

Clinical Characteristics of Fusarial Keratitis

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Abstract

Amongst corneal diseases, microbial keratitis is a major blinding disease. Eight cases of *Fusarium* keratitis were identified in central Taiwan. Eye pain was mostly noted at initial clinical presentation. All received the topical antifungal agent, and therapeutic lamellar keratectomy. Early diagnosis of fungal keratitis and its treatment are important in preventing complications. (J Intern Med Taiwan 2013; 24: 205-211)

Key Words: Corneal ulceration, Fungal keratitis, *Fusarium* sp.

Introduction

Corneal ulceration and ocular trauma account for 1.5 to 2 million new cases of monocular blindness every year, according to the World Health Organization report, and blindness is a major public health problem for developing countries¹. The etiological and epidemiological pattern of corneal ulceration varies. Srinivasan et al. reported that although 44% of corneal ulcers were caused by fungi², more than 70 species of filamentous fungi have been identified as etiological agents of fungal keratitis. Keratitis due to *Fusarium* infection was uncommon earlier, and such cases have emerged since 2011. Short et al. has proposed that plumbing systems might serve as a significant environmental reservoir of human-pathogenic isolates of *Fusarium*³. We conducted this study to identify the epidemiological features amongst patients with Fusarial keratitis in central Taiwan.

Materials and Methods

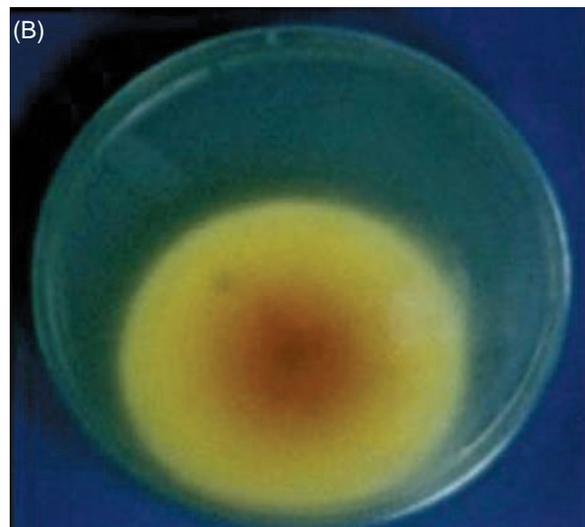
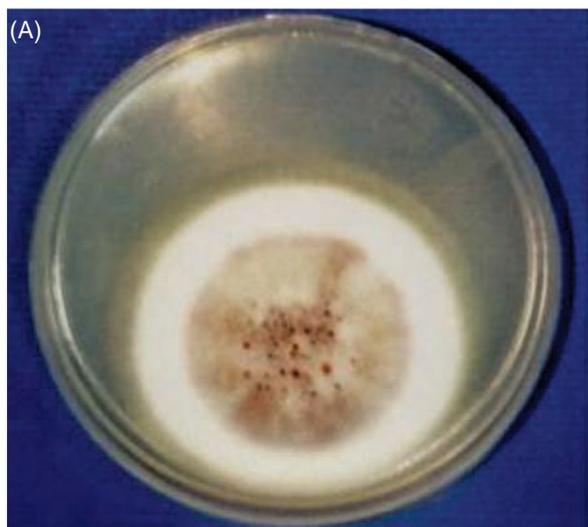
Population of Changhua is mostly served by the study hospital and has accumulated comprehensive clinical records since 1867. Changhua County (population 1,298,286 in 2013) is located in central Taiwan. The medical records of eight clinically diagnosed *Fusarium* keratitis patients during the time period from January 1st 2009 to December 31st 2011 were studied. Cases of *Fusarium* keratitis were identified using both the microbiology databases and medical records dataset by International Classification of Diseases, 9th edition, clinical modifications (ICD-9-CM) at study hospital. We entered into computerized indexes using the ICD-9-CM code number 370.05. Only cases with positive *Fusarium* isolates were reviewed. A medical chart exists for each case, from which medical diagnoses, surgical interventions and other key information from medical records are regularly abstracted.

