Case Report

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Disseminated Histoplasmosis in a Retropositive Young Male: A Case Report

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ABSTRACT

Disseminated histoplasmosis is caused by the dimorphic fungus Histoplasma capsulatum. This fungal infection is commonly seen in immunocompromised patients, especially in AIDS patients, children and elderly population. Here we present a case report of a 24-year-old male who was admitted with generalised fatigue and generalised lymphadenopathy. He was found to be retropositive on evaluation and FNAC of the node surprisingly revealed Histoplasmosis. Presence of these organisms were also seen on the peripheral smear which could be picked up only on reviewing the smear again. With this case report we wish to emphasize the need for careful and diligent search of these organisms in the peripheral smear.

Keywords: *Disseminated Histoplasmosis, Retropositive, FNAC, Peripheral Smear*

Introduction

Histoplasmosis is an opportunistic fungal infection found in humans with two clinical entities. [1] Histoplasmosis capsulati caused by *H. capsulatum* var *capsulatum* (Darling disease) was first described by S.T. Darling in 1905 [2] and *Histoplasmosis duboisii* caused by *H. capsulatum var duboisii*. [1] It is commonly seen in HIV patients, primary immunodeficiencies, other immunosuppressive disorders and in extreme of ages [3]. Prevalence rates of disseminated histoplasmosis ranged between 2-27% in United states and 29% in India. [1]

The clinical features of disseminated histoplasmosis are very similar to disseminated tuberculosis. [4] Fever, cachexia, hepatosplenomegaly, lymphadenopathy, pancytopenia and abnormal liver function tests are some of the commonest symptoms noted in both. [4] There is always a possibility of misdiagnosing it as tuberculosis due to overlapping clinico-radiological and histopathological features. [5] The definitive diagnosis is based purely on detecting histoplasmosis from patient's tissue sample or body fluids. [6] Early detection of the infection is important, so that treatment can be initiated at an early stage and complications can be avoided. [5]

Case Report

A 24-year-old male presented with one month history of low-grade fever associated with on and off chills and rigors, weight loss, malena, cough and dyspnea. He presented to our emergency department with generalized weakness, abdominal pain and vomiting which was noted for the past 5 days. He was empirically started on ATT from another hospital in the periphery with a clinical diagnosis of Tuberculosis. However, his condition continued to deteriorate.

On general examination, condition of patient was poor. He could sit up in propped up position with assistance. He had pallor, bilateral cervical lymphadenopathy and enlarged left axillary lymph node. Axillary node was 3x2cm, mobile and firm to touch. Pulse rate was 130 bpm, B.P - 80/ 40 mm Hg, Respiratory rate was 35-40/min, severely dyspnoeic. Per-abdomen examination revealed hepato-splenomegaly. Initial blood investigations on admission showed pancytopenia. RBC count - $1.27x10^6/\mu L$, hematocrit 7.2 %, hemoglobin 2.2 grams/dl, mean corpuscular volume 56.8 fl, mean corpuscular hemoglobin 17.7 pg, white blood cell count $4100x10^3/\mu L$ with a differential count of neutrophils 76%, lymphocytes 24% and platelets 45,000/ cumm, ESR was elevated 130mm/hr, renal parameters and LDH values were deranged. Chest radiography was normal, but ultrasonography of the abdomen revealed mild splenomegaly and periportal lymph nodes. (Figure 1,2) In view of the above said clinical findings a differential diagnosis of lymphoma and tuberculosis was kept in mind. Patient was extremely sick and was admitted to the intensive care unit.

Peripheral smear sent on day one of admission showed leucoerythroblastic blood picture. FNAC of the left axillary lymph node showed numerous macrophages with intracytoplasmic organisms. Our FNA differential diagnosis were *Leishmania donovani* and *Histoplasma capsulatum*. FNA smears showed basophilic crescent shaped nucleus (yeast forms, Figure 3) and no kinetoplast.

