Case Report

Keratomycosis after incidental spillage of vegetative material into the eye: Report of two cases

Ali Tabatabaee, Zahra Mohajernezhadfard, Farid Daneshgar, Mohammadreza Mansouri

Department of Ophthalmology, Eye Research Center, Farabi Eye Hospital, Tehran University of Medical Sciences, Tehran, Iran

Fungal corneal ulcers mostly occur after incidental corneal trauma by plant leaves in farm lands or the use of topical corticosteroids or antibiotics. The infection is more prevalent among farmers and harvesters and in some parts of the world is considered as an occupational disease; however, there have been a few reports on the occurrence of such ulcers in healthy individuals after incidental spillage of vegetative material into the eye. The importance of these ulcers is their long-term and refractory course, which makes the visual prognosis unfavorable in most patients, even after appropriate antifungal therapy or ocular interventions. Herein, we present two rare cases of fungal ulcers caused by incidental spillage of vegetative material into the eye while eating nuts and corn. We also discuss the diagnostic and therapeutic approaches, as well as visual outcome reviewing the relevant literature.

Keywords: Aspergillus, corneal ulcer, fungal, Fusarium

Introduction

Fungal corneal ulcers happen worldwide. They are especially seen in tropical areas as an occupational disease among farmers during harvest times or workers dealing with animal products.[1-4] Ocular trauma by plant skin or pieces of plant leaves are the most common facilitating factors.[5]

Different studies estimate the incidence of corneal ulcers from 17 to 44%,[1,4,6,7] which is apparently influenced by the geographic and epidemiological factors. The infection typically occurs in humid, warm, and windy seasons in tropical countries; which is the ideal atmosphere for the fungi to grow on plants.[8] Although the majority of plant fungi are saprophytic and are not harmful to the human, toxins of some fungi such as Aspergillus, Fusarium genera, Alternaria, or Mucor are known to be potential pathogens in human.[8]

Access this article online	
Quick Response Code:	Website: www.ojoonline.org
	DOI: 10.4103/0974-620X.116659

The most common pathogen varies according to the geographical region; however in most parts of the world, Fusarium species are considered to be the most causative organisms.[9-14] Aspergillus,[2,6,7,15-18] and to a lesser extent, Candida species[14,19] are the next most common fungi.

Topical use of corticosteroids and antibiotics after traumatic eye contact by the infected plants and the resultant local immunosuppression are the main possible risk factors.[5] Self-medication by topical steroids or antibiotics, insidious and gradual progression of infection, and delay in initiating antifungal therapy makes visual outcome unfavorable in most patients. These reasons, as well as difficulties to access professional healthcare in rural areas have made fungal corneal ulcers as one of the most important causes of blindness in developing countries.[4]

Case Reports

Case 1

History and physical examination

A 26-year-old male patient presented with gradual loss of vision in the right eye over the last 2 weeks. The patient had a history of incidental spillage of corn milk while eating corn into his right eye before the onset of his symptoms. There was no history of eye redness or mucopurulant eye discharge after the trauma. He had no history of drug consumption over the last 2 weeks and

Correspondence:
Dr. Zahra Mohajenezhadfard, Department of Ophthalmology, Eye Research Center, Farabi Eye Hospital, Tehran University of Medical Sciences, Tehran, Iran.
E-mail: zmfard@yahoo.com

past medical history was also negative. Visual acuity (VA) had decreased to hand motion in the involved eye. A 5.5 × 6 mm central ulcer with a gray-white dry appearing infiltrate, feathery margin, and satellite lesions characteristic for fungal keratitis was found during eye exam. An additional 1 mm hypopyon was also noted [Figure 1]. Other ocular exams were normal.

Laboratory evaluation

Corneal scraping was done to obtain smear and culture. Although the direct smear stained with gram staining revealed fungal mycelia, the culture became negative for fungus species within Sabouraud's environment.

