

FUNGAL KERATITIS: A STUDY FROM A MOROCCAN CENTER

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ABSTRACT

Context: Fungal keratitis is a serious condition, occurring most often on fragile corneas. In Morocco, we do not always have an optimal technical platform for the diagnosis of these pathologies, nor for therapeutic means, both pharmaceutical and surgical for their management.

Aim: Study the specificities of the epidemiology, diagnosis, treatment and prognosis of fungal keratitis in our Moroccan background.

Methods and Material: We reviewed all fungal keratitis cases between October 2014 and October 2016 in ophthalmology department A in Ibn Sina Hospital in Rabat.

Results: We reviewed 27 patients. Ocular trauma and local corticosteroid therapy were found in 37% and 44.4% of patients respectively. The mean time between the first clinical signs and the emergency department consultation was 21 days, and 66.7% of the patients were referred for non-improvement with antibiotic eye drops. The initial visual acuity ranged from 2/10th to no luminous perception. All patients received corneal scratching upon admission for diagnostic and therapeutic use. It confirmed the clinical suspicion of fungal keratitis in 51.9% of the cases. The evolution was marked by the occurrence of corneal perforation in 37% of patients, the persistence of a corneal opacity in 88.9% of the cases. An improvement in visual acuity was observed in 12 of our patients.

Conclusion: Fungal keratitis represent severe infections. In Morocco, like in many others countries, we have to adapt our diagnosis and therapeutic protocols according to our conditions. The mycological data are still insufficient, and most often confirm a strong clinical presumption. The prognosis is conditioned by an early diagnosis and the rapid initiation of an effective treatment..

Key-words: Fungal keratitis; Cornea; Ocular surface diseases; Voriconazole; Fluconazole

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KEY MESSAGES: Fungal keratitis are severe infections of the cornea. In Morocco, our resources are limited, both diagnostic and therapeutic. Based on the clinical and evolutionary characteristics of these infections and using therapeutic protocols based on voriconazole and fluconazole, we obtain results similar to those described in the literature.

INTRODUCTION

Fungal keratitis are serious corneal infections, which most commonly occur on fragile corneas [1-6] or on an immunosuppressed patient. Their diagnosis is based on a cluster of anamnestic, clinical, and microbiological arguments. It is often delayed,

sometimes aggravated by inadvertent corticosteroid therapy [7-10]. The corneal involvement is most often severe, and responsible for important sequelae that can compromise the visual prognosis of the affected eye [6, 11].

In Morocco, we do not always have an optimal technical platform for the diagnosis of these pathologies, nor for therapeutic means, both pharmaceutical and surgical (amniotic membrane graft, keratoplasty) for their management. The initial clinical aspect, as well as the evolution during the treatment, constitute key elements in our context, to evoke the diagnosis of fungal keratitis.

The aim of our study was therefore to study the characteristics of the epidemiological, diagnostic,

therapeutic and prognostic aspects of fungal keratitis in our Moroccan context.

SUBJECTS AND METHODS

We retrospectively collected the records of all the consecutive patients hospitalized in the ophthalmology department A of the specialty hospital of Ibn Sina University Hospital in Rabat, between October 2014 and October 2016, for fungal keratitis. The study was in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2000.

The inclusion criteria were as follows: patients with mycological evidence, and / or patients with at least three of the clinical signs strongly suggestive of fungal keratitis: Context of trauma by plant agent; An immunosuppression; An abscess with blurred, fluffy edges on a greyish, rough cornea; Micro satellite abscesses; Presence of flakes in the anterior chamber (Photo 1, 2, 3).

The non-improvement under antibiotic eye drops, then the improvement under antimycotic treatment was also retained as inclusion criterion.

The data collected for each patient were: age, sex, general and ophthalmological history, the wearing

of contact lenses or not, the circumstances of onset of keratitis, the date of onset of symptomatology and the time before their admission. We also clarified whether patients had received initial treatment, including local corticosteroids. In addition, we collected all the data from the initial clinical examination: the best visual acuity, the presence of an associated ocular surface disease, the clinical appearance of the abscess. All patients underwent corneal scraping for diagnostic and therapeutic purposes, for bacteriological and mycological examination.

All patients initially underwent ceftazidime and vancomycin fortified eye drops before reducing the doses after 48 hours. The antimycotic treatments were started either at admission or after no improvement under antibiotic eye drops alone (after verification of the liver function). The antimycotic treatments available to us were variable according to the periods: voriconazole administered in solution for injection or fortified eye drops, and fluconazole administered in solution for injection, or orally. The protocols used are detailed in Table I. An adjuvant treatment (ocular washes, cycloplegic wetting agents, more or less associated with acetazolamide hypotoniser) were systematically prescribed.