Hence a diagnosis of *Histoplasma capsulatum* was made. Collections of epithelioid histiocytes forming granulomas were also noted. Meanwhile patient turned seropositive for human immunodeficiency virus during evaluation. A repeat peripheral smear sent on day 2of admission showed similar organisms intracellularly and extracellularly. PAS stain highlighted the rim of these organisms (Figure 1,2). Review of day one smear also showed few organisms within the neutrophils. A blood culture study was advised for confirmation but isolation of Histoplasma capsulatum was not successful. Patient was started on IV Amphotericin B and corticosteroids. On the third day of treatment his condition worsened leading to adrenal crisis. He developed cardiac arrest, multiorgan dysfunction and expired.

Table 1: Cytomorphological features of fungi in the differential diagnosis of Histoplasma Capsulatum. [5,8]

S. No	Organism	Size	Morphology	Special stains
1.	Histoplasma capsulatum	2-4micrometer	Intracellular, round to oval spores with narrow neck budding	PAS
2.	Cryptococcus neoformans	4-12 micrometer	Tear drop shaped buds, distinct mucopolysaccharide capsule	PAS & Mucicarmine
3.	Blastomyces dermatitidis	8-15 micrometer	Broad based buds, thick double contoured cell wall.	PAS
4.	Leishmania donovani	2-4 micrometer	Small intracellular protozoa with a kinetoplast	------

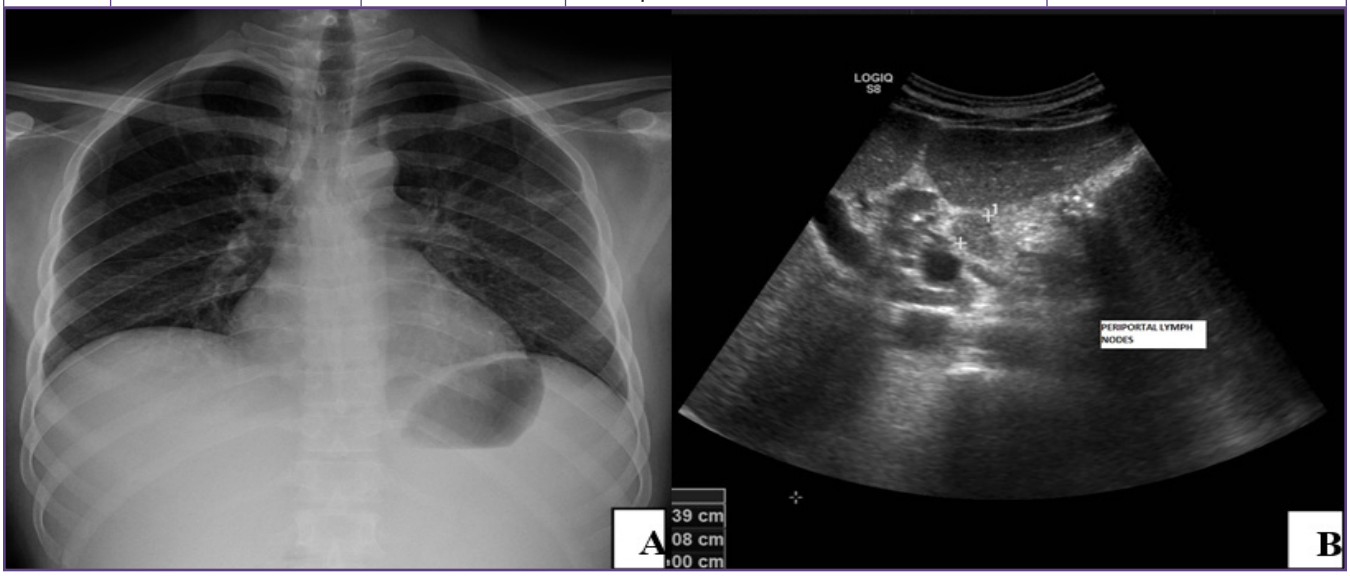

Fig. 1: a) Chest X-ray is normal, b) Ultrasonography shows periportal lymph nodes.

