

A Retrospective Study of Fungal Corneal Ulcers in the South Sharqiyah Region in Oman

*Thara Idiculla, George Zachariah, BR Keshav, Somansu Basu

دراسة استيعادية لتقرحات القرنية الناجمة عن الفطريات بالمنطقة الشرقية (جنوب) في عمان

ثارا ايديكوللا ، جورج زكريا ، بي آر كيشاف ، سومانسو باسو

المخلص: الهدف: دراسة معدل الحدوث ومعرفة عوامل الاختطار وتحديد الأحياء المجهرية السائدة وطرق علاج التقرحات القرنية الناجمة عن الفطريات . الطريقة: هذه دراسة استيعادية خلية للتقرحات القرنية للحالات التي عولجت في قسم العيون بمستشفى صور (عمان) للفترة من يناير 2004 إلى ديسمبر 2007 . تم مراجعة الملفات الطبية لاثنتين وثلاثين حالة ثبت إصابتها (عن طريق الزرع) بالتقرحات القرنية الناجمة عن الفطريات لمعرفة عوامل الاختطار ونتائج الفحوص المختبرية والاستجابة للعلاج. النتائج: من بين 242 حالة تعاني من قرحة القرنية كان 13.22% منها بسبب الفطريات . ومن بين 102 حالة موجبة بالزرع شكلت الفطريات (31.38%) منها . حازت الفطريات المِعْرَلَاوِيَّة (50%) والرَشَّاشِيَّة (34%) على الجزء الأكبر من الطيف الهيليبي الفطري . أما عوامل الاختطار فكانت كالآتي: استخدام الستيرويد الموضعي في 31.25% من الحالات وإصابات العين في (25%) منها . أكثرية الحالات (60.62%) استجابت لعلاج كيتوكونازول (2%) لوحده أو مع الأمفوتيريسين بي (0.15%) . الخلاصة: يبقى التقرح الناجم عن الفطريات سببا رئيسيا للعجز البصري . الاستخدام العشوائي لمستحضرات الستيرويد الموضعية وإصابات العين أهم عوامل الاختطار . الفطريات الخيطية من المسببات الأكثر انتشارا في هذه المنطقة . كان العلاج الموضعي بالكيتوكونازول والأمفوتيريسين فعالا جدا في معظم الحالات .

مفتاح الكلمات: قرحة القرنية، التهاب القرنية، الفطريات، مستنبتات الزرع .

ABSTRACT Objectives: To study the incidence, identify the risk factors and determine the predominant microorganisms and treatment regimen of fungal corneal ulcers. **Methods:** This was a retrospective analysis of corneal ulcers treated in the Ophthalmology Department of Sur Hospital, Oman, undertaken from January 2004 to December 2007. Medical and microbiology records of thirty two culture proven cases of fungal keratitis were reviewed for risk factors, laboratory findings and response to treatment. **Results:** Out of the total 242 corneal ulcers, 13.22 % were fungal. Among the 102 culture positive cases, 31.38 % were fungal isolates. *Fusarium spp* (50%) and *Aspergillus spp* (34.4%) predominated in the hyaline fungal spectrum. The important risk factors were topical steroid usage in 31.25 % of cases and ocular injury in 25 %. The majority of cases (90.62%) responded to 2% ketoconazole alone or in combination with 0.15% amphotericin B. **Conclusion:** Fungal ulcer remains one of the leading causes of visual disability. Indiscriminate use of topical steroids and ocular trauma are the most important risk factors. Filamentous fungi are common aetiological agents in this region. Topical ketoconazole and amphotericin B were very effective for most of the cases.

Key words: Corneal ulcer; Keratitis; Fungi; Culture media.

Advances in Knowledge

- Filamentous fungi are frequent causes of corneal ulcer in hot and dry climatic regions and it is imperative to keep a high level of suspicion.
- Direct wet mount potassium hydroxide (KOH) preparation is an essential screening test in corneal ulcers.
- Therapies with reconstituted antifungal agents are highly effective.
- Treatment has to be continued for a minimum of three to four weeks.

