“A fine needle aspiration cytology in time saves nine” – cutaneous phaeohyphomycosis caused by *Exophiala jeanselmei* in a renal transplant patient: Diagnosis by fine needle aspiration cytology

**ABSTRACT**
Infections by dematiaceous fungi are an emerging group of infectious diseases worldwide with a variety of clinical presentations. Though generally localized, they can disseminate in immunocompromised settings, therefore, early diagnosis and prompt therapy can prevent significant morbidity and mortality in these patients. Fungi of genus *Exophiala* are common causative organisms; however, *Exophiala jeanselmei* (*E. jeanselmei*) has not yet been reported from environmental sources in India. We present here the case of a renal transplant recipient who presented with an innocuous lesion on the foot, diagnosed on fine needle aspiration cytology (FNAC) as phaeohyphomycosis, and promptly treated with excision and antifungal therapy. To the best of our knowledge, this is the first case report from India of *E. jeanselmei* causing phaeohyphomycosis in a transplant recipient and highlights the role a cytopathologist can play in the timely management of such cases.

**Key words:** *Exophiala jeanselmei* (*E. jeanselmei*), fine needle aspiration cytology (FNAC), immunosuppression, phaeohyphomycosis

**Introduction**
Infections by dematiaceous fungi are an emerging group of infectious diseases worldwide, with a variety of clinical presentations both in immunocompetent and immunocompromised settings.[1] They are generally slowly progressive chronic localized infections but can disseminate in immunocompromised patients. Though many genera of these fungi can cause human disease, *Exophiala jeanselmei* (*E. jeanselmei*) is an uncommon cause. We present here the case of a renal transplant recipient who was diagnosed with cutaneous phaeohyphomycosis at an early stage by fine needle aspiration cytology (FNAC) and responded to treatment.

**Case Report**
A 48-year-old male patient underwent renal transplantation in March 2014. After 6 months he presented with a painless nodular swelling over the right ankle that had developed over 1.5 months. The patient had received basiliximab injection and had been on triple immunosuppression that...
comprised corticosteroids, tacrolimus, and mycophenolate mofetil.

On examination there was a 3 cm × 2 cm slightly-pigmented cutaneous nodule on the right ankle [Figure 1a] without any ulceration, discharging sinus, or tenderness. No regional lymphadenopathy was apparent and his systemic examination was within normal limits.

A fine needle aspiration of the lesion was subsequently done that yielded a pus-like material. On microscopy it showed dense mixed inflammation comprising numerous histiocytes, giant cells, and inflammatory granulation tissue [Figure 1b-d]. In addition, numerous pigmented branching and septate fungal hyphae were easily appreciable in the smears [Figure 1e]. A diagnosis of cutaneous fungal infection was rendered and the treating nephrologists informed immediately. The patient was subsequently admitted for antifungal therapy. Prior to the initiation of therapy, a second aspirate was sent for culture studies. Multiple darkly-pigmented hyphae were observed as well, on direct microscopy of skin biopsy using 10% potassium hydroxide. Cultures on Sabouraud dextrose agar (SDA) grew a dark, moist, olive-to-black yeastlike colony after 7 days of incubation that became dry by 14 days, exhibiting a mycelial fringe. Microscopic examination of the slide culture using a lactophenol cotton blue (LPCB) stain [Figure 1f] showed thin brown septate hyphae. The conidiogenous cells on hyphae were intercalary or rocket-shaped and brown, with inconspicuous annelated zones that were slightly tapering and smooth. The isolate produced narrow ellipsoidal conidia. The fungus was identified as *E. jeanselmei* on the basis of morphology and failure to grow at 40°C. It was differentiated from *Exophiala spinifera* (*E. spinifera*) that has very narrow long annelated zones of the conidiogenous cell, whereas *Exophiala dermatitides* (*E. dermatitides*) produces more yeastlike colonies and shows luxuriant growth at 40°C. Skin biopsy showed dense dermal aggregates of histiocytes and giant cells [Figure 1f] containing numerous thin-pigmented branching fungal hyphae [Figure 1g and h].

The fungal nodule was excised and a course of amphotericin B followed by itraconazole was given for 6 weeks. There has been no recurrent nodule subsequently to date.

**Discussion**

“Phaeo” in Greek means “dark,” therefore, phaeohyphomycosis means infection caused by dark-walled fungi. “Melanized”

![Figure 1: FNAC of nodule (a) reveals dense inflammation (b, c, d: Papanicolaou, ×100, ×200, ×1000, respectively) with pigmented hyphae (e: Papanicolaou, ×1000). Biopsy shows similar findings (f, g, h: H and E, ×100, ×1000, ×1000, respectively). Fungal profiles in SDA (i: LPCB, ×1000)
and “dematiaceous” are used synonymously as well. Melanin in the cell wall is implicated as an important virulence factor. Over 150 species and 70 genera of these fungi are implicated in human and animal diseases. These group of infections though rare, are being reported increasingly, both in immunocompromised and immunocompetent settings. Melanized fungi are ubiquitous in the environment, especially in the tropics and sub-tropics, inhabiting living and dead plant material and soil. However, certain fungi within the group are known to occupy specific “ecological niches” or “microenvironments.” Fungi of genus Exophiala are characterized as micro-extremophiles, wherein some species such as Exophiala xenobiotica can grow even in high concentrations of xylene and toluene.[13] E. jeanselmei is an uncommon cause of infection and though its presence in soil is well-known, it has not yet been reported from environmental sources in India.[3]

Infection usually results from traumatic implantation, but in many cases this history is not easily evident. Clinically, these infections may present as eumycetoma (chronic subcutaneous infection characterized by the presence of grains in tissue), chromblastomycosis (slowly progressive chronic subcutaneous mycosis defined histologically by the presence of muriform sclerotic bodies) or phaeohyphomycosis (all other presentations; superficial and deep) and are generally localized. Disseminated infections are rare outside immunocompromised settings. Diagnosis of melanized fungi as etiologic agents requires tissue demonstration of infection because growth in culture can commonly be due to environmental contamination.[1]

Infections from E. jeanselmei have been reported worldwide in a variety of clinical situations and sites including keratitis, epididymal infections, postrenal transplant, after lung transplant, hypersensitivity pneumonitis, and as well in immunocompetent hosts. From India, five cases reported could be identified in the literature, all of them being immunocompetent hosts, four presenting as mycetoma pedis,[3-6] and one as calcaneal osteomyelitis.[7] To the best of our knowledge, this is the first Indian case report of E. jeanselmei infection in an immunocompromised setting presenting as phaeohyphomycosis.

In a recent review of phaeohyphomycosis in solid organ transplant recipients, 40% (11/27 cases) were caused by Exophiala species. Death from fungal disease in their patients occurred only in cases with pulmonary and brain abscesses.[8] Another group reported overall mortality rate among the patients with skin and/or soft tissue infections or joint infections to be 7%.[9]

Multiple therapeutic options are available, depending on the immune status and extent of the lesion. Oral systemic therapy with an azole antifungal agent in conjunction with surgery is frequently employed, particularly in immunocompromised patients due to the inherent, though rare, risk of dissemination.

**Conclusion**

To conclude, this case report highlights the importance of regular follow-up and work-up of even innocuous lesions in a transplant setting and the role a cytopathologist can play in such a patient’s timely management.

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**Conflicts of interest**

There are no conflicts of interest.

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