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Special Article - Fungal Keratitis

Fungal Keratitis: A Clinical, Microbiologic and Histopathologic Diagnostic Challenge

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Introduction

Corneal perforation is a complication that is five times more likely to occur in fungal keratitis than in bacterial keratitis [1]. Although obtaining a positive corneal culture is the gold standard for identifying the microorganism [2], the culture-positive rate is only 60-70% in fungal keratitis [2,3].

We report a case of fungal keratitis in a contact lens wearer and the diagnostic and treatment challenges encountered. Only the second of three corneal scrapings showed Fusarium solani. The histopathological investigation of the excised corneal button was also difficult due to cell fragmentations following cornea perforation.

Case Report

A 20-year-old manpresented with one-month of presumed herpes simplexkeratitis of the left eye. There was no history of trauma or organic matter exposures, but he did shower with softcontact lenses. Visual acuity (Va) was 20/30. A 4.6-mm diametercorneal stromal infiltrate with satellite lesions and fimbriaeprotruding into the anterior chamberwere observed; there was no overlying epithelial defect (Figure 1). Amild AC reaction without hypopyon was evident. Gradual progression was notedduring treatment with oral valcyclovir, topical moxifloxacin and tobramycin/dexamethasone administered every 2 to 4 hours.

Corneal scraping was sent for Gram staining and cultures. Empiricantifungal, anti-acanthomebal and antibacterialtreatment were initiatedincluding topicalnatamycin (5%, hourly), topical amphotericin (0.1%, every 2 hours), oral voriconazole 200mg twice daily, topical Polyhexamethylene Biguanide (PHMB) (0.02% hourly), and topical moxifloxacin hourly. Oral valcyclovir was continued and topical corticosteroid was discontinued.

Four days after the initial visit, Vadecreased to 20/200 with significant worsening of thecorneal edemaand extension of the infiltrate into the central visual axis (Figure 2). Given the significant keratitis, thetopical corticosteroids were restarted once daily. Asecond corneal scraping was repeated. On day 9, acorneal biopsy of 150 microns was performed due to lack of clinical improvement.

At day 10, the second scraping's culturewas positive for Fusarium solani. Topical natamycin, topical amphotericinand oral voriconazole were continued. PHMB was discontinued andcorticosteroids was tapered. Microbiologic and histopathologic investigation of the superficial corneal biopsy did not reveal any organisms.

At 3-weeksfollow-up, hedevelopeda full-thickness corneal perforation. At this point the corticosteroidwas tapered to every third day. Emergent therapeutic penetrating Keratoplasty (PKP) was performed.Initial histopathological examination of the host deep corneal stroma showed fungal elements with spores. Due to concern that the spores represented acanthomeba, topical PHMB was restarted every 2 hours.

Further histopathologic examination reconfirmed the presence of septated filamentous hyphae with sporesand of keratic precipitates in the deep stroma close to Descemet's membrane; the endothelium was absent. These findings were consistent with fungal keratitis and topical PHMB was discontinued.

At 5-weeks post-PKP, then corrected Va was 20/60. There was no recurrence of fungal keratitis (Figure 4). Topical natamycin hourly and oral voriconazole were continued. Due to concern of fungal recurrence, corticosteroids were with held until post-operative day 17 at which point it was deemed safe to start corticosteroids four times daily.

Discussion

CL wear is a risk factor for microbial keratitis. Since differentiating the etiology of corneal ulcers based on clinical examination alone is challenging, diagnosis relies greatly on obtaining adequate corneal samples. In our case, the second of 3 corneal cultures was positive

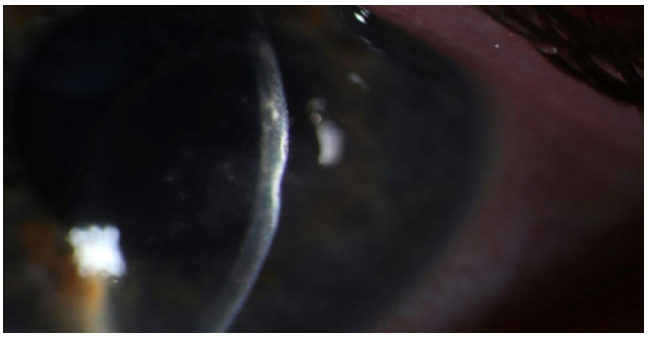

Figure 1: First presentation. Slit lamp biomicroscopic examination discloses satellite lesions in deep stroma and early thinning. There is minimal corneal edema.

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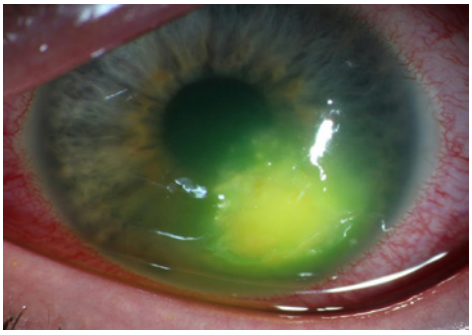

Figure 2: Dense stromal infiltrate with satellite lesions and increased corneal edema.

