Case Report

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Pathology Section

Disseminated Histoplasmosis: Case Report and Review

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ABSTRACT

Histoplasmosis is a systemic fungal disease. It is also called as Darling's disease, as it was first described by an American physician named Samuel Taylor Darling, in Panama. It is caused by the dimorphic fungus *Histoplasma capsulatum*. It is usually self-limiting or localized in immunocompetent individuals whereas in immunocompromised patients, it presents in disseminated forms. This infection is endemic to central and South-central United States.

Histoplasmosis infection is acquired by inhalation of fungal microconidia present in the contaminated soil. Asymptomatic dissemination of infection beyond the lungs is common. Infection heals spontaneously in most of the cases and in some cases it develops into pulmonary disease similar to tuberculosis. Dissemination and systemic involvement occurs in patients suffering from debilitating diseases and immunocompromised conditions. It is relatively uncommon in India with few sporadic cases getting reported and it is endemic in eastern part of India. In non-endemic parts, disseminated histoplasmosis is rarely suspected and there have been very few case reports. Awareness is required, as its presentation is similar to tuberculosis, especially when we have patients with compromised immune status. We are reporting, with consent, one such rare case of disseminated histoplasmosis in a 36-year-old male farmer from South India with acquired immunodeficiency syndrome and very low CD4 count of 17cells/µl with lymph node and bone marrow involvement. Awareness of this infection is essential in these cases as it is potentially lethal and adequately treated patients with antifungal agents carry better prognosis. In non-endemic areas Disseminated Histoplasmosis has to be differentiated from more common disease like tuberculosis, leishmaniasis or systemic malignancies.

Keywords: *Histoplasma capsulatum*, Oral thrush, Systemic histoplasmosis.

CASE REPORT

A 36-year-old male patient, farmer by occupation with history of fever and oral thrush was admitted in the Male Medical Ward at St. Martha's Hospital. He gave a history of fever since one year, loss of weight of 10 kg in the past three months and cough since 5 days. He had been diagnosed positive for HIV, 2 days prior to admission. Patient was a known alcoholic. He did not give any history of contact. There was a history of previous blood transfusion as he had low haemoglobin, although no work up had been done for low haemoglobin. On general physical examination, patient had pallor, grade 1 clubbing, presence of oral thrush and herpes labialis along with generalized lymphadenopathy. Auscultation revealed bilateral infrascapular crepitation.

Following differential diagnoses were thought of: Tuberculosis, lymphoma, histoplasmosis and Persistent Generalized Lymphadenopathy (PGL). Patient was explained about the rarity of illness and with consent we are reporting this case report.

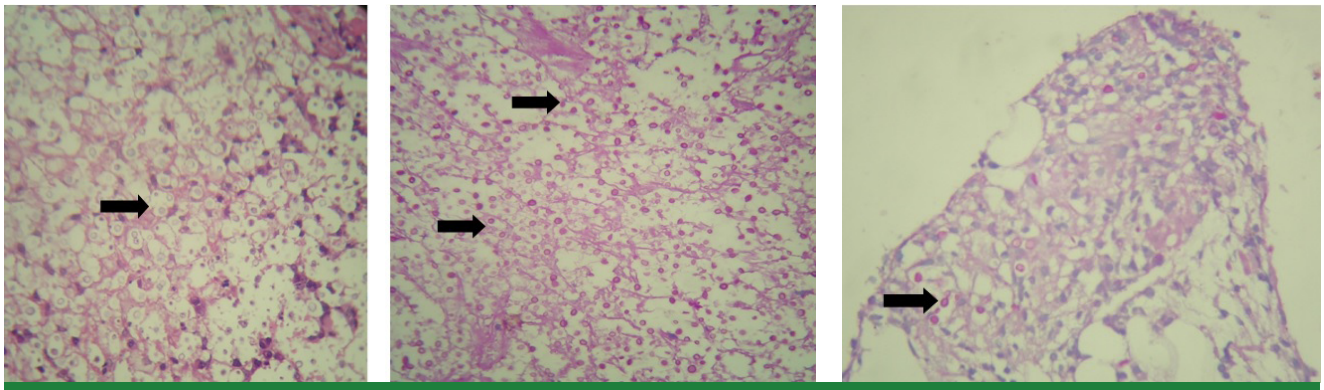
Patient was investigated : Haemoglobin 7.1g/dl, PCV - 21, ESR -90, urea -92, S.craetinine -2.39, ALP -220 u/l, GGT-228 u/l, Urine – albumin 2+, 24 hr. Urine protein – 942 mg HIV- Reactive (Elisa), CD4-17 cells/µl, sputum for AFB and Gene X-pert were negative. Ultrasonography showed mild splenomegaly, multiple discrete upper para-aortic lymph nodes.

FNAC of left cervical lymph node showed: few scattered inflammatory cells and occasional histiocytes and epithelioid like cells and caseous material.

