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## Case Report

# A rare case of progressive disseminated histoplasmosis with bone marrow involvement in an immunocompetent patient

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## ABSTRACT

Histoplasmosis is a rare entity in India and very few cases have been reported from eastern region of India like West Bengal and rarely cases from southern India as well. We hereby report a case of progressive disseminated histoplasmosis (PDH) from a non-endemic region of India (Eastern Utter Pradesh) and that too in an immunocompetent individual.

**Keywords:** Bone marrow, Histoplasmosis, Immunocompetent

## INTRODUCTION

Histoplasmosis is an infectious disease caused by Histoplasma capsulatum, a thermal dimorphic fungus. This infection is self-limited in immunocompetent people with low level of exposure whereas high level of exposure presents as flu-like illness, fever, chills, headache, myalgia, anorexia, cough dyspnea and chest pain.[1] The occurrence of disseminated histoplasmosis is most commonly seen even in immunosuppressed individuals.

However, there are a few case reports of this disease seen in immunocompetent individuals.[2]In India, 1st case of histoplasmosis was reported by Panja and Sen in 1952 and since then this infection is seldom reported from India.[3] The reason for this rarity is due to its clinical presentations being notoriously non-specific along with lack of awareness among physicians and lastly endemic fungal infections remain undiagnosed in India due to inadequate fungal laboratories and diagnostic facilities.

## CASE REPORT

35-years-old male, resident of Eastern Uttar Pradesh, unskilled manual labourers working in renovation and maintenance of old buildings was admitted to our hospital with chief complaints of fever on and off for 6 months associated with abdominal pain and weight loss. Fever was continuous, high grade, associated with chills and rigors and relieved by taking antipyretics. It was not associated with headache and vomiting. It was associated with epigastric pain which was non-radiating and increased more after taking food and associated with feeling of early satiety and fullness. Patient also had history of 3 episodes of epistaxis and hematuria 5 day back, for which patient visited a private hospital and symptoms subsided after taking some medication. In view of very low platelet counts discovered there on investigation, he was referred to our hospital. There was no significant past medical or surgical history except that during last 6 months he had shown to many physicians and took antibiotics for that. He had weight loss of 15 kg in last 5 months. Patient was a chronic alcoholic and a

chronic smoker. On general physical examination, he had mild pallor and bilateral pedal oedema. Abdominal examination revealed a soft abdomen with non-tender palpable liver, 4cm below the costal margin and a non-tender palpable spleen 8cm below the costal margin. A grade II ejection systolic functional murmur was heard at apical area. Rest of the general physical and systemic examination was within normal limit.

Laboratory investigations revealed haemoglobin of 8.4g/dl, total leukocyte count 3300/cmm with normal differential count but with thrombocytopenia (platelets count <20000/ml). Peripheral smear revealed RBC showing moderate anisopoikilocytosis with presence of microcytes, target cells with normochromic to mild hypochromic picture and thrombocytopenia with giant platelets. No parasites were seen. Urine routine and microscopy and renal function tests were all within normal limits. Liver function tests showed increase globulin and decrease in albumin (2 gm/dl) with reversed A: G ratio. Rest of the liver function test was within normal limit. 24-hours urine protein was 250 mg/day. Serum LDH was 2450 u/lt. PT and INR were within normal limit.

In view of fever, hepatosplenomegaly and thrombocytopenia, we kept Malaria/Enteric fever/Kala-Azar/Disseminated tuberculosis/CML or Lymphoma as differential diagnosis. RK 39, Malaria Antigen, ANA, HBsAg, Anti HCV and HIV were all negative. USG of abdomen showed hepatosplenomegaly with minimal ascites. CECT of thorax and abdomen showed para septal emphysematous change in bilateral upper lobes of lungs with hepatosplenomegaly and lymphadenopathy but grossly normal GI tract with no e/o tuberculosis or abscess.

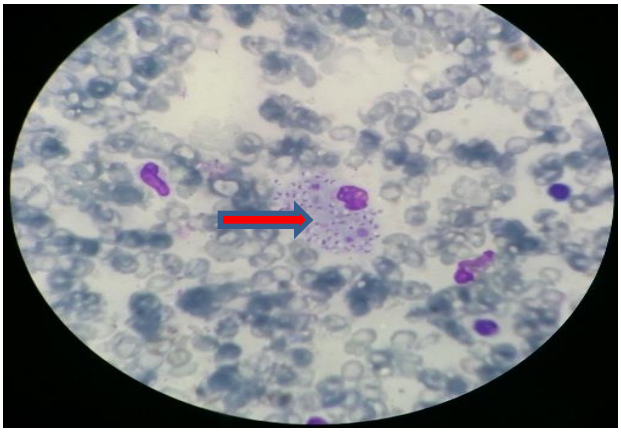

**Figure 1: Bone marrow aspiration (BMA)- BMA aspirate smears showing numerous yeast form of histoplasma within a histocyte (Leishman, 10X, Red arrow).**

