Cytological dilemma of a rare subcutaneous fungal infection: *Phaeoacremonium griseorubrum*

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**ABSTRACT**

Human disease caused by *Phaeoacremonium* species is rare. It was first reported in 1974 to cause subcutaneous tissue infection in the renal transplant recipient. Since then, only a few cases have been reported in the literature; however, underreporting is common in such cases due to incomplete or incorrect identification. Furthermore, some cases of subcutaneous infection in otherwise healthy patients may be asymptomatic and definitive identification of the etiological agent is not pursued. Identification of fungi at the species level is challenging by conventional methods; hence, final identification of fungi is based on culture. *Phaeoacremonium* has a very wide spectrum of presentation ranging from subcutaneous infections to fungemia and disseminated disease. We report a case of subcutaneous tissue swelling in an immunocompetent 55-year-old male, in whom etiology was traced to *Phaeoacremonium griseorubrum*. To the best of our knowledge, this report of *P. griseorubrum* causing human infection is second of its kind and the first from India. The patient did not respond well to oral itraconazole therapy and was advised surgical debridement with amphotericin B therapy.

**Key words:** Culture, fine-needle aspiration cytology, fungus, immunocompetent, *Phaeoacremonium griseorubrum*

**CASE REPORT**

A 55-year-old male patient working in a printing press presented in the surgical outpatient department with a single nodule at the left elbow for 3 years (Fig. 1). There was no history of trauma or any invasive procedure. The nodule was firm in consistency, erythematous, tender, and not fixed to the underlying structures. There was no recent increase in size or associated pain or bleeding from the nodule.

Routine laboratory investigations including hemogram, liver function tests, and kidney function tests were within normal limits. Further, investigations were performed including HIV (rapid kit tests), CD4 and CD8 cell counts and all were within normal limits suggesting immunocompetence of the patient. Fine-needle aspiration cytology (FNAC) was performed using a 22 gauge needle and 2 ml pus was aspirated. Smears stained with Giemsa and Papanicolaou stain revealed septate hyphae showing branching with inflammatory infiltrate comprising neutrophils, eosinophils, histiocytes, and multinucleated giant cells (Fig. 2a). Periodic acid–Schiff (PAS) stain was applied to the cytological material which confirmed the presence of septate branching fungus (Fig. 2b). Direct examination of the aspirate in 10% KOH showed the presence of branching septate hyphae (Fig. 3a). Gram stain showed the absence of bacteria. Ziehl–Neelsen stain for acid fast bacilli and TB Polymerase chain reaction were negative.

A provisional diagnosis of the fungal abscess was given on FNAC and patient was started with Itraconazole (antifungal) therapy. The aspirated material was sent for fungal culture. The aspirate was cultured on Sabouraud’s dextrose agar (SDA) and incubated at 37 and 25°C. Colonies appeared on SDA, which were initially yellowish on the obverse, but within 3 weeks became gray-black in color with blackish pigmentation noted on the reverse (Fig. 3b). The fungus was cultured on potato dextrose agar (PDA). On PDA, colonies were flat, short, woolly, violet-brown to reddish

**Phaeoacremonium** is a rare fungal infection. It can manifest as subcutaneous abscesses, cysts, or chronic or acute osteoarthritis in immunocompetent or immunocompromised patients. In an immunocompromised host, it may cause disseminated infection, fungemia, or endocarditis [1]. There are very few case reports of *Phaeoacremonium* as its morphological identification is difficult because the majority of species causing human infection were not described until recently. Most of the Phaeoacremonium species are plant pathogens, are able to grow at human body temperature and might be seen as human infections. To improve on our current knowledge of this fungal infection, each case needs to be exquisitely described.

Here, we present a case of *Phaeoacremonium griseorubrum* infection in an adult immunocompetent male and discuss the importance of morphological identification in reaching to the correct diagnosis.
gray toward the edge, and with gray woolly tufts; reverse violet-brown to reddish gray toward the edge. Colonies on Oatmeal Agar were flat, felt to powdery, and grayish orange to reddish gray.

On microscopy, the lactophenol cotton blue (LPCB) mount from colonies on PDA, revealed branched, septate hyphae occurring singly or in bundles of up to 7. Conidiophores were mostly short, occasionally branched, often constricted at the base. Phialides were terminal or lateral, mostly monophialidic. Conidia were mostly obovoidal, occasionally oblong-ellipsoidal or spherical (Fig. 3c and d). Maximum growth temperature was found to be 40°C. On this basis, the fungus was identified as *P. griseorubrum*.

