
CASE SERIES**Phaeohyphomycosis Masquerading As Epidermal Cyst – A Diagnostic Dilemma in Immunocompetent Hosts and Review of Literature**

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Abstract:

Phaeohyphomycosis is caused by a rare dematiaceous, pigmented, mycelia forming fungi. It is an opportunistic fungal infection in immunocompromised hosts. It can present with varied clinical manifestations, as subcutaneous infection to widespread fulminant disseminated disease. Here we present three cases of subcutaneous phaeohyphomycosis in immunocompetent hosts at unusual site – popliteal fossa, great toe and sole of the foot. Awareness of unusual clinical presentation of Phaeohyphomycosis can lead to early diagnosis which may help in prevention of wide spread dissemination of disease and fatal outcome.

Keywords: Phaeohyphomycosis, Exophiala-jeanselmei, dematiaceous fungi, Itraconazole

Introduction:

Phaeohyphomycosis refers to subcutaneous or systemic infection caused by saprophytic, dematiaceous and dark walled fungi. These are naturally occurring saprobes found in soil, wood and decomposing plants. This group encompasses more than 100 species and 60 genera of fungi [1-4]. Although uncommon, they can cause life threatening infection in both immunocompetent and immunocompromised hosts [5,6]. Common etiologic agents of phaeohyphomycosis belong to genera Wangiella, Alternaria and Exophiala [3,7]. These diseases can present with varied clinical presentation ranging from skin and subcutaneous

infections to allergic diseases like bronchopulmonary mycosis and chronic allergic sinusitis, brain abscess or can occur as a fulminant disseminated disease [4-7]. Predisposing conditions favoring growth of these opportunistic yeasts and moulds are use of broad-spectrum antibiotics, adrenal corticosteroid therapy, immunosuppressive drugs for organ transplantations, and chemotherapy for cancer, prosthetic heart valves, and contact lenses. Route of entry for these dematiaceous fungi is inoculation into skin or subcutis following minor trauma [1,2].

Here we report three cases of subcutaneous phaeohyphomycosis which occurred at unusual sites– popliteal fossa, great toe and sole of foot. Because of unusual presentation these infections can be misdiagnosed. In our case they were clinically mimicking benign cystic lesion and were clinically diagnosed as benign cyst and infected dermoid cyst respectively.

Case 1

A 40-year-old female presented in orthopedic OPD with vague swelling below right knee joint in the popliteal fossa since one year. There was no history of fever, diabetes mellitus and trauma. On examination, a well circumscribed, mobile soft to firm cystic swelling measuring 3.5×2.5cm was

noted. Skin over the swelling was unremarkable and swelling was slightly tender. Excision of the lesion was done and sent for histopathological examination.

On gross examination, pale, greyish white cystic structure was noted measuring 3.5×2.5cm (Fig. 1). Cut section showed cyst wall showed focal areas of necrosis on the inner surface. Microscopic examination of H&E stained slides showed cyst wall comprised of fibrocollagenous tissue along with chronic inflammatory cell infiltrate admixed with many foreign body type of giant cells and areas of necrosis. Many narrow based, septate, filamentous, retractile and brown colored hyphae were noted amidst the mixed inflammatory cell infiltrate (Fig. 2). Few sclerotic cells phagocytosed by multinucleate giant cell suggestive of muriform cell were also noted (Fig. 3). PAS stain demonstrated PAS positive hyphae of fungus (Fig. 4).

Case 2:

A 60-year-old male patient presented to surgery OPD with chief complaints of swelling of right great toe since one year. There was no history of Diabetes mellitus, HIV, trauma, thorn prick injury or fever. On examination, 3.5×3cm swelling was present on dorsal aspect of right great toe. Excision of the lesion was done and sent for histopathological examination.

On gross examination, pale white to brown cystic structure noted measuring 3.5×3×2cm. on cut surface, pale grey areas were noted. Microscopic examination revealed fibrocollagenous tissue along with multiple irregular aggregates of brownish septate hyphal forms with constriction at the septation. Also, noted foreign body type giant cells, foamy macrophages, chronic

inflammatory cell infiltrate and cholesterol cleft at foci. Diagnosis of phaeohyphomycosis was confirmed by demonstrating PAS positive fungal hyphae.

