

Original article:

Phaeohyphomycosis: Clinical, Epidemiological and Mycological profile in a tertiary care hospital from western Maharashtra

Dr Ashwini Dedwal*, Dr Swati Mudshingkar, Dr Sunil Bhamare, Dr Rajesh Karyakarte

Dept. of Microbiology, B.J. Govt. Medical College, Pune, Maharashtra, India

Corresponding author*

Abstract:

Phaeohyphomycosis is a disease caused by melanin producing fungus. A total of 150 samples were collected from patients suspected of phaeohyphomycosis. Processing was done as per standard mycological protocol. 15 samples (10%) showed growth of dematiaceous fungi with 10 (66.7%) correlation in direct smear and culture findings. *Exophiala spp.* (*Exophiala dermatitidis* and *Exophiala jeanselmei*) were most commonly isolated dematiaceous fungi (26.7%) followed by *Fonsecaea pedrosoi* (20%), *Cladosporium cladosporoides* (20%), *Alternaria spp.* (20%), *Phaeoacromonium spp.* (6.7%), *Cladophialophora bantiana* (6.6%). The incidence of dematiaceous fungi is increasing because of various empirical immunosuppressive interventions. Thus, isolation of fungi should be attempted when suspected and clinicians should be alerted on isolation and identification. The present study reiterates this fact and shows that prompt appropriate treatment by surgical excision alone or combined with azoles reduces morbidity.

Introduction

Phaeohyphomycosis is an uncommon fungal infection of skin and subcutaneous tissue caused by dematiaceous fungi or phaeoid fungi producing melanin giving brown pigmented hyphae and growth on culture commonly called as black fungus. Phaeohyphomycosis (from the Greek *phaios*, meaning dark) is a term coined by Ajello *et al.* [1-3] It is a mycotic disease caused by melanin containing fungus, characterized by the presence of phaeoid or dematiaceous (dark-walled) septate hyphae, pseudohyphae and sometimes yeast or a combination of all these in tissue. [2,3]

Clinical forms of phaeohyphomycosis varies from localized infections involving the skin and subcutis to invasive lesions involving paranasal sinuses, eyes, bones or central nervous system. Subcutaneous phaeohyphomycosis can clinically present as papulonodules, cysts or abscesses. In India, commonly associated genera with phaeohyphomycosis are *Exophiala*, *Phialophora*, *Cladosporium*, *Curvularia*, *Fonsecaea* and *Alternaria*. [4-6] It is a saprophyte found in soil, wood and plant material in tropical and subtropical areas. Subcutaneous infections usually occur following the traumatic implantation of fungal elements from contaminated soil, thorns or wood splinters.

Infection is more common in immunocompromised patients, very rarely in immuno-competent patient. Recently incidence of phaeohyphomycosis has increased due to increase in immunocompromised patients [2]. Superficial cutaneous and corneal manifestations of the mycosis are more frequent and develop among healthy

individuals. Cutaneous and systemic phaeohyphomycosis occur in immunocompromised patients. The laboratory diagnosis is first based on the morphological characteristics of the agents as observed by direct microscopic examination, culture on Sabouraud's dextrose agar and histopathologically, the lesions show brown-walled septate hyphae or yeast or a combination of both in tissue.

Data regarding this infection is scarce and in the form of case reports. This study was planned by considering the rarity of this mycosis which warrants describing the clinical, epidemiological, Mycological (diagnostic) and treatment outcome. This will aid in its immediate recognition and early treatment with reduced morbidity.

Material and Methods:

The present study was conducted over a period of 1.5 years (August 2018- January 2020). This was a prospective laboratory based study. A total of 150 samples were collected from patients suspected of phaeohyphomycosis from dermatology department of a tertiary care hospital. The clinical details like sex, age, race, predisposing diseases, anatomical location and time elapsed between the manifestation of the disease and its diagnosis were obtained from the clinicians/ patients.

Microbiological processing was done as per standard mycological protocol in mycology section of Microbiology department. The direct examination of the tissue fragments was performed by mounting and clarification in a solution of by 10% potassium hydroxide observed under microscope and findings of direct KOH mount recorded, and then some sample was streaked on Sabouraud's Dextrose Agar (SDA) medium with and without antibiotics at 37⁰ C and 25⁰ C. Once the growth was obtained on SDA, the macroscopic examination identified colony morphology varying from yeast-like to velvety (depending on the species) and olive-brown to black, when incubated at 25°C in Sabouraud agar with or without antibiotics. The cultures were maintained from two-four weeks. For the examination of microscopic morphology, the isolates were submitted to cultures in blades using potato agar (slide culture) was further identified by microscopically by LPCB (Lacto Phenol Cotton Blue) mount examination. The identification of genus and species was based on various morphological characteristics.

