Letters to the Editor

**Disseminated cryptococcosis**

Sir,

Cryptococcosis is mainly caused by two species of *Cryptococcus* that is, *C. neoformans* and *C. gattii*. Disseminated cryptococcosis is defined by a positive culture from at least two different sites or a positive blood culture.[1] We report a case with manifestations in lung and skin, with positive cultures from both sites identified as of the same fungus by DNA sequencing.

A 33-year-old male presented with a 3-month history of a nodule on the left upper eyelid and a 2-month history of productive cough. The nodule had enlarged gradually, after the onset of cough. There was no history suggestive of tuberculosis, acquired immunodeficiency syndrome (AIDS), idiopathic T-cell lymphopenia, diabetes mellitus, autoimmune disease, glucocorticoid use, high risk behavior or trauma. None of the family members had similar manifestations. Cutaneous examination revealed a dark red nodular plaque of size 1.5 cm × 1.0 cm with crusting, on the left upper eyelid [Figure 1].

Laboratory studies including a complete blood count, urinalysis and blood biochemistry were normal; blood and sputum cultures were negative. HIV screening was also negative. T-cell subset counts were not done. Histopathologic examination [Figure 2a] of the cutaneous lesion revealed numerous yeast cells in the dermis which stained positive with periodic acid-Schiff (PAS) [Figure 2b] and mucicarmine [Figure 2c]. Fungal culture [Figure 3] of the skin lesion yielded milky colonies in Sabouraud’s dextrose agar (SDA) medium. Mycological examination of the culture with India ink [Figure 4] was positive. Computed tomography (CT) of the chest revealed cavitary lesions in the left lung [Figure 5]. A fiber bronchoscopic biopsy was then done, and this revealed plenty of round organisms which stained positive with PAS and PAM (periodic acid-silver methenamine), suggestive of cryptococcus. Cryptococcus was also cultured from bronchoalveolar lavage fluid. Cerebrospinal fluid examination and a CT scan of the head were carried out, and both were normal. *C. neoformans* was identified in culture from both the skin and lung by multi-locus sequence typing, confirming disseminated cryptococcosis.

Risk factors for disseminated cryptococcosis include immunosuppression, malignancy, corticosteroid therapy, diabetes, and connective tissue disease.[2] None of these was present in our case, but he was a garbage collector and there might...
have been occupational exposure to Cryptococcus via soil, dust, sticks, or bird feces. Moreover, some case reports have reported disseminated cryptococcosis in immunocompetent patient.\[3,4\] Manifestations of cutaneous cryptococcosis are varied. Lesions may resemble molluscum contagiosum, or appear acneiform, nodular, herpetiform, cellullitic, or keloid-like.\[5\]

The management of cryptococcosis is not well-defined. Amphotericin B with or without flucytosine was considered the standard treatment in patients with disseminated cryptococcosis.\[6\] Fluconazole has been reported to be the most utilized treatment for cutaneous cryptococcosis, with a 600 mg daily dose for 40–60 days.\[5\] One report describes four pulmonary cryptococcosis patients initially treated with amphotericin B developing adverse reactions to it, and oral fluconazole then being used (600 mg daily for 4–5 weeks, followed by 400 mg daily for 10–12 weeks).\[7\] Non-central nervous system infection in HIV patients can also be treated with oral fluconazole 200–400 mg daily. If fluconazole is not tolerated, itraconazole 200–400 mg daily for 6–12 months may be used.\[6\] Our patient was treated with itraconazole 200 mg daily, after he failed to respond to fluconazole, 150 mg daily for 12 days, 800 mg daily for 1 day, followed by 400 mg daily for 10 days. Response to itraconazole was evident, with the skin nodule clearing, the cough improving and the lung cavity lesions found to have shrunk on a follow-up CT scan after 20 days of treatment. Unfortunately, he discharged himself against medical advice and was lost to follow up. This case suggests that itraconazole might be a good option for patients with lung and cutaneous involvement in C. neoformans infection.

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Sir,

Verruciform xanthoma is a rare benign mucocutaneous lesion which was first described by Shafer in 1971.[1] It usually presents as an asymptomatic, white or yellowish red plaque with a verrucous surface. However, polypoid, papillomatous and sessile lesions have also been reported. The condition has a predilection for the oral cavity.[1] Extraoral lesions have been reported, mainly involving the anogenital region.[2] Multiple lesions are extremely rare. Verruciform xanthoma has been reported in patients of bone marrow transplant who have graft versus host disease.[3] Though single lesions have been reported before,[4] we were unable to find any previous reports in the English literature of multiple verruciform xanthomas following bone marrow transplant, in the absence of graft versus host disease.

A 40-year-old man was evaluated for asymptomatic verrucous plaques on the upper gingiva and adjoining labial mucosa, and glans penis for 3 months. The lesions were slowly progressive. He had undergone allogenic bone marrow transplantation for chronic myeloid leukemia a year before the appearance of the lesions. The patient had received cyclosporine prophylaxis for graft versus host disease and was in complete hematological remission. Physical examination revealed a well demarcated, non-tender, pink to yellowish plaque with a verrucous surface, measuring 5 cm × 3 cm on the upper gingival mucosa, above the right incisor and canine and extending into the adjoining upper labial mucosa. Another yellowish sessile plaque measuring 3 cm × 2 cm was present on the glans penis [Figure 1a and b]. A differential diagnosis of condyloma acuminata was considered. Biopsy from both the lesions revealed stratified squamous epithelium with papillary proliferation, uniformly long bulbous rete ridges, areas of bright eosinophilic parakeratosis with neutrophilic exocytosis and a dense infiltrate of foamy macrophages in the papillary dermis [Figure 2a and b], confirming the diagnosis of verruciform xanthoma. A lipid profile was normal and polymerase chain reaction from the lesion was negative for human papillomavirus. The lesions were re-excised and topical imiquimod was applied to treat any possibility of a residual lesion.

The etiopathogenesis of verruciform xanthoma remains unclear. Postulated factors include immunologic factors, local inflammation and viral etiology. Ultrastructure and in situ hybridization from lesions of verruciform xanthoma have failed to demonstrate human papilloma virus making a viral etiology unlikely.[5] Immunologic factors were suggested based on the predominance of T-cell lymphocytes in the dermal infiltrate of verruciform xanthoma and a decreased number of Langerhans cells as compared to normal tissue.[5] A theory suggesting a role for a chronic inflammatory process in the development of verruciform xanthoma in patients with graft versus host disease proposed release of lipids from the phospholipid-rich cell membranes following epithelial tissue injury, which are engulfed by macrophages that later transform into foamy cells.[6] In our patient, presence of immunosuppression along with possible local irritation are probable factors involved in the pathogenesis of this disease.