Application to Patient Care

- There is a need to recognise the public health risks of corneal ulcers and educate the community to prevent this avoidable cause of blindness.
- The modifiable risk factors need to be understood to lessen the magnitude of fungal corneal ulcers.
- Any superficial corneal injury, especially with vegetable matter, has to be properly attended to.
- The application of native medicines and eye drops containing steroids should be avoided.

FUNGAL KERATITIS CAN POSE DIAGNOSTIC and therapeutic challenges for ophthalmologists. Although fungi cause only 5 to 10% of all corneal infections, devastating ocular damage can occur if they are not diagnosed promptly and treated effectively. Through a defect in the epithelial barrier, fungi may gain access into the corneal stroma where they can cause tissue necrosis and a host inflammatory reaction. In addition, they may penetrate through an intact Descemet's membrane. Once fungi reach the anterior chamber or spread to adjacent sclera, the infection becomes very difficult to control due to poor penetration of antimycotic agents.

The pattern of mycotic keratitis varies with geographic region according to the local climate.¹ Corneal ulcers with an indolent course, stromal infiltrates with a dry texture and feathery borders, satellite lesions, immune ring infiltrates and unlevelled hypopyon are highly suggestive of a fungal aetiology.² In cases of a negative smear or culture and where there is a high suspicion for fungal keratitis, a corneal biopsy should be considered. *In vivo* confocal microscopy is a useful adjunct to slit lamp biomicroscopy for supplementing diagnosis in most cases and establishing early diagnosis in many cases of non-responding keratitis. This is a non-invasive, high resolution technique which allows rapid detection of fungal hyphae in the cornea long before laboratory cultures can give conclusive results.³

METHODS

Case records of all corneal ulcers presented to Ophthalmology Department of Sur Hospital, Oman, in the four year study period from January 2004 to December 2007, were analysed retrospectively. A proper history regarding the events leading to ulcers was recorded and all the patients were subjected to a thorough clinical and microbiological examination at the time of presentation. Corneal scrapings, from the edge and base of the ulcers were subjected to complete micro-

biological examinations which included direct microscopic examination by 10% potassium hydroxide (KOH) solution and inoculation into various culture media. The wet preparations of KOH were examined under low magnification (x100) initially and then under high magnification (x400). Corneal scrapings were transferred directly from spatula to agar media by a series of C-shaped cuts on the media. Three different media were utilised: blood agar, chocolate agar and Sabouraud's dextrose agar with chloramphenicol (SDA). The SDA plates were incubated at 25°C for three weeks. Most of the patients were admitted. Visual acuity ranged from hand movement to 6/60. Only culture proven cases of fungal ulcers were included in this study and they were reviewed for risk factors, laboratory findings and response to treatment. The data obtained from the study were analysed using 95% level of confidence at 5% significance level.

RESULTS

There were a total of 242 cases of corneal ulcers in our study period of 4 years, out of which 13.32% (95% CI: 8.95% to 17.49%) were fungal. Among 102 culture positive cases, 32 (95% CI: 22.37% to 40.37%) were fungal and 70 were bacterial. The remaining 140 cases were culture negative. Among the 32 fungal corneal ulcers, 19 (59.37%) were in male patients and 13 (40.63%) in female ones. The incidence was highest in the age group above 60 years (62.5%).

Analysis of risk factors for fungal ulcers showed a history of steroid use in 10 patients, most in the elderly age group of 50-70 years. Five patients were on steroid treatment for unrelated eye problems and the remaining five were post operative cases on chronic steroid usage. The second commonest risk factor identified was ocular injury with plant debris in 8 patients. Among this group, two were children in the age group 10-15 years; the remaining six patients were elderly in the age group 50-75 years. Preexisting corneal pathol-

Table 1: Predisposing risk factors in fungal corneal ulcers

Factors	No. of cases	Age group	Percentage	Confidence Interval
Steroid use	10	50-70 years	31.25	95% CI: 15.19% to 47.31%
Ocular injury	8	10-75 years	25.00	95% CI: 10% to 40%
Preexisting corneal pathology	6	50-80 years	18.75	95% CI: 5.23% to 32.27%
Topical traditional medications	5	50-70 years	15.62	95% CI: 3.05% to 28.21%

ogy like corneal degenerative keratopathy and trachoma sequelae were seen in 6 patients in the age group 50-80 years. The use of topical traditional medications for minor eye diseases was another risk factor in 5 patients, all in the age group 50-70 years. The remaining 3 patients had no predisposing factors. Three were three diabetic patients, but all of them had additional predisposing factors [Table 1].

