Microbial keratitis: aetiological diagnosis and clinical features in patients admitted to Hospital Universiti Sains Malaysia

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ABSTRACT

Introduction: Corneal ulceration remains one of the major causes of blindness in developing countries, including Malaysia. Our objective is to determine the epidemiological characteristics, clinical features, risk factors and the aetiology of microbial keratitis in patients admitted to Hospital Universiti Sains Malaysia (HUSM).

Methods: All patients with microbial keratitis admitted to our hospital over a 16-month period from January 2004 to April 2005 were included in the study. Sociodemographic data and information pertaining to risk factors were recorded. All patients underwent examination with slit lamp biomicroscopy and corneal scrapings were sent for microbiological diagnosis.

Results: 42 patients were included in the study; 26 were male and 16 were female, with mean age of 44.5 (+/- 20.9) years. History of previous corneal trauma was present in 26 (61.9 percent) patients. Central location ulcers were more predominant (69 percent) than peripheral ulcers. Cultures from corneal scrapings were positive in 29 cases (69 percent). Of those individuals with positive cultures, 23 (79.3 percent) had pure bacterial infection, four (13.8 percent) had pure fungal infection and two (6.9 percent) had mixed growth. The most common bacterial pathogen isolated was *Pseudomonas aeruginosa* (40.5 percent), followed by *Streptococcus pneumoniae* (7.5 percent). Fungal pathogens which were isolated include *Fusarium* spp. (4.7 percent) and *Aspergillus* spp. (2.4 percent).

Conclusion: Central corneal ulceration is a problem among patients presenting with microbial keratitis in HUSM. It often occurs after corneal trauma. These findings have important public health implications for the treatment and prevention of visual morbidity due to an infective cause.

Keywords: blindness, corneal ulceration, eye infections, infectious corner ulcer, microbial keratitis, *Pseudomonas aeruginosa*

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INTRODUCTION

Microbial keratitis is a major cause of monocular blindness in developing countries. This represents only a small fraction of millions who suffer visual loss as a result of corneal trauma and subsequent microbial keratitis in the world.[1] Corneal scarring listed second only to cataracts as an important cause of blindness and visual impairment in many developing countries in Asia, Africa and the Middle East.[1] Based on the National Eye Survey conducted in Malaysia in 1996,[2] infectious corneal ulcer was found to be the fourth most common cause of blindness in Malaysia. Since the discovery of antibiotics and the advancement of medical technology, the incidence of microbial keratitis has been drastically reduced in developed countries. The incidence of microbial keratitis is still quite high in developing countries, mainly due to lack of medical awareness, or, in certain parts, due to inaccessibility to medical treatment.

In 1996, Gonzales et al reported on the incidence of corneal ulceration in the Madurai District, South India, yielding an annual incidence of 11.3 per 10,000 population.[3] The incidence of corneal ulceration in the Olmstead County, Minnesota, in eight years of study from 1980 to 1988, was 11.0 per 100,000 population, this is almost ten times less than in South India.[4] Malaysia, a developing country in the race to become a developed country by year 2020,

needs to move fast to eliminate mortality and morbidity due to infectious diseases, such as microbial keratitis. In order to eliminate or reduce the incidence of microbial keratitis, we need to identify a common causative organism as well as identify the important risk factors. The causative organisms not only differ from one country to another, or one region to another, but may also vary according to the source of economic income. For example, an agricultural-based economy will encounter more fungal-related keratitis, as compared to an industrial-based economy. The preventive strategy may differ from one area to another even in the same country. A customised strategy, is perhaps the best and most effective preventive measure.

We conducted a corneal ulcer registry in Hospital Universiti Sains Malaysia, one of the tertiary hospitals in Kelantan. Kelantan is a state in the northeast of West Malaysia, bordering Thailand, which is very much dependent on agriculture for its economic income. Our aim in this registry was to evaluate the clinical presentation, predisposing factors and microbiological diagnosis of microbial keratitis cases seen in our hospital. Based on this preliminary finding, we hope to be able to strategise our public awareness campaign in the future.

