

AFRICAN HISTOPLASMOSIS. REPORT OF THE FIRST CASE IN BRAZIL AND TREATMENT WITH ITRACONAZOLE(1)

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SUMMARY

We report the first case of African histoplasmosis diagnosed in Brazil. The patient was an immigrant from Angola who had come to Brazil six months after the appearance of the skin lesion. The skin of the right retroauricular area was the only site of involvement. The diagnosis was established by direct mycologic examination, culture and by histopathologic examination of the lesion. The patient was successfully treated with Itraconazole 100mg a day for 52 days. No recurrent skin lesions were observed during the ten month follow-up period.

KEY WORDS: African Histoplasmosis; *Histoplasma capsulatum* var. *duboisii*; Itraconazole.

INTRODUCTION

The African histoplasmosis is a mycosis caused by *Histoplasma capsulatum* var. *duboisii* that is prevalent in an area of Central Africa bordered by Uganda to the east, Dakar to the west, Sahara desert to the north and Kalahari desert to the south¹⁴.

This fungus is considered as a variant of *Histoplasma capsulatum* and the *Ajellomyces capsulatus* is the sexual state of the both fungi⁶. In the lesions, *Histoplasma capsulatum* var. *duboisii* presents as round fungus measuring 8 to 15 µm in diameter, while the *Histoplasma capsulatum* var. *capsulatum* usually measures 2 to 4 µm in diameter⁷.

The main differences between the classic and African histoplasmosis are:

1 - The classic histoplasmosis shows cosmopolitan distribution, usually involves lungs and mucosa, and rarely shows cutaneous or bone involvement.

2 - The African histoplasmosis occurs exclusively in Central Africa and involves the skin, lymph nodes and bone^{7,11,14,19,20}.

The reported cases of African histoplasmosis have been in either current or former residents of Africa¹⁹.

We report the first Brazilian case in a patient from Angola.

This is the second reported case in the South America, the first being from Chile in a patient who had lived in Ivory Coast (Africa) for three years¹².

CASE REPORT

CLINICAL HISTORY

The patient was a thirty six-year-old married black man from Luanda, who was communication technician and had worked in the Angola cities of Huambo, Benguela, São Salvadore and Uiji.

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He first noticed the skin lesion on the right retroauricular area in early 1985. He sought treatment in his country without success, and came to Brazil six months after the appearance of the lesion.

DERMATOLOGICAL EXAMINATION

The exam showed either single or grouped papules, nodules and ulcerated lesions in arciform distribution. The papules ranged from 3 to 4mm and the nodules from 1 to 1.2cm in diameter. The papules and nodules were skin colored and a few of the nodules were fluctuant. The ulcerated lesions showed purulent base and were covered by red-yellowish crust. (Fig. 1a.).

Mucosa, bones, joints, lymph nodes, liver, spleen and lungs showed no lesions.

LABORATORY EXAMINATION

The anti-HIV antibody test by ELISA method was negative.

RADIOLOGICAL EXAMINATION

Plain X-ray and CAT scan exams did not reveal involvement of the bone underlying the skin lesion.

Plain chest X-ray and full body bone survey showed no abnormalities.

Scintillography of full body and bone only revealed inflammatory cutaneous lesion on the right retroauricular area.

Abdominal ultrasonography revealed no abnormalities of the liver, spleen or the lymph nodes.

IMMUNOLOGICAL EXAMINATION

A - Serology

Ouchterlony immunodiffusion assay for Paracoccidioidomycosis, Histoplasmosis and Aspergillosis were negative.

Counterimmunoelectrophoresis and complement fixation reaction for histoplasmosis were negative.

B - Skin tests

PPD: 13mm

Trichophytin: 7mm

Paracoccidioidin: 6mm

Sporotrichin: 5mm

Levedurin: negative

Montenegro: negative

Varidase: 18mm

Histoplasmin: 49mm

DIRECT MYCOLOGIC EXAMINATION

The scraping smear of the right retroauricular lesion, cleared with 30% potassium hydroxide (KOH), showed oval shaped yeast cells disposed in chains, ranging from 9 to 15 μ m in diameter, with thick wall and narrow-based budding, characteristic of *Histoplasma capsulatum* var. *duboisii* (Fig. 1b).

