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Case Report

Cutaneous mucormycosis in a young, immunocompetent girl

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We report a case of cutaneous mucormycosis in a healthy, immunocompetent young girl (age 14 years). The patient had a 5-year history of a slowly enlarging, erythematous plaque with slight elevated, scaling, circinate borders on the right thigh. Histopathology showed a granulomatous infiltrate with broad, pale, non-septate hyphae. Mycological study identified *Mucor hiemalis* (Wehmer).

Keywords *Mucor hiemalis*, Brazil, mucormycosis, immunocompetent, thigh lesion

Introduction

Absidia, Mucor, Rhizomucor and *Rhizopus* of the order Mucorales (class Zygomycetes) are the most common etiologic agents of mucormycosis. While the cutaneous form of this disease is less described [1,2] than those occurring in other organs or systems (e.g., nasopharyngeal, cerebral, disseminated, pulmonary, intestinal), like these other presentations, it too is frequently seen as a complication of a number of conditions such as immunosuppression [3,4], diabetes [5,6], trauma [7,8], hematological disorders [9,10], organ transplantation [11,12], malignancies [13,14], premature newborns [15,16] and a variety of clinical disorders [17,18]. In a MEDLINE search of the relevant literature published over the last 30 years, cutaneous infections caused by *Mucor hiemalis* were reported on only two earlier occasions, i.e., one in a diabetic patient [5] and the other in a healthy young girl [19]. To our knowledge the case presented here represents the third case and the second involving a *Mucor hiemalis* infection in a healthy individual.

Case report

A 14-year-old girl presented with a 5-year history of a slowly enlarging erythematous and scaling plaque on her right thigh. The initial lesion was a small red papule that slowly enlarged to form a lesion that occupied almost the entire anterior aspect of the right thigh (Fig. 1A). There was no history of trauma or other definite precipitating factors.

Physical examination showed an erythematous, scaly, infiltrated, sharply demarcated plaque with petaloid borders on the right thigh. Routine laboratory tests including biochemistry, urinalysis, serological examination for HIV and syphilis were normal or negative, as were PPD and leishmanin skin tests. No fungal hypahe were observed in skin scrapings of the plaque lesion mounted on KOH. However, a fresh preparation of a biopsy fragment showed broad, branched, sparsely septate hyphae. Histopatology (H&E) of a biopsy specimen revealed slight acanthosis, as well as a superficial and deep granulomatous infiltrate composed by lymphocytes, macrophages and occasional giant cells (Fig. 2A, B & C). A few broad, nonseptate, pale staining hyphae lacking Splendore-Hoeppli phenomenon were

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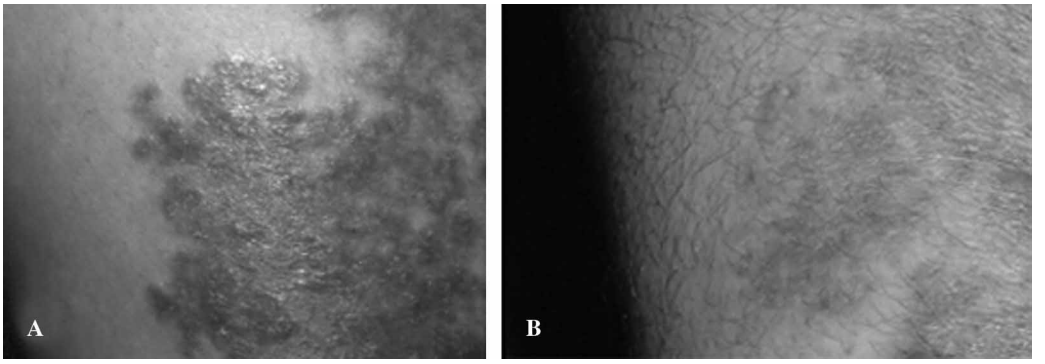

Fig. 1 (A) Initial lesion on thigh. (B) Healed lesion after Ampotericin B therapy.

seen in the infiltrate (Fig. 2D). The morphology of colonies recovered from a portion of a cutaneous biopsy which had been inoculated on MA 2% (Malt Extract Agar 2%) and incubated at 25°C was examined macroscopically and microscopically. The macroscopic observations revealed filamentous, buff yellow color colonies which grew up to 10 mm in height within 5 days. The reproductive structures examined microscopically consisted of: sporangiophores up to 11–14 μm in diameter, slightly branched sympodially; sporangia at first yellowish, then dark brown, with a diameter from 45–70 μm, with deliquescent, transparent walls; columellae globose when young (up to 34 × 39 μm in diameter) to ellipsoidal; sporangiospores ellipsoidal and smooth, yellow, variable in size 4–8 (12) × 2.5–5 μm. These findings allowed for a tentative identification of *Mucor hiemalis* (Wehmer) [20] (Fig. 3), which was confirmed at the Culture Collection INCQS (FIOCRUZ, Brazil) and deposited under the accession number INCQS 40258.

