

Clinical study and management of the fungal corneal ulceration

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Background: The corneal infection of fungal etiology is very common and comprising at least 50% of all culture-positive cases in India. Diagnosis and treatment of fungal corneal ulcers can be quite challenging because of the delay in seeking medical attention due to reduced symptoms in mycotic corneal ulcer and the limited antifungal agents available for ocular use and the deeper extent to which they can penetrate the corneal tissue. **Materials and Methods:** A study of 80 cases of fungal corneal ulcers was conducted in General Hospital attached to Medical College. A detailed history was taken and a thorough ocular and systemic examination were done. Microbiological work-up of corneal scrapings was done in all patients. All patients were given necessary topical and systemic antifungal drugs, antiglaucoma drugs, cycloplegics, and surgical treatment wherever needed by different consultants and followed up for a period of 8 weeks. **Results:** At the time of presentation 45% of patients had received different medications especially without microbiological workup. All patients were KOH positive and among them, 65% were culture positive. Different topical treatment combinations were used among them natamycin 5% suspension was used in all patients. Therapeutic penetrating keratoplasty and the conjunctival flap was done in one patient each. **Conclusion:** Agricultural activity and vegetative matter trauma was the commonest predisposing factor. Following treatment 77.5% ulcers healed with a visually significant corneal opacity, 20 % had perforation all of which were ulcers with full-thickness corneal involvement. In one non-healing ulcer penetrating keratoplasty was done.

Keywords: Cornea, Fungal Infection, Surgical therapy, Corneal Ulcer, Clinical study

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Introduction

The cornea is the principal refractive surface of the human eye and along with sclera forms the outermost coat of the eyeball. It constitutes up to one-sixth of the entire eyeball. Corneal ulceration occurs due to the host cellular and immunologic responses to

The offending agent which may be bacterial, viral, fungal, or protozoal organisms [1]. Sometimes it is sterile corneal ulceration, which may occur due to systemic dermatologic or connective tissue disease and chemical or thermal injuries. Blindness due to corneal infections is a serious problem next to cataract and fungal infections of the cornea have emerged as a major eye disease

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Globally. The corneal infection of fungal etiology is very common and comprising at least 50% of all culture-positive cases in India [2].

Compared with another infectious keratitis, fungal keratitis has a poor prognosis, due to not only the lack of effective treatment drugs and methods but also that fungi are different from other pathogens in pathogenesis. Prevention, early diagnosis, and early treatment of fungal keratitis can undoubtedly improve the curative effect and the prognosis of patients, and reduce the blindness rate [3,4].

Corneal blindness is responsible for 1.5 to 2 million new cases of monocular blindness every year in which ocular trauma and corneal ulceration are significant contributors. In a vast agricultural country like India, particularly where primary health care and referral systems are weak, minor eye injuries sustained in agricultural farms often lead to corneal ulceration of fungal etiology and loss of vision. The reported incidence of corneal ulceration in India is 1130 per million populations [5].

In the tropical countries, the commonest fungus is filamentous like *Aspergillus*, *Fusarium*, in temperate countries yeast fungus like *Candida* is common. Fungal pathogens also enter the cornea after an epithelial breach, following trauma or foreign body in the form of vegetative material or soil particles and after invasion incite a host inflammatory response [6].

The inflammatory response is less aggressive and slow compared to bacteria. The fungus secretes proteolytic enzymes and fungal antigens and toxins which facilitates their deeper stromal penetration and breach the descemet's membrane and thereby reach the anterior chamber where it forms a fungus-exudate-iris mass covering the pupillary area [6].

Diagnosis and treatment of fungal corneal ulcers can be quite challenging because of the delay in seeking medical attention due to reduced symptoms in mycotic corneal ulcer and the limited antifungal agents available for ocular use and the deeper extent to which they can penetrate the corneal tissue [7,8].

Isolation of the causative fungus from corneal ulcer takes weeks and thus the treatment cannot be dependent on the culture report in the majority cases. Hence, the treatment given is based on clinical diagnosis supported by detecting the presence of the fungus in KOH mounting/Giemsa

stain rather than on culture report; and a standard antifungal treatment protocol is followed in management [7]. Hence the present study is an attempt to study the clinical features, diagnosis, and management of fungal corneal ulcers.

Materials and Methods

Source of Data: The included patients were the patients attending the outpatient department of the Ophthalmology at the general hospital attached to the medical college. The totals of 80 patients diagnosed with the fungal corneal ulcers were included in the study. The college institutional ethical committee was informed about the study and the ethical clearance certificate was obtained from them before starting the study.

Inclusion criteria: A total of 80 cases diagnosed with fungal corneal ulcers were included in the study. All the patients who attended the outpatient department of the Ophthalmology were included in the study.