The patient came to follow-up after 6 weeks. Swelling still persisted; however, it was reduced in size. Hence, he was advised surgical debridement with amphotericin B therapy.

DISCUSSION

*Phaeoacremonium* was first reported in 1974 as causing subcutaneous tissue infection [2]. They are chiefly planted pathogens, growing as endophytes infecting woody plants [3]. They are dematiaceous fungi characterized by the presence of melanin and melanin-like pigments. It has varied clinical presentations including subcutaneous infections [2,4], eumycetoma [5], osteomyelitis [6], arthritis, endocarditis, and disseminated disease-causing fungemia. Minute trauma may cause implantation of the pathogen in the body [7]. However; generally, the patient is unaware of the trauma causing subcutaneous infection. Our patient also presented as a subcutaneous infection and did not give any history of trauma.

FNAC was done and smears examined revealed septate hyphae showing branching along with inflammatory infiltrate and multinucleated giant cells. The emphasis was given on morphology of hyphae and spectrum of fungal organisms such as mucor and Aspergillus was kept in the differential diagnosis. In view of the absence of granulomas, other giant cells rich lesions such as tuberculosis, leprosy, rhinoscleroma, actinomycosis, rhinosporidiosis, sarcoidosis and granulomatosis with polyangiitis, giant cell reparative granuloma, and giant cell tumor were easily excluded. The absence of nuclear grooving was helpful in ruling out Langerhans cell histiocytosis. Aneurysmal bone cyst (ABC) was excluded as pus was aspirated in our case and smears were not bloody as in the case of ABC. Demonstration of inflammatory reaction determines that the organism represents the infection and not the contamination [8]. Similarly in our case, the presence of dense inflammatory reaction in the background suggested infection. FNAC provides a reliable generic diagnosis of inflammation and inflammatory infiltrate with foreign body giant cells with or without necrosis. Fungi may be seen intracellularly or extracellular. Special stains such as PAS and Masson Fontana (MF) further aid in the identification of fungal hyphae. Melanin pigment is highlighted on MF in dematiaceous fungi.

Fungal culture is necessary for the correct identification of the species and is aptly complemented by cytomorphology. Reliable species identification is not always immediately therapeutically essential but is vital for any detection of consistent, specific
patterns related to disease progression, treatment response, or environmental sources of infectious inoculums. Very few cases of Phaeoacremonium have been described in the literature.

Phaeoacremonium is an uncommon cause of fungal infection, and its appropriate identification may be difficult. High index of suspicion is required to diagnose the case, so that early treatment can be given to prevent complications, especially among immunocompromised individuals. An extensive search of published literature, it was revealed that only two cases of P. griseorubrum causing human infection have been reported in the past and this case is first of its kind from India. This may be attributed to the fact that majority of the species causing human infection go unreported. Although difficult, identification of different Phaeoacremonium species can be done based on cultural and microscopic features. General characters common to all Phaeoacremonium species include flat and predominantly felty colonies with wooly texture. Most of the colonies are brown in color with shades varying from pale to dark brown. Similarly, pink colored colonies vary in shades ranging from pale to dark pink. The mycelium consists of septate hyphae either single or in bundles of fascicles of 10 or fewer individual hyphae. The morphological characters that prove most useful in further distinguishing species include a combination of conidiophore morphology, phialide type and morphology, besides colony color on malt extract agar, PDA, and maximum growth temperature. Dark pink colonies on Oatmeal agar, short (0–4 septate), mostly unbranched conidiophores with constriction at the base, mostly obovoidal conidia and the maximum growth temperature of 40°C, helped identify the fungus as P. griseorubrum [3].

CONCLUSIONS

The goal of this case report is to emphasize on the early diagnosis of subcutaneous fungal infections which can be managed conservatively, preventing morbidity and mortality in these patients. Cytology being an easily available procedure can be used as initial diagnostic modality in subcutaneous and sinonasal fungal infections. Microbiology is a very useful aid in such cases. Cytology in conjunction with culture obviates the need of diagnostic biopsy and allows rapid diagnosis.

REFERENCES


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