Initially the patient was treated with itraconazole (200 mg per day) over 10 months with no improvement. Another culture inoculated at this time with a biopsy fragment from the lesion again yielded the same pathogen. Terbinafine (250 mg per day) was then added to the treatment over the next 6 months, but there was

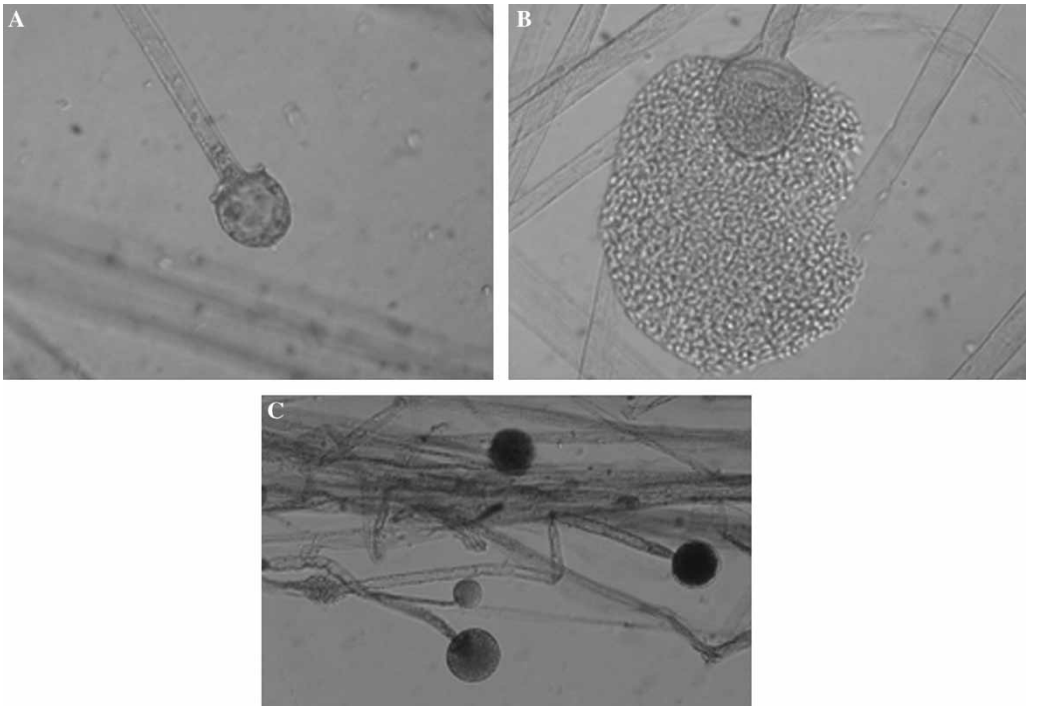

Fig. 2 (A) Slight acanthosis and cellular infiltrate in upper and mid dermis (H&E, ×100). (B) Cellular infiltrate in deep dermis (H&E, ×100). (C) Granulomatous nature of cellular infiltrate with giant cell (arrow) (H&E, ×100). (D) Broad, branching, non-septate hypha in the infiltrate (H&E, ×1000).

