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Case Report

Pathology Section

Pheohyphomycosis in Renal Transplant Recipient Presenting as a Rare Case of Submandibular Salivary Gland Swelling

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ABSTRACT

Renal transplant patients are at high risk of developing various infections causing morbidity and mortality. Invasive fungal infection has been recognized as a significant complication of organ transplantation. The major fungal infections in these patients are due to *candida, aspergillus* and mucormycosis. However, infection because of infrequently encountered fungi like hyaline molds, dematiaceous filamentous fungi and zygomycetes are increasing in immunocompromised hosts. Dematiaceous fungi are recognized pathogens in organ transplant recipients with skin and soft tissue infection. We report the case of a 37-year-old man, a renal transplant recipient who developed an asymptomatic dematiaceous fungal infection in submandibular salivary gland. He recovered after excision and antifungal therapy.

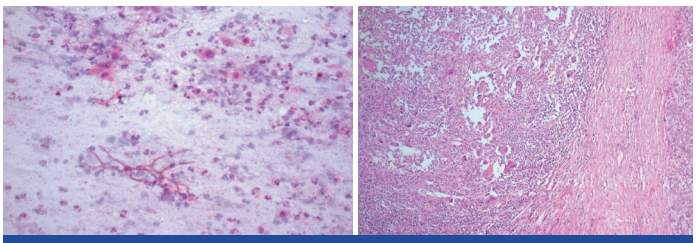
Keywords: Dematiaceous fungi, Pheohyphomycosis, Solid-organ transplantation

CASE REPORT

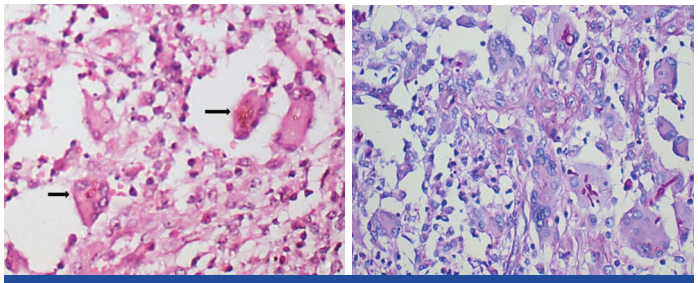
A 37-year-old renal transplant recipient underwent Live Donor Renal Transplant (LDRT) with mother's kidney in 2006. He lost this graft to chronic rejection after 2 years inspite of triple immunosuppression of Tacrolimus 0.04 mg/kg/day, Azathioprine 50 mg/day, and Prednisone 10 mg/day. He underwent second transplantation in 2009 with wife's kidney (haplo-identical). He had been maintaining stable graft function with serum creatinine around 1.4 mg/dL with the same triple immunosuppression. At 3 years post-transplant he developed Post-Transplantation Diabetes Mellitus (PTDM) with complains of dysuria and urinary retention. Ultrasonography of abdomen and MRI were suggestive of prostatic abscess. About 120ml of pus was drained out by trans-urethroscopy and was subjected to microbiological studies. *E.coli* sensitive to Meropenom and Levoflox were isolated. He was treated with these drugs.

Three months later he complained of swelling in the left sub-mandibular region. On examination a well-defined, non-tender and freely mobile lump of size 3x3cm was observed in the left submandibular region. Fine needle aspiration cytology (FNAC) showed polymorphonuclear cells, lymphoctes, macrophages and foreign body giant cells along with aseptate fungal hyphae and buds [Table/Fig-1]. Excision biopsy of tissue showed salivary glands with large number of foreign body giant cells forming granulomas, scattered areas of necrosis with nuclear debris and aseptate fungal hyphae and buds [Table/Fig-2] with haematoxylin-eosin stain and Periodic acid–Schiff stain [Table/Fig-3,4]. He was treated with antifungal agent Voriconazole.

