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CASE REPORT/CAS CLINIQUE

Late occurrence of *Histoplasma duboisii* cutaneous and pulmonary infection 18 years after exposure

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Pulmonary histoplasmosis

Summary We report an imported case of *Histoplasma capsulatum* var. *duboisii* (*H. duboisii*) infection in a white French woman revealed by cutaneous lesions of the scalp, 18 years after her last stay in West and Central Africa. Asymptomatic bilateral pulmonary infiltrates were discovered on thoracic computed tomography. Skin biopsy allowed the positive diagnosis showing the typical yeasts; culture of biopsy specimens was positive for *H. capsulatum*. In the absence of criteria of severity, the patient was treated for one year with oral itraconazole 400 mg/day. The outcome was favourable, skin and pulmonary lesions resolved slowly. The follow up is 5 years without relapse after the end of treatment. This case illustrates the possibility of late occurrence of *H. duboisii* infection, many years after exposure and the major importance of asking any patient for travelling or residency in tropical countries.

MOTS CLÉS
Histoplasmose africaine ;
Histoplasma capsulatum

Résumé Nous rapportons un cas importé d'infection à *Histoplasma capsulatum* var. *duboisii* (*H. duboisii*) chez une femme française de race blanche, révélée par des lésions cutanées du cuir chevelu, 18 ans après son dernier séjour en Afrique Centrale et de l'Ouest. Des infiltrats pulmonaires asymptomatiques ont été découverts par un scanner thoracique. Le diagnostic a été affirmé par l'examen histologique montrant les levures caractéristiques et la culture d'une

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biopsie de peau. En l'absence de critères de gravité, la patiente a été traitée par l'itraconazole administré per os pendant un an à la posologie de 400 mg par jour. L'évolution a été favorable, les lésions cutanées et pulmonaires régressèrent lentement. Le recul est de 5 années après la fin du traitement sans rechute. Cette observation illustre la possibilité de réactivation d'une infection à *H. duboisii* de nombreuses années après la contamination et l'importance de l'interrogatoire pour tous les patients à la recherche d'un séjour, même ancien, en zone tropicale.

Introduction

African histoplasmosis due to *Histoplasma capsulatum* var. *duboisii* is a rare fungal infection occurring most often in immunocompetent patients. In France, cases are imported from endemic area of Western and Central Africa and Madagascar Island. The main sites of infection are the skin, the lymph nodes and the bones, but other visceral localizations such as lungs and disseminated forms have been reported. The diagnosis relies on direct mycological examination and histopathology of pus or biopsy material disclosing typical lemon-shape large yeasts and on positive culture. We report an unusual case of African histoplamosis involving the scalp and the lungs and characterized by its occurrence 18 years after the last stay in endemic area.

Case Report

A 60 year-old French woman was referred to the department of dermatology in September 2007 for lesions of the scalp (Fig. 1a).

The skin lesions appeared six months earlier at the site of a minor traumatism without any cutaneous wound. Physical examination showed three keratotic and infiltrated papules located on a plaque measuring 5 by 2 cm on left fronto-temporal area (Fig. 1a). Clinical examination was otherwise normal, the patient had no fever nor adenomegaly and general health was preserved. She took no immunosuppressive medication and she had no evolutive disease that may affect her immune status. However, she had been treated for a right breast cancer by tumorectomy followed by breast radiotherapy without chemotherapy one year before presentation. Her medical history included also primary tuberculosis infection in 1953 (medically treated during several months), an hydatiform mole and cigarettes heavy smoking at 30 packs/year with mild broncho-pulmonary chronic obstructive disease. She had lived abroad for 17 years for professional reasons (1971—1988) mainly in Western and Central Africa (Mali, Ivory Cost, Cameroon, Burundi and Rwanda). She came back in France in 1989 from Rwanda and then made only tourism travels of short duration in Asia and South America.

Histopathologic examination of the skin biopsy showed a granulomatous infiltrate without necrosis in the dermis, with giant cells containing numerous yeasts (Fig. 1b). PAS (Periodic Acid Schiff), Grocott and Alcian blue staining identified the large ovoid thick-walled yeasts (8—15 μm) very suggestive of *H. duboisii*. Mycologic direct examination of the skin biopsy found the same large typical yeasts (Fig. 1c) Tissue culture for fungi on Sabouraud's dextrose agar yielded cottony white buff colonies. Microscopic examination showed septate hyaline hyphae with tuberculate chlamydospores. CRP value was 6 mg/L, CD4 lymphocytes count was 1130/mm^3 and the protein electrophoresis was normal. HIV, HCV antibody testing was negative. Histoplasma serology for antibodies by immune-diffusion test was negative. *Histoplasma* Antigen Detection test, not available in our country, was not performed. Galactomannan test detection (Platellia Aspergillus EIA, BioRad, Marnes La Coquette, France) was negative. Skull X-ray found no osteolytic lesions. Although the patient had no pulmonary signs or symptoms, because of a chronic obstructive broncho-pulmonary disease COBP) a systematic thoracic computed tomography was performed and disclosed bilateral nodular and interstitial lesions predominating in the right lung (Fig. 1d), adrenal glands were normal. Gastric aspiration and broncho-alveolar lavage found no pathogen micro-organisms and cultures were negative, particularly for *H. duboisii* and mycobacteria. The cytologic examination of the bronchial lavage showed 99% of macrophages and 1% of neutrophils, thus excluding lymphocytic radiation pneumonia.

The patient was treated with itraconazole 200 mg twice a day—with Coca Cola — during 12 months without side effects. The healing of the lesions of the scalp was slowly obtained in 8 months (Fig. 2) After 2 months of treatment, antifungal plasma levels were satisfactory: itraconazole: 2.3 mcg/mL and hydroxy-itraconazole: 2.9 mcg/mL Thoracic computed tomography performed at the end of the treatment showed marked regression of infiltrates with only minimal interstitial lesions considered as scars. Follow up without relapse after the end of treatment was 5.5 years.

Discussion

African histoplasmosis caused by *H. capsulatum* var. *duboisii* is an endemic mycosis in Western and Central Africa, between the tropics of Cancer and Capricorn and Madagascar Island [7—11,13,17,21].

The prevalence of histoplasmosis due to variety *duboisii* has not been established but less than 300 cases are reported in the literature, among them nearly 50% occurred in Nigeria [3,4,6,8,10,12,13].

Reports of cases are scarce in Europe, and all are imported [1,10,11,21]. Most of its ecology and pathogenesis remain unknown. The main route of acquisition is not known, it is presumed to be inhalation from the soil, although a primary pulmonary infection has not been demonstrated. Telluric contamination by direct cutaneous inoculation is a