METHODS

All patients with microbial keratitis seen in our eye clinic, and subsequently admitted to the eye ward, over a 16-month period from January 2004 to April 2005, were included in this registry. Microbial keratitis was defined as a loss of the corneal epithelium, with underlying stromal infiltration and suppuration associated with signs of inflammation with or without hypopyon. Diagnosis was made according to International Classification of Diseases (ICD)-10, H-16.0 to H-16.9.

Every patient underwent a comprehensive ophthalmology examination, including slit lamp biomicroscopical examination, and characteristics of the ulcer. The site and size of the ulcer, as well as the severity of the ulcer, were documented. Both peripheral and central ulcers were included. The central corneal ulcer was defined as an ulcer involving the central 4-mm diameter of the cornea, which is the optical axis of the eye or the pupillary area (approximately 4 mm). The size of the ulcer was determined as small when the size was less than 2 mm, moderate when the size was between 2 mm and 4 mm, and large when it was larger than 4 mm. The best corrected visual acuity was taken using the Snellen chart. Systemic examination was also carried out when necessary. The recruited patients were queried on the possible risk factors of the keratitis, which include ocular and systemic comorbidity.

Corneal scraping was performed, under aseptic technique, on all patients. The specimens were sent for gram stain, direct fungal smear and inoculated directly onto blood agar, chocolate agar, McConkey agar for bacterial isolation, and Sabaroud's dextrose agar for fungal culture. The cultures for the patients' contact lenses and their cleaning solutions were also done when their usage was indicated. For all cases, treatment was commenced empirically with broad spectrum topical antibiotics immediately after the diagnosis was made. Subsequent treatment was tailored according to the microbiological diagnosis and sensitivity results. The final visual acuity was defined as the visual acuity on discharge from the ward.

RESULTS

42 patients were included in this study, 26 (62%) were male with the mean age of 44.5 ± 20.9 years (range 2–81 years). The majority of them were Malays (95%); this was representative of the ethnic distribution of the local population. 25 (60%) patients had sought medical treatment elsewhere prior to presentation. 16% of them were on topical and oral medication, whereas 11% were on a single topical antibiotic which mostly comprised Chloramphenicol, Gentamycin or Neomycin, while 5% were on combined antibiotic and corticosteroid drugs such as Neomycin and Dexamethasone. A history of recent eye injury was obtained from 26 (62%) patients. Injury involving vegetative materials, such as paddy stalk, wood and grass, contributed to 30% of cases. Nine (21%) of the patients wore contact lenses. History of chronic use of topical steroid eye drops due to allergic conjunctivitis was obtained from four (10%) patients. Three patients (7%) had ocular pathology, such as dry eyes, blepharitis, exposure keratopathy and proptosis (Table I).

In this study, we found central ulceration in 29 (69%) cases, and 27 (64%) had moderate to large ulcers. Culture-positive ulcers were found in 29 (69%) cases. Of these 29 patients, pure bacterial growth was present in 23 (79.3%) patients and pure fungal growth in four (13.8%) patients. Of the 29 culture-positive cases, five grew gram-positive

Table I. Risk factors to the development of microbial keratitis.

Risk factor	No. of cases (%)
Corneal trauma/injury	26 (62)
Contact lens usage	9 (21)
Topical steroid eye drops	4 (10)
Ocular pathology	(7)
Total	42 (100)

organisms and 18 cultures grew gram-negative organisms. *Pseudomonas aeruginosa* was the commonest bacteria isolated, followed by *Streptococcus pneumoniae*. Other organisms were *Klebsiella pneumoniae, Streptococcus sangius* and *Bacillus cefilius*. A total of four fungal species were cultured; two grew *Fusarium* spp., one *Aspergillus* spp., and one *Penicillium* spp. (Table II).

Table II. Positive cultures from corneal scraping specimens.

