Journal de Mycologie Médicale xxx (2018) xxx–xxx

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Cas clinique/Case report

Disseminated histoplasmosis diagnosed in the bone marrow of an HIV-infected patient: First case imported in Tunisia

N. Fakhfakh [a,b,*], R. Abdelmlak [b,d], S. Aissa [b,d], A. Kallel [a,d], Y. Boudawara [a,d], S. Bel hadj [a,d], N. Ben Romdhane [c,d], H. Touiri Ben aissa [b,d], K. Kallel [a,d]

[a] *Laboratory of Parasitology-Mycology, Rabta Hospital, Jabbari street, 1007 Tunis, Tunisia*
[b] *Infectious diseases ward, Rabta Hospital, Tunis, Tunisia*
[c] *Laboratory of Hematology, Rabta Hospital, Tunis, Tunisia*
[d] *Université de Tunis El Manar, faculté de médecine de Tunis, Tunis, Tunisia*

ARTICLE INFO

Historique de l'article :
Received 19 October 2017
Accepted 12 February 2018

Keywords:
Disseminated histoplasmosis
HIV-seropositive patient
Histoplasma capsulatum var. *capsulatum*
Imported case
Tunisia

ABSTRACT

Histoplasmosis is a fungal infection caused by a dimorphic fungus, *Histoplasma capsulatum*. We report a first case of disseminated histoplasmosis in a 34-year-old woman, infected with human immunodeficiency virus (HIV), originating from Ivory Coast and living in Tunisia for 4 years. She was complaining from fever, chronic diarrhoea and pancytopenia. The *Histoplasma capsulatum* var. *capsulatum* was identified by direct microscopic examination of the bone marrow. She was treated by Amphotericin B, relayed by itraconazole. Even though a regression of symptoms and normalization of blood cell count (BCC), the patient died in a respiratory distress related to CMV hypoxemic pneumonia.

1. Introduction

Histoplasma capsulatum is the causative fungus of a spectrum of diseases affecting both the immunocompetent and the immunocompromised host with initial lung involvement [1]. The immunocompromised condition of HIV patients is associated to high prevalence of histoplasmosis [1]. Past infection in immunocompetent patients results in partial protection against disease effects if they are re-infected [2].

This fungus is a dimorphic ascomycete that grows in its hyphal form in soil and bird. Upon inhalation of spores, *H. capsulatum* transforms into the pathogenic yeast phase. This form replicates within macrophages that carry the yeast from lungs to virtually any organ [3,4]. Isolation of the fungus can be achieved on special media, such as Sabouraud agar, following incubation at 25 °C for 6 to 12 weeks [5].

Two human types have been described according to infectious agent involved: *H. capsulatum* var. *capsulatum* for American type and *H. capsulatum* var. *duboisii* for African type who is less common [6].

The definitive diagnosis of histoplasmosis requires isolation of the *H. capsulatum* on specific culture media or visualization in direct examination using specific fungal staining techniques. Non-culture methods have also been developed and include antibody or antigen detection, although there is an increase in false-negative results in disseminated forms [5].

Histoplasmosis is common in endemic areas, which are the USA and South parts of Asia and Africa [7]. However, several cases can occur in non-endemic areas, where the fungus is very rare like in Europe [8]. In Tunisia, no native cases have been reported but the introduction of imported cases is possible. The growth of economic and commercial exchanges with a great number of countries, mainly of Africa, as well as the increase in travelers, leads to the occasional occurrence in our countries of exotic pathology, like histoplasmosis. Cases of disseminated histoplasmosis may be fatal even in an immunocompetent individual, so, the diagnosis must be obtained early by mycological examinations [9].

There are no published cases of histoplasmosis even in immunocompromised patient in our country. We report the first case of imported disseminated histoplasmosis in Tunisia.

2. Case

M.Z. was a 34-year-woman, unknown HIV infected, admitted to the infectious diseases ward of Rabta Hospital of Tunis, in May 2017, two months after delivery, with a history of chronic diarrhoea and weight loss over the last 6 months. She was

* Corresponding author. Laboratory of Parasitology-Mycology, Rabta Hospital, Jabbari street, 1007 Tunis, Tunisia.

https://doi.org/10.1016/j.mycmed.2018.02.008
1156-5233/

originating from Ivory Coast and living in Tunisia for 4 years. Physical examination found fever at 38 °C, impaired general status, global dehydration and hepatosplenomegaly. The biological evaluation showed a hypokalemia at 1.6 mmol/L, functional renal insufficiency and normochromic normocytic anemia (8.7 g/dL). HIV-Serologic test was positive, virus load was 409,500 copies/mL and CD4 T-lymphocyte count was 2 cells/mm^3. Serology of hepatitis and leishmaniasis were negative. Blood cultures identified *Salmonella sp*. CT scan showed normal pulmonary parenchyma, necrotic intraabdominal adenopathy, peritoneal effusion, hepatomegaly and thrombosis of primary iliac venous. The diagnosis of minor salmonellosis and disseminated tuberculosis was retained. The patient received tuberculosis treatment (isoniazid-rifampicin-ethambutol-pyrazinamid) and Ceftriaxon. Seven days after, she developed a deep pancytopenia. The bone marrow smear stained with May-Grünwald stain (MGG) performed in the Laboratory of Hematology in Rabta Hospital concluded to the absence of malignancy and the presence of intracellular microorganism that do not fit with *Leishmania*. Then, smears were sent to Laboratory of Parasitology-Mycology for identification. Microscopic examination showed intracellular small budding yeasts, ovoid, from 2 to 4 μm, typical of *Histoplasma capsulatum* variety *capsulatum* (Fig. 1).

