Case Report

Disseminated cutaneous phaeohyphomycosis due to *Cladophialophora bantiana*

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ABSTRACT

Cladophialophora bantiana is a neurotropic dematiaceous fungus which only rarely affects the skin. We report a case of disseminated cutaneous phaeohyphomycosis caused by *Cladophialophora bantiana* in an immunocompromised female who presented with multiple pyogenic granuloma-like nodules, dermatophytosis-like plaque, and subcutaneous cysts on the upper and lower extremities without systemic involvement. Biopsy revealed black yeasts resembling sclerotic bodies and culture yielded irregular, velvety, grey colonies with black reverse. Excisionof the nodules and treatment with oral itraconazole 100 mg twice daily resulted in complete clinical resolution within two months, following which itraconazole was administered for another 4 months.

Key words: *Cladophialophora bantiana,* cutaneous, phaeohyphomycosis, pyogenic granuloma like nodules

INTRODUCTION

Phaeohyphomycosis was a term introduced by Ajello *et al.* in 1974 to denote infections caused by a variety of dematiaceous fungi characterized by pigmented hyphae in the tissue. Many cases were previously misdiagnosed as chromoblastomycosis especially in the absence of tissue cultures. There are very few reports of localized cutaneous phaeohyphomycosis due to *Cladophialophora bantiana*, a neurotropic fungus.[1]

CASE REPORT

A 38-year-old female presented with multiple skin tumors of 2 months duration, with recurrent episodes of bleeding from the lesions. There was no previous history of trauma. Her medical history included membranous glomerulonephritis and nephrotic syndrome for which she had been on oral corticosteroids and cyclosporine for the past 8 months.

General examination showed features of Cushing's syndrome with truncal obesity and facial hypertrichosis. Dermatological examination revealed multiple reddish dome shaped and flat surfaced nodules of size ranging from 2 × 2 cm to 7 × 8 cm over both lower limbs resembling pyogenic granulomas [Figure 1]. There was an erythematous plaque with scaling along the borders and a clear centre over the lateral border of the left foot mimicking dermatophytosis [Figure 2]. In addition, there were two cystic swellings on the base of the left middle finger and the dorsum of the left hand [Figure 3].

Laboratory investigations including complete blood cell count, liver and renal function tests were within normal limits except for a raised erythrocyte sedimentation rate (ESR) of 80mm/h. Screening for

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hepatitis B, hepatitis C and human immunodeficiency virus, as well as serology for antinuclear and anti double-stranded DNA antibodies were negative. Chest X-ray and electrocardiogram were normal. An ultrasonogram of the abdomen and computed tomography scan of the brain and chest were normal indicating that there was no systemic dissemination.

Scrapings from the plaque and wet mount examination revealed septate hyphae. Biopsy from a nodule revealed hyperkeratosis, acanthosis, hemorrhage, and ulceration with a dense inflammatory infiltrate in the dermis. There were large black spores within and outside giant cells suggestive of chromoblastomycosis [Figure 4a and b]. Pigmented fungal elements in the form of pseudohyphae were detected with Periodic acid Schiff and Masson–Fontana stains [Figure 4c]. Fungal culture of aspirate and tissue samples from the cysts, nodules, and plaque yielded irregular, velvety, gray colonies with black reverse within 7 days of incubation [Figure 5a]. Microscopy showed plenty of septate hyphae with unicellular microconidia branching at acute angles surviving incubation upto 40°C [Figure 5b]. All these features were characteristic of *Cladophialophora bantiana*.

The two larger nodules were surgically excised and the patient was treated with oral itraconazole, 100mg twice daily. Two months after initiating treatment, there was complete resolution of all the lesions. However, itraconazole was continued for a total of 6 months in order to ensure eradication of the infection. There has been no sign of recurrence during 1 year of follow-up.

