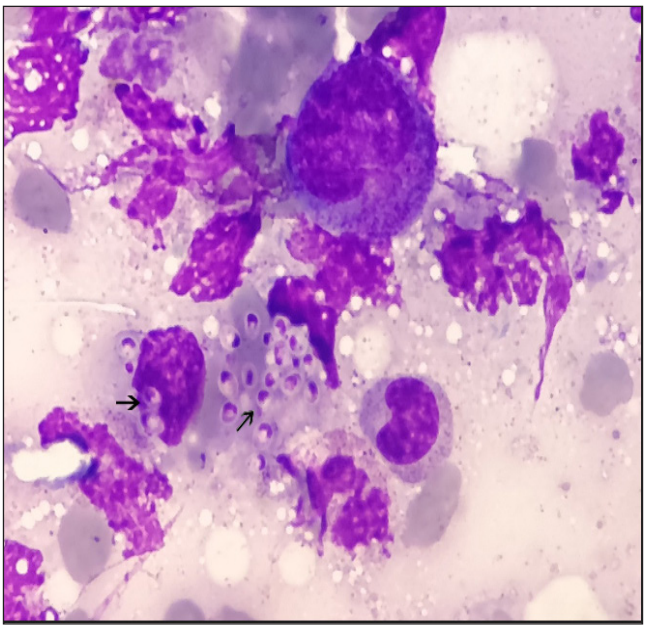

Fig. 1: Bone marrow aspirate showing multiple yeast cells of *Histoplasma capsulatum*

Serological tests for Hepatitis B and C, Syphilis and Toxoplasma were negative. Urine and stool routine microscopy were normal. Her blood culture, both aerobic and anaerobic, and urine cultures were sterile. Sputum for Acid Fast Bacilli (AFB) also tested negative. Her chest radiograph was within normal limits. Contrast Enhanced Computed Tomography (CECT) chest and abdomen was normal except for hepatosplenomagaly.

She was thus diagnosed to have HIV-1 infection (WHO clinical stage IV) with progressive disseminated Histoplasmosis. IV Liposomal Amphotericin B was started and continued for 2 weeks and after that was switched over to oral Itraconazole 200 mg twice daily. She was counselled about drug adherence and was restarted on anti-retroviral *therapy* (Tenofovir Disoproxil Fumarate, Lamivudine and Efavirenz) one week after starting Liposomal Amphotericin B. Co-trimoxazole was also started as prophylaxis against Pneumocystis jiroveci.

With treatment her clinical condition improved and her Hemoglobin levels, total leucocyte count and platelet count increased gradually and levels of Alkaline phosphatase declined. She was discharged on Oral Itraconazole, anti-retroviral therapy and Co-trimoxazole prophylaxis.

DISCUSSION

Histoplasmosis is caused by a thermally dimorphic fungi Histoplasma capsulatum. Deficiency in cellular immunity is the most important predisposing risk factor for Histoplasmosis. Such conditions include HIV infection, post organ transplantation, Corticosteroid use, cytotoxic chemotherapy and use of other immunosuppressive drugs(2). In Immunocompromised patients Histoplasmosis present as a disseminated disease (Progressive Disseminated Histoplasmosis). In India the disease is mostly reported from its northern and north-eastern part. There has been a significant increase in the number of cases reported from India in last one decade (3).

In HIV patients the most important risk factor for the development of Histoplasmosis is low CD4 count. A CD4 count < 200 cells/μL increases the risk of Histoplasmosis in HIV patients and the incidence rate increases proportionally to the level of CD4 decline(4). Our patient had a baseline CD4 count of 159 cells/μL and was poorly adherent to the medication which predisposed her to acquiring the diseases.

Progressive Disseminated Histoplasmosis present as prolonged fever, weight loss and fatigue. Pulmonary symptoms in the form of cough and breathlessness is found in about 50% of the patients. Hepatosplenomegaly and lymphadenopathy is seen in around 25% of the patients(5). Pancytopenia is also a well described feature of disseminated histoplasmosis and is more likely to occur in immunocompromised patients than immunocompetent patients(6).

Direct demonstration of the organism in various tissues as well as culture of all the involved tissue are the gold standard for diagnosis of Histoplasmosis. For patients with disseminated disease samples from blood, bone marrow, liver, skin lesions or other involved tissue can be used for diagnosis(2).

This case emphasises the importance of considering Progressive Disseminated Histoplasmosis as a differential diagnosis in any HIV patient presenting with prolonged fever. Presence of pancytopenia should strengthen the suspicion of this potentially treatable opportunistic infection.

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