Case Report

Demodex mite infestation of unknown significance in a patient with rhinocerebral mucormycosis due to Apophysomyces elegans species complex

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Demodex mites have been reported in the past as a cause of facial rash in immunosuppressed patients. Here, we report an interesting case of possible demodicosis associated with rhinocerebral mucormycosis. The association of mites with a fungus was detected on direct microscopic examination of the scrapings of a nasal ulcer. The mite and the fungus were identified as Demodex folliculorum and Apophysomyces elegans species complex, respectively.

Introduction

Two members of the mite family, Demodex folliculorum and Demodex brevis, inhabit the pilosebaceous unit. These mites were previously thought to be harmless commensals occurring permanently on the human skin. However, results from recent studies claimed that the mites may be associated with pityriasis folliculorum, rosacea, perioral dermatitis, seborrhoeic dermatitis, pustular eruption, blepharitis, seborrhoeic alopecia and other skin lesions (Zhao et al., 2011). Data also exist on severe infestation and increased severity of demodicosis in immunosuppressed individuals (Seyhan et al., 2004). Herein, we report a case of a patient with rhinocerebral mucormycosis who had severe Demodex infestation of unknown significance.

Case report

A 45-year-old man, with a recurrent giant cell tumour of the left radius with lung metastasis, had received six courses of chemotherapy with the ifosfamide, carboplatin and etoposide regimen and palliative external radiotherapy (20 Gy for 5 fractions) to the lung mass. He received oral prednisolone (40 mg daily) for the past 8 months for breathlessness, and irregular treatment with insulin for 5 years on account of diabetes mellitus. He presented with progressive swelling and redness of the face, and had difficulty in breathing for 10 days. Swelling and redness were associated with itching. Dyspnoea was present throughout the day and was not associated with any positional variation. Upon general physical examination the patient was drowsy and had laboured breathing, bilateral eyelid swelling and periorbital oedema. He also had erythema, erosions and woody, hard induration of the cheeks and upper lip. A large palatal ulcer (1 × 2 cm) with a necrotic base in the anterior two-thirds of the palate and a small ulcer with a necrotic base on the nasal septum were observed. The patient had reduced air entry in the left lung fields. The rest of the physical examination was within normal limits. A provisional diagnosis of rhino-orbital-cerebral mucormycosis, angio-oedema, Cushing’s syndrome and superior vena caval syndrome was made. Laboratory investigations revealed leukocytosis (count 29 900 μl⁻¹), raised levels of aspartate aminotransferase and alanine aminotransferase (244.2 U l⁻¹ and 942.2 U l⁻¹, respectively), hyperglycaemia (340 mg dl⁻¹), hypokalaemia (2.8 mEq l⁻¹), hypocalcaemia (7.29 mg dl⁻¹), hypochlorae mia (88.6 mEq l⁻¹) and hypoproteinaemia (4.68 g dl⁻¹). Other biochemical and haematological parameters were within normal limits. A potassium hydroxide wet mount (10 %) examination of the nasal scrapings from the base of the necrotic ulcer revealed the presence of 4–6 mites per low-power field (Fig. 1a) and broad aseptate hyaline hyphae (Fig. 1b). The mites were 0.3–0.4 mm long, with four legs and a long striated posterior segment. The detailed examination of the size and morphology of the mites identified them as D. folliculorum. Culture of nasal scrapings on Sabouraud dextrose agar (SDA) medium yielded white cottony, mycelial colonies after 4 days of incubation at 37 °C. As there was no sporulation on the SDA, water agar culture was carried out to induce sporulation. Microscopic examination of the squash preparation of the water agar culture after 10 days of incubation at 30 °C showed pauciseptate hyphae, unbranched sporangiohyphae, pyriform sporangia with funnel-shaped apophyses. Sporangiospores were elongated and smooth walled. Based on these features, the isolate was identified as Apophysomyces elegans complex. The isolate was later subjected to molecular identification by amplifying the...
**Discussion**

