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Fungal corneal ulcers: our 5-year experience in Bintulu

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Abstract

Purpose: The aim of this study is to investigate the epidemiological and aetiological pattern of fungal corneal ulcers treated in Hospital Bintulu, Sarawak.
Study design: Cross-sectional study.
Methods: This study is based on the data collected from clinical records of patients with culture-positive fungal corneal ulcer who presented to Hospital Bintulu from 2016 to 2020. Data was analysed using descriptive statistical methods.
Results: A total of 13 patients had fungal corneal ulcer. Males (84.6%) were more commonly affected compared to females (15.4%). The age of the patients ranged from 19 to 67 years. The commonest age group involved was 21–40 years, constituting more than half of the patients (53.8%). The mean age of the patients was 38 years old. *Fusarium* sp. was isolated in eight of them (61.5%), all of which had a history of palm oil dust insertion into the eye prior to presentation. Other fungal pathogens found include *Phellinus noxius* sp. in two cases (15.4%) as well as *Ascomyces* sp., *Nectriaceae* sp., and *Colletotrichum trunchatum* sp. in one case each (7.6%). Hypopyon was seen in eight cases (61.5%), where six cases were caused by *Fusarium* sp. while *Ascomyces* sp. and *Nectriaceae* sp. contributed one case each. Mixed fungal and bacterial infection was seen in two cases (15.4%).
Conclusion: This study showed that *Fusarium sp.* is the commonest pathogen causing

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fungal corneal ulcer and affects predominantly young male plantation workers. The establishment of a proper framework to educate as well as strict enforcement of occupational safety may reduce the incidence of this disease in the population.

Keywords: blindness, fungal corneal ulcer, fungal keratitis, fungi, *Fusarium*

Ulser kornea akibat jangkitan kulat: pengalaman 5 tahun di Bintulu

Abstrak

Tujuan: Matlamat kajian ini adalah untuk menyiasat pola epidemiologi dan etiologi jenis kulat penyebab ulser kornea yang dirawat di Hospital Bintulu, Sarawak.
Reka bentuk kajian: Kajian keratan rentas.
Bahan dan kaedah: Kajian ini adalah berdasarkan data yang dikumpul daripada rekod klinikal pesakit dengan ulser kornea yang positif kultur untuk kulat, yang menerima rawatan di Hospital Bintulu daripada 2016 sehingga 2020. Data dianalisis menggunakan kaedah statistik deskriptif.
Keputusan: Sejumlah 13 pesakit mempunyai ulser kornea akibat jangkitan kulat. Lelaki (84.6%) adalah lebih kerap mendapat jangkitan ini berbanding wanita (15.4%). Umur pesakit yang terlibat adalah di antara 19 hingga 67 tahun. Umur 21-40 tahun merupakan julat umur yang paling berisiko dan mereka ini merangkumi lebih separuh daripada jumlah pesakit yang terlibat. Purata umur pesakit adalah 38 tahun. *Fusarium sp.* telah dikenalpasti dalam 8 pesakit (61.5%) di mana kesemua pesakit mempunyai sejarah kemasukan habuk kelapa sawit ke dalam mata sebelum hadir ke hospital untuk rawatan. Patogen kulat lain yang ditemui termasuk *Phellinus noxius sp.* dalam 2 kes (15.4%) serta *Ascomyces sp., Nectriaceae sp.* dan *Colletotrichum trunchatum sp.* dalam 1 kes setiap satu(7.6%). Kehadiran nanah (hypopyon) dilihat dalam 8 kes (61.5%) di mana 6 kes disebabkan oleh *Fusarium sp.* manakala *Ascomyces sp.* dan *Nectriaceae sp.* masing-masing menyumbang satu kes. Jangkitan kulat dan bakteria bercampur dilihat dalam 2 kes (15.4%).
Kesimpulan: Kajian ini menunjukkan bahawa *Fusarium sp.* adalah patogen yang paling kerap menyebabkan ulser kornea akibat jangkitan kulat dan kebanyakannya melibatkan pekerja ladang lelaki yang masih muda. Pembentukan satu rangka kerja yang boleh memberi kesedaran dan pengetahuan serta penguatkuasaan ketat keselamatan pekerjaan boleh mengurangkan kejadian penyakit ini di daerah Bintulu.