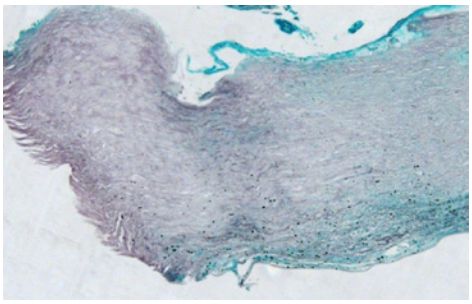

Figure 3A: Numerous spores near the deep margin of the perforation. The fungi are deeply situated near descemet's membrane below (Grocott GMS stain, original magnification x 50).

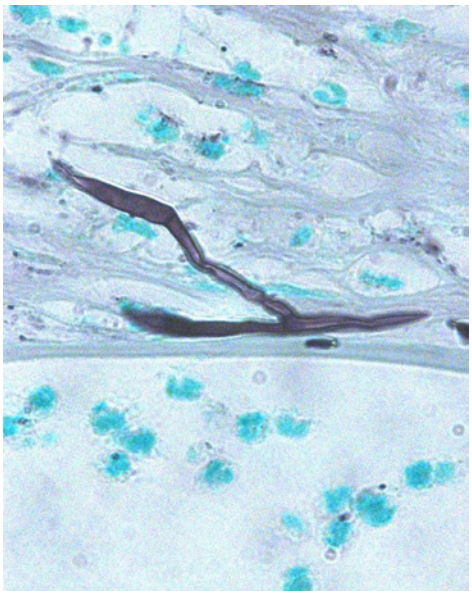

Figure 3B: Septated, branching hyphae next to Descemet's membrane. There are also several polymorphonuclear leukocytes along Descemet's membrane (Grocott GMS stain, original magnification x 50).

for filamentous fungus, but speciation was not available until10 days following treatment initiation. The rate of positive culture from corneal scrapings in fungal keratitis ranges from 31.3 to 69.6% [4,5]. Since the yield of fungal cultures is low, histopathological examination is essential when the microbiology results are unclear. The initial

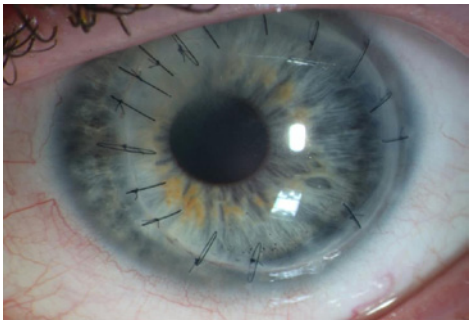

Figure 4: 5 Weeks post-penetrating keratoplasty shows no signs of graft rejection or recurrence of fungal keratitis.

superficial biopsy was negative because it was not deep enough to reach the microorganisms situated in the deep stroma. The second histopathological examination of the excised corneal button from the PKP confirmed fungal keratitis, but could not definitively rule out co-infection with acanthomebadue to the fragmentation of cells. Overall this case demonstrates the microbiological and histopathological diagnostic challenges of fungal keratitis.

Fusarium solani is among the most refractory causes of fungal keratitis [6-8]. The recommended medical treatment for Fusarium keratitis is natamycin 5% drops [9]. Despite appropriate treatment, primary treatment failure has been reported to be as high as 31% in fungal keratitis [5]. Surgical intervention is required in a significantly larger number of patients with fungal keratitis than bacterial and parasitic keratitis [10]. In our case, there was a one-month delay from symptom onset to treatment initiation; topical tobramycin/dexamethasone was initially used. Use of corticosteroids in that first month likely masked his symptoms but promoted fungal growth. Corticosteroids have been well-known to increase the risk of infectious complications in fungal keratitis [11]. Although our patient was started on natamycin hourly during his initial visit at our center, the deep location of fungal elements within the stroma reduced the penetration of the natamycin. Overall, the one-month delay in treatment initiation, initial use of corticosteroids, and the depth of fungal penetration into the deep stroma all likely contributed to the perforation seen in our case. As detrimental as corticosteroids are to fungal Keratitis, the sudden withdrawal of steroids may have contributed to the perforation by allowing a sudden rise in uncontrolled inflammation. Although it is only speculative, it may have been more desirable to have tapered the corticosteroids during first four days instead of abrupt cessation.

Prolonged use of topical corticosteroids is a major risk factor for recurrence of post-PKP infectious keratitis [12]. As an alternative cyclosporine may have both suppressive effects on fungal growth as well as immunosuppressive effects, but it cannot be considered as a sole agent in prophylaxis against graft rejection. Corticosteroids still remain the gold standard [12]. However, as demonstrated in our case, it may be prudent to delay their use until there is reasonable certainty that there is no recurrence of AC or corneal fungal infection. Topical cyclosporine was not used in our case.

Our case illustrates the diagnostic and treatment challenges of fungal keratitis. Only the second of three corneal scrapings showed

Fusarium solani. The histopathological investigation of the excised corneal button was also challenging due to cell fragmentations following cornea perforation. The sudden reduction of erroneously used corticosteroids should be done with caution as the resultant inflammation can promote corneal melting.

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