**List of abbreviations**

EBER: Epstein-Barr virus-encoded RNA
CD: Cluster of differentiation
TIA: T-cell intracellular antigen
GrB: Granzyme B
EBNA: Epstein-Barr virus nuclear antigen
VCA: Epstein-Barr virus capsid antigen

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# Candidal granuloma in a renal allograft recipient

Sir,

The incidence of candidiasis has increased considerably over the past four decades with the surge of HIV/AIDS, diabetes, cancer and frequent use of chemotherapeutic agents, broad-spectrum antibiotics, steroids, immunosuppressive medications and indwelling medical devices. Although *Candida albicans* is historically the most prevalent species causing human candidiasis, non-*albicans Candida* species such as *Candida glabrata, Candida tropicalis* and *Candida parapsilosis* are being increasingly identified globally. This is attributed to the advances in diagnostics and availability of molecular identification techniques.[1] Candidal granuloma is an uncommon presentation of candidal infection, and here we report such a case caused by *Candida parapsilosis*.

A 58-year-old male presented with a slowly enlarging warty growth over the upper lip for 1 month. Examination revealed a solitary verrucous plaque of size 3x4 cm located over the right lateral aspect of the upper lip at the mucocutaneous junction extending into the mucosa [Figures 1 and 2]. The clinical differentials included verrucous squamous cell carcinoma, cutaneous tuberculosis and deep fungal infections like chromoblastomycosis and blastomycosis. The patient had undergone renal transplant for diabetic nephropathy four years ago and was currently receiving 5mg/d of oral prednisolone and 250 mcg/d of oral tacrolimus. All routine laboratory investigations were normal except for elevated serum creatinine (2 mg/dl) and HbA1c (9%). Serology for the human immunodeficiency virus was non-reactive.

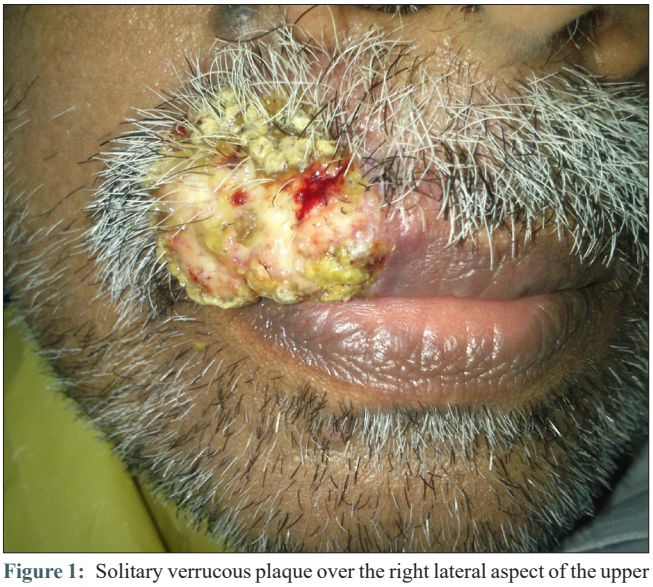

**Figure 1:** Solitary verrucous plaque over the right lateral aspect of the upper lip extending into the mucosa

A potassium hydroxide mount from a scraping of the skin lesion did not show any fungal spores or hyphae.

Histopathological examination of the growth revealed epithelioid cell granulomas with Langhans type giant cells admixed with inflammatory infiltrate in the dermis, suggestive of an infective granuloma [Figures 3 and 4]. Acid-fast staining was negative for organisms; however,

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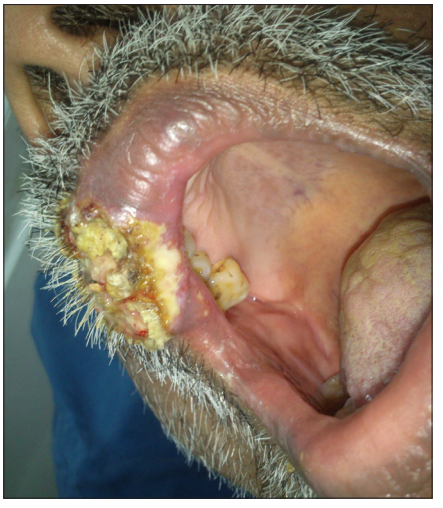