Rhinocerebral mucormycosis was suspected in this individual, as he was poorly compliant to diabetic therapy and had necrotic ulcers on the palate and nose. The diagnosis was confirmed by the presence of broad hyaline aseptate hyphae on microscopy and the isolation of the *A. elegans* species complex from the nasal scraping sample. Invasive mucormycosis is commonly caused by species of *Rhizopus*, *Lichtheimia* and *Rhizomucor*, and less commonly by species of the genera *Mucor*, *Apophysomyces*, *Saksenaea*, *Cunninghamella*, *Cokeromyces* and *Syncephalastrum* (Chakrabarti *et al.*, 2010). However, recent studies have shown that the genus *Apophysomyces* is a species complex comprising more than one species (Alvarez *et al.*, 2010). *Apophysomyces* is an emerging pathogen in tropical countries such as India, as it is increasingly isolated from cases of mucormycosis (Chakrabarti & Singh, 2011). In India the *A. elegans* complex is the second most frequently isolated agent from mucormycosis patients (Diwakar *et al.*, 2007). It commonly causes cutaneous and subcutaneous mucormycosis in immunocompetent hosts. Local wound contamination with soil or plant detritus after an accident is the single most common risk factor. Though it is not known how this patient became infected with this agent that caused rhinocerebral mucormycosis, inhalation of spores from contaminated air is expected. The patient was immunosuppressed, as he had undergone radiotherapy, was on long-term steroids and was poorly compliant to anti-diabetic therapy. Uncontrolled diabetes mellitus is the most predominant risk factor for mucormycosis in India and overshadows the other risk factors (Chakrabarti *et al.*, 2010).

A high density of *Demodex* mites was found in the nasal scraping of the base of a necrotic ulcer in this patient. The significance of the mite infestation could not be evaluated as the patient left the hospital against medical advice 2 days after the initiation of therapy. *Demodex* mites belong to the family *Demodicidae*, of which two closely related species, *Demodex folliculorum* and *Demodex brevis*, infest man.

A new term demodicosis has been coined to denote patients with facial dermatosis who have a *Demodex* density of five mites cm$^{-2}$ from one surface biopsy or ten mites cm$^{-2}$ from two successive surface biopsies at the same site (Hay, 2010). Severe demodicosis has been reported in a number of patients with AIDS, haematological malignancies and allogeneic bone marrow transplants, and those undergoing long-term corticosteroid, pimelolinus and erlotinib therapy. The etiopathogenesis of severe infestation has been attributed to suppression of cell-mediated immunity and secondary lymphocyte depletion, leading to an increased number of parasites in the skin (Seyhan *et al.*, 2004). Our patient had erythema, erosions and induration on the face with pruritus. Though we did not attempt to detect the mites on the face, the mites were detected in the nasal ulcer only. The necrotic tissue at the site of infestation and immunosuppressed condition of the host might have allowed unhindered proliferation of these mites and the subsequent skin manifestation.

The treatment guideline for demodicosis in humans is not available. Several clinicians used systemic antiparasitic agents like ivermectin and metronidazole (Holzchuh *et al.*, 2011; Román-Curto *et al.*, 2012). The topical preparations like ointment permethrin, metronidazole, pilocarpine gel, tea tree oil, mercury oil and crotamiton have also been used (Bikowski & Del Rosso, 2009; Gao *et al.*, 2005). In the present case study a turpentine wash was initiated as the mites were initially confused with maggots.

The assumption that *Demodex* mites were the cause of facial rash in this patient could not be confirmed as the patient left hospital against medical advice. To the best of
our knowledge, this is the first case of possible demodicosis associated with invasive mucormycosis. This case reflects the need for greater awareness about demodicosis amongst clinicians and laboratory physicians managing immunosuppressed patients. Future studies are also needed to examine the possible role of diabetes mellitus in the predisposition of demodicosis.

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References


