



Case Reports

Fusarium Keratitis Treatment and Management: A Case Series of Emerging Organism

Rajashri Patil¹, Sahjid Mukhida^{1,2*}, Jyoti Ajagunde¹, Chanda Vyawahare¹, Nageswari Gandham¹, Shital Algule¹

¹ Department of Microbiology, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Dr. D. Y. Patil Vidyapeeth, Pimpri, Pune, Maharashtra, India -411018

² Department of Microbiology, GMERS Medical college, Junagadh, India -362001

* Corresponding author's email: drssmukhida@rediffmail.com

ABSTRACT

Article history:

Received 7 March 2024

Accepted 12 May 2024

Available online 1 August 2024

<https://doi.org/10.47723/yvaagd47>

Keywords: Fusarium, keratitis, emerging organism, fungal keratitis

Infectious keratitis may be caused by viruses, bacteria, parasites, and fungi. Noninfectious can be caused by injury to the cornea, dryness of the cornea, allergies, and improper use of contact lenses. Fungi commonly responsible for corneal ulcers are *Aspergillus* (most common), *Candida*, and *Fusarium*. Both *Aspergillus* and *Fusarium* account for about one-third of all traumatic infectious keratitis. In the current case series, we submit 4 cases of *Fusarium* keratitis. A microbiological investigation like KOH mount is an important test that can confirm the presence of the fungal infection in samples. Topical and systemic anti-fungal treatment combinations give better outcomes in fungal keratitis patients. Culture is the gold standard, and *Fusarium* species are rapid growers. All suspected patients should be screened for fungal culture in their primary visit to prevent further complications and disability.



This article is an open access article distributed under the

terms and conditions of the Creative Commons Attribution (CC BY) license

<http://creativecommons.org/licenses/by/4.0/>

Introduction

The word keratitis simply it means inflammation of cornea. It will clinically present as corneal ulcer. Keratitis may be infectious or noninfectious. Infectious keratitis may be caused by viruses, bacteria, parasites, fungi. Noninfectious can be caused by injury to cornea, dryness of cornea, allergies, improper use of contact lenses (1).

Due to majority of people are agriculture workers and some environmental factors (tropical environment) keratomycosis is common in India. Here male population is commonly affected than females due to more outdoor exposure(2). When keratitis is caused by a fungal agent, it is called mycotic keratitis, which can be caused by numerous fungi. Most commonly isolated organisms are filamentous

fungi (*Aspergillus*, *Fusarium*, *Alternaria*, *Curvularia*); yeast (*Candida* and *Cryptococcus*) and some dimorphic fungi (*Histoplasma*, *Coccidioides*). Fungi commonly responsible for corneal ulcer are *Aspergillus* (most common), *Candida*, and *Fusarium*. Both *Aspergillus* and *Fusarium* account for about one-third of all traumatic infectious keratitis (3). *Fusarium* spp. belongs to a mould group. *Fusarium* species are abundant in air, soil, and plants. Injudicious use of antibiotics and steroids disturbs the symbiosis of between bacteria and fungi then fungi start acting as a pathogen which were previously symbiotic saprophytes, colonize when defenses of eye abolished by corneal trauma with vegetative material contaminated with fungi, use of steroids, and predisposes the patient to fungal infections. Major risk factors for *Fusarium* keratitis are contact lens wear, trauma, ocular

surface diseases, lid diseases, and post-ocular surgery. It is characterized by acute ocular pain, foreign body sensation in eye, diminished vision, corneal ulceration, and/or stromal infiltrates (4,5).

Although it is treatable but it has fulminant course as they showed high resistance with many antifungal agents, hence sometimes leads to deeper penetration into vitreous causing panophthalmitis, sometimes in severe cases nucleation is needed (6). *Fusarium* keratitis is more destructive and less responsive to treatment hence stances therapeutic challenges (7). In current case series we are presenting 4 cases of the *Fusarium keratitis*.