Exclusion criteria: all those patients who were non-complaints, not available for follow up were excluded from the study. Detail history of all the patients was recorded followed by a detailed clinical examination as per the decided proforma. For the better follow up the patients were advised to get admitted to the hospital. Examination of the anterior segment and corneal ulcer was done in detail with the help of a slit lamp biomicroscope. The sample for microbiological investigations was obtained by corneal scrapings. The cornea was anesthetized using 0.5% proparacaine solution and scraping was done using a sterile No. 15 Bard-Parker blade from the margins of the corneal ulcer.

The following microbiological investigations were done immediately:

01. Gram's stain
02. 10% KOH preparation
03. Bacterial culture using blood agar and chocolate agar. Sensitivity was done using the disc diffusion method if organisms were isolated.
04. Fungal culture was done using Sabouraud's dextrose agar medium. Culture reports were declared negative at the end of 14 days.

Management of the patients proceeded on an urgent basis and broadly classified as

01. Medical
02. Surgical

Medical management: After obtaining the reports of positive 10% KOH preparation, topical antifungal drugs like natamycin 5% eye suspension, fluconazole 0.3% eye drops were used hourly for the first 48 hours and then decreased to 2nd hourly. Initially, only natamycin suspension was used if the smear showed the presence of septate hyphae, and the response was noted. If the smear showed pseudohyphae then fluconazole eye drops were also added. In some cases which were not responding to natamycin alone, fluconazole eye drops were added. Topical therapy was continued at least 3rd hourly for at least 2 weeks after healing of the ulcer.

Along with the above drugs, topical cycloplegic like atropine 1% eye drops were used initially 8th hourly and then tapered according to the response. Antiglaucoma medications like topical timolol maleate 0.5% eye drop and acetazolamide 250 mg tablets were prescribed wherever necessary. In some cases, topical antibacterial drops like moxifloxacin 0.3% were used on the basis of Gram's stain report showing evidence of bacterial infection also.

Systemic antifungal therapy was used in corneal ulcers with deep stromal involvement, ulcers extending to the limbus, or any evidence of anterior chamber involvement. Fluconazole 200 mg tablets were given twice a day for at least a period of 15 days. Before starting systemic fluconazole liver function tests were done. Supportive therapy like vitamin A capsules (5000 IU per day) was given.

Surgical Management

01. Debridement of the ulcer: This procedure was performed under topical anesthesia on a slit lamp using Bard-Parker blade No. 15. This was done daily to help better penetration of drugs until the ulcer showed a decrease in infiltration.
02. Conjunctival Flap: The technique used was Gunderson's total conjunctival flap. It was done in one case of non-healing ulcers with small perforation.
03. Therapeutic penetrating keratoplasty: It was done in case of nonhealing ulcers after adequate medical therapy for a period of four weeks. Along with the surgical mode of treatment, the necessary antifungal, antiglaucoma, and cycloplegics were continued. The patients were examined on days 1, 2, 3, followed by the first, second, third, fourth, fifth, and sixth week. At each follow-up ulcer, details and visual acuity was recorded.

Results

A total of 80 patients were included in the study. The following observations were done and the results were obtained. The majority of patients were in the age group of the working population i.e., from 21 -65 years. It was least in very young and old patients. The majority of the patients in this study were male (58) and the rest of the patients were females (22).

Occupation of the patients was as follows; most of the patients were farmers (46), followed by homemaker (12), others (10) category which included other professions like students and engineers, shopkeepers (7), carpenters (3), and one manual laborer in that order. Owing to the residence of the patients 62 were from the rural area and the rest of the 18 patients were from urban areas. Results showed that no prior treatment was received by 44 patients included in the study, patients who had taken antibiotics were around 22, in 6 patients combination of antibiotics with antifungal was given, 4 patients received steroids, the antibiotic and antiviral combination was given in 2 patients and 2 patients were in another category.

The history when recorded gave the history of trauma to the eye with various agents. Trauma with the vegetative matter was the main reason in the majority of patients i.e. 24 patients, in 22 patients there was the history of stone fallen in the eye, in 20 patients there was a history of trauma with other agents like animal tail, dust, and fingernail, no history of trauma was seen in 14 patients. In the present study, the maximum ulcers were found centrally in 44 patients, paracentrally the ulcer was located in 24 patients, and in 12 patients the ulcers were found peripheral in location. In this study 20 patients had only fungal elements positive in Gram's stain, 22 patients had bacteria positive, 8 had both fungal elements, and bacteria positive, and 20 had no organisms.

The study showed that 50 patients were not treated with any systemic antifungal. A total of 26 patients were put on systemic fluconazole 200mg tablets for at least a period of 2 weeks. Two patients were put on oral itraconazole 200mg BD tablets and two patients were treated with oral terbinafine 250 mg tablets OD. In the maximum number of patients i.e. 72 patients ulcer debridement was done. Two patients underwent therapeutic penetrating keratoplasty was done and in two patients conjunctival flap was done. In 4 patients no surgical

Treatment was done. The present tables show that 52 of patients had visual acuity between PL, PR + to 3/60 and at 8 weeks 42 of patients had visual acuity in that range.