Kata kunci: buta, Fusarium, keratitis kulat, kulat, ulser kornea kulat

Introduction

Corneal ulcerations are described as corneal epithelium loss with underlying infiltration and suppuration of the stroma associated with signs of inflammation with or without the presence of hypopyon.[1] Corneal ulcers have been acknowledged as one of the most common causes of preventable blindness, second only to cataract in tropical countries.[1,2] In developing countries, approximately 1.5 to 2 million new cases of monocular blindness every year are partly attributed to corneal ulceration.[3] The causative organisms that infect the cornea includes bacteria, viruses, fungi, and parasites.[2]

Fungal keratitis forms a prime component of this disease spectrum and its incidence has been noted to vary from 17% to 36% in various regions worldwide.[4] Various clinical series set in tropical, warm climates such as south Florida, Africa, the Middle East, South Asia, India, and Singapore have described the predominance of fungal keratitis.[5] While India recorded an incidence rate of 44% to 47% due to its tropical climate, Ghana reported an incidence of 37.6 %.[6,7] This is followed by Bangladesh, 36%, and subsequently by south Florida and Nepal with a rate of 35% and 17%, respectively.[7] Geographic regions with temperate climates, however, showed a low incidence as depicted by Great Britain and northern United States.[7]

More than 105 species, classified into 56 genera have been recognized as the causative agents of mycotic keratitis.[8-10] Filamentous fungi, mainly *Fusarium* sp. and *Aspergillus* sp., as well as yeast-like fungi, particularly *Candida* sp., are the two medically important forms of fungi identified.[10] Fungal infections of the cornea often exhibit yellowish-white or greyish-white infiltrates with soft, creamy, raised exudates at the base of the ulcer.[7] Hypopyon is present in 55% of cases, hyphate edges or feathery borders are seen in 70% of cases, and satellite lesions appear in 10% of patients.[7] However, some fungal infections tend to mimic other types of stromal inflammation, posing a challenge in choosing the treatment regime.[6] In addition to the clinical findings, laboratory diagnosis by detection of fungal pathogens on direct microscopy and their isolation by culture is crucial.[6] Prompt diagnosis and treatment are essential to save vision and prevent complications such as endopthalmitis.[10] While current advances in diagnosis and pharmacological treatment are in place, 15–27% of patients still require surgical interventions such as keratoplasty, evisceration, or enucleation due to advanced disease at presentation or failure of medical treatment.[4]

The ophthalmological services in Bintulu Hospital receive emergency eye referrals from many interior primary care facilities. Cases of corneal ulcers contribute to the number of referrals apart from trauma and thus present an opportunity to study the disease from a single health facility. This study is intended to investigate the epidemiological and aetiological pattern of fungal corneal ulcers treated in Hospital Bintulu, Sarawak.

Methods

This study was conducted in compliance with ethical principles outlined in Declaration of Helsinki as well as Malaysian Good Clinical Practice Guideline and has obtained ethical clearance from the country's Medical Research and Ethics Committee. In this cross-sectional study, case records of all patients with fungal corneal ulcers who presented to the Department of Ophthalmology of Bintulu Hospital, Sarawak in the 5-year study period from January 2016 to December 2020, were analysed. All patients underwent a thorough medical history with complete clinical and microbiological examination during presentation. After a clinical diagnosis of infectious corneal ulcer was made, corneal scrapings were taken under slit lamp from the edge and base of ulcers, and were smeared onto two separate slides for direct microscopic examination with gram stain and 10% KOH preparation. Corneal scrapings were also directly inoculated onto Sabouraud agar for fungal culture, and McConkey agar, blood agar, and chocolate agar for bacterial culture.

A fungal corneal ulcer diagnosis was achieved after a positive result in gram stain or culture agar. All patients were started on empirical treatment; the treatment was modified according to response and microbiological tests. Information on possible predisposing factors, demographic data, microbiology results, treatment received, treatment continuity, and visual outcome at the end of 3 months or at the completion of the treatment (whichever happened earlier) were collected from the case records and analysed. Visual impairment of the affected eye was classified according to the International classification of Diseases 11, where the patient is defined to have no visual impairment when visual acuity (VA) is 6/12 and better; mild impairment when VA is worse than 6/12 but better than or equal to 6/18; moderate impairment when VA is worse than 6/18 but better than or equal to 6/60; severe visual impairment when VA is worse than 6/60 but better than or equal to 3/60; and the affected eye is defined as blind when VA is worse than 3/60.[11] Patients with incomplete data in case records, immune-compromised patients, and those who were partially treated prior to presentation were excluded. Descriptive analysis was used in this study.

Results

In the span of 5 years, from January 2016 to December 2020, a total of 13 patients were treated for fungal corneal ulcer. The first 3 years, from 2016 to 2018, recorded only one case each year. Subsequently there was a surge to six cases in 2019 and a slight drop to four cases in 2020. Males (84.6%) were more commonly affected compared to females (15.4%) (Table 1). Foreigners comprised 69.2% of total patients, with the majority coming from Indonesia. The age of the patients ranged from 19 to 67 years old (Table 2). The commonest age group involved was 21–40

Table 1. Gender and ethnicity distribution of fungal corneal ulcer cases

Gender	Ethnicity				Total
	Malay	Iban	Chinese	Foreigner	
Male	1	2	0	8	11
Female	0	0	1	1	2

Table 2. Age distribution of patients with fungal corneal ulcers

Age distribution (years)	Total
0–20	2
21–40	7
41–60	2
61–80	2

years, constituting more than half of the patients (53.8%). The mean age of the patients was 38 years old.