Culture

Part of the material was incubated at room temperature in Sabouraud-dextrose agar. After 25 days of incubation a slow growing colony with a fluffy white aspect and brown reverse was observed. The micromorphology of the colony placed between a glass slide and a coverslip and stained with lactophenol-cotton-blue showed hyaline septate and branched mycelia; 8 to 15 μ m macroconidia with thick wall, either smooth or tuberculate or digitate were seen within the conidiophores (Fig. 1d).

HISTOPATHOLOGICAL EXAMINATION

H&E and Gomori: A fragment of skin showing an ulcer covered with fibrinopurulent exudate. In the upper reticular dermis there is a marked band-like inflammatory infiltrate composed of lymphocytes, histiocytes, eosinophils, giant cells of Langhans and foreign body type forming granulomata.

Within the giant cells and the surrounding tissue, there are round or oval shaped, birefringent organisms disposed in chains which is characteristic of African histoplasmosis (Fig. 1c).

EVOLUTION AND TREATMENT

The patient was treated with Itraconazole 100mg a day for 52 days with a complete regression of the lesions and without recurrence after 10 months of follow-up.

DISCUSSION

The African histoplasmosis is a rare deep mycosis with fewer than two hundred cases

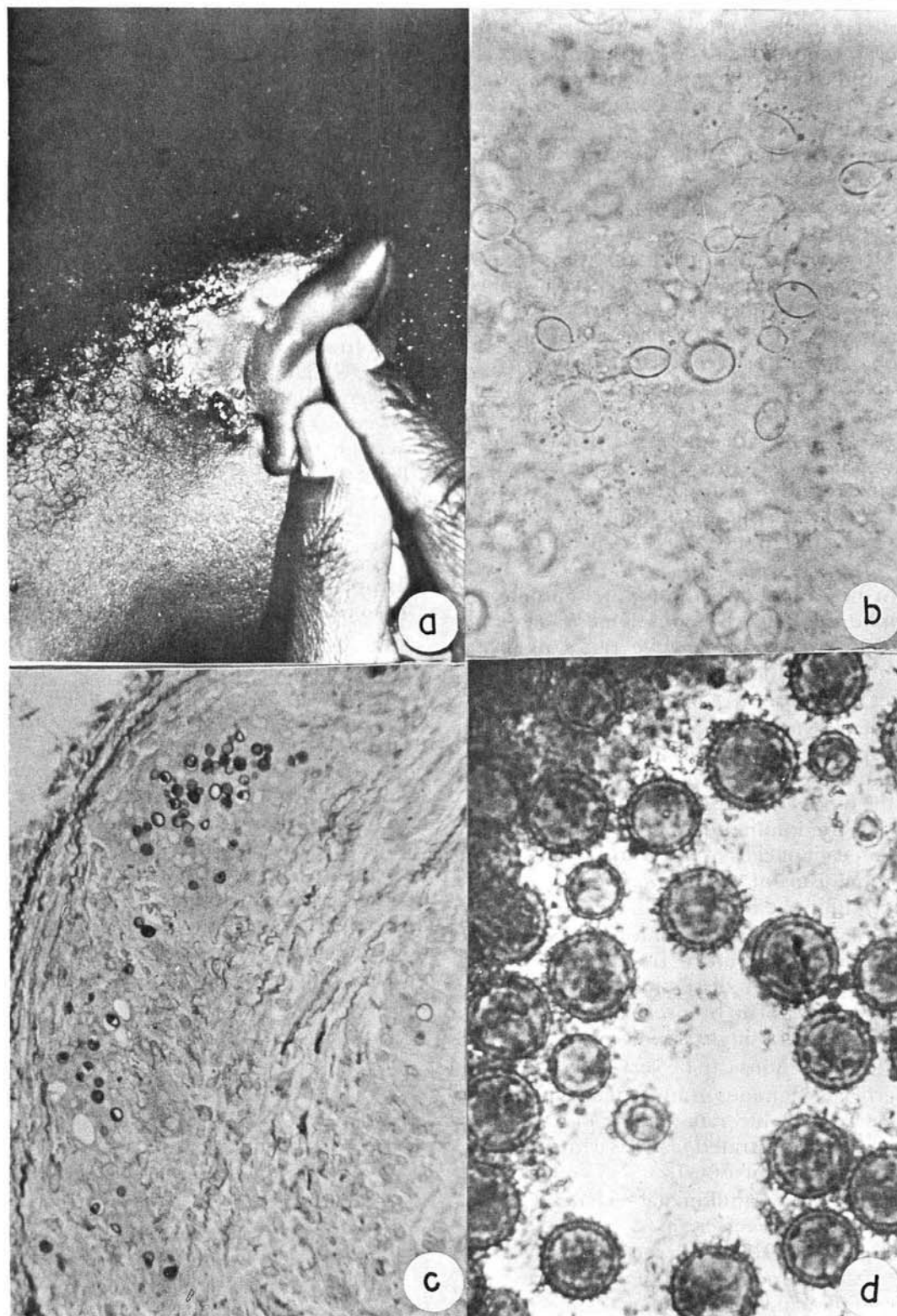


Figure 1 - a) Papules, nodules and ulcers covered by crust; arciform distribution; b) Parasites in chains, with thick wall, direct mycologic examination, cleared with 30% KOH; c) Yeast-like cells clustered within the reticular dermis. Gomori. Original magnification X100; d) Numerous tuberculate macroconidia incubated at room temperature. Original magnification X1000.

reported in the literature^{1,16}. To this date, there are seven reported cases of African histoplasmosis in the American continent; three cases are from USA, one from Canada, two from Cuba and one from Chile^{5,8,11,12,15,17,18}. According to ODDO et al.¹², the Argentinean case¹⁰ would have been caused by *Histoplasma capsulatum* var. *capsulatum* with large and small forms in the tissue.

All reported cases of African histoplasmosis in the American continent occurred in persons who had either lived or traveled to the endemic area^{7,8,11,12,15,17,18,19}. The mode of transmission of the disease remains unknown^{15,20}. The men are affected three times more often than the women⁴.

The definitive diagnosis of African histoplasmosis is made by direct mycologic examination, culture and by histopathological examination^{13,20}, while the immunological tests (serological tests and skin tests) have small diagnostic value^{2,4}.