So further a bone marrow aspiration was planned which revealed normal cellularity, M: E ratio was 2:1 with normal erythropoiesis and megakaryocytes. Myeloid series of cells were seen in all stages of maturation. Histiocytes were prominent. Many intracellular and extracellular yeast forms of histoplasma were noted which showed PAS positivity (Figure 1 and 2). However, Langhans bodies or LD bodies were not detected on aspirate slides. Bone marrow aspirate stained by Ziehl Nielsen stain was done and showed no acid-fast bacilli. Guided FNAC of abdominal lymph also revealed many yeast forms of histoplasma. CD 55 and CD59 for PNH were also negative.

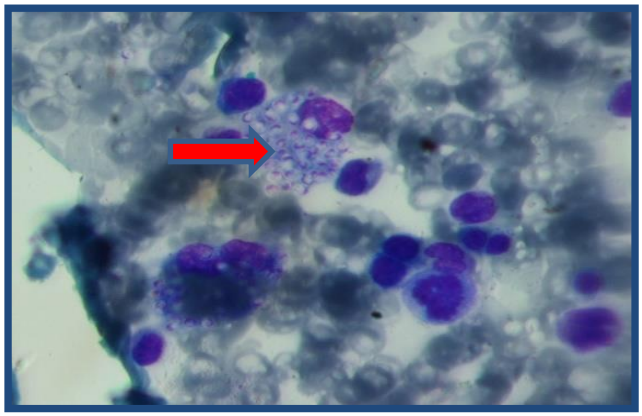

**Figure 2: High power view of smear showing numerous yeast form of Histoplasma heighted by PAS stain (Periodic acid Schiff, 40X, Red arrow).**

Bone marrow culture for *S. Typhi* and Tuberculosis was negative. Isolation of the fungus was achieved on special media (Sabouraud agar) and growth of histoplasma capsulatum was detected after 6 weeks. Bone marrow biopsy also revealed numerous yeast form and extracellular histoplasma along with eosinophilic prominence and scattered myeloid and erythroid series cells (Figure 3 and 4).

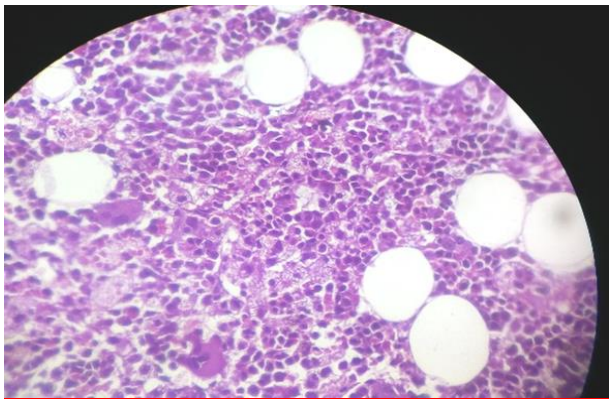

**Figure 3: Section from bone marrow biosy (BMB) shows hematopoietic cells comprising of myeloid and erythroid series cell and extracellular yeast form of histoplama (H and E,10X).**

Since the HIV status was negative so we asked for immunological profile of the patient. His CD4 count was 640 cells/ul (Normal-500-1200 cells/ul) and the levels of

IgA (80mg/dl), IgM (200mg/dl) and IgG (873mg/dl) were all within normal limit. A Colonoscopy was planned but the patient refused for that.

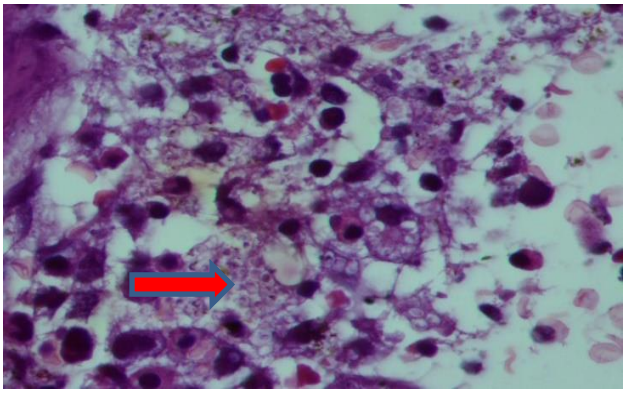

Figure 4: High power view of BMB showing numerous yeast form and extracellular histoplasma along with eosinophils prominence and scattered myeloid and erythroid series cells (H and E,40X, Red arrow).

