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Case Report

# Fever, Pancytopenia and Intracellular Eukaryotic Microorganisms in a Bone Marrow Aspirate

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## CLINICAL IMAGE

A 58 year-old female from Cambodia travelling to France for Waldenström's macroglobulinaemia treatment. She had systemic lupus erythematosus and anti- phospholipid syndrome with history of sub-acute fever, corticosteroid-responsive prolonged thrombocytopenia associated with immunosuppression induced by chemotherapy. She was admitted to the hospital for non-obstructive acute pyelonephritis. The laboratory findings revealed pancytopenia with moderate anemia (hemoglobin 8.7 G/dL), leucopenia (white blood cell count 3.64 $10^9$/L), and severe thrombocytopenia (6.$10^9$/L) initially attributed to late toxicity of chemotherapy, thrombocytopenic purpura, or macrophage activation syndrome. Culture of blood and urine samples did not yield bacteria and testing for human immunodeficiency virus were negative. Smears from a bone marrow aspirate were prepared and stained with Wright-Giemsa (Figure 1A) showing a moderate cell density with megakaryocytes and numerous macrophages in the cytoplasm of which, intracellular 2 µm-long bodies with internal purple staining suggestive of a nucleus were observed. Treatment with liposomal amphotericin B was started and symptoms resolved with a rapid clinical improvement. The patient remained completely asymptomatic with normal laboratory parameters 1 month post treatment. The microscopic aspect was highly suggestive of histoplasmosis. Silver staining of bone marrow smears and à culture that resulted positive a few weeks later confirmed the diagnosis of disseminated histoplasmosis.

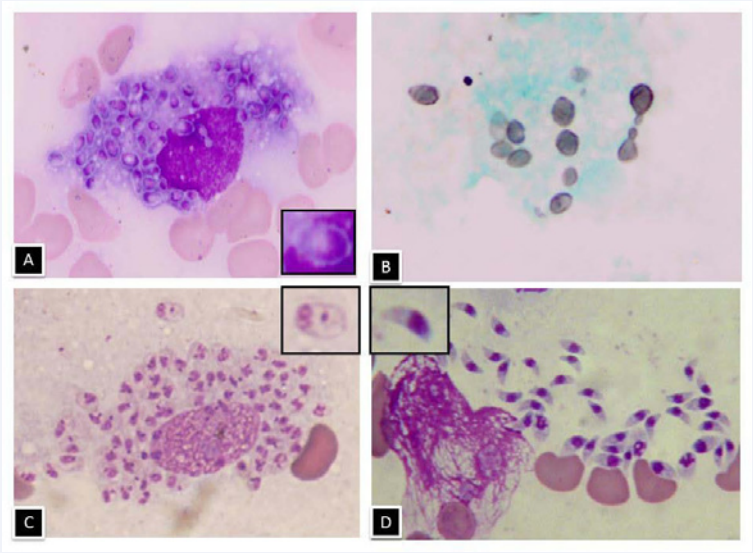


**Figure 1** Wright-Giemsa stained smear of the bone marrow of a 58- year-old woman who presented with sub-acute fever and pancytopenia. (Black bars = 10µm) (A). Silver staining smear of a bone marrow that revealed *Histoplasma capsulatum* yeasts (B) Wright-Giemsa stained smear of a bone marrow infected with *L. donovani.*(C). Wright-Giemsa stained smear of a bone marrow infected with *T. gondii.*(D).

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## DISCUSSION

The observation of 2-4 µm oval, narrow-based budding elements on Wright-Giemsa stained smears is highly suggestive of histoplamosis. However, other micro-organisms resemble *H. capsulatum* in tissues [1]. *Histoplasma capsulatum*, *Leishmania donovani s.l.* and *Toxoplasma gondii* are the three main eukaryotic microorganisms that can cause sub-acute fever with pancytopenia. Both *L. donovani* and *T. gondii*can display morphological aspects similar to yeasts of *H. capsulatum* on a Giemsa-stained smear. Pseudo- capsulated *H. capsulatum* (Figure 1.A, arrowhead) and *L. donovani* amastigotes that infect human macrophages are similarly ovoid, and are almost identical in size (Figure 1.C). Robust morphological identification of *Leishmania* amastigotes requires the association of à cell membrane, a basophilic staining nucleus and à rod-shaped intensely stained kinetoplast (Figure 1.C, arrowhead). *T. gondii* tachyzoites rapidly invade and multiply in many mammalian cell types and are sometimes observed in human macrophages. They are crescent-shaped, approximately 5-7 µm long, with pale blue staining cytoplasm and pink nucleus (Figure 1.D, arrowhead). Silver staining of smears confirmed the diagnosis of histoplasmosis by showing the yeast wall (Figure 1.B, arrowhead). Silver does not stain protozoan plasma membranes. The diagnosis was further consolidated by a serum positive *Aspergillus* galactomannan index which is known to cross react during invasive histoplasmosis and, a few weeks later, by the appearance of *H. capsulatum* hyphae with microconidia and characteristic tuberculate macroconidia formed on short, hyaline, undifferentiated conidiophores in culture (Sabouraud medium, 25°C, under humidified, aerobic conditions, strict confinement). PCR analyses for *T. gondii* and *Leishmania spp* were both negative. Treatment of disseminated toxoplasmosis is with either pyrimethamine-sulfonamide or cotrimoxazole [1,2]. The first-line treatment of both disseminated histoplasmosis and visceral leishmaniasis is liposomal amphotericin B, but regimens differ. In India, a single infusion of 10 mg/kg cures visceral leishmaniasis due to *L. donovani* in more than 95% of cases [3], whereas a longer induction therapy with higher cumulative dose followed by maintenance therapy with azole therapy is essential for sustained cure of disseminated histoplasmosis [4,5]. The patient had a sustained response to treatment with liposomal amphotericin B, followed by oral azoles (itraconazole switched to posaconazole after 14 days) for one year. Immediate microscopic identification of *Histoplasma capsulatum* facilitated a prompt, adapted treatment without waiting for the results of antigen/antibody detection, PCR and culture.

## REFERENCES

1. Hill PMRS. Toxoplasmosis. Hunter's Tropical Medicine and Emerging Infectious Disease. 9th edn. 2012; 10: 1111-1190.
2. Robert-Gangneux F, Darde ML. Epidemiology of and diagnostic strategies for toxoplasmosis. Clin Microbiol Rev. 2012; 25: 264-296.
3. World Health Organization. Control of the leishmaniases. World Health Organ Tech Rep Ser. 2010; (949):xii-xiii, 1- 186, back cover.
4. Chastain DB, Henao-Martinez AF, Franco-Paredes C. Opportunistic Invasive Mycoses in AIDS: Cryptococcosis, Histoplasmosis, Coccidiodomycosis, and Talaromycosis. Curr infect Dis Rep. 2017; 19: 36.
5. Kauffman CA. Histoplasmosis. Clinics in Chest Med. 2009; 30: 217-225.

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