In the laboratory investigations, the positive cultures obtained were corroborated with positive KOH results. In direct microscopy, branching and septate hyphae were identified in 24 cases (75%). *Fusarium spp* was the most common fungi isolated (50%) followed by *Aspergillus spp* (34.4%). Apart from filamentous fungi, 2 cases were yeast infection [Table 2].

TREATMENT AND OUTCOME

The initial treatment given was ketoconazole 2% drops hourly with 14 (43.75%) cases responding well. The remaining 18 (56.25%) patients, who had unfavourable response after the third day, were given a combination of 2% ketoconazole and 0.15% amphotericin B. Fresh preparations were reconstituted every third day. Daily examination was done with clinical documentation of the size, extent and anterior chamber reaction. Frequency of instillation was gradually tapered as the ulcers improved. Treatment was continued for a minimum period of three weeks. Six patients, who had lesions extending to the limbus and with thinning of cornea, were given oral ketoconazole 200mg twice daily for 7 days in addition to the combination drops. Twenty nine patients (95% CI: 80.53% to 100.73%) responded well to this regimen. Visual acuity improved in 15 patients, while it remained the same in 12 patients and deteriorated in 5 patients. The ulcers worsened in 3 patients and they were referred for further treatment to a tertiary centre. Patients who were on native medication presented late with extensive ulcers. These patients needed a longer period of treatment

and their outcome was dense scarring.

DISCUSSION

Even though fungal corneal ulcers are comparatively uncommon, they cause devastating ocular damage if not managed properly.² Our study shows an incidence of fungal keratitis (13.22%) comparable with other studies. In a similar study conducted in a tertiary referral centre in Baghdad, an 18.7% incidence of fungal keratitis was reported.⁴ Filamentous fungi like *Fusarium*, *Aspergillus* and *Penicillium* were the predominant isolates in our study. World wide, *Aspergillus* is the most common cause of mycotic keratitis. *Fusarium* species are the most common cause of fungal corneal infection in the southern United States (45.76%), while *Aspergillus* species followed by *Fusarium* are the most common isolates in India.^{5,6,10} The Baghdad study showed *Aspergillus* in 56.8% and *Fusarium* in 27%.⁴ Our study shows a higher incidence of *Fusarium* (50%) followed by *Aspergillus* (34.4%). This may be due to the fact that the *Fusarium* species is commonly found in soil and plants and most of our patients were from a rural background.

When the risk factors were analysed, the highest risk factor noted was steroid usage (31.25%) followed by ocular trauma (25%). A similar study of fungal keratitis in Melbourne showed chronic steroid usage in 31.4% and ocular trauma in 37%.⁷ Corneal injury associated with outdoor activities with plant or soil material is a high risk factor for fungal keratitis. In a study of fungal keratitis in northern Iran, trauma with plant debris and straws were noted in 28.6% of patients with fungal keratitis.⁸ Other predisposing factors noted were ocular surface disorders in 18.75% and use of native medications in 15.62%. A study of fungal keratitis at Wills Eye Hospital, Pennsylvania, USA, reported chronic ocular surface disease in 41.7%.¹¹ In a study from a rural area of India, usage of traditional medi-

Table 2: Fungal Culture: Species grown

Species grown	No of cases	Percentage	Confidence Interval
Fusarium spp	16	50 %	95% CI: 32.68% to 67.32%
Aspergillus spp	11	34.4%	95% CI: 17.92% to 50.84%
Penicillium spp	3	09:4%	95% CI: -0.72 to 19.48%
Candida spp	2	06.2%	95% CI: -2.14 to 14.64%

cations like human milk, leafy extracts and oil were reported in 47% of corneal ulcer patients.^{12,13}