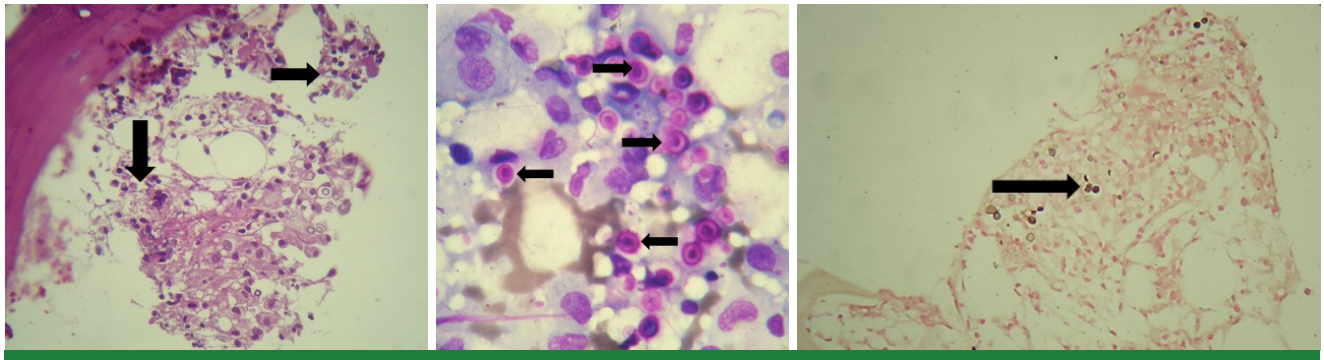
Patient underwent lymph node biopsy and bone marrow aspiration and biopsy. Lymph node biopsy [Table/Fig-1&2] showed completely effaced architecture of lymph node with aggregates of lymphoid cells. Numerous PAS positive capsulated yeast forms resembling histoplasma are noted throughout lymph node. No granuloma seen.

Bone marrow aspiration: Smears showed a hypocellular marrow with presence of increased histiocytes and intracellular capsulated yeast like bodies morphologically consistent with histoplasmosis [Table/Fig-3].

Bone marrow biopsy: Sections showed spicules of bone



[Table/Fig-1,2]: Lymph node biopsy showed completely effaced architecture of lymph node with aggregates of lymphoid cells. Numerous PAS positive capsulated yeast forms resembling histoplasma are noted throughout lymph node. No granuloma seen (H&E, PAS stain, x 10).
[Table/Fig-3]: Bone marrow aspiration smear showing a hypocellular marrow with presence of increased histiocytes and intracellular capsulated yeast like bodies consistent with histoplasmosis (Leishman stain, x 100)



[Table/Fig-4-6]: Sections showed spicules of bone with intervening marrow spaces showing normal marrow. Histiocytes are increased in number.PAS and GMS stain showed few capsulated yeast forms resembling histoplasma (H&E, GMS & PAS stain, x 10).

with intervening marrow spaces showing normal marrow. Histiocytes are increased in number. Special stain studies with PAS and GMS stain showed few capsulated yeast forms resembling histoplasma [Table/Fig-4-6].

Course in the Hospital: Patient was hospitalised for 2 weeks. Initially started on IV Monocef, Azithromycin (MAC), and Fluconazole. TB was ruled out and patient was started on ART. Even though the drug of choice is Amphotericin B, patient had HIV Associated Nephropathy (HIVAN), hence started on Itraconazole for 2 weeks. Patient was discharged after 2 weeks in a stable state and suggested to have follow up at ART centre.

DISCUSSION

Histoplasmosis is a granulomatous fungal infection of the reticuloendothelial system caused by the thermally dimorphic fungus, *Histoplasma Capsulatum* [1,2]. The organism is present in soil contaminated with bird droppings and chicken feathers. Infection is through inhalation of micro conidia and mycelial fragments present in the contaminated soil. It is self-limiting most of the times and causes potentially lethal infection in immunocompromised patients, patients on cytotoxic drugs, hematologic malignancies and with debilitating diseases [1-3]. It can either present as pulmonary histoplasmosis or as progressive disseminated histoplasmosis [1,2,4,5]. In patients with HIV infection the CD4 count of < 150 cells/ul increases the risk of disease and its dissemination [4,6]. The most common physical findings include fever, night sweats, fatigue dyspnoea, hepato-spleenomegaly and lymphadenopathy [7]. In India sporadic cases are reported and is considered to be endemic in certain areas of East India [3,6,8]. It mimics other clinical conditions like tuberculosis, lymphoma, malignancies [9]. Our patient with agricultural background had risk factors of exposure to soil and AIDS with CD4 count 17 cells/µl [10]. High degree of suspicion of histoplasmosis like rare opportunistic infections is very much necessary in present situation of AIDS pandemic, even in non-endemic parts of the world. A timely diagnosis and appropriate medical intervention will result in a good prognosis. Disseminated histoplasmosis is uncommon in non-endemic areas of India with clinical course and features overlapping with other systemic diseases like tuberculosis and malignancy [5,9]. Early diagnosis and treatment is vital as this condition carries high mortality and

tests like bone marrow aspiration can help in early diagnosis. The infection responds well to antifungal agents and lifelong maintenance therapy may be required in AIDS especially if CD4 counts remains <150cells/µl. Histoplasmosis should be a differential diagnosis in immunosuppressed patients with unexplained fever, weight loss, hepatomegaly and chest findings, if not responding to anti-TB treatment [5]. Bone marrow examination has a 75% sensitivity in diagnosing fungal pathogens in HIV patients [5,6,8].

The differential diagnosis to be considered are Leishmaniasis, other fungal infections like Candidiasis, Cryptococcosis, Blastomycosis and Pneumocystis infection or systemic malignancy [7].

CONCLUSION

Awareness of the histoplasmosis disease is essential as it is still rare in non-endemic areas of India and the clinical features are similar to other common systemic illness like tuberculosis and malignancy. The early diagnosis and early initiation of treatment with the antifungal agents helps to have better prognosis.

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