**Figure 2:** Solitary verrucous plaque over the right lateral aspect of the upper lip extending into the mucosa

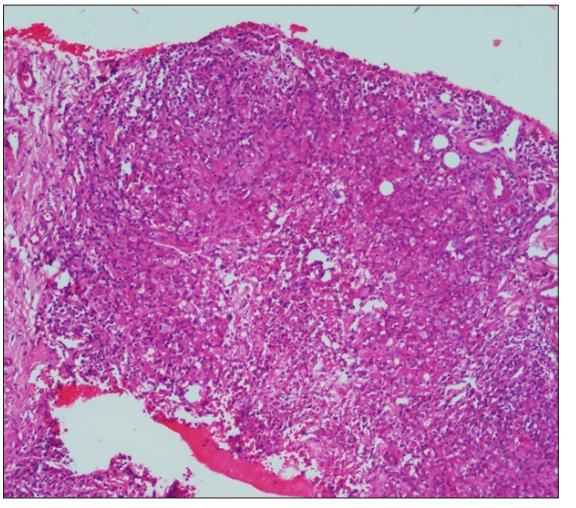

**Figure 3:** Epitheloid cell granulomas with Langhans type giant cells admixed with inflammatory infiltrate in the dermis (Haematoxylin-eosin ×100)

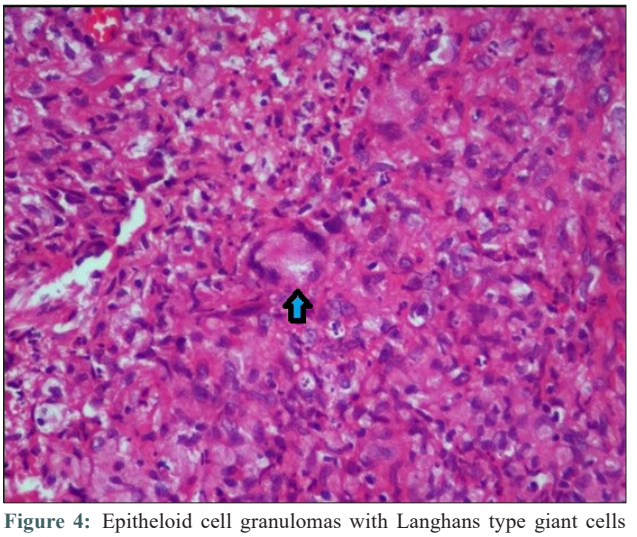

**Figure 4:** Epitheloid cell granulomas with Langhans type giant cells (blue arrow) (Haematoxylin-eosin ×400)

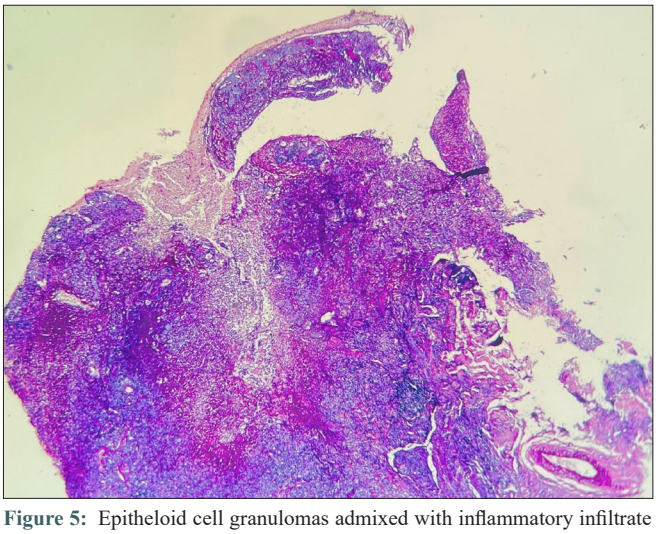

**Figure 5:** Epitheloid cell granulomas admixed with inflammatory infiltrate in the dermis (Periodic acid-Schiff stain ×40)