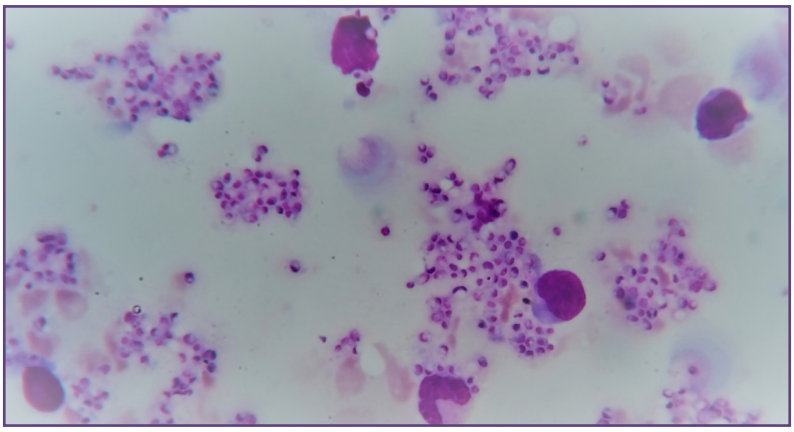

Fig. 2: Histiocytes filled with yeast-like organisms with crescent like eccentric chromatin (Giemsa stain, X400).

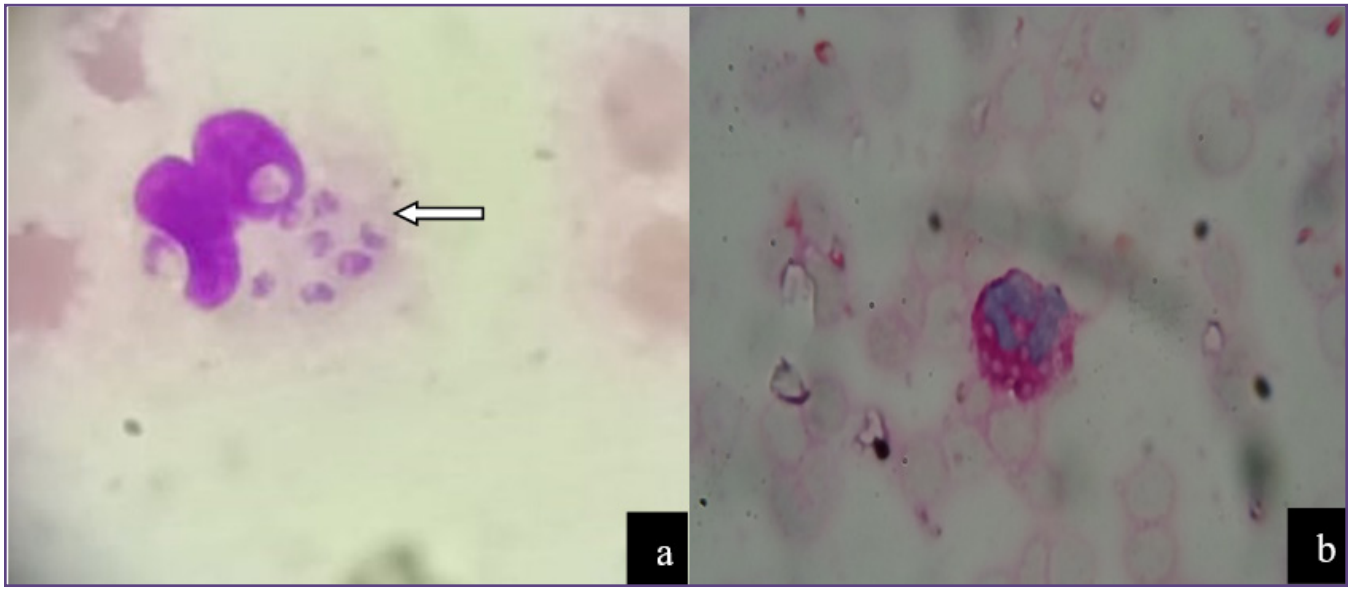

Fig. 3: a) Peripheral smear showing neutrophil with multiple yeast like organisms – white arrow (Leishman stain, X1000), b) The rim is highlighted with PAS stain (PAS stain , X1000).