Management

The patient was treated with a high suspicion for filamentous fungal keratitis. Oral ketoconazole (400 mg/day), fortified antibiotic eye drop (voriconazole and amphotricin), topical steroid eye drop (betamethasone, twice daily), and dicloptin eye drop (every 6 h) were prescribed for two weeks. Due to the lack of response to the initial treatment, two intrastromal injections of voriconazole (50 µg/0.1 cm^3) were performed within 8 days. The patient was discharged with the aforementioned drugs after relative response with corneal epithelialization and decreased infiltration. Follow-up session after 2 and 4 weeks revealed no better VA than hand motion after the initiation of therapy. The enlargement of the previous ulcer (6.5 × 7 mm) with central thinning, hypopyon of 0.5 mm, and protective ptosis were also evident. Due to no obvious improvement, direct smear and culture was obtained again, which became positive for mycelia and Fusarium species, respectively [Figure 1]. The patient underwent two intrastromal injections of variconazole in 5 days. VA was only light perception afterwards. Two weeks after the last injection, tectonic penetrating keratoplasty was done and the patient was treated with fortified eye drop including amphotericin and natamycin and topical flucortison and chloramphenicol eye drops. Forty days later, the graft was rejected. VA appeared to be as equal to 1 m finger count. Examination revealed suture loosening, corneal edema, infiltration, and keratic precipitates (KPs). The patient was again treated by fortified natamycin, prednisolone (oral: 75 mg/day), and non-preservative steroid eye drop. The next day, suture removal and resuturing was done and topical prednisolone and ciprofloxacin eye drops were added to previously administered drugs. The patient was on treatment for 4 weeks. By the end of the month, edema and infiltration were subsided, VA was increased to 2 m finger count and the patient was discharged with cyclosporine (oral: 200 mg/day) and fortified eye drop (natamycin). During a 2 year follow-up, VA remained unchanged.

Case 2

History and physical examination

A 48-year-old female patient presented with redness and pain in the right eye. She had a history of incidental spillage of nut water into her right eye while eating nuts 11 days ago. She was also on medication as a diabetic case from several years ago. Over the last 11 days, she had been treated in another center with homatropin, NaCl, gentamycin eye drops, and ketoconazole (oral). Examination revealed decreased VA to be as equal as hand motion in the right and 6/10 in her left eye. A 4 + injection was noted within conjunctiva. A 4 × 5 mm central corneal ulcer with feathery margin and dry appearance was noted. Associated hypopyon was less than 0.5 mm [Figure 2].

Laboratory investigation

Direct smear and culture from the ulcer was positive for mycelia and Aspergillus species, respectively.

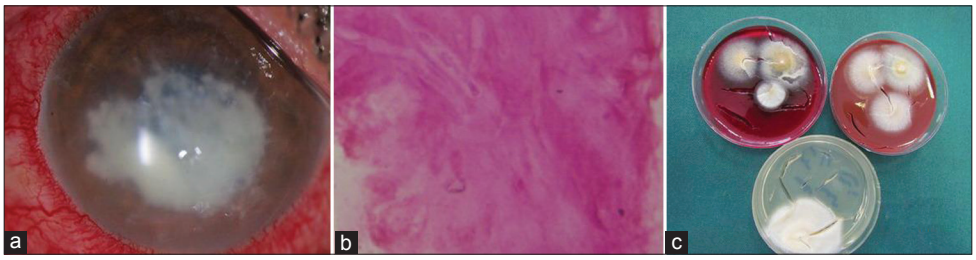

Figure 1: (a) Slit photograph of the right eye showing central corneal infiltration with a size of 5.5 × 6 mm with feathery margin, dry appearance, and typical satellite lesions characteristic for fungal keratitis. (b) Photomicrograph of gram staining of the specimen (×40) reveals mycelia in favor of fungal keratitis. Culture was negative. (c) Delayed repeat culture (after 1 month) became positive in blood agar (top left), chocolate agar (top right), and Sabouraud's dextrose agar (down) environments

