



Histoplasma capsulatum in peripheral blood neutrophils

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Case report

A 45-year-old female presented with chief complaints of moderate- to high-grade fever for 4 months associated with drenching night sweats. Physical examination revealed hepatosplenomegaly, 10 and 12 cm below costal margins, respectively. Her complete blood count showed anemia (78 g/L), thrombocytopenia ($20 \times 10^9/L$), and total leukocyte count ($4.6 \times 10^9/L$). The differential leukocyte count (DLC) at presentation was as follows: neutrophils 80%, lymphocytes 13%, eosinophils 04%, monocytes 01%, myelocytes 01%, and metamyelocytes 01%. The patient had a history of seronegative rheumatoid arthritis and was taking methotrexate or azathioprine intermittently. A peripheral blood smear obtained on admission showed a few neutrophils with one to multiple, small, intracellular yeast-like organisms with crescent-like eccentric chromatin. The organisms were ovoid in shape and surrounded by a cytoplasmic halo (Fig. 1a; original magnification $\times 1000$, Leishman stain). Periodic acid–Schiff (PAS) stain highlighted the rim of these organisms. These features are consistent with diagnosis of *Histoplasma capsulatum* var. *capsulatum*. Subsequent bone marrow aspiration and biopsy were performed which revealed numerous histiocytes filled with *H. capsulatum* yeast forms. Some of the histiocytes show hemophagocytosis (Fig. 1b and c; original magnification $\times 1000$, May–Grünwald Giemsa and Gomori-methenamine silver stain). The patient was treated with amphotericin B and showed remarkable clinical improvement.

H. capsulatum is acquired by the inhalation of conidia or mycelial fragments [1]. Disseminated histoplasmosis is

a severe and often fatal opportunistic infection, when left untreated, among patients with immunodeficiency that includes patients with acquired immunodeficiency syndrome (AIDS), those with hematologic malignancies, and those on immunosuppressive therapy. Our patient was on treatment with azathioprine intermittently for her medical condition. There are various tests which can be used to diagnose *H. capsulatum* infection, including mycology cultures, histopathological examination, polymerase chain reaction–based methods, and serological tests. The morphological identification of distinctive 2- to 4- μm , oval, narrow base budding yeast forms with surrounding halo (clear zone) corresponding to the cell wall allows a tentative diagnosis of *H. capsulatum* var. *capsulatum* infection. The cell wall is highlighted with PAS and GMS stains. In addition, clustering of yeast forms within macrophages is an important diagnostic feature of *Histoplasma* infection. *Leishmania* and *Candida glabrata* can mimic *H. capsulatum* var. *capsulatum* morphologically; however, *Leishmania* amastigotes are oval bodies, mostly present intracellularly in macrophages and macrocytes, 2–3 μm in length, have rod-like body called kinetoplast oriented right angle to the nucleus, and absence of peripheral halo as noted in *Histoplasma*. *Candida glabrata* does not cause a clinical syndrome similar to histoplasmosis, usually results in suppurative inflammatory response, and depict size heterogeneity compared with *H. capsulatum* var. *capsulatum* and mostly extracellular distribution of organisms [1, 2].

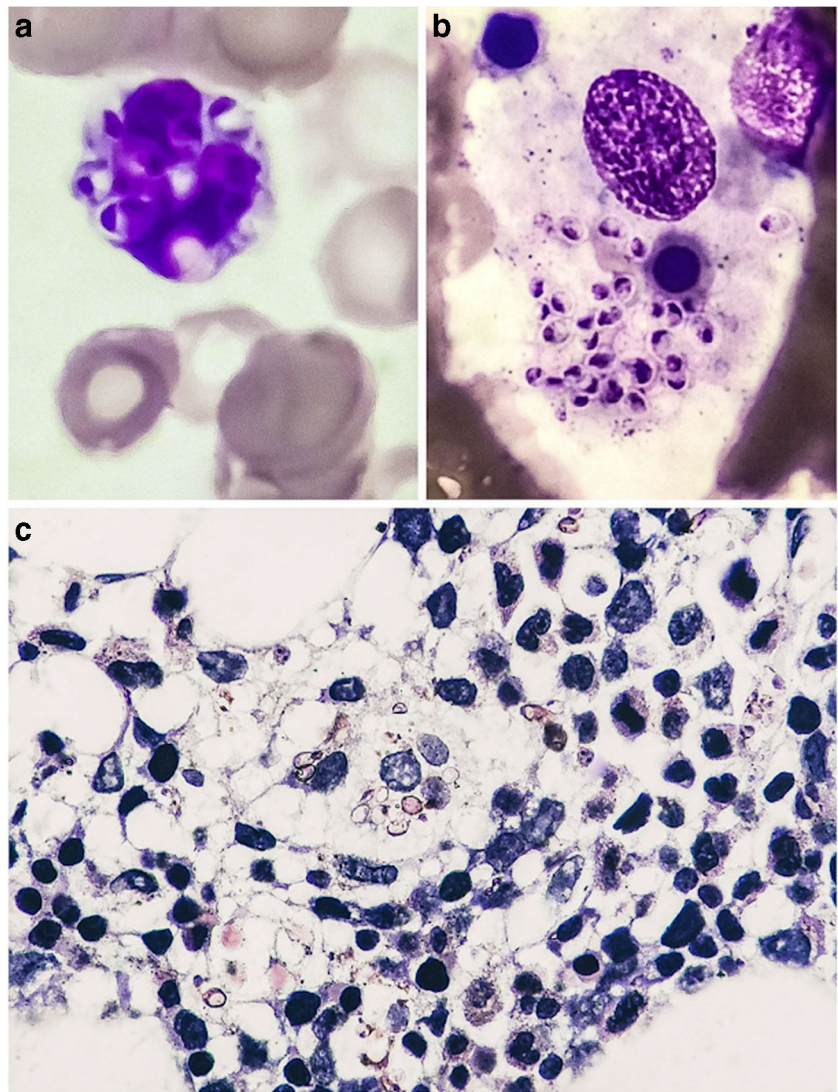
The peripheral blood histoplasmosis is uncommon and a few case reports have been published [3, 4]. The secondary hemophagocytosis is a well-known complication of disseminated *H. capsulatum* infection [5].

This case highlights the significance of careful examination of peripheral blood smear to pick up clinically useful rare findings.

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Fig. 1 **a** Neutrophil with multiple yeast-like organisms with crescent like eccentric chromatin (1000×, Leishman stain). **b, c** Histiocytes filled with *H. capsulatum* yeast forms (original magnification 1000x, May-Grunwald Giemsa and Gomori-Methenamine silver stain)



Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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