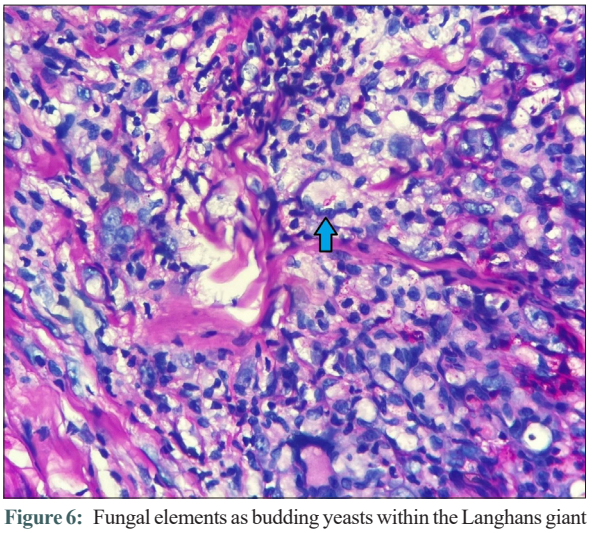

**Figure 6:** Fungal elements as budding yeasts within the Langhans giant cells (blue arrow) in the granuloma (Periodic acid-Schiff stain ×400)

periodic acid–Schiff stain demonstrated fungal elements as budding yeasts within the Langhans giant cells within the granuloma [Figures 5 and 6]. Mantoux test and bacterial and mycobacterial tissue cultures were negative. Tissue fungal culture grew *Candida parapsilosis* on Sabouraud agar which was susceptible to fluconazole, voriconazole, amphotericin B and itraconazole [Figure 7].

Based on the antifungal susceptibility, fluconazole was started at a dose of 100 mg daily for one week. A significant improvement was observed, so fluconazole was continued at an alternate day regimen for the next three weeks which resulted in a near-complete resolution with no relapse at the end of three months [Figures 8 and 9]. Fluconazole can potentially increase the blood levels of tacrolimus and prednisolone augmenting their side effects. A nephrology consultation was taken before starting fluconazole and dose adjustment was not deemed

**Figure 7:** *Candida parapsilosis* colonies on Sabouraud agar

**Figure 8:** Near-complete resolution post-treatment with fluconazole

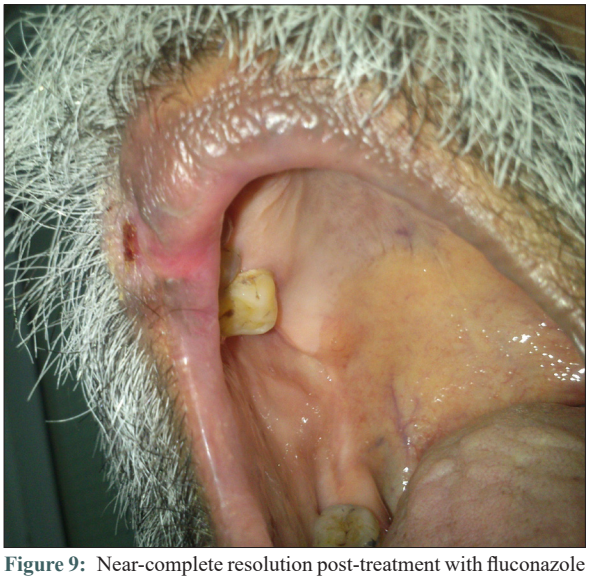

**Figure 9:** Near-complete resolution post-treatment with fluconazole

necessary for any drug. Serum creatinine was monitored during treatment and no worsening was noted.