In the present case, the counter immunoelectrophoresis and the complement fixation reaction were negative, while the skin tests showed preservation of cellular immunity, including the strongly positive *histoplasmin* test.

The *Histoplasma capsulatum* var. *duboisii* is a dimorphic fungus. Usually, the organisms are abundant in the purulent secretion, abscesses or in the biopsy of the skin lesions¹⁴. The organisms are predominantly seen within the multinucleated giant cells of the granulomata, while the organisms of the *capsulatum* variant are present within the histiocytes¹².

Clinically, there are two forms of African histoplasmosis: the more frequent localized form and the rarer disseminated form. The most frequent form of presentation of this disease is that of a single skin lesion²⁰.

The skin lesions can be very polymorphic:

- superficial cutaneous granulomata – papules and nodules that ulcerate and/or produce arciform lesions; infiltrated plaques with eczematoid or psoriasiform aspect.
- Subcutaneous granulomata – characterized by nodules and abscesses.
- Osteomyelitic lesions with secondary involvement of the skin – subcutaneous abscesses, giant granulomata and fistulas⁹.

In regard to evolution and treatment, the localized lesions show periods of remissions and relapses and may show a spontaneous

cure¹⁸. The disseminated form is serious and can even be fatal if not treated¹⁴.

Several therapeutical modalities have been used:

- Surgical treatment for localized form^{7,14}.
- Amphotericin B, used alone^{2,4,5,8,13} or in association with rifampicin^{4,11} or with clotrimazole⁴ or with miconazole⁴, is the drug of choice, specially in the disseminated form.
- Imidazole derivatives such as clotrimazole, miconazole and ketoconazole were efficacious^{2,12,17,18}.
- The Itraconazole was first used by DUPONT & DROUHET³ in a 66-year-old Zaire man who received 100mg a day for six and a half months with cure within two months. In the present case, the patient was cured with a dose of 100mg a day for 52 days.

RESUMO

Histoplasmose Africana. Relato do primeiro caso no Brasil e tratado pelo Itraconazol.

Relata-se o primeiro caso de histoplasmose africana diagnosticado em nosso meio, em indivíduo angolano que imigrou para o Brasil seis meses após o início das lesões. Quadro clínico de forma localizada exclusivamente na pele na região retro auricular direita. O diagnóstico foi estabelecido através do exame micológico direto, cultura e exame anátomo-patológico. Houve sucesso terapêutico com a administração de itraconazol, na dose de 100mg/dia durante 52 dias. Não houve recidiva do quadro cutâneo no seguimento clínico do doente após 10 meses de interrupção do tratamento.

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