Fusarium sp. represented the highest proportion of fungal pathogen, accounting for eight patients (61.5%). Other fungal pathogens found included *Phellinus noxius* sp. in two cases (15.4%), *Ascomyces* sp., *Nectriaceae* sp., and *Colletotrichum trunchatum* sp. in one case each (7.6%). Hypopyon was seen in eight cases (61.5%): six cases were caused by *Fusarium* sp., while *Ascomyces* sp. and *Nectriaceae* sp. contributed one case each. Mixed fungal and bacterial infection was seen in two cases (15.4%).

Table 3 summarizes the preceding trauma and isolated organisms among patients. Oil palm dust was found to be the most common source of trauma in our patients. A total of nine patients (69.2%) claimed to have experienced dust particles from palm oil fruit or leaves falling into their eye before their painful ordeal begun. Most of them were Indonesian palm oil workers and none of them wore goggles or personal protective gear. Of these patients, Sabouraud culture grew *Fusarium* sp. in eight and the remaining one grew *Nectriaceae* sp. A patient whose preceding trauma was contact lens was infected with *Phellinus noxius* sp., while *Colletotrichum trunchatum* sp. was isolated from a patient injured by a plant branch while gardening. The remaining two patients were unsure of any presence of trauma.

Table 4 summarizes the percentage of visual impairment among patients. More than one-third (38.5%) of our cases were blind (as per ICD 11) in the affected eye at the time of discharge or default to follow-up. Severe visual impairment affected 7.7% cases. Recovery with no visual impairment was observed in 30.7% of patients, while the remaining 15.4% and 7.7% were categorized under moderate and mild visual impairment, respectively. Patients presented to the hospital at an average of 6.9 days after onset of symptoms and a regrettable 69.2% either requested an “at own risk” discharge or defaulted follow-ups prior to treatment completion.

Table 3. Preceding trauma and organisms isolated from the corneal ulcers

Organism	Preceding trauma				Total
	Palm oil dust	Contact lens	Plant branch	Unknown	
Fusarium sp.	8	0	0	0	8
Nectriaceae sp.	1	0	0	0	1
Ascomyces sp.	0	0	0	1	1
Colletotrichum trunchatum sp.	0	0	1	0	1
Phellinus noxius sp.	0	1	0	1	2
Total	9	1	1	2	13

Table 4. Percentage of patients with visual impairment at the time of discharge or default to follow-up according to severity as per ICD 11

Severity	Visual impairment (%)
None (VA 6/12 and better)	30.7
Mild (VA worse than 6/12 but better than or equal to 6/18)	7.7
Moderate (VA worse than 6/18 but better than or equal to 6/60)	15.4
Severe (VA worse than 6/60 but better than or equal to 3/60)	7.7
Blindness (VA worse than 3/60)	38.5

VA: visual acuity

Discussion

The prevalence of fungal corneal ulcer from various fungal pathogens has been estimated to be 1.3/100,000 people in Malaysia.[12] Most studies have addressed the role of geographic and climate variation in the predominance of certain fungal agents.[1,4,6,13-14] Bintulu, being a region with tropical climate, has been seeing a rise in fungal corneal ulcers. Therefore, it is crucial to identify the commonest fungal pathogen, correlate with risk factors, and manage the diseases before it progresses into a fulminating infection leading to blindness. While treatment of this debilitating disease has been costly and burdensome, the final visual outcomes are often

guarded.[15] The ability of fungal infections to masquerade as other infections leads to delayed diagnoses and makes treatment more challenging.

Fusarium sp. was the commonest species found to have infected our patients. This concurs with many previous studies that have yielded similar results.[16-18] It is important to note that all patients whose fungal isolates were *Fusarium* sp. were Indonesian palm oil workers in Sarawak. Agriculture is closely related to the incidence of fungal corneal ulcer in many countries.[19-21,20] Initial history from these patients revealed that symptoms were preceded by traumatic injury caused by palm oil dust or leaves while working. *Fusarium* sp. is known to be found in almost all ecosystems and commonly infects agricultural crops, therefore explaining our findings.[22] In addition, this species is said to be found in organic debris and all plant parts, from highest flowers to deepest roots.[23] Interestingly, a study in Malaysia on crown disease, a disease affecting palm oil trees that has been reported from palm oil plantations worldwide, isolated five different types of *Fusarium* sp. from palm oil leaves.[24] Moreover, a study has quoted that humid and warm climates are favourable to the growth of this fungus, which explains its prevalence in this part of the world.[25]

