

Corneal Fungal Keratomycosis - A Therapeutic Challenge: A Case Report

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Abstract

Objective: To report a case of fungal keratitis caused by *Fusarium* species.

Result: A 57 year old man presented with painful blurring of vision of his left eye. There was presence of dry corneal ulcer with irregular borders, hypopyon and anterior chamber cell activity. An initial diagnosis of bacterial keratitis was made and was started on topical ceftazidime and topical ciprofloxacin. When corneal scraping revealed hyphae the diagnosis was revised to fungal keratitis and he was started on topical amphotericin B 0.15%. He developed corneal toxicity due to amphotericin B and antifungal was changed to topical fluconazole 5%. His ulcer slowly healed with a final visual acuity of 6/36.

Conclusion: Treatment of fungal keratitis remains a challenge and the use of topical anti fungal remains a mainstay. However the side effects of corneal toxicity secondary to the medications also needs to be given importance.

Keywords: *Fusarium* keratitis; Fungal; Keratitis; Fluconazole; Amphotericin B

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Introduction

Fungal keratomycosis is the infection of the cornea that can lead to devastating visual outcome. Leber reported the first case of fungal keratitis in 1879 [1]. Since then, there have been an increasing number of fungal keratitis cases. Malaysia is a developing country based mainly on agriculture. Hence, more fungal keratitis patients are encountered in our setting. A study by Mohd Tahir et al., [2] found that the prevalence of fungal keratitis in the east coast of Malaysia was 25.27%. This was comparable to the neighboring countries of Singapore and Thailand [3, 4].

Fungal keratitis normally occurs in warm climates [5]. These are opportunistic pathogens that are able to penetrate corneal stroma due to traumatic disruption of the epithelium [6]. Risk factors for fungal keratitis are male, history of ocular trauma and use of corticosteroids [7]. The most common fungal pathogen is *Fusarium* species followed by *Aspergillus* and *Candida* [8]. Clinically, fungal keratitis caused by *Fusarium* is similar to other fungal infections but its prognosis is worse [9].

The medical management of fungal keratitis is a worldwide challenge. This is attributed the the wide range of fungal pathogens, variations geographically and the delay in diagnosis [10, 11].

We report a case of fungal keratitis caused by *Fusarium* that developed corneal toxicity to topical amphotericin B.

Case Report

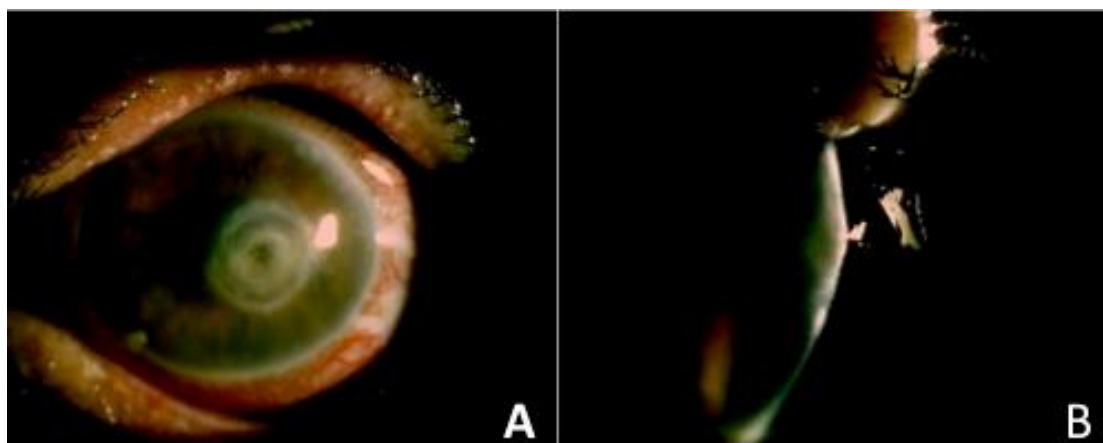
A 57 year old previously fit man presented with painful blurring of vision of his left eye for 5 days duration. It was associated with redness but no eye discharge. There was history of an insect entering his eye a day prior to the onset of symptoms. He initially presented to a general practitioner and was prescribed with topical eye drops containing corticosteroids. His symptoms worsened after the instillation of the eye drops.

On examination, visual acuity was 6/9 in his right eye and hand movements in his left eye. A central grey white, dry appearing corneal ulcer measuring 3.5mm x 4.0mm in diameter with irregular borders was seen. There were no obvious feathery edge or satellite lesions. A hypopyon of 1mm and anterior chamber cell activity of grade 3 was noted. Other ocular examinations were normal. An initial diagnosis of infective keratitis of bacterial origin was made. He was started empirically on topical fortified ceftazidime hourly and ciprofloxacin hourly, topical atropine 1% daily and oral Vitamin C 1 gram daily.

Corneal scraping done revealed fungal hyphae and culture showed the existence of *Fusarium sp.* The diagnosis was revised to fungal corneal ulcer. He was then started on topical amphotericin B 0.15% hourly and topical fortified ceftazidime was withdrawn. Topical ciprofloxacin was reduced to 2 hourly.