Case 3:

A 41-year-old male patient presented to the surgery outpatient department with chief complaints of swelling on the posterior aspect of left sole since one and half year. There was no history of thorn prick injury, trauma or fever. Mild tenderness was present over the swelling. On examination, soft swelling measuring 4×2cm was noted. Swelling was not adherent to the underlying tissue. Excision of the lesion was done and sent for histopathological examination.

Gross examination of the tissue received revealed, multiple pale brown tissue bits along with a cystic structure measuring 4×2×0.5cm. Microscopic examination of the cyst wall revealed fibrocollagenous tissue showing many ill formed granulomas, aggregates of foamy macrophages, lymphocytes, foreign body type and Langhans type of multinucleate giant cells along with central areas of brownish necrotic debris showing pigmented filamentous hyphae. Diagnosis of phaeohyphomycosis was made by demonstration of filamentous pigmented hyphae on PAS stain.



Fig. 1: Pale Brown Cystic Structure

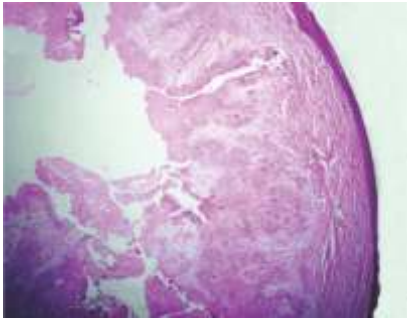


Fig.2: Cyst Wall Lined by Fibrocollagenous Tissue [H&E, 40X]

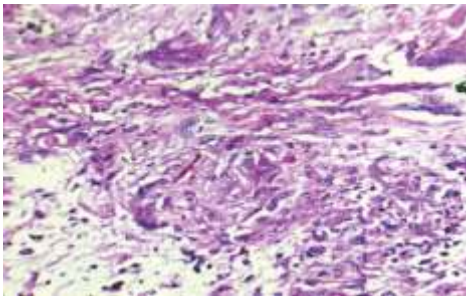


Fig.3: Photomicrograph showing Narrow Based, Septate, Filamentous, Refractile and Brown Colored Hyphae [H&E, 40X]

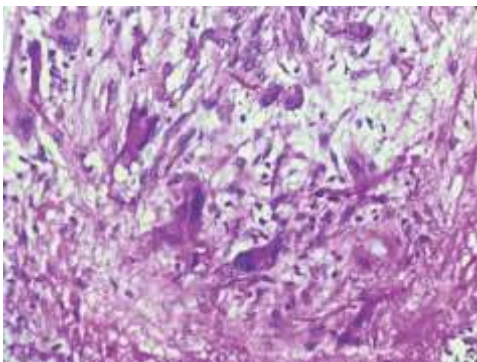


Fig.4: Photomicrograph showing PAS positive Fungus Hyphae [PAS, 400X]

Discussion:

The term phaeohyphomycosis was coined by Ajello *et al.* in 1974 for melanin containing filamentous fungi [1,8]. Incidence of phaeohyphomycosis was reported as 1:1, 00,000 /year

in a study conducted by Rees *et al.* [9]. A study conducted by Ben-Ami *et al.* showed increased incidence rate of phaeohyphomycosis from 1.0 to 3.0 cases per 1, 00,000 patients/year during the study period from 1989 to 2008 [5].

This infection is caused by inhalation and exogenous inoculation at the site of minor trauma. The infection from skin or subcutaneous site can disseminate to other sites/organs [1-5]. The melanin produced by this fungus acts like a virulence factor, which evades host immune system by scavenging free radicals and hypochlorite, also it inhibits enzyme production by phagocytes. Due to this reason these fungi can cause infection in immunocompetent hosts [4, 3]. As these are opportunistic fungi, clinical outcome depends on the immune status of the host. In immunocompetent host, presentation is more of chronic, localized and superficial with subcutaneous cyst formation, while, deep seated, extensive, and disseminated and life threatening mode of presentation is seen in immunocompromised patients [8].

In the study done by Severo *et al.* out of 18 patients 12 patients had immunocompromised history while in 4 cases Phaeohyphomycosis was noted in immunocompetent patients [10]. In our study all 3 patients were immunocompetent and there was no history of Diabetes mellitus, HIV or immunosuppressive therapy.