Tables I: Treatment protocols used

	Protocol 1	Protocol 2	Protocol 3	Protocol 4
Treatment used	Voriconazole , solution for IV infusion of 200mg	Voriconazole fortified eye drops 1%, (10mg/mL)	Fluconazole , solution for IV infusion of 200mg	Fluconazole 200mg, oral
Day 1	Dose of charge at 400mg / 12h	Hourly Instillation	Dose of charge at 400mg / 12h	Dose of charge at 400mg / 12h
From day 2	Infusion of 200mg / 12h	Instillation hourly for 48h then decrease to 1 drop / 2h	Infusion of 200mg / 12h	2 tablets per day of 200 mg
Continuation of treatment	Variable according to the evolution: between 8-21 days	Variable according to the evolution: between 7-10 days	Variable according to the evolution: between 8-21 days	Variable according to the evolution: between 3-6 months
Maintenance treatment	Fluconazole per os at a dose of 2 tablets / day of 200 mg for 3 to 6 months according to the evolution			

Patient outcomes were also examined, including complications such as corneal perforation, corneal opacity, visual acuity and the mean follow-up duration.

RESULTS

Twenty-seven patients were included. The mean age was 51 years, with a male predominance of 63%. The profession of farmer was found in 22.2% of cases, and 29.6% of our patients had diabetes. Only one patient wore cosmetic contact lenses.

Ocular trauma was found in 37% of patients, 25.9% per plant agent and 11.1% per telluric agent. In 66.7% of the cases, patients had been seen by a first ophthalmologist, treated by antibiotic eye drops, and referred to our hospital for non-clinical improvement. Forty-four percent of patients (n=12) received local corticosteroids.

The mean duration between the onset of symptoms and hospital admission was 21 days. The initial visual acuity varied between 2/10th to absence of luminous perception. On initial clinical examination, an ocular surface disease with blepharitis and/or meibomitis was found in 66.6% of cases. All patients had diffuse conjunctival hyperaemia associated to an abscess with an average axis of 5.5 mm and a minor axis of 4.4 mm. Microsatellite abscesses were found in 51.9% of the cases. On average, the anterior chamber was the site of a hypopion reaching 22% of its height, with fluffy flakes in 40.7% of the cases. Two of our patients were admitted with corneal perforation.

Systematic corneal scratching with direct examination alone confirmed fungal keratitis diagnosis in 51.9% of the cases. A B-mode ultrasonography was performed in 70.4% of our patients, especially when the vitreous was not

visible on the initial examination, and revealed 2 cases of associated endophthalmitis, which benefited specific treatment.

There was an improvement in the visual acuity in 12 patients with an average gain of 1.2 lines, and a decrease in the size of the abscess with a major axis of 2.8 mm and a minor axis of 2.2 mm . Corneal perforation occurred in 37.5% of patients despite the use of a therapeutic lens in the pre-rupture stage in 14.8% of cases. Of these patients, two patients received blepharography, and one patient was gutted.

Our patients were followed for an average of 2, 3 months. Eighty eight percent of them had corneal scar opacity, and 70,4% of all of them retained posterior synechias despite the instillation of cycloplegics.

DISCUSSION

In our series, we found 27 cases of hospitalized fungal keratitis over a period of 2 years, an average of 13.5 cases per year. The published western series found much smaller averages [12]. Conversely, Kibret et al.[13] found an average of 69 cases / year of fungal keratitis in Ethiopia (Table III).

Table II : Patients' characteristics / * Mean (standard deviation) / ** Percentage (number)

Variables	Results
Age*	51 (17)
Sex	
Male**	63 (17)
Female**	37 (10)
Risk Factors	
Diabetes**	29,6 (8)
Farmer**	22,2 (6)
Corticosteroids**	44,4 (12)
Circumstances of occurrence	
Trauma by plant agent**	25,9 (7)
Trauma by telluric agent**	11,1 (3)
Contact Lens**	3,7 (1)
Ocular surface disease**	66,7 (18)
Delay between start of signs and consultation (days)*	21,7 (15)
Patients referred for failure of ambulatory care **	66,7 (18)
Clinical signs	
Major axis of the abscess (mm)*	5,5 (2,2)
Small axis of the abscess(mm)*	4,4 (1,9)
Ulcer fluorescein positive**	70,4 (19)
Micro satellite abscess**	51,9 (14)
Corneal Perforation**	7,4 (2)
descemetocoele **	14,8 (4)
Hypopion (level) *	0,22 (0,24)
Flakes in anterior chamber**	40,7 (11)
Mycological data	
Yeasts on the Direct mycological exam**	33,3 (9)
Filaments on the Direct mycological exam**	18,5 (5)
Negative direct mycological exam**	48,1 (13)
Negative culture	100 (27)