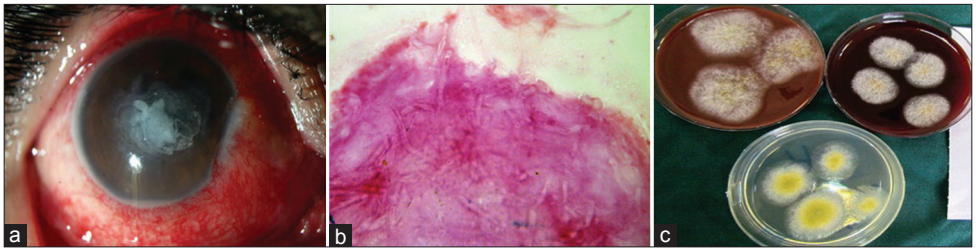

Figure 2: (a) Slit photograph of the right eye demonstrating central corneal infiltration measuring around 4 × 5 mm with feathery margin, dry appearance, and satellite lesions in favor of fungal keratitis. A small hypopyon (less than 1 mm) is also noted within anterior chamber. (b) Mycelia were found in gram staining of the corneal specimen. (c) Culture became positive in chocolate agar (top left), blood agar (top right), and Sabouraud's dextrose agar (down) environments

Management

The patient was treated with ketoconazole (200 mg/day, oral), doxycyclin (100 mg/12 h, oral), amphotricin, homatropin, and vitamin C eye drops. Follow-up session at one month showed resolved fungal keratitis and partial improvement in right VA (1/10). Due to the development of neurotrophic ulcer and persistent epithelial defect (PED) in the cornea, the patient underwent amniotic membrane transplantation (AMT) and was discharged. Follow-up at 1 year revealed no further improvement in VA.

Discussion

Fungal infection is not only considered as a threat to agricultural products, but also is of utter importance to the farmers and harvesters dealing with infected farming products. Weather condition and geographical characteristics of some tropical areas can contribute to the endemic fungal keratitis, especially during harvest time.[4,5]

Risk factors for keratomycosis include occupation (agriculture), male sex, age between 30 and 59 years, history of ocular trauma, and self-medication.[20]

Incidental ocular trauma by plant leaves or vegetative materials is a facilitating factor in most patients, which can lead to fungal keratomycosis and corneal ulcer after the release of cytotoxins. The inflammatory reaction occurs after the release of mycotoxin and proteolytic enzymes, which are responsible for the catastrophic corneal melting in some patients.

More than 70 molds and yeasts are believed to cause keratomycosis.[21] Although the main fungi varies according to the geographical area, in tropical areas, hyaline molds, such as Aspergillus and Fusarium species are more prevalent than phaeoid dematiaceous fungi.[22-24] Fungi are opportunistic organisms, which are able to penetrate conrneal stroma after traumatic disruption of the natural defensive barrier of the cornea (epithelium). Most of these fungi are saprobic and cannot cause any infection, because of cellular and humeral defensive mechanism of the host;[25] however, self-medication by topical steroids and antibiotics will increase the risk of infection due to local immunosuppression.

The predominant fungi responsible for corneal ulcers vary according to the epidemiological and climatic factors. For instance, Fusarium species are the most common fungi in Ghana,[24] south Florida,[1] and south India;[26] while Aspergillus and Candida are the most prevalent fungi in other countries.[27,28]

Filamentous fungi are believed to cause up to one-third of traumatic corneal infections.[29] These fungi are also found within the corneal stroma after surgical trauma, such as penetrating keratitis (PK) or radial keratotomy.