Table-1: Oral systemic antifungal treatment

Drugs	No. of cases
Fluconazole	26
Itraconazole	2
Terbinafine	2
No treatment	50
Total	80

Table-2: Surgical treatment of patients

Procedure	No. of cases
Debridement	72
Conjunctival flap	2
Therapeutic Penetrating keratoplasty	2
No surgical treatment	4
Total	80

Table-3: Visual activity at presentation

Day 1 activity	No. of cases
PL,PR+ - 3/60	52
4/60 - 6/60	8
6/36 - 6/6	20
Total	80

Table 4: Visual activity at the end of 8 weeks

Day 1 activity	No. of cases
PL,PR+ - 3/60	42
4/60 - 6/60	12
6/36 - 6/6	26
Total	80

Discussion

A fungal corneal ulcer classically presents as a dry, raised lesion with crenate or feathery borders, presence of satellite lesions, and a hypopyon. Conventional methods for the diagnosis of fungal keratitis include staining of tissue scrapings with Gram-stain, 10% potassium hydroxide (KOH) wet mount, lactophenol cotton blue, Giemsa, or calcofluor white [9]. KOH is one of the most commonly performed direct microscopy procedures for the detection of fungi since it is a rapid and inexpensive procedure. It has a sensitivity of 61-94% and specificity of 91-97% for detecting fungus [9]. Risk factors that can predispose to fungal keratitis include contact lens wear, eye trauma with the vegetative matter, previous ocular surgery, topical steroid use, and immunosuppression. Patients with a fungal corneal ulcer will complain of

Eye pain, light sensitivity, red eyes, and possibly reduced vision [10].

At the presentation, a significant proportion of patients (45%) received various topical medications like antibiotics, antivirals, and steroid eye drops like dexamethasone and others like topical instillation of butter to relieve symptoms. Among them, only antibiotics were used by 27% of patients. The probable reason for this was that these drugs were readily available over the counter and compounded diagnosis of fungal etiology in the peripheral centers. 7.5 % of patients received a combination of antibiotic and antifungal, 5 % steroid eye drops, and 3% combination of antibiotic and antiviral. Fifty-five percent of patients received no prior treatment. Two patients who were using steroids in this study had undergone prior surgical treatment. One of the two underwent corneal tear repair and the other had prior cataract surgery.

All patients in this study were 10% KOH positive because that was the chosen inclusion criteria for the recruitment of patients in the study. Gram's stain was done to find out the bacterial etiology in case of mixed infections. In this study, 62.5% of cases were pure fungal isolates whereas 37.5% were mixed infections. In Nath R et al [11] study 8.7% of cases were mixed infections. Out of the 80 patients, 52 patients were fungal culture-proven, which agrees with two other studies. The percentage of agreement in the Chowdhary et al [12] study was 62% and Nath et al study was 65.2%. Gram's stains as a diagnostic aid in mycotic keratitis were positive in 47.5 % whereas it was positive in 60 % of cases in the Chowdhary et al study. Sharma et al [13] opined that KOH positive cases could be considered as fungal ulcers irrespective of the fungal culture positivity. The probable cause of this may be due to the presence of non-viable fungal elements at the time of culture but the exact cause in our cases could not be ascertained.

Despite the availability of several antifungal agents, fungal keratitis continues to have poor visual prognosis because of the resultant corneal scar of varying density. Sixty five percent of patients had VA ranging from PL, PR+ to 3/60 at presentation. Most of them were central in location. Only 10 patients had improvement and moved to the 4/60 to 6/60 visual acuity group. 10% of patients had visual acuity in the range of 4/60 to 6/60. In the present study, 20 patients had visual acuity between 6/36 to 6/6 at presentation. These ulcers

Were either paracentral or peripheral in location and involved the anterior stroma or mid stroma. All of them healed and at 6 weeks follow up they had at least one line improvement in visual acuity with 32.5% patients with visual acuity 6/36 or better. In Tanure et al [14] study, 54% of patient's final visual acuity of 6/36 or better. This underscores the emphasis on intensive treatment and sustained follow up. Among 80 patients, 62 healed with corneal opacity, 16 had a perforation of the cornea whereas in the Nath et al study 69 (43.9%) healed with corneal opacity, 19 (12.1%) cases had perforation, and 2(1.3%) cases developed endophthalmitis.

Conclusion

There was no significant difference in the healing of ulcers between patients who were already on topical treatment at presentation and no prior treatment because only one patient was on indigenous medicine.

What does the study add to the existing knowledge

Surgical debridement of the ulcer in the initial stages helps in reducing microbiological load and drug penetration. However, caution has to be exercised in ulceration with thin floors. Penetrating keratoplasty should be resorted to in nonhealing ulcers and perforated ulcers subject to the availability of healthy donor corneas.

Author's contribution

Dr. Minal M Patel: Concept, study design, and manuscript preparation

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