Protocols of treatment	
Protocol 1**	33,3 (9)
Protocol 2**	11,1 (3)
Protocol 3**	3,7 (1)
Protocol 4**	51,8 (14)
Clinical evolution	
Best major axis of the abscess (mm)*	2,8 (2,1)
Best minor axis of the abscess (mm) *	2,2 (1,9)
Corneal Perforation **	37 (10)
Phtyse**	7,4 (2)
Duration of hospitalization (days) *	21,3 (8,2)
Long-term complications	
Corneal patch**	88,9 (24)
Posterior synechiae **	70,4 (19)

Table III. Number of reported cases of fungal keratitis in the literature

Publications	Duration	Number of fungal keratitis	Country
Our Data	2 years	27	Rabat-Morocco
Kibret and al. ^[13]	One year	67	Ethiopia
Bharathi and al ^[1]	3 years	1095	South India
Zbiba W and al ^[5]	5 years	30	Cap Bon
Galarreta and al ^[7]	13 years	30	London- England
Saha and al. ^[16]	One year	110	West Bental, India

The high recruitment of our unit can be explained by the high proportion of patients referred after failure of ambulatory therapy (antibiotics eye-drops), since most of our provincial hospitals in Morocco have only ambulatory ophthalmic activity.

Predisposing factors were similar to those reported in the literature. The fungal keratitis occur preferentially on traumatized or pathological corneas [3,13-18], or in case of immunosuppression [13,14,17,19,20]. Furthermore, we found a high proportion of patients with diabetes (29.6%), and it would have been interesting to analyse the glycemic balance to further investigate this association. The use of local corticosteroids is found in the majority of published series, further aggravating fungal keratitis and making it more difficult to manage [7,9,19,21].

The delay between the onset of symptoms and the diagnosis of fungal keratitis was long (21.6 days). The diagnosis of fungal keratitis is rarely evoked in the first place, and patients are first treated for bacterial keratitis, before the diagnosis of fungal keratitis is rectified due to corneal worsening. It is comparable to Rondeau et al.[19] (mean: 14 days. 1 to 60 days). This delay in diagnosis is the cause of a severe corneal involvement explaining the difficulties of care on the one hand, and the length of hospitalization period on the other hand. In our series, patients were hospitalized on average for 21.3 days, which is comparable with the series of Rondeau et al.[19] (16 days). The American series

of Tanure et al.[21] found a lower hospital stay, an average of 9 days. This is explained by the preferential use of therapeutics in eye drops, whereas in our case, a majority of patients received intravenous infusion solution, considering the initial severity of the lesions.

For mycological diagnosis, we did not have during the period of study in our hospital a mycology laboratory for the immediate cultivation of the samples. The systematically performed corneal scraping was addressed for direct examination which made it possible to demonstrate yeasts or filaments strongly suggestive of fungal keratitis. This explains our inability to determine the germs involved. Nevertheless, it seems that yeasts are more frequently found (33.3%), which corresponds to the data obtained by other Western series[19,21]. This higher frequency could be explained by the more temperate climate of our countries, unlike the tropical countries where the filamentous frequency is higher [1,15,16,22–24].

In Morocco amphotericin B [14,25,26], or natamycin[18,26–31] are not available. We have therefore used various alternative therapeutic protocols, preferably based on fluconazole, when a yeast was suspected, and voriconazole when the infection appeared secondary to filamentous [32]. This makes our care much more difficult, and we have to adapt to our sometimes difficult conditions.

There was a high rate of corneal perforations (37%) in our series, due to delayed diagnosis, and corneal fragility. Nevertheless, unlike the Western series[7,14,19,21,33] where keratoplasty is accessible, in our country it is not. Long-term results therefore show a high rate of residual corneal opacity. One patient in our series had an evisceration, indicated because of the association of fungal keratitis and endophthalmitis. It is comparable with the Tunisian series of Anane et al.[34] and the Indian series of Garg et al.[20]. Despite difficult conditions, the management of fungal keratitis in our care unit meets the recommendations accepted by all. The delayed diagnosis, due to the two-stage management, and the circumstances of the occurrence of these infections on fragile corneas, makes the prognosis of these affections darker. Nevertheless, the results obtained are comparable to data from the literature, with an adaptation of the protocols according to available diagnosis and therapeutic options, in particular voriconazole and fluconazole.

CONCLUSION

Fungal keratitis represent severe infections. In Morocco, like in many others countries, we have to adapt our diagnosis and therapeutic protocols according to our conditions. The particular clinical features of mycotic disease are of great help in diagnostic. The mycological data are still insufficient, and most often confirm a strong clinical presumption. The prognosis is conditioned by an early diagnosis and the rapid initiation of an effective treatment, in order to avoid the frequent, sometimes even blinding complications of these infections.

Conflicts of Interest: None

Statistical analysis used: Descriptive statistics

Settings and Design: Retrospective study.

Fungal keratitis: a retrospective study

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