Case 1:

A 32 years old male patient presented to ophthalmology OPD with complaint of the headache from last 1 month. He was unable to sleep or work properly. He also had the complaint of blurred vision in left eye. He was a fruit seller who visited farms frequently. Patient was earlier visited physician and neurology department and he was referred to ophthalmology after clinical evaluation. His vitals were within normal limits. During the eye examination, ulceration was noted in the corneal part. Whitish gray elevated slough was observed in the cornea. Patient was belonging to young age and did not have any co morbidity or immunocompromised condition. Ophthalmologist suspected the infective keratitis. Corneal scrapping was planned and respective culture plates were ordered from microbiology laboratory. Cornea was scraped and sample inoculated on Chocolate agar, Subaroud Dextrose Agar (SDA), and on Plain slide for KOH mount. Sample immediately transport. to microbiology laboratory for investigation. During the KOH mount investigation, branched septate fungal hyphae was observed. Findings were informed to the clinicians. They started empirical antifungal therapy on the basis of the KOH mount. Next day patient had severe headache and temporary vision loss complaint. Ophthalmologist planned to corneal removal with Therapeutic penetrating keratoplasty (TPK). On 3rd day, cornea was removed and keratoplasty was done. Figure 1A and 1B show the pre- and post-operative condition of the patient's eye. Removed corneal material was sent to microbiology laboratory for further investigation. At this time, same type of fungal elements was observed in KOH mount. Sample was processed as per standard operating procedures of the laboratory. After 2 days of the inoculation of corneal scrapping, scanty fungal growth was observed on SDA media.

On 5th day of inoculation, fungal growth was matured. Colonies were whitish gray with pink in center. Lactophenol Cotton Blue (LPCB) mount was made from growth and observed under low and high-power field lens of microscope. Branched hyaline septate hyphae along with curved macroconidia and oval microconidia. *Fusarium oxysporum* was reported on the basis of morphology in LPCB. (Figure 2 and 3 show the *Fusarium* species culture on SDA and morphology in LPCB) Patient was shifted from empirical therapy to Itraconazole 200mg/BDS along with 1% topical Voriconazole eye drops for 4 weeks. On the 3rd week follow-up patient was improving, headache and blurred vision complaint were resolved around 80%.

Case 2:

A 41 years villager female was referred by periphery hospital to tertiary care eye center with suspicious infective etiology. Patient had loss of vision from last 4-6 weeks in right eye. Clear discharge was observed in right eye. She had normal vision with left eye. She also had history of headache. She was recently diagnosed as Type-2 diabetes and on diet control. No medical management prescribed by physician for diabetic control. Her other investigation with vitals were within normal limit. During the physical examination of eye, traumatic injury evidence was observed. Patient was housewife but she had history of trauma 1.5 month back during the cooking in

village. Corneal scraping kit was ordered and cornea was scrapped. Collected material inoculated on Blood agar, MacConkey agar, SDA agar and Plain slide for KOH mount. Septate, branching fungal hyphae was observed in KOH mount. Findings were informed to clinicians. Within 48 hours of inoculation, white cottony colony was grown on blood agar and MacConkey agar media. Same type of growth also observed on SDA agar too. Further LPCB done where fungal structure observed same like case-1. *Fusarium oxysporum* was reported. On 5th day of surgery, 14 suture intact, donor corneal graft was on places, blood stain over endothelial at 4'o clock place. Patient was shifted from empirical therapy to organism specific treatment same like case-1. Patient was discharged after 1 week with oral medicine prescription. During the follow-up patient was improving, headache and blurred vision complaint were resolved around 60%.

Case 3:

A 59 years old male come to ophthalmology OPD with complaints of loss of vision of left eye from last 15 days. Patient does not have any comorbid condition like Tuberculosis, DM, Bronchial Asthma or Hypertension. He did not have any surgical history in past. During the detail history examination, patient had accidental traumatic injury 2-3 weeks ago. After 3 days of the trauma, redness was observed in his left eye. Patient rubbed his eye due to irritation which made his vision blurred. Patient was visited periphery physician who prescribed antibiotic eye drops and refer to another tertiary care hospital. In another tertiary care hospital did the corneal scraping but further investigation details were not available with patient. Tertiary care hospital prescribed the Gatifloxacin and Natamycin but patient not improved. After 3 days treatment patient took Discharge Against Medical Advice (DAMA) and came to our tertiary care hospital for further investigation and treatment. During the ocular examination edema was observed on left eye. Around 8 x 8 mm size corneal ulcer with central corneal thinning and feathery margin infiltrate around the ulcer base taking stain. Endothelial plaques were present with 0.5 mm hypopyon. Corneal sensation was absent and fundus not visualized. TPK was performed. All pre-operative and post-operative measure were taken and corneal debride material was sent for microbiological investigation.

