ORIGINAL RESEARCH PAPER

Volume-7 | Issue-7 | July-2018 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

KERATOMYCOSIS CAUSED BY PIGMENTED FUNGI

Ophthalmology

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ABSTRACT

Keratomycosis is a major cause of blindness, especially in the developing world. A major proportion of these are caused by fungi, of which pigmented fungi is a good number. Pigmented fungal corneal ulcers may present with surface pigmentation, helping in diagnosis but the presumptive treatment is usually started after evaluation of smears made from scrapping samples. Aggressive treatment with topical anti-fungals help accelerated healing in most of them but few still worsen and need therapeutic keratoplasty. In this study, we evaluated the cases of pigmented Keratomycosis presenting in a tertiary care center for various factors like demographic details, risk factors, clinical characterstics, response to treatment and prognosis.

KEYWORDS

fungal keratomycosis, fungal corneal ulcers, pigmented fungal corneal ulcers, *Curvularia*, pigmented keratomycosis

Introduction

Corneal ulcer is a major cause of corneal blindness. Fungal keratitis represents 30 to 40 % of all culture positive infections.[1] Fungal corneal infections are higher in tropical and semitropical areas. These infections follow trauma, especially with vegetative matter. Filamentous fungi are the most common causative organisms. A convenient method of classifying fungal isolates has been reported in the ophthalmic literature. It includes four diagnostic/laboratory groups: yeasts which include *Candida* spp.; filamentous septated fungi, which include both nonpigmented hyaline hyphae (*Fusarium* spp. and *Aspergillus* spp.) and pigmented dematiaceous hyphae (*Alternaria* spp. and *Curvularia* spp.); filamentous nonseptated fungi, which include *Mucor* spp.; and other fungi. Fusarium and Aspergillus sp are the most common organisms followed by pigmented fungi. Curvularia species are dark pigmented soil fungi and are the most predominant cause of pigmented keratomycosis[2].

Table 1: Classification of fungi

Yeast	Filamentous septated	Filamentous nonseptated
	***Nonpigmented hyphae* (*hyaline*)**	
Candida species *albicans, parapsilosis, krusei, tropicalis, guillermondii* *Trichosporonbeigelii* *Pichiaohmeria* *Cryptococcus uniguttulans* *Malassezia restricta* *Blastoschizomy cescapitatus*	*Fusarium* species*solani, oxysporum, moniliforme, episphaesia* *Aspergillus* species*fumigatus, flavus, terreus, glaucus, niger* *Acremonium* species *Cylindocarpon* species *Paecilomyces* species *Scedosporiumapiosperum*(*Pseudoallescheriaboydii*) *Trichophytonmentagrophytes* *Arthrographiskalrae* *Beauveriabassiana*	*Mucor* species*Rhizopus* species
	***Pigmented hyphae*(*dematiaceous*)**	
	Alternaria species *Curvularia* species *senegelensis, verruculosa* *Cladosporium* species *Colleotricum* species *dematium, gloeosporoides* *Exopiliaphilophora* *Histoplasma capsulatum* *Lasiodiplodiathreobromae* *Scytalidium* species	

The purpose of this study was to analyze the risk factors, clinical features, response to treatment and prognosis of this group of fungal keratitis.

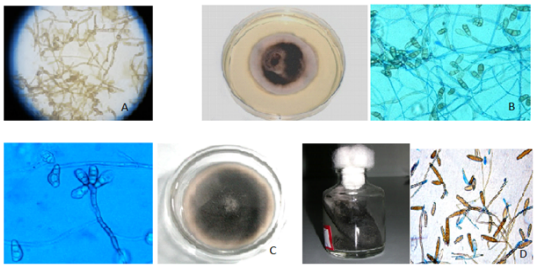
Materials and methods

All patients having infectious keratitis in the period January 2014 to December 2017 were analysed. Patients with culture proven fungal keratitis were included in the study. The analysis was based on demographic features like age, sex and occupation. Risk factors like diabetes, steroid use or immunosuppression, trauma and the traumatic agent were documented. Prior therapy such as native treatment (unhygienic methods of foreign body removal, use of unproven native treatment), antibiotics, antifungal, steroids was also noted. The size of ulcer, depth of stromal infiltrate, presence of hypopyon, and presence of pigmentation were assessed on slit lamp evauation.

Corneal scrapping samples were evaluated with Gram's stain and in KOH mount. For culture, samples were inoculated in blood agar and Sabaraud's dextrose agar. Cultures were considered significant if there was confluent growth at the site of inoculation, and if it corresponded to the direct microscopic findings. The growth was identified by colony morphology and microscopic appearance fungal hyphae and conidia in lactophenol cotton blue mount. The isolate was considered dematiaceous, if fungal colonies were pigmented-black or brown and lactophenol mount showed pigmented hyphae and conidia.

All patients were started initially on hourly use of topical 5% Natamycin eyedrops and 1% Voriconazole eyedrops. Patients were reviewed at regular intervals (based on severity of ulcer) and treatment was modified or tapered based on the response. Cure was defined as healing of the epithelium and early scar formation (absence of infiltrate, absence of anterior chamber reaction, vascularisation. Time taken for initial healing response was noted. Therapeutic keratoplasty was advised in cases which did not respond to medical management or worsened to the stage of impending or frank perforation.