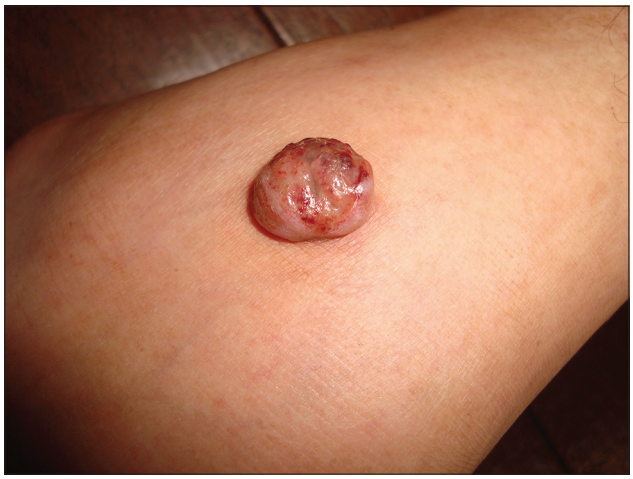

Figure 1: Reddish dome shaped nodule resembling pyogenic granuloma

DISCUSSION

Fungal infections produce diverse clinical features that pose difficulty in diagnosis and management. Phaeoid or pigmented fungi cause a diverse group of infections which includes chromoblastomycosis producing sclerotic bodies, eumycetomas producing grains and phaeohyphomycosis which forms yeast-like cells, pseudohyphae, hyphae or a combination of these in the infected tissues. Most infections follow inoculation of the fungus from soil or wood into abraded skin.[2]

Phaeohyphomycosis is known to occur in four clinical categories: superficial, cutaneous or corneal, subcutaneous, and visceral forms. Superficial infections include black piedra and tinea nigra. Cutaneous diseases are similar to dermatophytosis. Subcutaneous infection causes a solitary abscess, "phaeohyphomycotic cyst" usually over the extremities. More than 100 species have been implicated as causative agents of which the most common are *Exophiala, Alternaria, Bipolaris, Curvularia*, and *Wangiella*.[3]

Disseminated phaeohyphomycosis with multiple cystic lesions and systemic involvement is rare and is usually seen in immunocompromised patients.[3] A report from India describes disseminated lesions in four patients, of whom two patients had both cysts and warty plaques. The causative agents included *Phialophora dermatidis, Exophiala jeanselmi*, and *Alternaria alternata*.[1] Dissemination occurs as a result of hematogenous spread from a primary focal infection. Melanin is a virulence factor that acts as