Microbiological investigations were processed as per the previous cases protocol. Scanty fungal growth was observed on SDA media within 48 hours which confirmed on LPCB mount as *Fusarium oxysporum*. Report was conveyed to the ophthalmologist. After 7 days of the surgery, post-operative sub conjunctival hemorrhage present all over with chemosis present, 16 interrupted sutures present radially at donor host junction. Stomal and graft host junction edema present along with discharge. Clinician change the treatment but improvement not seen. Patient took DAMA. Clinician prescribed the topical and systemic antifungal treatment same like case-1 on discharge but we lost the follow-up.

Case 4:

A 60 years old male patient present with diminution of vision in left eye from 3 months. Patient was apparently alright 3 months back, but latter he developed diminution of vision which was sudden onset, progressive, and painful in nature. Patient was using spectacles for distant and near vision from last 2 years. Patient had history of watery discharge and redness in left eye. He doesn't have history of flashes flattens, halos or double vision. He can tolerate the light flash. He gave history of foreign particles in left eye before 3 months. He didn't had comorbidity like hypertension, Bronchial asthma, epilepsy but he recently diagnosed DM before 3 months ago. On ocular examination, HMCTF sign found positive. Chronic indolent refractory ulcer with sever thinning was noted. Multifocal scatter infiltrate around the ulcer

base. Endothelial plaques were present with 0.5 mm hypopyon. TPK was performed under local anesthesia. All preoperative and post operative measure were taken and corneal debride material was sent for microbiological investigation.

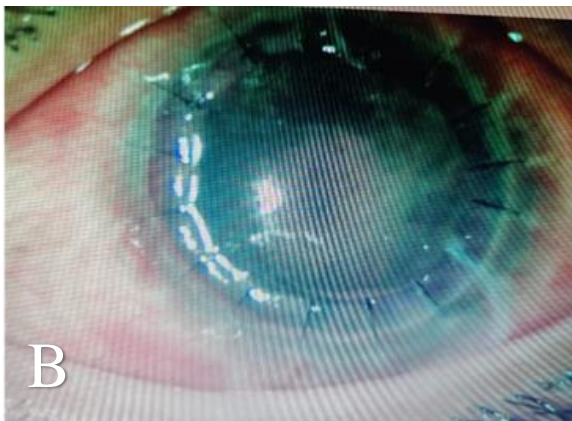
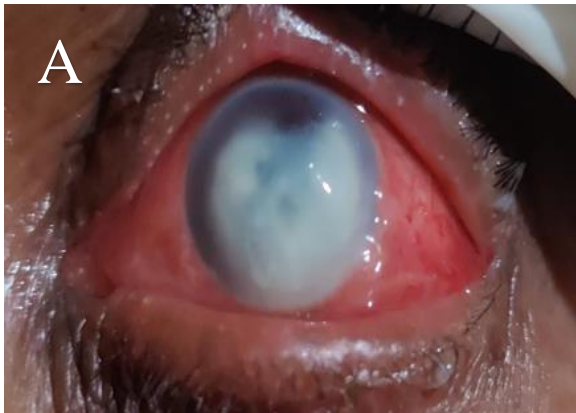


Figure- 1: Pre and Post operative corneal view of fungal keratitis. **A:** Pre operative fungal keratitis, **B:** Post operative Fungal Keratitis



Figure 2: Fusarium growth on Subaroud Dextrose Aga



Figure 3: Fusarium on LPCB mount

Microbiological investigations were processed as per the previous cases protocol. *Fusarium species* growth was observed on the SDA medium within 48 hours which confirmed on LPCB mount. Report was conveyed to the ophthalmologist. On 3rd of surgery, 18 suture intact, donor corneal graft was on places, blood stain over endothelial at 4'o clock place. Patient was shifted from empirical therapy to culture specific therapy. On 4th day of surgery, patient was discharged with oral treatment and advice for regular follow-up. He regularly visited hospital for follow-up and improving 80% at the 3rd week follow-up.