Organisms isolated	No. of cases (%) (n = 29)
Gram-positive	
Streptococcus pneumoniae	3 (10.3)
Streptococcus sangius	1 (3.4)
Bacilllus cefilius	1 (3.4)
Gram-negative	
Pseudomonas aeruginosa	17 (58.6)
Klebsiella pneumoniae	1 (3.4)
Mixed growth (bacterial)	2 (6.9)
Fungus	
Fusarium spp.	2 (6.9)
Aspergillus spp.	1 (3.4)
Penicillium spp.	1 (3.4)

Table III. Visual acuity of patients (n = 42) at initial presentation (admission) and discharge.

Visual acuity	On admission No. (%)	On discharge No. (%)
6/6–6/18	7 (16.7)	13 (30.9)
6/24–6/60	18 (42.9)	19 (45.2)
Counting fingers	1 (2.4)	0 (0.0)
Hand movement	11 (26.2)	6 (14.3)
Perceived light	5 (11.9)	2 (4.8)
Did not perceive light	0 (0.0)	2 (4.8)

At the end of the treatment, 13 patients (30.9%) had attained vision of 6/6 to 6/18, 19 patients (45.2%) had visual acuity of 6/24 to 6/60. Six patients had visual acuity of hand movement and another two with light perception (Table III). 37 (88%) of our patients had healed ulcers with corneal opacity. One patient with fungal infection had corneal perforation, and another one had progressed to endophthalmitis and was subjected to inadvertent evisceration. Persistently high intraocular pressure was observed in one patient who needed a prolonged anti-glaucoma treatment.

DISCUSSION

Although there was already a report on culture positive bacterial microbial keratitis in Johor Bahru, Malaysia,[5] we believe the difference in geographical location and economic income plays a sufficiently important role to warrant the setup of our present study. Moreover, this previous study was a retrospective study, with a high possibility of inaccurate determination of the size of the keratitis, as well as missing data. In addition, the study emphasised only bacterial microbial keratitis. Generally, developing countries have a higher incidence of microbial keratitis than more developed countries, such as the United States.[4,6] In regions where agricultural work is more common, vegetative material-induced corneal trauma is the major cause of microbial keratitis.[3] In contrast, in the more developed countries where contact lenses are widely used, contact lens usage is the major contribution to microbial keratitis.[4,7]

Male patients in their mid-40s contributed to the majority of our patients, with a male-to-female ratio of 3:2. Presumably, they are at a greater risk for eye injury in occupational and/or recreational settings. Furthermore, with their propensity for risk taking behaviour, males are less likely to wear eye protection. In 83.3% of our cases, the eyes were unprotected at the time of injury.[8] However, in countries where contact lens usage is more prevalent as a risk factor, female patients predominate.[7] Similar findings were also noted in Malaysia, where young female patients were found to be more prone to contact lens-related bacterial keratitis. The final visual outcome is usually good.

Before their initial presentation, 60% of all patients had consulted primary healthcare providers and were using either antibiotics or a combination of antibiotics and steroid eye drops. 11% used topical antibiotics alone and 5% used a combination of antibiotics and corticosteroids. These partially-treated microorganisms were often difficult to culture,[9] which may contribute to a lower percentage of positive culture (29 cases, 69%) in our study. These figures compare favourably with the studies conducted in South India[10] and Ghana,[11] where 68.4% and 57.3% of cultures were positive, respectively. But this does not approach the 80% isolation rate reported in Nepal by Upadhyay et al.[12] Although more than half of their patients received previous treatment, their yield rates remained high. This was primarily due to multiple scrapings from the area of ulceration and to a lesser extent, the use of several enriched cultured media for inoculation.