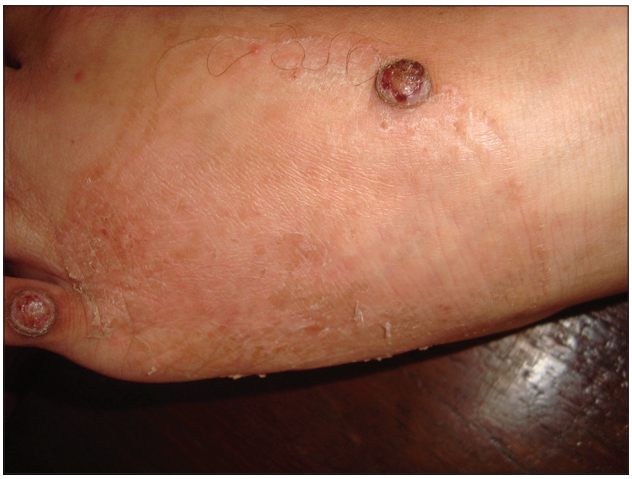

Figure 2: Erythematous plaque mimicking dermatophytosis

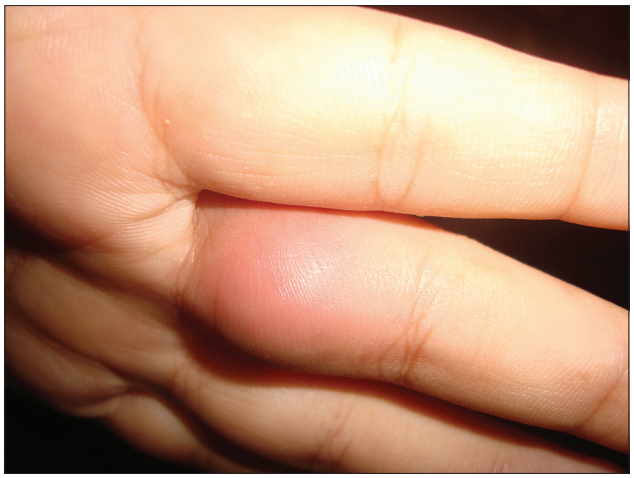

Figure 3: Subcutaneous cyst of the finger

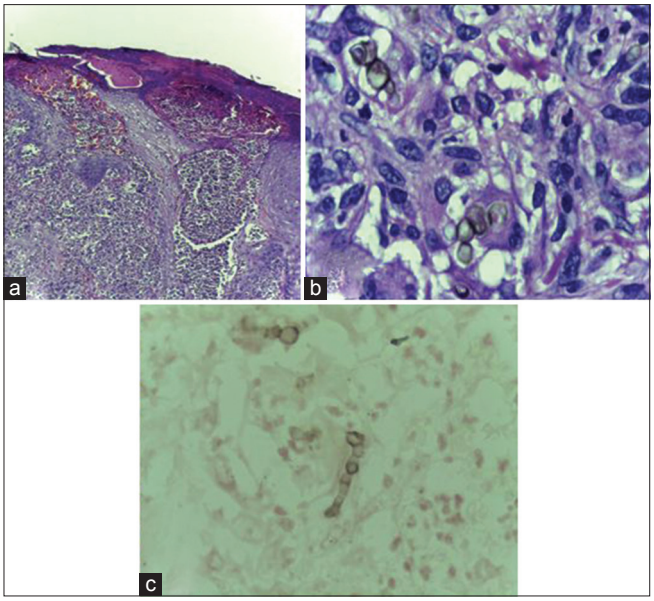

Figure 4: (a)Hyperkeratosis, acanthosis, hemorrhage in the epidermis, and dense inflammatory infiltrate in the dermis, H and E, ×100 (b) Large black spores within and outside giant cells, H and E, ×400 (c) Pseudohyphae, Masson–Fontana stain ×400

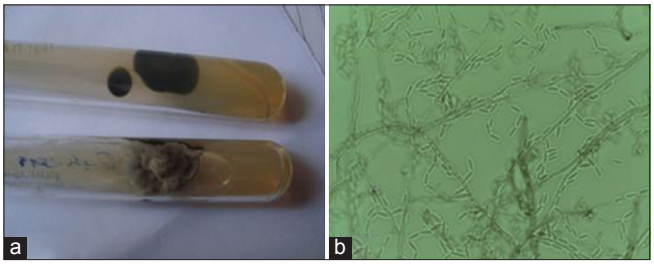

Figure 5: (a) Irregular, velvety, gray colored colonies with black reverse, (b) septate hyphae with unicellular microconidia branching at acute angles, ×400

an antioxidant against oxidative bursts produced by phagocytes. It also binds to the host hydrolytic enzymes that target fungal plasma membrane.[4]

Phaeohyphomycosis differs from chromoblastomycosis in the appearance of the etiological agent as brown-black hyphae in the tissues of the former and sclerotic bodies in those of the latter. Among the etiological agents of phaeohyphomycosis, *Exophiala dermatidis* is known to produce sclerotic bodies - like rounded structures in the tissue.[1]

Cladophialophora bantiana is predominantly a neurotropic fungus causing phaeohyphomycosis in the central nervous system of both humans and animals.[4] There are very few reports of cutaneous infection due to *Cladophialophora bantiana*.[1] The skin lesions known to be caused by *Cladophialophora bantiana* include papulo-nodules, plaques, nodules with pustules, nodules with sinuses, and ulcerative lesions.[5-9]

Cladophialophora bantiana elicits a blastomycosis-like tissue reaction or forms a phaeomycotic cyst. The pigmented fungal elements seen with hematoxylin–eosin stain include septate hyphae, pseudohyphae, globose to oval yeast like cells, budding cells and spherical cells with prominent septations. The latter resemble sclerotic bodies but differ in having thinner cell walls, a single planate septum, and stain black with Masson–Fontana stain.[9] The fungus grows within 7–8 days on routine fungal culture media at room temperature, at 37°C and at temperatures higher than 40°C. The colonies mature within 15 days of incubation and show a velvety texture and olivaceous gray to brown colour with a black reverse. The fungus shows hyaline-to-brown, septate hyphae and have smooth walled, single-celled, pale olivaceous, ellipsoidal to spindle-shaped conidia arranged in long, strongly coherent chains.[10]

Our patient did not have a history of antecedent trauma but was immunocompromised due to long-term steroids and cyclosporine. Three types of morphological patterns, pyogenic granuloma-like nodules, dermatophytosis-like plaques, and subcutaneous cysts, coexisted in our patient. We were unable to find any previous reports of pyogenic granuloma - like lesions caused by *Cladophialophora bantiana*.

Physicians should consider cutaneous phaeohyphomycosis in the differential diagnosis of plaques, nodules, and cysts in the skin, especially in the setting of immunosuppression. The characteristic

colonies and morphology of the fungus help to identify the species facilitating early diagnosis and management, which may prevent systemic dissemination and lead to a favorable outcome.

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