A 5-year retrospective review of fungal keratitis in the region of Cap Bon

La kératite fongique dans la région du Cap Bon : une étude rétrospective de 5 ans

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Summary

Introduction. — Microbial keratitis is a serious ocular infection and a leading cause of morbidity and blindness worldwide.

Methods. — A retrospective review of the charts of 30 patients (30 eyes) diagnosed with presumed or culture-proven fungal keratitis among 100 patients with infectious keratitis. All patients initially received hourly 0.5% Amphotericin B eye drops. Systemic antifungal agents consisted mainly of oral Fluconazole. After treatment, a healing time of less than 3 weeks from presentation was considered a good result. Mean follow up was 10.4 months.

Results. — Risk factors for fungal keratitis included ocular trauma in 13 patients (43.3%). Stromal infiltration was seen in 100% of patients. Satellite lesions were noted in 6 eyes (20%) and an immune ring was noted in 3 cases (10%). The most commonly isolated agent was Fusarium in 9 eyes (50%), followed by Aspergillus in 6 eyes (33.3%), and Candida in 2 eyes (11.1%). At the end of follow up, final visual acuity varied from no light perception to 20/20. The significant predictors were initial visual acuity, size of infiltrate at presentation, male gender and advanced age.

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Introduction

Microbial keratitis is a serious ocular infection and a leading cause of morbidity and blindness worldwide. Many microorganisms can cause infectious corneal ulcers. Among them are bacteria, viruses and fungi.

The diagnosis of fungal keratitis is usually based on culture and stain of the corneal scrapings. Environmental factors (humidity, rainfall, wind) greatly influence the frequency of fungal keratitis.

The aim of this study was to describe the clinical and microbiological spectrum of fungal keratitis over the last five years in a referral center in the region of Cap Bon, Tunisia, North Africa.

Methods

A retrospective review of the charts of 30 patients (30 eyes) diagnosed with presumed or culture-proven fungal keratitis among 100 patients with infectious keratitis between January 2010 and December 2015 at the department of Ophthalmology of the University Hospital of Nabeul in Tunisia. Detailed data were collected from medical records including: socio-demographic features, onset of symptoms, systemic disease, previous treatment, visual acuity at presentation, ocular examination findings (size of epithelial defect after staining with fluorescein, size and depth of the stromal infiltrate, satellite lesions, immune ring, presence of hypopyon, associated ocular conditions such as blepharitis, dacryocystitis, trichiasis), treatment modalities, and clinical outcome.

In all cases, corneal scrapings were aseptically performed from the corneal ulcer using a spatula under direct vision through slit lamp. The scraping material obtained was inoculated in different solid and liquid media.

After corneal scraping, all patients initially received 0.5% Amphotericin B every hour. Systemic antifungal agents consisted mainly of oral Fluconazole (800 mg the first day then 400 mg a day). It was used in cases with deep stromal infiltration and severe anterior chamber reaction. Voriconazole (topical, oral and intrastromal injection) was used in some cases after the result of microbiological findings.

The consultation period ranged from 1 to 25 days with an average of 12.7 days. The antifungal treatment was started as soon as the positivity of the direct exam and/or culture, within 4 to 30 days of the onset of symptoms. Additional procedures were undertaken for patients not responding to

Conclusion. — The key element in the diagnosis of mycotic keratitis is clinical suspicion on the part of the ophthalmologist. However, because of the potential serious complications, it is essential to identify the exact pathogen so as to initiate appropriate treatment in time and to thus improve the prognosis of this condition.

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medical therapy and they included therapeutic penetrating keratoplasty and evisceration. After treatment, a healing time of less than 3 weeks from presentation was consid-
ered good result. If no response was noted within 1 week, treatment should be reevaluated. The mean follow up was 10.4 months (1 month to 24 months).

Results

The mean age of our patients was 48.9 years (15 to 84 years). There was male predominance: 17 males (56.6%) and 13 females (43.4%).

Risk factors for fungal keratitis included ocular trauma in 13 patients (43.3%), with a vegetal matter in 9 patients (30%), diabetes in 3 cases, corticoid treatment in 1 case, larynx cancer in 1 case, cataract surgery in 3 cases, trichiasis in 2 cases, dacryocystitis in 1 case and contact lens in 1 case. Trauma occurred significantly in those working outdoors than in those who were indoors. Eight (8) of our patients with ocular trauma were farmers. A high incidence of mycotic keratitis was observed from April to July.