In spite of vegetation- or agricultural-related ocular trauma (62%) being the major predisposing factor of microbial keratitis in our setting, 79.3% of the corneal ulcers were of bacterial origin and only 13.8% were of fungal origin. This is in contrast with a study conducted in South India, an agricultural-based state where almost half of their cultures had grown fungal organisms.[10] Thylefors,

in his study, observed that in developing countries, superficial cornea trauma during agricultural work often leads to rapidly progressing corneal ulceration and visual loss.[13] Even though the amount was not accurately known, he estimated that up to 5% of all cases of blindness were due to, or at least half a million individuals worldwide have lost their sight secondary to, eye injury. Others have reported similar results in several population-based studies carried out in Africa and Asia.[11,14-17] In South Florida, *Fusarium* spp. was the most common culture positive among fungal keratitis cases.[18]

Interestingly, we found that *Pseudomonas aeruginosa* was the most common isolate, which is similar to other studies.[1,4,9,11] However, in these other studies, the major risk factor was contact lens usage (34%). *Pseudomonas aeruginosa* is a common inhabitant of soil, water and vegetation,[15] and may still be the main pathogen following vegetation-related corneal injury. Similar findings were seen in a study done in a more urbanised state of Malaysia.[5] We believe that *Pseudomonas aeruginosa* could be the true infection source of microbial keratitis in our setting. This is evident from the positive cultures and its sensitivity to standard antibiotics. Furthermore, without the presence of fungal hyphae on gram staining, polymicrobial infection is unlikely.

Although most patients had received previous treatment from general practitioners or through self-medication, none of our patients were on any type of traditional eye remedy. In contrast, in a study done in South India, 37.3% of their patients were on traditional or herbal topical treatment.[10] Potential fungal or bacterial contamination from traditional medicine poses a real problem with possible detrimental effects on the development and progression of corneal ulcer.[10] However, there is still a possibility that our patients do not disclose their encounters with traditional healers. Self-prescribed medication also impose a dangerous impact on the progression of microbial keratitis. This is compounded by their availability as over-the-counter non-prescription drugs in Malaysia. Misdiagnosis by the primary eye-care provider, without consultation from an ophthalmologist, leading to the prescription of the wrong combination of antibiotics and steroid eye drops, is another important risk factor in the progression of this blinding disease. In view of these factors, our future preventive strategies must not only create public awareness on microbial keratitis, but also include refresher ophthalmic courses for general practitioners, especially on the appropriate prescription of antibiotics and steroid eye drops.

Of the non-traumatic risk factors, contact lens usage contributed to 21% of all cases. Erie et al reported, in a Minnesota study, that the cases of ulcerative keratitis associated with contact lens usage increased from zero percent in the 1950s and 1960s to 32% in the 1970s and 52% in the 1980s.[4] These figures were directly related to the increasing usage of contact lenses either for refractive correction or cosmetic purposes. Other causes are steroid eye drops and ocular pathology, such as dry eyes, blepharitis, and exposure keratopathy.[1,7,11-13] Tanure et al found that chronic ocular surface disease was the main risk factor for fungal keratitis in their series.[19] Interestingly, all our patients had no systemic predisposing factors that could contribute to an ulcer development, except for a single patient who has poorly-controlled diabetes mellitus.

Our study also revealed that 69% of our patients had a centrally-located ulcer, in which 88% of them healed with a central corneal opacity. This contributed to the poor visual acuity of most patients. Only 12% of them attained 6/18 visual acuity and better. However, this is not a true reflection of the best visual outcome; perhaps with penetrating keratoplasty, this percentage could be higher. Retrospective study of fungal keratitis in Singapore showed that almost half of their cases required therapeutic penetrating keratoplasty due to the involvement of central large persistent ulcers.[20]

This study has illustrated that microbial keratitis and corneal opacity are important potentially blinding conditions in a developing nation; this can be a setback to the economic growth of the country. This knowledge is essential to define the magnitude of the problem, in terms of healthcare costs and the socioeconomic burden of blindness. An efficient public health programme for rapid referral, diagnosis, treatment and ultimately, the prevention of microbial keratitis, in the population at risk, is vitally important.

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