The specimen from cornea obtained was directly smeared on a labeled slide of 10% KOH wet mount, Gram's stained and incubated directly in solid media (10% sheep blood agar, Sabourand's Dextrose agar) in a row of C-shaped streaks. The Sabourand's dextrose plates were observed for 21 days in room temperature. Any growth obtained was further identified by microscopic aspects of texture, pigmentation, mycelium arrangement and conidium types by lactophenol cotton blue mount. The culture was considered positive if the growth of the same fungal species was found in more than one solid media.

Results

Eight patients were diagnosed as having fungal keratitis based on clinical findings as well as microbiological reports of fungal filaments in KOH mount, Grams staining and fungal culture. The demography and clinical presentations of 8 *Fusarium* keratitis patients have been shown in

Table 1. The ratio of male to female was 1:3. The mean patient age was 65 years, and elderly patients (>65 years) were more frequently affected (5/8, 62.5%). The mean admission days were 9.6 days. No obvious predisposing factor could be identified in 6 patients, except for contact with dirt in 2 patients. The initial clinical presentations included eye pain (5/8), foreign body sensation of eye (4/8), blurred vision (1/8) and photophobia (1/8). The underlying diseases included hypertension (3/8), coronary artery disease (1/8), and hepatoma (1/8). The physical examination included corneal stromal infiltration decreased with desmatocoele (8/8), perforated corneal ulcer (1/8), and anterior chamber flat with exudate (1/8). Three patients showed positive KOH smear of corneal scrapings for fungi. All of the eight patients showed positive culture for *Fusarium* keratitis (Supplement). All 8 patients received the topical antifungal agent (0.1% amphotericin B 1 gtt q1H, 0.2% fluconazole 1 gtt q 1H) at initial stage. Two patients received amphotericin-B 0.0025 mg



Supplement

Culture of *Fusarium* sp.

Figure 1. A pure culture obtained from a single hyphal tip isolation. Colony growth diameters on Sabouraud dextrose agar after incubation in the dark for 4 days at 25°C. Culture pigmentation on Sabouraud dextrose agar after incubation for 10-14 days with a daily exposure to light. The macro morphology shows typical colony color for a hyaline hyphomycete, id est any color except brown, olivaceous black or black. Top picture (A) shows chocolate pigmentation and gray colony. Bottom picture (B) shows cream-color pigmentation and yellow colony.

Table 1. The demography and clinical presentations of 8 *Fusarium* keratitis patients

Case number/ age/sex/eye	Insult to cornea	Initial complains / Diagnosis of eye	VA initial	Severity of corneal stromal infiltration/ Corneal condition	Surgical intervention	VA last follow-up	Complications	Admission duration/ (days)/ Total follow-up duration(months)	Eye, outcome
1/71/F/L	Unknown FB	eye pain(14 D)/MCU (os), PCU(os)	HM	3.0 x 2.5mm, central/ epithelial defect	LK, AMT, patch graft	CF	negative	18/18	AMT
2/59/F/R	Dirt	foreign body sensation (7 D)/MCU (od)	0.1	2.2 x 2.2mm, paracentral/ epithelial defect	LK	0.2	negative	7/3	Recovery
3/83/F/L	Unknown FB	red eye(7 D), foreign body sensation (7 D)/ PCU(os)	0.1	2.2 x 1.5mm, central/ epithelial defect	LK	0.3	Glaucoma, PAS	6/6	Recovery
4/54/M/R	Unknown FB	eye pain(3 D), foreign body sensation (3 D)/ MCU (od)	0.1	3.0 x 2.5mm, central/ epithelial defect	LK	0.3	negative	17/3	Recovery
5/68/F/L	Unknown FB	eye pain(7 D)/ corneal leukoma (os), MCU (os)	0.2	3.0 x 1.8mm, peripheral/ epithelial defect	LK	0.4	negative	7/4	Recovery
6/67/F/R	Unknown FB	eye pain(7 D), blurred vision(7 D), ocular congestion (7D)/ MCU (od)	0.3	1.5 x 1.5mm, peripheral/ epithelial defect	LK	0.4	negative	10/3	Recovery
7/43/M/R	Unknown FB	eye pain(28 D), photophobia(28 D)/ MCU (od)	0.1	3.0 x 2.5mm, peripheral/ epithelial defect	LK	0.2	negative	7/3	Recovery
8/73/F/R	Dirt	foreign body sensation (1 D)/MCU (od)	0.1	5.0 x 2.5mm, paracentral/ epithelial defect	LK	0.1	Glaucoma, PAS	7/6	Recovery

Abbreviations: AMT: amniotic membrane transplantation; CF, counting finger visual acuity; FB, foreign body; HM, hand motion visual acuity; LK, lamellar keratectomy; MCU: mycotic corneal ulcer; PAS, peripheral anterior synechiae; PCU: perforated corneal ulcer; VA, visual acuity.