Candidal granuloma, a rare form of cutaneous candidiasis, was first reported by Hauser and Rothman in 1950; occurring in a chronic, recurrent form mostly in children and mainly involving face, scalp and oral mucosa.[2] It is an acute inflammatory process involving the epidermis, dermis and mucosa resulting in profound granulomatous reaction histologically and hyperkeratotic lesions clinically.[3]

Disequilibrium between cell-mediated and humoral immunity along with defective phagocytic activity is the possible immunological basis of Candida granuloma formation.[4]

Non-*albicans Candida* species of late are gaining notoriety as the causative agents of varied forms of candidiasis from superficial to systemic. Recent studies show *Candida parapsilosis* as the commonest isolated non-*albicans Candida* species mainly causing superficial candidiasis with no reports so far of candidal granulomas.[1,5]

Diversity among *Candida* species in terms of virulence and variable susceptibility to antifungals makes species identification crucial for therapeutic decisions. The factors attributed to the virulence of *Candida parapsilosis* are adherence to the host cells, formation of potent biofilms, secretion of enzymes aspartic proteinases, phospholipases and lipases, and higher avidity for buccal epithelial cells causing aggregates on epithelial surfaces.[1] A recent study reported that the global incidence of *Candida parapsilosis* isolates' susceptibility to oral fluconazole is 96.5%.[5]

Although chronic mucocutaneous candidiasis is widely prevalent, candidal granulomas are seldom described and the present case illustrates one such instance in a renal allograft recipient who responded well to fluconazole. In immunocompromised individuals, atypical presentations of infections are not uncommon and as the underlying diseases are also associated with increased morbidity, favourable outcomes depend on early diagnosis and treatment.

#### Declaration of patient consent

Patient's consent not required as patient's identity is not disclosed or compromised.

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#### Conflict of interest

There are no conflicts of interest.

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# An unusual case of nasal chromoblastomycosis progressing to squamous cell carcinoma in a non-endemic region

Sir,

Chromoblastomycosis is a slowly progressive granulomatous mycosis of the skin and subcutaneous tissue, caused by inoculation of dematiaceous fungi mainly affecting the lower limbs. The infection is common in tropical and subtropical regions, but there have been several cases reported in temperate regions.[1] Early diagnosis and treatment is necessary as long-standing cases can rarely undergo malignant transformation into squamous cell carcinoma.[1] Herein, we report an unusual case of chromoblastomycosis in Tunisia, anon-endemic area,occurring at a distant site from the original lesion and progressing into squamous cell carcinoma.

A 60-year-old man from North Tunisia, a masseur in a Turkish bath presented to our department in 2006 with an infiltrated plaque on the right thigh. He had a history of trauma at the same site two years back at work. There was no history of travel to tropical areas. The histopathological examination revealed the presence of fungal elements. Mycological examination confirmed the diagnosis of chromoblastomycosis but the species was not identified. He was treated with terbinafine (500 mg/day) for three months. There was a significant decrease in the size of the lesion, but he was lost to follow-up. Eight years later, he presented with a reddish fleshy mass in the left nasal cavity associated with mucopurulent discharge. Over the past three months, the mass rapidly increased in size and extended to involve the nasal dorsum. On examination there was a 4 × 3 cm ulcero proliferative nasal tumour with irregular edge surmounted by telangiectasia on the nasal dorsum and left nasal cavity [Figure 1a]. Dermoscopy revealed a vascular pattern with polymorphous vessels [Figure 1b]. Cervical lymph nodes were not palpable. On the right thigh, there was a 12 × 13 cm erythematous to verrucous plaque interspersed with areas of atrophy and depigmentation [Figure 2]. Clinically, the differential diagnoses of tumour form of chromoblastomycosis and squamous cell carcinoma were considered. Biopsies were performed at different sites of the nasal and the thigh lesion. Histological examination of the biopsy specimens taken from the margin of the nasal lesion revealed the presence of fungal elements within a granulomatous reaction with mixed inflammatory infiltrate [Figures 3a and 3b]. The same histopathological findings were noted in the thigh lesion.

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