Fusarium infection might occur in healthy individuals after ocular trauma or in the presence of ocular foreign body. Some authors believe Fusarium is the most common cause of keratomycosis worldwide;[9,10,13] however, the consensus is that the most common fungi varies as the geographical condition differs.[10] Corneal ulcers caused by Fusarium species are typically suppurative and ulcerative.[30] In one recent study, the most predominant species was found to be *Fusarium solani*.[13] Fusarium keratitis is refractory to treatment, and especially solani species has a worse prognosis than other fungi and can lead to corneal sloughing and visual loss.[31]

Genus Aspergillus is believed to be the second most common cause of fungal keratitis. *Aspergillus flavus* is the most prevalent pathogen among this species.[32] Other members of the genus also can rarely cause fungal keratitis.[33] Other fungi species might also rarely cause keratitis and include *Carvularia lunata*[34] and Colletotrichum.[35,36] These fungi typically cause milder clinical course than Fusarium; however, Culvularia keratitis might spread in immunocompromised patients and cause systemic involvement.[37]

Fungal keratitis has been reported as an occupational disease among farmers in different countries; such as USA,[1] Thailand,[38] and India.[5] Tropical climate in these areas, which is the ideal atmosphere for plant fungi to grow in, as well as wind blowing during harvest time; which increases the risk of traumatic corneal contact with already infected plant leaves; pieces of vegetables or vegetative material are believed to be the two most facilitating factors. Incidental contact between the cornea and plant products can destroy the epithelial barrier and fungus can infiltrate the corneal stroma and initiate its pathogenesis. In India, for example, up to 46.8% of central corneal ulcers are due to pure fungal infection.[39] The figure is estimated to be 36% in Bangladesh,[7] 17% in Nepal,[6] 35% in south Florida,[1] and 56% in Ghana.[25]

The results of one study in India revealed that Fusarium infection is responsible for nearly half of keratomycosis cases, while Aspergillus was only found in 16% of cases.[4] Dematiaceous fungi including filamentous pigmented organisms, such as Culvularia and Cladosporium were found in 13.5% of cases, while hyaline fungal species include 9.6% of patients.

In some cases, the exact fungus is hardly ever to be diagnosed and for some cases, it is even more difficult to spot the genus of organism.[4,39] For these cases the initiation of empirical antifungal therapy is suggested.

The coincidence of bacterial and fungal keratitis is not an uncommon phenomenon, because both infections share common facilitating factors. Even, the incidence of coinfection might be more than expected. In one study,[40] up to 42.8% of fungal keratitis cases showed bacterial coinfection; however only 20% of cases were confirmed by laboratory exam. The rate of coinfection is 3.16 times more with yeast keratitis than filamentous fungal keratitis.[40] The result of the latter study confirmed that the possibility of culture to become positive is 80% in blood agar,

77% in chocolate agar, and 74% in Sabouraud agar plates.[40] Gram positive cocci were the most common bacterias (51%) in coinfection. Other studies have estimated the prevalence of bacterial coinfection from 5 to 60%.[41-43] This wide discrepancy is possibly due to the difference between risk factors, climate, access to healthcare facilities, and the sensitivity of culture environments.

Conclusion

Fungi are a threat to vision. Ocular trauma in farm lands and incidental spillage of vegetative material into the eye are two major causes for the entrance of fungal innoculum into the corneal stroma. As presented herein, the visual outcome of such ulcers might be disappointing due to the fact that these ulcers are resistant to most of treatment modalities. Instant ophthalmological care and meticulous follow-up should be taken in the event of incidental spillage of vegetative material into the eye. This should include appropriate smear and culture taken with a high suspicion for fungal organisms and initiating empirical antifungal therapy for symptomatic cases until the results of smear and culture are known. When fungal mycelia are found in the smear, therapy should be continued even when the culture is negative. Repeat smear and culture might be necessary in the absence of clinical response. Despite these prompt attempts, the visual outcome might not be as satisfactory as bacterial ulcers.