Figure 1: A. KOH mount showing pigmented fungal filaments, B. *Bipolaris sp*. (on culture medium and lactophenol cotton blue), C. *Curvularia sp*. (lactophenol cotton blue staining and appearance on culture medium), D. *Exserohelium sp*. (colony morphology and appearance on lactophenol cotton blue)



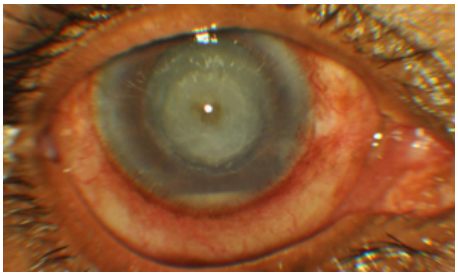
Results

In the study period of 3 years, 267 cases were culture positive for fungi and of these, 58 were caused by pigmented fungi. Most of the patients with pigmented fungal ulcers were in the age group of 41 to 60 years and 37 out of 58 were male patients. Trauma (62.5%) with organic matter, and soil were the most common predisposing factor and 86% (50/58) were actively involved in farming. Most of the patients presented within 2 weeks of the illness. 65 % (38/58) of the patients had some form of previous treatment before presenting to our hospital (mostly antibiotics). Only 2 patients were diabetics and 3 patients were using topical steroids. None of them had used native treatment.

Table 2: Age distribution of patients with pigmented fungal corneal ulcers

Upto 20 years	2
21 to 40	12
41 to 60	32
61 to 80	12

Figure 2: Fungal corneal ulcer with surface pigmentation



All patients had symptoms of redness, watering, photophobia, and decreased vision of variable severity at initial examination. At the time of presentation 31 out of the 58 cases had unaided vision of 6/24 and better, 20 patients were able to 3/60 and less. All the patients had clinical picture of yellow white, dry raised infiltrate with feathery hyphate margins. The stromal infiltrate size varied from 3 mm to 9 mm with 22 patients having more than 5mm diameter stromal infiltrate at presentation. 6 patients had severe stromal thinning at presentation and were advised therapeutic keratoplasty. One patient had a foreign body (paddy) in the cornea, which grew Bipolaris sp. on culture. Another patient had an infected bandage contact lens. The characteristic pigmentation of the corneal ulcer was noted in 35% of the cases. 19 cases had hypopyon at initial visit.

Septate branched filaments were identified on microscopy either in KOH smear and Gram's staining in all 58 cases. *Curvularia sp*. (26 cases) was the most common fungus followed by *Bipolaris sp*.(21), *Exserohilum sp*.(8), *Alternaria* (1) and unidentified dematecious fungi (2).

Treatment was started with topical 5% Natamycin drops, 1% Voricanozole drops , Itraconazole ointment, atropine eye ointment, antiglaucoma medications. Systemic antifungal like fluconazole were started based on response during follow up. The average duration of treatment (early scar formation) was 21 to 30 days. 42 patients resolved well with medical management, 3 needed anterior chamber wash with intra-stromal and intra-cameral voriconazole injection, 8 needed therapeutic keratoplasty. 5 patients were lost to follow-up.

Discussion

In our study, non-pigmented fungi were the most common (67%) etiologic agents of keratomycosis. Pigmented fungi form the second largest group (30%). This is similar to the previous reports on the incidence of corneal infections. Sengupta et al [3] reported 31.37% of pigmented keratomycosis, Garg et al [4] reported 15%, Bharathi et al[5] showed 25% from south India, and Chowdhary et al[6] reported 29% incidence of Curvularia keratitis from North India.

Most of our patients belonged to rural community and involved with agricultural work. This means more exposure to the soil fungus Curvularia. Though from rural background, none of them were on native medicines. Most of them had sought some form of medical consultation before consulting us. Patients who had presented early had better visual acuity and responded to therapy better. Those with advanced stage of presentation did not respond well and had to undergo therapeutic graft.

The characteristic clinical pigmentation was seen in 20 out of the 58 patients. This is much higher from what was reported by Sengupta et al[3] (14.5%), Garg et al[4] (27%). Presence of pigmentation is an easy way of identifying this group and we can start early multidrug treatment. The clinical significance of macroscopic pigmentation as a potentially helpful sign for the diagnosis of keratitis of dematiaceous fungal cause was earlier put forward by Berger et al[7]. Only dematiaceous fungi cause such pigmentation and it can be concluded that in the presence of pigmented infiltrate, the ophthalmologist could promptly start anti-fungal therapy. This information is useful to ophthalmologists treating cases of infectious keratitis on an empirical basis.

Amongst the pigmented fungi, Curvularia sp. was the predominant pathogen. This is very similar to the other studies.[3,4] All patients were started on 5% natamycin suspension at hourly frequency and 1%voricanazole eye drops hourly, and itraconazole eye ointment at night. 77.5 % of our patients responded well, suggesting that use of multidrug treatment hastened recovery. In the previous studies, natamycin alone was the first line of treatment, and newer drugs like voricanazole was not used.

In conclusion, pigmented fungi are emerging significant pathogens in keratomycosis. Prompt multi drug therapy accelerates recovery and results in better prognosis.

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