Our mean age of 38 years old does not follow trends in other studies performed worldwide, where the mean ranged from 40 to 56.1 years of age.[26-29] The lower figure may be attributed to the fact that most of the study subjects were young palm oil plantation workers. According to a study conducted in east Malaysia in 2019, the mean age of palm oil plantation workers was 30 years old, with males dominating the industry by 80%.[30] Male preponderance in this infection was evident with a male-to-female ratio of 5.5:1, mostly related to occupational ocular trauma. Men are also known to be more actively involved in outdoor activities and frequent contact with soil and nature, predisposing them to a greater exposure to fungal pathogens.[17]

Infection involving *Fusarium* sp. and *Aspergillus* sp. is a significant risk factor for hypopyon, a common finding in fungal keratitis.[31] Ocular examination findings in our study revealed hypopyon in 61.5% subjects. In China, Xu *et al.* observed hypopyon in 52.6% of fungal keratitis patients, while Shi *et al.* noted hypopyon in 47.9% of patients diagnosed with fungal keratitis.[31-32] A similar study in Mexico revealed hypopyon in 65.5% patients with *Fusarium* keratitis.[33] In this study, we noticed hypopyon in 75% of patients with *Fusarium* keratitis. On that account, hypopyon may be considered as a clinical indicator for commencing empirical antifungal regime after correlation with presenting history, which may improve prognosis of this debilitating disease.

According to the ICD 11, 38.5% of our patients were classified as blind and 7.7% as severely visually impaired in the affected eye at the time of discharge or default to follow-up. This was further worsened by a high “at own risk” discharge and default to follow-up rate of 69.2%, with 77.8% of defaulters being foreigners. The financial constraints following the need for a long hospital stay, travelling for follow-up, and costly antifungal medications may be contributing factors for this high rate, especially among foreigners. A study based on medical treatment for Fusarium keratitis reported that patient may require long hospital stay with an average of 31.5

days with a mean fee of USD 1,559.39.[34] The need for frequent travel for follow-up in certain cases may also be a major barrier, particularly for those travelling from the interiors of Sarawak. Furthermore, in severe cases such as corneal perforation, patients are required to travel approximately 1,200 km to west Malaysia by flight for a penetrating keratoplasty.

Bintulu has the third largest palm oil plantation in Sarawak, with foreigners comprising 47% of the workers employed.[35] As observed in our study, most of our patients were foreign palm oil plantation workers. A study done in west Malaysia reported that most palm oil plantation workers are on low incomes.[30] Many palm oil companies subscribe insurance for their employees. However, some faile to do so, leading to inability to afford medical expenses when unfortunate events occur. This problem arises commonly among foreigners who commonly request an "at own risk" discharge to return to their native country for further treatment, as observed in many of our study patients. Some studies have also addressed socioeconomic status as a potential risk factor of fungal corneal ulcers; this should be taken into account considering the fact that Sarawak has recorded a gross household income lower than the national average in the nation's recent socioeconomic report.[2,9,36] Tackling these financial burdens may lead not only to a reduction of fungal corneal ulcer cases but also improve prognosis of those suffering from this disease.

Most palm oil workers are not provided with protective gear for use at work.[30] According to national guidelines, the Department of Occupational Safety and Health (DOSH) Malaysia stressed the need for personal protective equipment wear for pesticide sprayers in the agricultural field, whereas there were no clear guidelines for fresh fruit harvesters.[37] Within palm oil plantations, DOSH should create awareness and enforce the use of protective goggles as preventive measures also among fresh fruit harvesters, now that it is evident that trauma from palm oil dust is a major preceding factor for fungal corneal ulcers. A direct referral pathway to specialist hospitals from these plantations via their DOSH team may also hasten the commencement of treatment, as patients only present to the hospital 6.9 days after initial symptoms. Early treatment may reduce ocular morbidity, reduce duration of hospitalization, and increase national work productivity.

Conclusion

This study showed that the *Fusarium* sp. was the commonest pathogen causing fungal corneal ulcers and affected predominantly young male plantation workers. The establishment of a proper framework to educate as well as strict enforcement of occupational safety may reduce the incidence of this disease in the population.

Declarations

Ethics approval and consent to participate

This is a retrospective study of the medical records of patients in Hospital Bintulu from 2016 to 2020. This study adhered to the tenets of the Declaration of Helsinki and ethical approval was obtained from the Medical Research and Ethics Committee, Ministry of Health Malaysia (Research ID: 59201).

Competing interests

The authors declare no conflicts of interest with respect to the publication of this article.

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