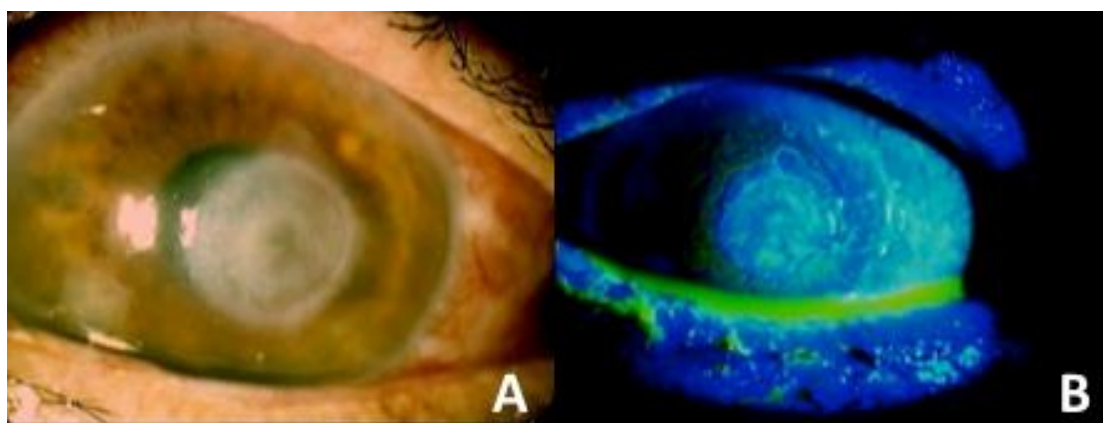
The ulcer responded initially to treatment. However 2 weeks after commencement of treatment, there was presence of microbullae and epithelial edema. This progressed to a central descemetocele 4 weeks after treatment (Figure 1). He was put on a bandage contact lens. Topical amphotericin B was stopped and replaced with topical fluconazole 5% three times a day.

Figure 1: Central corneal ulcer (A), showing a central descematocele with a bandage contact lens in situ. The central descematocele healed (B) with thickened stromal fibrosis (lateral view).



His ulcer slowly healed with central corneal opacity (Figure 2). Topical fluconazole 5% was continued for 12 weeks with gradual taper. Three months after treatment, his best-corrected final visual acuity was 6/36. He was offered penetrating keratoplasty, but due to financial constraints he was unable to proceed with the surgery.

Figure 2: Healed corneal ulcer (A) with central dense opacity. On fluorescein staining (B), there is no uptake of stain seen.



Discussion

Fungal infection to the eye can cause devastating visual outcomes. In tropical countries, the commonest cause of fungal keratitis is filamentous in origin [12]. Diagnosing and treating can pose a challenge as fungal keratitis is often mistaken for other causes of inflammatory keratitis.

In our case, the patient was initially treated empirically for bacterial keratitis. Studies to aid diagnosis of fungal keratitis have reported that a longer history of symptoms, dry raised surface with serrated margins, presence of endothelial rings and anterior chamber involvement was more common in fungal keratitis [3, 12]. Our patient had a dry appearing corneal ulcer with hypopyon that suggest a fungal origin. However, the acute history of symptoms and the lack of satellite lesion or endothelial rings were more suggestive of bacterial keratitis.

A study by Florakis et al., [13] noted that a reliable diagnosis couldn't be made by clinical appearance alone. Furthermore, geographical distribution of bacterial and fungal keratitis varies. Hence clinicians do not have a similar clinical experience [14]. However, there are studies that found growth of microorganisms only occurs in 40% to 60% of cases where culture is obtained [15, 16]. Therefore, in addition to clinical acumen, it is imperative to have corneal scrapings to aid in the diagnosis. In addition, as these patients will be on long term anti fungal treatment; microbiological result is needed prior to committing to treatment [17].

Our patient had been initially treated with topical corticosteroids that made his condition worse. Corticosteroid use has been known to ease the penetration of pathogens into the eye [18]. In addition, the history of an insect entering the eye would have caused an initial injury to the epithelium, initiating an ulcer.

In our case, topical amphotericin B was changed to fluconazole 5% due to the development of central descematocele. Amphotericin B, a polyene; combines with cell membrane ergosterols to induce cell membrane structural changes. A study on toxicity of antifungal agents on stratified human cultivated corneal epithelial sheets by Kimakura et al., [19] found that topical amphotericin B had the highest ocular toxicity compared to topical primaricin and voriconazole. It has been thought that its ocular toxicity is due to its binding to human cholesterol cells [20].

In contrast, topical fluconazole has lesser toxicity than amphotericin B [21] and shows variable susceptibility to *Fusarium* species [22]. Though management of fungal keratitis focuses primarily on the antifungal activity, but importance should also be given to the effects of corneal toxicity to prevent severe ocular toxicity.

Topical ciprofloxacin was continued in our patient after obtainment of the culture results. Van Babbekke et al., [23] found that antibiotics mainly fluoroquinolone and aminoglycoside are efficacious against fungal infections. Fungal pathogens have high levels of topoisomerase [24] and the inhibitory effect of fluoroquinolone on topoisomerase potentiates the antifungal effect [23]. In addition, Stergiopoulou et al., [25] reported that ciprofloxacin interacts with antifungal agents to aid the activity of antifungal agents.

We did not add a systemic antifungal for our patient. A randomized control trial done in 2008 to compare the effectiveness of 1% topical itraconazole versus 1% topical itraconazole and oral itraconazole found no significant advantage when systemic antifungal was added [26]. Sonogo-Krone et al., [27] concurred with this study; where they recruited 23 patients comparing topical fluconazole versus topical and oral fluconazole. They did not find significant difference in the clinical outcome. On contrary, a prospective randomized study by Parchand et al., [28] found that a combination therapy is useful in severe fungal keratitis patients. Therefore, though topical antifungal therapy is the standard treatment for fungal keratitis; the addition of systemic antifungal may offer benefit in resistant or severe keratitis [29].

Conclusion

Diagnosing and treating fungal keratitis remains a difficult task. It is important for accurate diagnosis to be made early as to tailor therapy appropriate to the microbiological evidence and to optimize the patients' visual outcome. However, it needs to be noted that the visual outcome might not be as satisfactory despite early treatment.

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