Table 2. Literature review for *Fusarium* keratitis

Author	Year	Country	Patient number	Purpose	Risk factors	Microbiology (number)	Treatment	Outcome	References
Panda A	1997	India	211	epidemiologic and microbiologic evaluation.	improper contact lens wear and the use of specific contact lens solutions	Fusarium (23)	NM	NM	Panda A, et al. <i>Cornea</i> 1997; 16: 295-9.
Gopinathan U	1991-2000	India	1352	epidemiological features and laboratory results of 1,354 cases of fungal eyes; keratitis	Ocular trauma predisposed to infection in 736 (54.4%) of 1,354 cases of fungal eyes;	Fusarium (506)	NM	NM	Gopinathan U, et al. <i>Cornea</i> . 2002; 21: 555-9.
Tanure MA	1991-1999	Pennsylvania, USA	24	report the spectrum of fungal keratitis	Predisposing factors included chronic ocular surface disease (41.7%), contact lens wear (29.2%), atopic disease (16.7%), topical steroid use (16.7%), and ocular trauma (8.3%)	Fusarium sp (6)	Six patients had penetrating keratoplasty	13 eyes (54.1%) had the best corrected	Tanure MA, et al. <i>Cornea</i> . 2000; 19: 307-12.
Lin HC	2005	Taiwan	18	report the experience of fungal keratitis	Twig, 3;Vegetable material, 3; Unknown FB, 3; Pterygium surgery, 1; SCL, 1; Glaucoma surgery, 1; Grass, 1; Bamboo, 1; Dirt, 1; Trichiasis, 1; Lime, 1; Spider web, 1	Fusarium (18)	Group A (n=13), debridement, lamellar keratectomy; Group B(n=5), lamellar keratectomy combined with amnioticmembrane transplantation	The mean re-epithelialisation time was 12.67 days	Lin HC, et al. <i>International Journal of Clinical Practice</i> 2005; 59: 549-554.
Dahlgren Matthew	2007	U.S.	104	molecular genotyping of isolates from the Singapore outbreak	The positive predictive value of clinical diagnosis is 45% (95% CI, 17%–77%) for 13 fungal keratitis	20 with <i>Pseudomonas</i> sp, 13 with fungi, 9 with <i>Acanthamoeba</i> sp	NM	NM	Dahlgren MA, et al. <i>Am J Ophthalmol</i> . 2007; 143: 940-944.
Roland Jureen,	2008	Singapore	66	fungal keratitis caused by members of the <i>Fusarium solani</i> species complex	improper contact lens wear and the use of specific contact lens solutions	fungal keratitis caused by members of the <i>Fusarium solani</i> species complex	NM	NM	Jureen R, et al. <i>BMC Infect Dis</i> . 2008; 8: 92.

Table 2. Literature review for *Fusarium* keratitis (continued)

Author	Year	Country	Patient number	Purpose	Risk factors	Microbiology (number)	Treatment	Outcome	References
Bullock John	2009	US	483	root cause analysis of the <i>Fusarium</i> keratitis epidemic of 2004-2006	storage temperatures of contact lens	<i>Fusarium sp</i>	NM	NM	Bullock JD, Trans Am Ophthalmol Soc. 2009; 107: 194-204.
Ferrer Consuelo	2011	Spain	27	assess the utility of polymerase chain reaction in diagnosing fungal keratitis	NM	NM	NM	NM	Ferrer C, et al. J Ophthalmic Inflamm Infect. 2011;1:15-22.
Lin HC	2012	Taiwan	33	To evaluate the treatment outcomes and costs of early keratectom	NM	<i>Fusarium</i> Keratitis (13)	13 patients, receiving early keratectomy; 20 patients, treating medically	Disease duration and median hospitalization costs per patient are lower in the early keratectomy group	Lin HC, et al. PLoS One. 2012; 7: e42126

Notes: NM meant "no mention in the article".

intra-cameral injections. One patient received 1% voriconazole q 1 H, and also received intra-vitreous voriconazole injections. Two of them received oral ketoconazole, and one patient received oral fluconazole. All of them received lamellar keratectomy, and one received amniotic membrane transplantation. All of them recovered gradually.