Exophiala jeanselmei species are the most common etiological agent for cutaneous or subcutaneous cyst or abscess formation in immunocompetent host, resulting from direct inoculation following trivial trauma [7, 10, 11, 12]. Morphologically these may present in varied forms like pigmented or non-pigmented, septate, irregular branching hyphae, short hyphal segments and occasionally chlamydoconidia like structures [1, 3,

5, 7]. The differential diagnosis for pigmented fungi is chromoblastomycosis and eumycotic mycetoma. In former, black, pigmented sclerotic bodies are diagnostic along with muriform cells with septation along one or two planes in different levels, whereas, in mycetoma, micro-colonies of hyphae in the shape of grains are seen in the tissue [10].

Diagnosis of subcutaneous phaeohyphomycosis is made based on demonstration of pigmented fungi by careful histopathological examination, special stains like PAS and Gomori methenamine silver stain and culture. Phaeohyphomycosis can be treated by different antifungal agents like flucytosine, ketoconazole, itraconazole and fluconazole [7, 11, 13]. In two cases, following

surgical excision, treatment with oral itraconazole was given for 1 month and 6 months follow up showed no remission. In second case patient was lost for further follow-up.

Conclusion:

Differential diagnosis of phaeohyphomycosis should be kept in mind for adult patient, irrespective of immune status, presenting as lower limb subcutaneous cyst or nodule with or without history of prior trauma. Rarity of this disease, can lead to misdiagnosis and if untreated it may advance to fatal outcomes such as wide spread fulminant/disseminated disease especially in immunocompromised patients.

References

1. Ajello L, Georg LK, Steigbigel RT, Wang CJ. A case of phaeohyphomycosis caused by a new species of *Phialophora*. *Mycologia* 1974; 66(3):490-8.
2. Ajello L. Hyalohyphomycosis and phaeohyphomycosis: two global disease entities of public health importance. *Eur J Epidemiol* 1986; 2(4):243-51.
3. Jakkan MS, Agashe VM, Soman R, Almeda A. Subcutaneous Foot Phaeohyphomycosis due to *Alternaria alternata*. *J Foot Ankle Surg (Asia-Pacific)* 2015; 2:44-6.
4. Revankar SG. Dematiaceous fungi. *Mycoses* 2007; 50(2):91-101.
5. Ben-Ami R, Lewis RE, Raacl II, Kontoyiannis DP. Phaeohyphomycosis in a tertiary care cancer center. *Clin Infect Dis* 2009; 48(8):1033-41.
6. Revankar SG. Phaeohyphomycosis. *Infect Dis Clin North Am* 2006; 20(3):609-20.
7. Silveira F, Nucci M. Emergence of black moulds in fungal disease: epidemiology and therapy. *Curr Opin Infect Dis* 2001; 14(6):679-84.
8. Kathiah R, Selvakumar S, Sundaram KM, Rajalakshmi V. Phaeohyphomycosis, Emerging as a common cause of Diagnostic Dilemmas. *Int J Med Health Sci* 2014; 3(2):150-2.
9. Rees JR, Pinner RW, Hajjeh RA, Brandt ME, Reingold AL. The epidemiological features of invasive mycotic infections in the San Francisco Bay area, 1992-1993: results of population-based laboratory active surveillance. *Clin Infect Dis* 1998; 27(2):1138-47.
10. Severo CB, Oliveira F de M, Pilar EFS, Severo LC. Phaeohyphomycosis: A clinical-epidemiological and diagnostic study of eighteen cases in Rio Grande do Sul, Brazil. *Mem Inst Oswaldo Cruz* 2012; 107(7):854-8.
11. Sadigursky D, Nogueira e Ferreira L, Moreno de Oliveira Corrêa L. Phaeohyphomycosis infection in the knee. *Rev Bras Ortop* 2016; 51(2):231-4.
12. Rossetto AL, Dellatorre G, Pêrsio RA, Romeiro JCDM, Cruz RCB. Subcutaneous phaeohyphomycosis on the scrotum caused by *Exophiala jeikei*: case report. *An Bras Dermatol* 2010; 85(4):517-20.
13. Kathiah R, kumar S, Sundaram KM, Rajalakshmi V. Phaeohyphomycosis, Emerging as a common cause of diagnostic dilemmas. *Int J Med Health Sci* 2014; 3(2):150-2

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