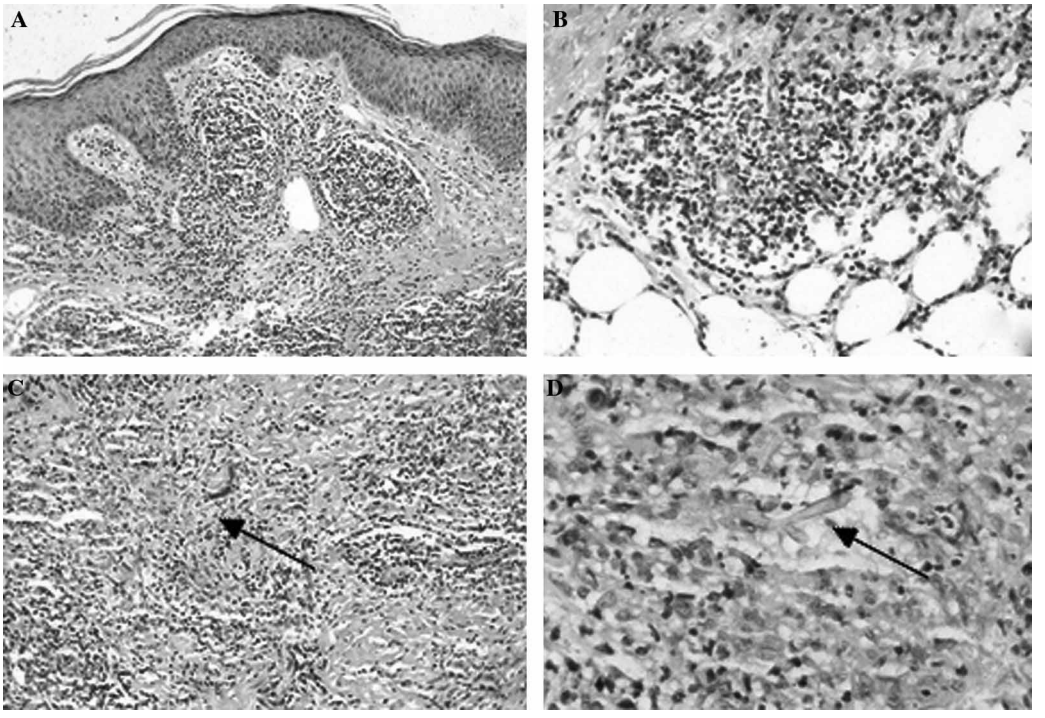

Fig. 3 (A) Columella (cotton blue, ×400). (B) Senescent sporangium, sporangiospores and collumella (cotton blue, ×400). (C) Sporangia (cotton blue, ×200).

still no improvement in the patient's condition. At the end of this treatment, microscopic examination of a portion of another biopsy showed a granulomatous infiltrate with no hyphae, but biopsy fragments yielded colonies of the same suspected etiologic agent in culture. A new treatment regimen with intravenous application of Amphotericin-B was initiated at a dose of 50 mg, three times a week followed by a single dose of 50 mg per week. After a cumulative dose of 1.6 g, the lesion was clinically healed leaving a sequel of brown macule (Fig. 1B). A last biopsy made 2 months after the end of the therapy showed cicatricial tissue with no granulomas or hyphae and cultures inoculated with portions of the biopsy were negative. Therefore, the patient was considered healed.

Discussion

The most commonly encountered members of the family Mucoraceae belong to the genera *Absidia*, *Mucor* and *Rhizopus*, which are generally associated with decaying vegetation and soil. Human exposure occurs in the majority of cases by inhalation of airborne spores, but ingestion or direct inoculation through the skin have also been described as possible portals of entry. While cutaneous mucormycosis is uncommon and represents only 10% of reported cases [19], it has been more recently recognized with increasing frequency [21,22]. Roden *et al.* in a recent review covering 929 zygomycosis cases, including mucormycosis and enthomophthormycosis, pointed out cutaneous involvement as the presenting pattern in 176 cases (19%) of all cases. The authors considered that cutaneous inoculation may have been previously underestimated [23]. Most of the cutaneous cases are represented by acute cellulitis or gangrene [24,25], primarily in immunosuppressed and severely diabetic patients. Traumatic inoculation may also be the antecedent to cutaneous involvement as in the reported cases of those affected by the Southeast Asia tsunami [4,6,8].

Our case is quite similar to that described in 1991 by Prevoo and associates in The Netherlands [19] in that both involved young girls in excellent general health conditions, presenting with superficial lesions having only slightly elevated circinate and squamous borders resembling tinea corporis. Our case had a 5 year course and the patient did not refer to a trigger event and denied any kind of traumatic event prior to the development of the lesion. However, the one presented by Prevoo and associates had an evolution of 10 months and in this instance there was a history of insect bite that could have inoculated the spores into the skin. Histopathology showed no vascular involvement such as invasion and/or infarction. In a

MEDLINE search of the literature published over the last 30 years, this particular fungus was found only on two previous occasions, i.e., a Brazilian case in a diabetic patient in 1990 [5] and the Dutch case mentioned above [19]. To our knowledge this is the third case in the literature and the second detected in a healthy individual.

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