The time between the onset of symptoms and presenta-
tion varies from 2 to 15 days (mean of 7.4 days).

Ocular symptoms included blurred vision in 25 patients (83.3%), ocular redness in 15 patients (50%), and ocular pain in 21 patients (70%). Initial visual acuity ranged from neg-
ative light perception to 20/20 (mean = 20/320). It was less than 20/200 in 24 eyes (80%), more or equal to 20/200 in 6 eyes (20%).

The corneal ulcer was central in 21 patients (70%) and peripheral in 9 patients (30%). The size of the corneal lesion was ≤ 2 mm in 23.3% (7 patients) of cases, between 2 and 5 mm in 50% of cases (15 patients) and ≥ 5 mm in 26.7% of cases (8 patients). The mean size was 3.2 mm.

Stromal infiltration was seen in 100% of patients. It was deep in 17 eyes (56.6%). Satellite lesions were noted in 6 eyes (20%) and immune ring was noted in 3 cases (10%). Hypopion was seen in 19 cases (63.3%) (Fig. 1). Of the 30 patients with fungal keratitis, 18 were culture positive cases. The most commonly isolated agent was Fusa-
rium in 9 eyes (50%), followed by Aspergillus in 6 eyes (33.3%), Candida in 2 eyes (11.1%) and Acremonium in 1 eye (5.6%) (Fig. 2).

All patients were treated with topical antifungal agents: Amphotericin B in 21 cases and voriconazole in 9 cases. Twenty-two patients were treated with systemic antifun-
gal agents. Twelve patients were treated with Fluconazole (Triflucan), 6 patients with Ketoconazole (Nizoral) and 4 patients with oral Voriconazole (VFend).

In one case, penetrating keratoplasty was performed because of corneal perforation due to Fusarium solani. Two eyes underwent evisceration.

At the end of follow up, final visual acuity varied from negative light perception to 20/20 (mean = 20/125). It was less than 20/200 in 16 eyes, or equal to 20/200 in 14 eyes. Visual acuity improved in 19 eyes (63.3%), remained the same in 6 eyes (20%) and worsened in 5 eyes (16.6%) (Fig. 3). Corneal perforation was seen in 5 eyes (16.7%), sequelar corneal opacities were seen in 20 eyes (66.7%).

The significant predictors were initial visual acuity, pre-
sentation infiltration size, male gender and older age.

Discussion

Microbial keratitis is a serious ocular infection that can cause corneal scarring and opacification.

Data from previous studies in different geographic areas showed a large discrepancy in the proportion of fungal keratitis, and in the respective causative agents. This propor-
tion varies from 6% to 53% [1]. The difference may be explained by several factors like climate, age, sex, geographical and socioeconomic conditions. The infection is rare in temperate areas and more common in warm and humid environments [2]. In our study, this frequency was estimated to be relatively higher 29% than the frequency in other regions of Tunisia because of the humid climate and the predominance of agricultural work in the region of Cap Bon.

The mean age of our patients was 48.9 years with male predominance. The most important risk factor was ocular trauma with vegetable matters. Fungal corneal ulceration is usually more common in men which is consistent with findings of studies by Basak et al. [3], Srinivasan et al. [4]. The higher incidence rates seen in men in our study may be due to the higher exposure to injury during fieldwork compared to women.

Many risk factors of fungal keratitis have been reported. In developing countries, ocular injury from plant parts is a major predisposing factor, unlike in developing countries, contact lenses are reported to be more common [5]. Association of fungal keratitis with use of corticosteroids and diabetes mellitus has been reported earlier [6]. In our study, ocular trauma was identified as a risk factor for fungal corneal infection in 43.3% of cases, diabetes was found in 10.3% of cases, contact lens in 3.4% of cases and corticoste-
roids’ use in 3.4% of cases.