References

1. Leisengang TJ, Forster RK. Spectrum of microbial keratitis in south Florida. Am J Ophthalmol 1980;90:38-47.
2. Chander J, Sharma A. Prevalence of fungal corneal ulcers in northern India. Infection 1994;22:207-9.
3. Polack FM, Kaufman HE, Newmark E. Keratomycosis. Medical and surgical treatment. Arch Ophthalmol 1971;85:410-6.
4. Srinivasan M, Gonzales CA, George C, Cevallos V, Mascarenhas JM, Asokan B, *et al*. Epidemiology and aetiological diagnosis of corneal ulceration in Madurai, south India. Br J Ophthalmol 1997;81:965-71.
5. Lin SH, Lin CP, Wang HZ, Tsai RK, Ho CK. Fungal corneal ulcers of onion harvesters in southern Taiwan. Occup Environ Med 1999;56:423-5.
6. Upadhyay MP, Karmacharya PC, Koirala S, Tuladhar NR, Bryan LE, Smolin G, *et al*. Epidemiologic characteristics, predisposing factors, and etiologic diagnosis of corneal ulceration in Nepal. Am J Ophthalmol 1991;111:92-9.
7. Dunlop AA, Wright ED, Howlader SA, Nazrul I, Husain R, McClellan K, *et al*. Suppurative corneal ulceration in Bangladesh: A study of 142 cases examining the microbiological diagnosis, clinical and epidemiological features of bacterial and fungal keratitis. Aust N Z J Ophthalmol 1994;22:105-10.
8. De Lucca AJ. Harmful fungi in both agriculture and medicine. Rev Iberoam Micol 2007;24:3-13.
9. Dignani MC, Anaissie E. Human fusariosis. Clin Microbiol Infect 2004; 10(Suppl 1) 67-75.
10. Dóczi I, Gyetvai T, Kredics L, Nagy E. Involvement of Fusarium spp. in fungal keratitis. Clin Microbiol Infect 2004;10:773-6.
11. Guarro J, Gene J. Opportunistic fusarial infections in humans. Eur J Clin Microbiol Infect Dis 1995;14:741-54.
12. Mselle J. Fungal keratitis as an indicator of HIV infection in Africa. Trop Doct 1999;29:133-5.
13. Naiker S, Odhav B. Mycotic keratitis: Profile of Fusarium species and their mycotoxins. Mycoses 2004;47:50-6.
14. Tanure MA, Cohen EJ, Sudesh S, Rapuano CJ, Laibson PR. Spectrum of fungal keratitis at Wills Eye Hospital, Philadelphia, Pennsylvania. Cornea 2000;19:307-12.
15. Deshpande SD, Koppikar GV. A study of mycotic keratitis in Mumbai. Indian J Pathol Microbiol 1999;42:81-7.
16. Kumari N, Xess A, Shahi SK. A study of keratomycosis: Our experience. Indian J Pathol Microbiol 2002;45:299-302.
17. Panda A, Sharma N, Das G, Kumar N, Satpathy G. Mycotic keratitis in children: Epidemiologic and microbiologic evaluation. Cornea 1997;16:295-9.
18. Sundaram BM, Badrinath S, Subramanian S. Studies on mycotic keratitis. Mycoses 1989;32:568-72.
19. Rondeau N, Bourcier T, Chaumeil C, Borderie V, Touzeau O, Scat Y, *et al*. Fungal keratitis at the Centre Hospitalier National d"Ophthalmologie des Quinze-Vingts: Restropective study of 19 cases. J Fr Ophtalmol 2002;25:890-6.
20. Verghese S. Post traumatic fungal keratitis caused by Acremonium recifei. Indian J Pathol Microbiol 2010;53:587-8.
21. Prajna NV, Rao RA, Mathen MM, Prajna L, George C, Srinivasan M. Simultaneous bilateral fungal keratitis caused by different fungi. Indian J Ophthalmol 2002;50:213-4.
22. Vijaya D, Sumathi, Malini. Keratomycosis due to Fusarium Oxysporum-A case report. Indian J Pathol Microbiol 2001;44:337-8.
23. Basak SK, Basak S, Mohanta A, Bhowmick A. Epidemiological and microbiological diagnosis of suppurative keratitis in gangetic West Bengal, Eastern India. Indian J Ophthalmol 2005;53:17-22.