Discussion

Keratitis can affect any gender of the patients but most commonly affect the male patients due to their more chance to exposure to traumatic material which mostly found in the villages and farms. On current case series 3 out of 4 patients were male. Findings are similar to the study conducted by Chidambaram J et al where they reported keratitis majority (64%) in male.(8) Keratitis caused due to trauma various material like, wooden dust, wooden stick, trauma due to woods. In study conducted by Thomas PA et al reported fungal keratitis due to traumain their study. In current case series, 3 out of 4 patients had trauma due to exposure of the risky material which were most probably responsible for keratitis infection. They also reported predisposing factors like corticosteroids and contact lens wearing in their patients (3).

Age variation was found in current study. Adult age and older age patients were reported fungal keratitis in current study while study conducted by Chidambaram J et al found mean age 50 years (37-60 years)in their patients which is similar to current case series. We not found fungal keratitis in pediatric age group patients (8).

Keratitis can be caused by bacteria, fungal and viral .Gurnaniet al. and Ahmad B et al. reported in their study about bacterial and viral keratitis. In contrast Chidambaram J et al study have only 7.53% bacterial keratitis and they not reported any viral keratitis case (8-10) .Prevalence of fungal keratitis in among all keratitis patients were 5.3 % in study conducted by Cariello AJ et al. In contrast, Chidambaram J et al reported 75.79% prevalence of fungal keratitis in their study (6, 9).

Table 1: Combine details for all patients

	Case-1	Case-2	Case-3	Case-4
Gender	Male	Female	Male	Male
Age	32 years	41 years	59 years	60 years
Infected eye	left eye	right eye	left eye	left eye
Occupation	Fruit seller	Housewife	Carpenter	Retired
Living area	Villager	Villager	Villager	Villager
Exposure history	Visited farm	h/o traumatic injury to eye while cooking 1.5 month back	Accidental traumatic injury before 2-3 wks	h/o foreign particle dm since last 3 months
Clinical features	Blurred vision in lt eye	Loss of vision of right eye for 4-6 weeks h/o headache	Irritation of left eye, loss vision of left eye	Water discharge and redness of left eye
Duration of symptoms	1 month	4-6 weeks	15 days	2 years.
Comorbidity	No	Type 2 diabetes	No	Type 2 diabetes
Spectacles status	No	No	No	Yes
Size of ulcer	Multifocal scatter infiltrate	Multifocal scatter infiltrate	8 X 8mm	Multifocal scatter infiltrate
Another eye situation	Normal	Normal	Normal	Normal
Blood Pressure	110/80mmHg	120/90 mmHg	136/100 mmHg	130/98 mmHg
HB (g/dL)	13.2	12.8	13.3	11.2
TLC (per μL)	8200	8500	8500	9500
RBS (per μL)	5.2	4.6	5.1	4.8
ESR (mm/hour)	12	15	10	13
CRP (mg/dL)	3.2	4.8	6.2	5.1
Type of specimen	Corneal scrapping	Corneal scrapping	Corneal scrapping	Corneal scrapping
KOH mount findings	Branched septate fungal hyphae	Branched septate fungal hyphae	Branched septate fungal hyphae	Branched septate fungal hyphae
Duration of growth on culture	5 days	2 days	2 days	2 days
Organism	Fusarium oxysporum	Fusarium oxysporum	Fusarium oxysporum	Fusarium spp
Definitive treatment	Itraconazole 200mg bd+1% tropical voriconazole for 4 weeks	Itraconazole 200mg bd+1% tropical voriconazole for 4 weeks	Itraconazole 200mg bd+1% tropical voriconazole for 4 weeks	Itraconazole 200mg bd+1% tropical voriconazole for 4 weeks
Surgical procedure	TPK	TPK	TPK	TPK
Post-operative treatment	Itraconazole 200mg bd+1% tropical voriconazole for 4 weeks	Shifted to oral medication	Shifted to oral medication	Shifted to oral medication
Discharge on post-operative day	Day 7	Day 8	Patient took DAMA on day 7	On 4 th day of surgery
Patient outcome	80% symptoms resolved	60% symptoms resolved	Improvement not seen	Improved 80%
Follow-up	3 weeks	4 weeks	Patient lost follow up	3 weeks

Fungal keratitis can be caused by *Fusarium* species, *Candida* species and *Aspergillus* spp. In current case series all the keratitis cases were due to *Fusarium* species. Study conducted by Cariello AJ et al reported, *Fusarium* species (51.9%) followed by *Candida albicans* (10.7%) and *Aspergillus* species (9.1%) as a common cause of the fungal keratitis while Chidambaram J et al reported *Fusarium* sp. (39%) and *Aspergillus* sp. (18%) commonly. (8,11) Vélez M et al reported pigmented mycotic keratitis caused by *Aspergillus fumigatus* however none of our case have isolate the *Aspergillus* species (12).