Discussion

Histoplasmosis is an airborne disease caused by dimorphic fungus *H. capsulatum*, which is acquired by inhalation of particles from the soil infected by bird or bat droppings. [7,8] Histoplasma infection primarily involves the reticuloendothelial system. [5] Clinical manifestation often resembles tuberculosis leading to diagnostic difficulty. [4,7,8]

A similar diagnostic dilemma was there in our case too, which led to the patient being subjected to an early course of anti-tuberculous drug therapy from the periphery. Since he showed no recovery and his condition deteriorated, he was referred to our centre. Case reports by Asim Qureshi and Gupta P et al, mirrors this diagnostic dilemma. [7,8] Histoplasmosis and tuberculosis are frequently noted in patients with advanced HIV accounting to 8-15% in some countries. [9] As the symptoms are non-specific for histoplasmosis and indistinguishable from tuberculosis, it complicates the clinical diagnosis and treatment. [10]

Satya vara prasad et al and Hye Won jeong et al mentions in their respective case reports about co-infections in HIV patients, similar to our case. [4,5] In healthy patients, exposure to histoplasma micronidia, individuals often are asymptomatic or develop mild influenza like illnesses with fever, headache and non-productive cough. [4] Whereas in, immunosuppressed individuals the fungal organism spreads through the blood and disseminates to other organs like bone marrow, brain, lymph node, spleen, kidney and pancreas leading to disseminated histoplasmosis. [5,11] This includes patients with acquired immunodeficiency syndrome (AIDS), hematologic malignancies, transplant recipients and those on corticosteroids. [12] The diagnostic difficulty is usually between histoplasmosis, leishmaniasis and cryptococcus neoformans in cytology. *Histoplasma capsulatum* is appreciated as round to oval yeast bodies with a thin outer halo and an eccentrically placed crescent shaped basophilic nucleus. [13] *Leishmania donovani* cytologically is seen as an intracellular protozoon with a rod-like body called kinetoplast oriented right angle to the nucleus. [13] Cryptococcus organism is noted as an encapsulated yeast with a clear halo. [5] So it is very important to differentiate between them in order to diagnose correctly.

Other cytomorphological differential diagnosis includes *Blastomyces dermatitidis* and *Coccidiodomycosis immitis*. [5,8] Size of the organism, cytomorphology, localization and special stains are few features that distinguishes these fungi from each other (Table 1). [5,8]

FNAC is a simple, safe and quick technique aiding in the initial diagnosis and prompting early treatment. [8] Culture is a useful tool and remains the gold standard in diagnosing histoplasmosis, because it allows isolation and characterization of fungus. [14] Brain heart infusion incubated at 25 degree celsius are ideal to support the growth of the organism. [15] However it requires prolonged incubation which takes up to 8 weeks. [14] Cases of disseminated histoplasmosis show a positivity rate around 50 % in blood and BM cultures, according to various studies. [4] Our case yielded negative culture result.

A very interesting finding in our case is the presence of histoplasma organisms in the peripheral blood which

was seen inside the neutrophils and monocytes. This feature is noted commonly in immunocompromised host. [5] A case report by Christine mentions the utility of peripheral blood examination where histoplasmosis can be identified in patients with HIV at the terminal phase. [6] Secondary hemophagocytosis is a known complication of disseminated H. capsulatum infection. [13]

Conclusion

Disseminated histoplasmosis in retropositive patients poses high morbidity rate if not promptly treated. Its close differential diagnosis is tuberculosis. A wide range of clinical manifestations is possible in this condition. Although isolation of Histoplasma capsulatum from culture is the gold standard for confirmation, a simple lymph node FNAC can also render a diagnosis. In our case, a retrospective analysis of the peripheral smear revealed the presence of these organism in the neutrophils, which was initially missed on evaluation. With this case report we look forward to share our experience and increase the clinician's awareness to this entity.

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Competing Interests

None Declared

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