Discussion

Our study is the first to describe *Fusarium* keratitis in central Taiwan. Risk factors include injury to the cornea, a history of corneal trauma with vegetable matter or organic matter, and usage of contact lens^{2,4}. Steroid use as initial therapy has been reported in 1–30% of patients having microbial keratitis². We reviewed the literature for *Fusarium* keratitis, and have summarized it in Table 2. In our study, two of eight patients had contacted with dirt, and others did not have any risk factors. Short et al. has proposed that plumbing systems might serve as a significant environmental reservoir of human-pathogenic isolates of *Fusarium*, and in the study found that 66% of sinks and 80% of buildings surveyed yielded at least one *Fusarium* culture³. Short et al. stated that some major *Fusarium* types were frequently isolated from plumbing drains³. Out of eight patients, a few maybe have acquired the *Fusarium* infection from the environment, such as plumbing systems.

Early diagnosis of *Fusarium* keratitis is not easy. Direct examination of smears from corneal scrapings examined by 10% KOH wet mount preparation and/or gram stain continue to be an important mode of identifying causative organism in patients with microbial keratitis. In our study, three (37.5%) patients showed positive KOH smear of corneal scrapings for fungi. The sensitivity of KOH and gram stain in preliminary identification of fungal filaments has also been reported in other studies^{5,6}.

Keratitis due to *Fusarium* infection was uncommon before 2011, and many such cases have

emerged since then. *Fusarium* sp. were the third major etiologic agents (10.81%) of fungal keratitis in Saha's study⁷. Sharma's studies have implicated *Fusarium* species (37–62%) as major pathogens, with dematiaceous fungi being the cause in 8 – 16.7% of patients with fungal keratitis⁵. *Fusarium* keratitis is the main etiological organism responsible for mycotic keratitis (43%) in south India. Factors other than climatic conditions, such as altered local defense mechanisms and immune suppression as well as environmental reservoirs of *Fusarium* in plumbing systems may also be responsible for the incidence of *Fusarium* infection.

Surgical intervention, in the form of therapeutic keratoplasty, continues to be an important mode of management. In our study, all patients needed therapeutic lamellar keratectomy. Regina L et al. reported from Texas that out of 29 *Candida* keratitis patients, 15 patient (51.72%) required surgical intervention, of which 13 patient had therapeutic penetrating keratoplasty and 2 eyes needed enucleation⁸. Vemuganti et al. reported that maximum fungal species identified from corneal buttons after therapeutic keratoplasty were *Fusarium* sp.⁹. In our study, it was seen that all patients suffering from *Fusarium* species infections required a surgical intervention. Lin HC described early keratectomy in moderate *Fusarium* keratitis may reduce length of hospital stay, hospital costs, and perforation rates¹⁰. Lin's study supports our results.

Our study summarized the profile of fungal pathogens responsible for corneal ulceration in Central Taiwan. Topical therapy and oral therapy are not always sufficient to eradicate infection in patients with *Fusarium* keratitis. Therapeutic keratoplasty continues to remain an important treatment modality. Particular care should be taken in identification of the pathogenic organism on

basic microbiological procedures, so as to initiate appropriate therapy. Early diagnosis and treatment of fungal keratitis are important in preventing complications and loss of vision. Also, keratitis due to *Fusarium* infection needs to be considered in mycotic keratitis.

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镰刀黴菌性角膜炎臨床特性

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摘 要

眼角膜疾病是導致病患失明的主要疾病。我們報導八例镰刀黴菌性角膜炎 (Fusarium keratitis) 病例。在最初的臨床表現主要出現眼睛疼痛。所有病患都接受局部抗黴菌抗生素治療與角膜切削術。镰刀黴菌性角膜炎的早期診斷與治療，對於預防併發症的發生是很重要的。