24. Chander J. Textbook of Medical Mycology. 2nd ed. Pune: Mehta Publishers; 2002. p. 309-17.
25. Hagan M, Wright E, Newman M, Dolin P, Johnson G. Causes of suppurative keratitis in Ghana. Br J Ophthalmol 1995;79:1024-8.
26. Bharathi MJ, Ramakrishna R, Vasu S, Meenakshi, Palaniappan R. Aetiological diagnosis of microbial keratitis in South India-A study of 1618 cases. Indian J Med Microbiol 2002;20:19-24.
27. Jones BR. Principles in the management of oculomycosis. XXXI Edward Jackson Memorial Lecture. Am J Ophthalmol 1975;79:719-51.
28. Saha R, Das S. Mycological profile of infectious keratitis from Delhi. Indian J Med Res 2006;123:159-64.
29. Kumar A, Pandya S, Madan M, Kavathia G. Keratomycosis with superadded bacterial infection due to corticosteroid abuse-A case report. J Clin Diagn Res 2010;4:2918-21.
30. Thomas PA. Current perspectives on ophthalmic mycoses. Clin Microbiol Rev 2003;16:730-97.
31. Richardson MD, Warnock DW. Fungal Infection: Diagnosis and Management. Oxford: Wiley-Blackwell; 2012. p. 156-61
32. Manikandan P, Do'czi I, Kocusube' S, Varga J, Németh TM, Antal Z, *et al*. Aspergillus species in human keratomycosis. In: Varga J, Samson R, editors. Aspergillus in the Genomic Era. Wageningen: Wageningen Academic Publishers; 2008. p. 293-328.
33. Kredics L, Varga J, Kocusube' S, Dóczi I, Samson RA, Rajaraman R, *et al*. Case of keratitis caused by Aspergillus tamarii. J Clin Microbiol 2007;45:3464-7.
34. Børve J, Stensvand A. Use of a plastic rain shield reduces fruit decay and need for fungicides in sweet cherry. Plant Dis 2003;87:523-8.
35. Cano J, Guarro J, Gené J. Molecular and morphological identification of Colletotrichum species of clinical interest. J Clin Microbiol 2004;42:2450-4.
36. Fernandez V, Dursun D, Miller D, Alfonso EC. Colletotrichum keratitis. Am J Ophthalmol 2002;134:435-8.
37. Safdar A. Curvularia-favorable response to oral itraconazole therapy in two patients with locally invasive phaeohyphomycosis. Clin Microbiol Infect 2003;9:1219-23.
38. Imwidthaya P. Mycotic keratitis in Thailand. J Med Vet Mycol 1995;33:81-2.
39. Sharma S, Srinivasan M, George C. The current status of Fusarium species in mycotic keratitis in south India. Indian J Med Microbiol 1993;11:140-7.
40. Pate JC, Jones DB, Wilhelmus KR. Prevalence and spectrum of bacterialco-infection during fungal keratitis. Br JOphthalmol 2006;90:289-92.

41. Leck AK, Thomas PA, Hagan M, Kaliamurthy J, Ackuaku E, John M, *et al*. Aetiology of suppurative corneal ulcers in Ghana and south India, and epidemiology of fungal keratitis. Br JOphthalmol 2002;86:1211-5.
42. Laspina F, Samudio M, Cibils D, Ta CN, Fariña N, Sanabria R, *et al*. Epidemiological characteristics of microbiological results on patients with infectious corneal ulcers: A 13-year survey in Paraguay. Graefes Arch Clin Exp Ophthalmol 2004;242:204-9.
43. Khanal B, Deb M, Panda A, Sethi HS. Laboratory diagnosis in ulcerative keratitis. Ophthalmic Res 2005;37:123-7.

Cite this article as: Tabatabaee A, Mohajernezhadfard Z, Daneshgar F, Mansouri M. Keratomycosis after incidental spillage of vegetative material into the eye: Report of two cases. Oman J Ophthalmol 2013;6:122-6.

Source of Support: Nil, **Conflict of Interest:** None declared.