Reconstituted topical 2% ketoconazole and 0.15% amphotericin B were very effective for most of the cases. Fresh preparations were reconstituted on every third day and instilled hourly as ready made antifungal drops were not available.^{4,9} Most cases of corneal ulcers presented in this study were already on topical antibiotics and this may explain the high percentage of culture negative cases. Filamentous fungi are common aetiological agents for fungal keratitis in our region. Hence this study is useful to institute appropriate empirical antifungal therapy based on this scenario.

CONCLUSION

Fungal keratitis presents both diagnostic and management challenges for the clinician. Infection due to filamentous fungi is a frequent cause of corneal blindness and remains as a major ophthalmological problem. Corneal injuries need to be treated and managed properly. Indiscriminate use of steroid drops and the application of native medicines for unrelated eye problems may provide an environment for fungal growth. A wet smear of 10% KOH preparation is an essential screening test for corneal ulcer.⁸ Mycotic lesions are often recalcitrant and require many weeks of medical treatment. Reconstituted antifungal drops are equally as effective as commercial antifungal drops which are not readily available in this region. It is imperative to maintain a high level of suspicion for fungal keratitis, so that appropriate therapy can be instituted immediately.

CONFLICT OF INTEREST: None declared

SOURCE OF FUNDING: Sur Hospital, Oman

REFERENCES

1. Khairallah SH, ByrneKA, Tabbara KF. Fungal keratitis in Saudi Arabia. *Doc Ophthalmol* 1992; 79:269-76.

2. Kim MC, Karp CL. Managing fungal keratitis. *Amer Acad Ophthalmol, Eye Net Magazine*, March 2001.
3. Gupta N, Tandon R. Investigative modalities in infectious keratitis. *Ind J Ophthalmol* 2008; 56:209-13.
4. Al-Shakarachi F. Initial Therapy for suppurative microbial keratitis. *BJO* 2007; 91:1583-87.
5. Agarwal PK, Roy P, Das A, Banerjee A. *Ind J Ophthalmol* 2001; 49:173-6.
6. Gopinathan U, Garg P, Fernandes M, Sharma S. The epidemiological features and laboratory results of fungal keratitis: a 10-year review at a referral eye care center in South India. *Cornea* 2002; 21:555-9.
7. Bhartiya P, Daniell M, Constantnou M. Fungal Keratitis in Melbourne. *Clin Experiment Ophthalmol* 2007; 35:124-30.
8. Shokohi T, Nowroozpoor-Dailami K, Moaddel-Haghighi T. Fungal Keratitis in patients with corneal ulcer in Sari, Northern Iran. *Arch Iran Med* 2006; 9:222-7.
9. Yavas GF, Oztürk F, Küsbeci T, Cetinkaya Z, Ermis SS, Kiraz N, et al. Antifungal efficacy of voriconazole, itraconazole and amphotericin B in experimental fusarium solani keratitis. *Graefes Arch Clin Exp Ophthalmol* 2008; 246:275-9.
10. Chander J, Singla N, Agnihotri N, Arya SK. Keratomycosis in and around Chandigarh: a five-year study from a north Indian tertiary care hospital. *Ind J Pathol Microbiol* 2008; 51:304-6.
11. Tanure MA, Cohen EJ, Sudesh S, Rapuano CJ, Laibson PR, et al. Spectrum of fungal keratitis at Wills Eye Hospital, Pennsylvania. *Cornea* 2000; 19:307-12.
12. Prajna V, Pillai MR, Manimegalai TK, Srinivasan M, et al. Use of traditional eye medicines by corneal ulcer patients. *Ind J Ophthalmol* 1999; 47:15-18.
13. Bialasiewicz A, Shenoy R, Thakral A, Al-Muniri A, Shenoy U, Al-Mughairi Z. Microbial keratitis: A 4 year study of risk factors and traditional/complimentary medicines in Oman. *Ophthalmologie* 2006; 103:682-87.