Over a follow-up of 2 years he was asymptomatic, and had stable graft function with S.Cr of 1.35 mg/dL on Sirolimus 1 mg/day and Prednisone 5mg/day.



[Table/Fig-1]: Fine needle aspiration cytology (FNAC) showed polymorphonuclear cells, lymphocytes, macrophages and foreign body giant cells along with aseptate fungal hyphae and buds. Hematoxylin-eosin stain (H&E), 40x. **[Table/Fig-2]:** Salivary glands with large number of foreign body giant cells forming granulomas. H&E, 40x.



[Table/Fig-3]: Multinucleated giant cells (arrow) engulfing brown colour fungal elements. H&E, 40x. **[Table/Fig-4]:** Multinucleated giant cells engulfing fungal elements. Periodic acid - Schiff stain, 40x.

DISCUSSION

Transplantation, although is the most preferred therapeutic modality for patients with end organ failure, it is associated with morbidity and mortality secondary to infections and malignancy due to life-long immunosuppression. Infection after Solid-Organ Transplantation (SOT) accounts for nearly half of the deaths occurring in this group of patients in India. The spectrum of infection, their chronological occurrence and the risk factors are different from those of developed nations. Prevalence of deep tissue mycoses is 3.8% to 6.1% and is associated with nearly 70% mortality. The major fungal infections include aspergillosis, candidiasis and mucormycosis [1].

Dematiaceous fungi are being increasingly recognized as human pathogens, particularly in immunocompromised patients. Lesions could be superficial, cutaneous, subcutaneous, disseminated or invasive lesions [2,3].

Pheohyphomycosis is caused by dematiaceous fungi characterized by mycelial form with brown-black pigment, conidia or both. It should be distinguished from other specific pathological conditions associated with dematiaceous fungi which include chromoblastomycosis caused by group of fungi that produce characteristic sclerotic bodies in skin and soft tissue. Dematiaceous fungi are commonly seen in tropics as mycetoma in deep tissue infection, usually of the lower extremities characterized by the presence of mycotic granules. These fungi are found in solid and plant pathogens. Infection may follow inhalation or traumatic implantation of the fungus [2]. In recent years they have been highly recognized as important pathogens in immunocompromised individuals, and infections with these organisms have been reported in SOT recipients [4]. Underlying diabetes mellitus may also play a

role in their causation [5]. Our patient was immunocompromised as he underwent Renal Transplantation (RT) twice with Triple immunosuppression, along with development of PTDM.

Clinical presentation of dematiaceous fungal infection in SOT recipients is distinct from that of other common fungal infections like candida, aspergillus and mucormycosis encountered after transplantation. Infection by dematiaceous fungi usually occurs early in post-transplant period and presents predominantly as systemic invasive infection [6,7]. However, when it occurs late, nearly 2 years post-transplant, it usually presents as skin/soft tissue infection. Our patient presented with systemic involvement of submandibular salivary gland without involving other tissues like skin [7]. RT recipients have low incidence (1-14%) of invasive fungal infections than the liver and pancreas transplant [7,8].

Involvement of submandibular gland without any superficial or deeper tissue is very unusual. Singh et al., observed that nearly 50% of renal, 23.5% of liver and heart transplants and 3% of small bowel transplant recipients were infected by dematiaceous fungi; of these nearly 76% had skin involvement. None of the RT recipients had systemic involvement [3].

Halaby et al., reported one RT recipient with skin infection of lower extremities [9]. Maha Yahin et al., reported three cases of subcutaneous skin infection with pheohyphomycosis of lower extremities in RT recipients [10].

Dematiaceous fungi are generally highly susceptible to Intraconazole. Surgical resection is also recommended, as in our case who underwent excision under the cover of antifungal therapy.

CONCLUSION

Dematiaceous fungi are being increasingly reported as pathogens and will likely assume an important role as opportunistic pathogens in SOT recipients. Early diagnosis and prompt treatment can help in reducing the mortality rate in such cases.

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