*Treatment*

Patient was started on Liposomal amphotericin -B at a dose of 3-5 mg/kg/day for 4 weeks and then oral Itraconazole at a dose of 200 mg daily which was continued for 6 months. There was marked improvement in his symptoms without any complications or side effects of Amphotericin-B and he was discharged on oral Itraconazole after 6 weeks of hospital stay.

*Outcome and Follow-Up*

The patient responded very well to the treatment and has not shown any new or recurrent infection on follow up since last 8 months and has gained weight of 14 kg.

## DISCUSSION

Histoplasmosis is a disease of western part of the world primarily caused by Histoplasma capsulatum. It is mainly of three types-acute primary, chronic cavitary and progressive disseminated.[4] PDH is rare in immunocompetent individual. This infection by itself is very rare in India; however, few cases have been reported from different region in the eastern and southern parts of the country.[5,6] Our patient was a native of a non-endemic region of northern part of India. The common presentation of this disease is fever with abdominal pain, weight loss, hepatosplenomegaly, lymphadenopathy; oral ulcerations, anaemia and thrombocytopenia.[7] Fungal culture remains the gold standard for diagnosis although they can often be negative, the reason for which has been stated before.[1]

In progressive disseminated histoplasmosis, thrombocytopenia and other cytopenia are hallmark of bone marrow involvement but rarely reports of patients presenting with isolated thrombocytopenia the present case has been reported.[8-11]

Pathogenesis of thrombocytopenia in histoplasmosis according to Des Prez et al.[12] has been found to be that the yeast from H. capsulatum activates the platelets resulting in serotonin release reaction and aggregation without the involvement of the complement pathway. The plasma cofactors which are involved are Ig G which is necessary for induction of release reaction. Our patient was an inhabitant of eastern part of Utter Pradesh, which is endemic for kala-Azar and malaria. Above that he had no obvious immunodeficiency state. This case highlights the fact that although progressive disseminated histoplasmosis is very rare cause of fever of longer duration that too in immuno-competent individuals in India but it should be kept in mind as a differential diagnosis whenever other often sought of differential causes of PUO are ruled out.

## CONCLUSION

Progressive disseminated histoplasmosis is an uncommon disease in immunocompetent individuals specially from non-endemic regions. In patient presenting with long duration fever and hepatosplenomegaly in India the obvious provisional diagnosis is disseminated tuberculosis, kala azar, chronic malaria, lymphoma, leukemia, and HIV-AIDS. Histoplasmosis is a rare cause with similar manifestation and should be kept as a differential diagnosis. Early diagnosis and prompt treatment only can prevent lethal complications.

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## REFERENCES

1. Dodd K, Tompkins EH. A case of histoplasmosis of Darling in an infant. Am J Trop Med. 1934;14:127-37.
2. Sayal SK, Prasad PS, Sanghi S. Disseminated histoplasmosis: Cutaneous presentation. Indian J Dermatol Venereol Leprol. 2003;69:90-1.
3. Panja G, Sen S. A unique case of histoplasmosis. J Indian Med Association. 1954;6:257-8.
4. Sood N, Gugnani HC, Batra R, Ramesh V, Padhye AA. Disseminated histoplasmosis (a case report). J Postgrad Med. 1983;29:270-3.
5. Sanyal M, Thammaya A. Skin sensitivity to Histoplasma in Calcutta and its neighbourhood. Indian J Dermatol Venereol Leprol. 1980;46:94-8.
6. Mukherjee AM, Khan KP, Sanyal M, Basu N. Histoplasmosis in India with report of two cases. J Ind Med Assoc. 1971;56:121-5.
7. Mukherjee A, Tangri R, Verma N, Gautam D. Acute disseminated histoplasmosis in an immunocompetent patient. J Bras Pneumol. 2004;30:1-6.

8. Kauffman CA. Histoplasmosis: a clinical and laboratory update. Clin Microbiol Reviews. 2007;20:115-32.
9. Subramanian S, Abraham OC, Rupali P, Zachariah A, Mathews MS, Mathai D. Disseminated histoplasmosis. J Association Physicians India. 2005;53:185-9.
10. Hood AB, Inglis FG, Lowenstein L. Histoplasmosis and thrombocytopenic purpura: transmission by renal homotransplantations. Canadian Med Association J. 1965;93:587-92.
11. Armitage JO, Sheets RF. Idiopathic thrombocytopenic purpura. J American Med Association. 1977;237:23-4.
12. Des Prez RM, Steckley S, Stroud RM, Hawiger J. Interaction of Histoplasma capsulatum with human platelets. J Infectious Dis. 1980;142:32.

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