Results:

A total of 150 samples were collected from patients suspected of Phaeohyphomycosis from dermatology department of a tertiary care hospital. The clinical details like sex, age, race, predisposing diseases, anatomical location and time elapsed between the manifestation of the disease and its diagnosis were obtained from the clinicians/ patients.

Table 1 The distribution of samples collected from Phaeohyphomycosis cases was as follow (n=150)

Sample (N=150)	No	%
Skin biopsy	60	40%
Nasal biopsy/scrapings	38	25%
Corneal scraping	20	13%
Skin scraping	15	10%
Nail clipping	10	7%
Discharging grains	5	3%
Submandibular abscess	2	1%
Total	150	

Incidence of Phaeohyphomycosis was more common at average age of 45 years with age ranging from 11 to 71 years. Infection was more common in males 10 (66.7%) of cases and in females 5 (33.3%). Clinically 10 (66.7%) of cases showed some kind of immunosuppression.

Table 2 The distribution of samples culture positive from Phaeohyphomycosis cases (n=15)

Sample (n=15)	No	%
Skin biopsy	7	46.7 %
Nasal biopsy/scrapings	1	6.7 %
Corneal scraping	1	6.7 %
Skin scraping	1	6.7 %
Nail clipping	2	13.3 %
Discharging grains	2	13.2 %
Submandibular abscess	1	6.7 %
Total	15	

Out of 150 samples 15 samples (10%) showed growth of dematiaceous fungi. When we compared direct smear and culture findings it showed correlation in 10 (66.7%) of cases, out of 15 samples which showed growth in 10 cases direct KOH mount showed fungal filaments.

Table 3: Commonly isolated dematiaceous fungi isolated from suspected Phaeohyphomycosis cases

Dematiaceous fungi (n=15)	Sample	No	%
<i>Exophiala</i> spp (<i>Exophiala dermatitidis</i> 2 and <i>Exophiala jeanselmei</i> 2)	Biopsy tissue, Submandubular abscess	4	26.7 %
<i>Fonsecaea pedrosoi</i>	Sinus biopsy, Biopsy tissue,	3	20 %
<i>Alternaria alternaria</i>	Grain, Biopsy tissue, Skin scraping	3	20 %
<i>Cladosporium cladosporoides</i>	Granules from sinus, Nail clipping, Corneal scraping	3	20 %
<i>Phaeoacremonium</i> spp	Skin biopsy	1	6.7 %
<i>Cladophialophora bantiana</i>	Nail clipping	1	6.6 %
Total		15	

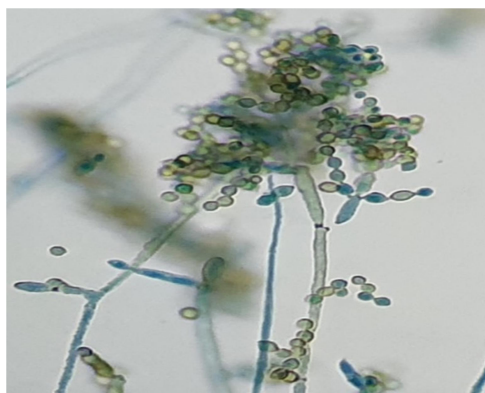


Figure no 1: *Fonsecaea pedrosoi* produces septate, dark brown hyphae with pale brown, erect, septate conidiophores branching at apices and conidia are brown and barrel-shaped



Figure no 2: *Exophiala dermatitidis* produces septate, branched hyphae with poorly differentiated conidiogenous structures present with numerous oval conidia piled up at the edge.

Discussion:

Phaeohyphomycosis, chromoblastomycosis and mycetoma are three types of mycosis caused by dematiaceous fungi. Phaeohyphomycosis is a rare cutaneous, subcutaneous or systemic infection that contains brown pigmented mycelial elements in tissue, which differs from the chromoblastomycosis and mycetoma by absence of sclerotic cells and grains.[3,7] These fungi are often found in soil, wood and plant as saprophytes in tropical and subtropical areas. It is more commonly found in northern and southern part of India, which provide ideal environment for their growth. Northern and Southern part of India has ideal environment for these type of fungi thus these infections are commonly found in this areas.