Microbiological investigation like KOH mount is an important test which can confirm the presence of the fungal infection in samples. However, presence of the organism in KOH mount doesn't confirm the species of organism, their live or dead status and it is not much sensitive in case of improper sample collection. Clinician can choose the empirical therapy on base of KOH mount findings. (13) Culture is the gold standard and confirmatory test to identify the proper organism and test for anti-fungal susceptibility in view of treatment selection; however it takes time from 2 days to 1 month to grow on artificial culture media (14). *Fusarium* is a fast-growing fungal organism. In current case series, growth was appeared within 3-4 days of the sample inoculation (15).

Among the *Fusarium* genes, *F. solani* reported as a most common cause of keratitis in De Hoog et al study while we are reporting all 4 cases of keratitis due to *c.* In contrast, Guarro J et al reported rare case of *Fusarium polyphialidicum* in their case reports. Prompt and accurate diagnosis of the causative organism is that much important to choose the definitive treatment against the organism. Not only organism identification but on-time conveying the results of culture is also important. Without informing the clinicians, treatment cannot be continued blindly (16,17).

Treatment outcome can vary patient to patient due to their time lapse after exposure, duration of the symptoms, treatment initiation and confirmatory treatment implementation, surgical procedure and post-surgical care; and also, determination of the patient and their family members. In current case series, 3 out of 4 cases had good outcome with improving reports and rest one patient we lost the follow-up due to patient and their family members impassion.

Topical and systemic anti-fungal treatment combination give better outcome in fungal keratitis patients. In current case series, itraconazole 200mg/BDS along with 1% topical voriconazole eye drops combination for 4 weeks inhibit the fungal growth and improve the patients. Post-operative care is also important to reduce the chance of other hospital and surgical site bacterial infection in the patients (18-20).

Conclusion

Fungal keratitis caused by *Fusarium* species are much common, but it can be more emerging if not treated on time. Their prompt diagnosis and treatment can save the patient's vision to become lifetime impairment. Culture is gold standard and *Fusarium* species are rapid grower. All suspected patients should be screen for fungal culture in their primary visit to prevent further complication and disability.

Funding

This research did not receive any specific fund.

Conflict of Interest

The authors declare that they have no competing interests.