The patient received Amphotericin B deoxycholate (1 mg/kg/day) for two weeks, relayed by Itraconazole (400 mg/day) with normalization of the BCC. After 3 weeks of treatment, the patient presented consciousness impairment with multiple brain abscesses at cerebral CT scan, advocating cerebral toxoplasmosis. She received pyrimethamin, sulfadiazin and dexamethason as toxoplasmic treatment. Because of the endemic tuberculosis in Tunisia, necrotic lymph nodes and pancytopenia, she was retained under tuberculosis treatment. One week later, a treatment based on tenofovir-emtricitabin and efavirenz was started. After an initial 2 weeks improvement, she presented a respiratory distress. A CMV hypoxemic pneumonia was suspected because of long duration of dexamethason, and the patient received ganciclovir 10 mg/kg/day. The CMV viral load was very high (14,000 copies/mL). Triglycerides, ferritinemia, fibrinogen and CRP were not high. She died one week after.

3. Discussions

Disseminated histoplasmosis is an opportunistic infection associated with immunosuppressed status, mainly HIV infected patients [10]. Other risk factors include transplantation, chronic renal disease, use of corticosteroids and immunosuppressive agents [11,12]. Some cases are seen with immunocompetent patient [7,13,14].

Most infections occur after inhalation of fungal spores from the environment; dissemination can be acute or can occur years after the initial exposure [15].

In *Histoplasma capsulatum* var. *capsulatum*, most of the cases are asymptomatic in immunocompetent person; those with symptoms usually present with self-limited respiratory infection [9,16].

Variety duboisii has tropism for lymph nodes, skin and bones. It is classically associated with cutaneous lesions (nodules, ulcers) and osteolytic bone lesions, especially affecting the skull, ribs, and vertebrae [17].

Disseminated form is defined by the presence of an extrapulmonary focus; the most common clinical findings are fever, weight loss, cough, lymphadenopathy, hepatomegaly, splenomegaly and anemia [18].

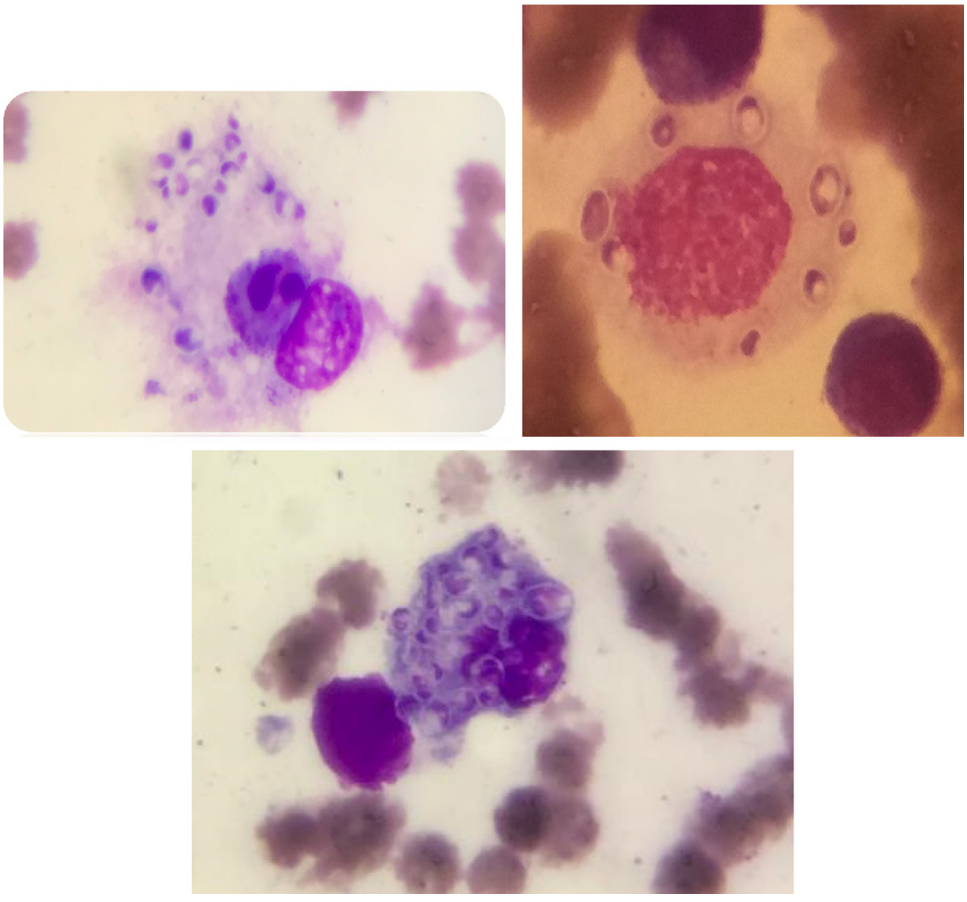

Fig. 1. Intracellular *Histoplasma capsulatum* var. *capsulatum* within histiocytes seen on the bone marrow smear staining (MGG stain, × 100).

Please cite this article in press as: Fakhfakh N, et al. Disseminated histoplasmosis diagnosed in the bone marrow of an HIV-infected patient: First case imported in Tunisia. Journal De Mycologie Médicale (2018), https://doi.org/10.1016/j.mycmed.2018.02.008