On examination, fungal ulcer is a central elevated discoid ulcer with irregular, undermined edges. Satellites lesions can be seen around the edge of the ulcer and they indicate the extension of the fungus. They were found in 20% of cases of our study and in 6.18% in cases in the study of Rajpal et al. [7].
Hypopion, which refers to deposits of white blood cells in the anterior chamber, signifies severe anterior segment intraocular inflammation. More than half of the patients with severe fungal keratitis develop hypopion during the clinical course [8]. It was seen in 63.3% of cases in our study. Immune ring is typical of fungal origin. It was found in 2.2% of cases in the study of Rajpal et al. [7] and in 10% of cases of our study.

More than 105 species of fungi, classified in 56 genera, have been identified as the etiological agents of fungal keratitis [9].

Aspergillus, Fusarium and Curvularia are the more frequent among filamentous fungi, while Candida albicans is the most common form of yeasts. Ocular infection with Candida almost exclusively occurs in patients with ocular or systemic disease. The filamentous fungi do rarely penetrate an intact epithelium and are often secondary to epithelial defects caused by trauma, contact lenses or ocular surface disease [10]. Our study shows a higher incidence of Fusarium (50%), followed by Aspergillus (33.3%). These incidences are different of those of a study in USA, in which, Fusarium accounted for 33% of all fungal keratitis cases [11]. This may be due to the fact that the Fusarium species are commonly found in soil and plants and most of our patients were from a rural background.

Eleven of our cases (36.6%) were culture negative. Khater et al. found that 15.5% were negative in spite of their typical clinical findings and their improvement with antifungal therapy [12]. Other methods for fungus identification should be considered: PCR, confocal microscopy, anterior segment OCT. PCR is more sensitive than stain and culture methods. Confocal microscopy also plays a role in diagnosis of fungal keratitis. SDAS-OCT imaging provided a range of characteristic patterns that could be used as an additional tool in the diagnosis of fungal microbial keratitis [13].

A recent Cochrane Database systematic review of medical interventions for mycotic keratitis (an update of a review in 2005) analyzed nine randomized controlled trials involving 568 participants who were randomized to various comparisons (1% topical Itraconazole versus 1% topical Itraconazole and oral Itraconazole, Voriconazole 1% versus natamycin 5%). It was concluded that based on the available literature, there is no evidence to suggest that any particular drug is more effective than any other in the management of mycotic keratitis [14].

In our study, two of our patients have an infection that did not heal under Amphotericin B and recovered after adjunction of topical Voriconazole. In these cases, the fungal agent was Fusarium. In many instances, topical use of those drugs was not sufficient alone to treat those cases and so adjunctive treatment were described: subconjunctival injections of Fluconazole and Amphotericin B and intrastromal injection of Voriconazole [15]. In our study, intrastromal injection of voriconazole was used in one case with good results.

A recent study sought to analyze the predictors of outcome in mycotic keratitis. Older age and a larger infiltrate size at presentation significantly predicted a longer time
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Figure 3. Evolution of fungal keratitis. Anterior segment photography (left) and fluorescein stain (right): a: fungal ulcer with an important stromal infiltration and hypopion indicating a more advanced infiltration; b: aggravation after topical Amphotericin B; c: healing of the infection 1 week after voriconazole intrastromal injection.

to re-epithelialization and worsened 3-month visual acuity [16]. In our study, the final visual acuity depends on presentation visual acuity and on the size of the ulcer. From the 16 patients with final visual acuity inferior to 20/200, 8 had an ulcer superior to 5 mm (50%) and 14 (87.5%) had an initial visual acuity inferior to 20/200. Furthermore, in our study, the two patients who underwent evisceration were male. The visual acuity was less than 1/10 and the ulcer size was more than 5 mm in the two cases.

The major limitations of this study arose from its retrospective nature. First, all the data came from medical records, the information of treatment of some patients outside of our department was not available, and some details such as use of corticosteroids and risk factors were potentially missed in our records.

Conclusion

The key element in the diagnosis of mycotic keratitis is the clinical suspicion by ophthalmologists. However because of the potential serious complications, it is crucial to identify the exact etiology of corneal ulcer to institute appropriate therapy in time. Improvement in our care system is important in preventing blindness due to fungal keratitis in the region of Cap Bon characterized by humid climate and agricultural work.

Disclosure of interest

The authors declare that they have no competing interest.
References