References

- [1] Cabrera-Aguas M, Khoo P, Watson SL. Infectious keratitis: A review. *Clinical & Experimental Ophthalmology*. 2022;50(5):543-62. <https://doi.org/10.1111/ceo.14113>
- [2] Bharathi MJ, Ramakrishnan R, Meenakshi R, Padmavathy S, Shivakumar C, Srinivasan M. Microbial keratitis in South India: influence of risk factors, climate, and geographical variation. *Ophthalmic epidemiology*. 2007;14(2):61-9. <https://doi.org/10.1080/09286580601001347>
- [3] Thomas P, Kalamurthy J. Mycotic keratitis: epidemiology, diagnosis and management. *Clinical Microbiology and Infection*. 2013;19(3):210-20. <https://doi.org/10.1111/1469-0691.12126>
- [4] Ung L, Bispo PJ, Shanbhag SS, Gilmore MS, Chodosh J. The persistent dilemma of microbial keratitis: Global burden, diagnosis, and antimicrobial resistance. *Survey of ophthalmology*. 2019;64(3):255-71. <https://doi.org/10.1016/j.survophthal.2018.12.003>
- [5] Qiao GL, Ling J, Wong T, Yeung SN, Iovieno A. *Candida* keratitis: epidemiology, management, and clinical outcomes. *Cornea*. 2020;39(7):801-5. <https://doi.org/10.1097/ico.0000000000002306>
- [6] Winiarczyk M, Borkowska A, Mackiewicz J. *Fusarium* keratitis as a growing problem—case report and literature review. *Annals of Agricultural and Environmental Medicine*. 2021;28(3):409-13. <https://doi.org/10.26444/aaem/128682>
- [7] Ting DSJ, Ho CS, Deshmukh R, Said DG, Dua HS. Infectious keratitis: an update on epidemiology, causative microorganisms, risk factors, and antimicrobial resistance. *Eye*. 2021;35(4):1084-101. <https://doi.org/10.1038/s41433-020-01339-3>
- [8] Chidambaram JD, Venkatesh Prajna N, Srikanthi P, Lanjewar S, Shah M, Elakkiya S, et al. Epidemiology, risk factors, and clinical outcomes in severe microbial keratitis in South India. *Ophthalmic epidemiology*. 2018;25(4):297-305. <https://doi.org/10.1080/09286586.2018.1454964>
- [9] Gurnani B, Kaur K. Bacterial Keratitis. (Updated 2022 Dec 6). In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2022 Jan-.
- [10] Ahmad B, Patel BC. Herpes Simplex Keratitis. (Updated 2022 Aug 1). In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2022 Jan-.
- [11] ariello AJ, Passos RM, Yu MCZ, Hofling-Lima AL. Microbial keratitis at a referral center in Brazil. *International ophthalmology*. 2011;31:197-204. <https://doi.org/10.1007/s10792-011-9441-0>

- [12] Vélez M, Balparda K, Díaz AM. A rare pigmented keratitis caused by *Aspergillus fumigatus*. *International Journal of Ophthalmology*. 2015;8(1):208. <https://doi.org/10.3980%2Fij.issn.2222-3959.2015.01.37>
- [13] Rathi VM, Thakur M, Sharma S, Khanna R, Garg P. KOH mount as an aid in the management of infectious keratitis at secondary eye care centre. *British Journal of Ophthalmology*. 2017;101(11):1447-50. <https://doi.org/10.1136/bjophthalmol-2017-310241>
- [14] Kozel TR, Wickes B. Fungal diagnostics. *Cold Spring Harbor perspectives in medicine*. 2014;4(4):a019299. <https://doi.org/10.1101/cshperspect.a019299>
- [15] Nucci M, Anaissie E. *Fusarium* infections in immunocompromised patients. *Clinical microbiology reviews*. 2007;20(4):695-704. <https://doi.org/10.1128/cmr.00014-07>
- [16] Hoog Gd, Guarro J, Gene J, Figueras MJ. *Atlas of clinical fungi 2000*.
- [17] Guarro J, Rubio C, Gené J, Cano J, Gil J, Benito R, et al. Case of keratitis caused by an uncommon *Fusarium* species. *Journal of clinical microbiology*. 2003;41(12):5823-6. <https://doi.org/10.1128/jcm.41.12.5823-5826.2003>
- [18] Szaliński M, Zgryźniak A, Rubisz I, Gajdzis M, Kaczmarek R, Przeździecka-Dolyk J. *Fusarium* keratitis—review of current treatment possibilities. *Journal of Clinical Medicine*. 2021;10(23):5468. <https://doi.org/10.3390/jcm10235468>
- [19] Sharma N, Sahay P, Maharana PK, Singhal D, Saluja G, Bandivadekar P, et al. Management algorithm for fungal keratitis: the TST (topical, systemic, and targeted therapy) protocol. *Cornea*. 2019;38(2):141-5. <https://doi.org/10.1097/ico.0000000000001781>
- [20] Zhao X, Tong Y, Wang X, Zhang X, Chen S, Lu H. Comparison of the ocular penetration and pharmacokinetics between natamycin and voriconazole after topical instillation in rabbits. *Journal of Ocular Pharmacology and Therapeutics*. 2018;34(6):460-7. <https://doi.org/10.1089/jop.2017.0139>

To cite this article: Patil R, Mukhida S, Ajagunde J, Vyawahare C, Gandham N, Algule SA. *Fusarium* Keratitis Treatment and Management: A Case Series of Emerging Organism. *Al-Kindy College Medical Journal*. 2024;20(2):152-157. <https://doi.org/10.47723/yvaagd47>