In India 18 cases of subcutaneous Phaeohyphomycosis have been reported affecting various body parts.[8] In the present study we could identify 15 culture positive cases of Phaeohyphomycosis from different samples collected from 150 suspected patients. Phaeohyphomycosis is caused by brown pigmented fungi having melanin in their cell walls. Melanin acts as a virulence factor because of its scavenging effects over free radicals and hypochlorite's produced by phagocytic cells, and moreover it binds to hydrolytic enzymes. This may be the explanation for infection in immunocompetent hosts.[9] Mode of transmission of infection is usually trauma by vegetative mater. In the present study also the most common mode of transmission was trauma by vegetative matter (in 60% of patients). In many of the cases, presumed source of infection is due to inoculation of fungus by some kind of trauma by vegetative matter or some road traffic accidents. Many showed Delayed presentation of symptoms due to dormant infective nidus under the grafted wound which overtime went on to become symptomatic. There are other cases in literature suggesting similar sequence of events. A case report by Kaell et al. had mentioned a case where a patient had a glass injury to the knee in childhood and several years later, this nidus was likely a source of the acute fungal arthritis observed in this case (*Phaeoacremonium parasiticum*).[10] Since it is a ubiquitous fungus

with increasing incidence after trauma, it should also be remembered that it is often misdiagnosed as carcinomatous non healing ulcer.

The diagnosis of Phaeohyphomycosis primarily depends on careful examination of lesions on direct KOH examination and after that on culture by doing LPCB mount, pathological examination.

In the present study *Exophiala* (*Exophiala dermatitidis* and *Exophiala jeanselmei*) were most commonly isolated dematiaceous fungi(4) followed by *fonsesea pedrosoi*(3), *Cladosporium cladosporoides*(3), *alternaria spp*(3), *phaeoacromonium spp*(1), *cladophialophora bantiana*(1). In a study by Varun Sundaramoorthy et al,¹² *Cladophialophora bantiana*, *Cladosporium cladosporoides*, *Cladosporium sphaerospermum*, *Phialophora oxyspora*, and *Exophiala spinifera* fungi were isolated. The European society of Clinical Microbiology and Infectious diseases recommends Itraconazole, Voriconazole and Posaconazole as common treatment options (11). In the present study, Itraconazole was commonly given with improvement in conditions for superficial infections. In deep seated infections along with Itraconazole, Voriconazole with local surgical debridement was offered with no recurrence rate.

Conclusion:

Phaeohyphomycosis infections are increasing now days due to increased interventions leading to immunosuppression of some or other kind, thus Phaeohyphomycosis should be considered in the differential diagnosis. Standard fungal identification methods are still common modalities to diagnose Phaeohyphomycosis infection. Azoles are the drug of choice with some other combinations to treat dematiaceous infections. Further studies are suggested to look for commonly isolated fungi and to identify different treatment modalities in disseminated infections.

References:

1. Ajello L, Georg LK, Steigbigel RT, Wang CJ. A case of phaeohyphomycosis caused by a new species of Phialophora. *Mycologia* 1974;66:490-8.
2. Kwon-Chung KJ, Bennett JE. Phaeohyphomycosis. In: Kwon, Chung KJ, Bennett JE, editors. *Medical mycology*. Philadelphia: Lea and Febiger 1992; p. 620-77.
3. Rossmann SN, Cernoch PL, Davis JR. Dematiaceous fungi are increasing cause of human disease. *Clin Infect Dis* 1996;22:73-80.
4. Sharma NL, Mahajan V, Sharma RC, Sharma A. Subcutaneous phaeohyphomycosis in India – A case report and review. *Int J Dermatol*. 2002;41(1):16-20.
5. McGinnis MR. Chromoblastomycosis and phaeohyphomycosis. New concepts diagnosis and mycology. *J Am Acad Dermatol* 1983; **8**: 1–6.
6. Murray, P., K. Rosenthal and M. Pfaller, 2012. *Opportunistic Mycoses: Phaeohyphomycosis*. Murray: Medical Microbiology, 7th Edn., Elsevier Health Sciences, London, pp: 694-9
7. Fader RC, McGinnis MR. Infections caused by dematiaceous fungi: Chromoblastomycosis and phaeohyphomycosis. *Infect Dis Clin North Am* 1988;2:925-38.
8. Kiran Kumar K, Kaveri Kallekeri. Phaeohyphomycosis. *Indian J Pathol Microbiol* 2008;51:556-8.
9. Revankar SG. Phaeohyphomycosis. *Infect Dis Clin North Am* 2006;20:609-20.
10. Kael AT, Weitzman I. Acute monoarticular arthritis due to Phialophora parasitica. *Am J Med* 1983;74:519-22.

11. Chowdhary A, Meis JF, Guarro J, et al; European Society of Clinical Microbiology and Infectious Diseases Fungal Infection Study Group; European Confederation of Medical Mycology. ESCMID and ECMM joint clinical guidelines for the diagnosis and management of systemic phaeohyphomycosis: diseases caused by black fungi. Clin Microbiol Infect 2014; 20 (Suppl 3):47–75.
12. Varun Sundaramoorthy, General Medicine, Frederico Duarte, General Medicine, Promila Mohan Raj, Joy S Michael, and Priscilla Rupali. Phaeohyphomycosis: A 10-Year Review (2006–2016). Open Forum Infect Dis. 2017 Fall; 4(Suppl 1): S86.

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