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10.4103/tjo.tjo_93_20

Ocular sporotrichosis from a tertiary referral center in Malaysia and review of literature in Southeast Asia

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Abstract:

Ocular sporotrichosis is rare in Malaysia and Southeast Asia and is increasingly reported in endemic areas of Brazil and Peru. We describe six cases of ocular sporotrichosis involving the bulbar conjunctiva and lid with a literature review on ocular sporotrichosis in Southeast Asia. In these series, four patients presented with similar findings of granulomatous lesion at the palpebral conjunctiva within 1–3 weeks. There was one case mistakenly diagnosed as conjunctival concretion due to its multiple yellowish nodules on the palpebral conjunctiva and another case as chalazion due to swelling of the lower lid. All patients showed immunocompetence. Four patients had an immediate contact with sick cats, one patient had a history of skin scratched by a healthy cat, and another patient had a history of gardening without direct contact with cat. Culture from conjunctival biopsy obtained from five patients and from ruptured lower lid nodules of one patient yielded *Sporothrix schenckii*. The patients were successfully treated with oral itraconazole 200 mg twice daily. Two patients developed symblepharon after completing treatment, while four patients showed good results without any sequelae.

Keywords:

Conjunctival sporotrichosis, granulomatous conjunctivitis, ocular sporotrichosis, *Sporothrix schenckii*, sporotrichosis

Introduction

Sporotrichosis is a worldwide cutaneous fungal infection by *Sporothrix schenckii*, a dimorphic fungus commonly found in contaminated soil, dead plant, and leaf matters.^[1] The fungus was inoculated and transmitted into the human body by breach in the skin due to bites or scratches by a contaminated feline or cat.^[1] Direct inoculation on the traumatized skin area by outdoor activities such as gardening is the other possible route of entry.^[1] Ocular involvement is rare, but the number of reported cases is increasing in endemic areas in Brazil and Peru.^[2] Eyelid nodules and granulomatous conjunctivitis are the most common reported presentation in the eye.^[3,4]

There was sporadic distribution of cases from Asian countries, and the data were limited. A PubMed literature search from 2014 up to the present reported the largest number of cases only in China and sparse distribution of ocular sporotrichosis in Japan, Thailand, and Malaysia.^[3,5-7] Northeast China had the highest number of reported cases of all published data.^[3] Availability and variability of their diagnostic tools cause a higher number of cases who were diagnosed in Jilin province area in China than other regions.^[3]

We believed that the number of cases is underreported from Southeast Asian countries. Malaysia and its neighbors are tropical countries with high humidity and preponderance to fungal infection. Furthermore, its ocular presentation

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How to cite this article: Ahmad-Fauzi S, Abd-Manan N, Yusof NS, Ibrahim M, Mohamad SA, Muhammed J. Ocular sporotrichosis from a tertiary referral center in Malaysia and review of literature in Southeast Asia. Taiwan J Ophthalmol 2022;12:237-41.

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Submission: 22-10-2020
Accepted: 21-12-2020
Published: 29-03-2021

mimicked those of common eye diseases, such as conjunctivitis and lid abscess, leading to undiagnosed and unreported cases. In the present study, we report the case series of ocular sporotrichosis in Malaysia and review the literature on ocular sporotrichosis in Southeast Asia. Thus, this reported case series will aid in epidemiology data and help ophthalmologist make a timely diagnosis and prevent devastating ocular sequelae.

Case Reports

Case 1

A 61-year-old man, a gardener, presented with 1-week duration of right eye redness and mucopurulent discharge with no history of prior trauma. Ocular examination revealed multiple lobulated granulomatous conjunctival reactions in the bulbar and palpebral conjunctiva with mucopurulent discharge [Figure 1a and b]. An initial diagnosis of pseudomembrane bacterial conjunctivitis was made, which was treated with antibiotic eye drops for 2 weeks. However, the symptoms persisted. He was admitted to the ward, and conjunctival biopsy was taken from temporal bulbar conjunctiva. Empirical intravenous amoxicillin/clavulanic acid and topical ciprofloxacin and ceftazidime therapy was started, but his condition remained the same. On the 11th day of admission, eye swab culture and sensitivity yielded *S. schenckii*. Histopathological examination (HPE) from conjunctival biopsy showed necrotic tissue infiltrated by neutrophils, lymphocytes, and few macrophages. The periodic acid-Schiff (PAS) and Grocott-Gomori methenamine silver (GMS) stains are negative for fungal bodies. A revised diagnosis of ocular sporotrichosis was made. The patient was treated with itraconazole 200 mg twice daily for 6 months. The patient showed clinical improvement with resolved conjunctival

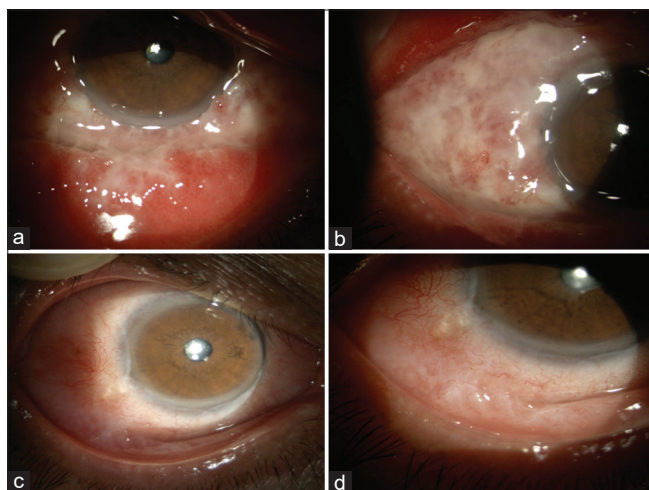


Figure 1: Multiple lobulated granulomatous conjunctival nodules at the palpebral and bulbar conjunctiva with mucopurulent discharge (a and b). Resolution of the conjunctival nodules after completed treatment (c) with symblepharon formation (d)

lesions [Figure 1c] and symblepharon formation over the inferior conjunctiva [Figure 1d].

Case 2

A 24-year-old woman presented with a 2-day history of left eye discomfort with multiple lobulated lesions at the superior palpebral conjunctiva [Figure 2a]. She had a history of contact with sick cats at home. However, there was no specific history of injury. Ocular sporotrichosis was presumed. Conjunctival biopsy was sent and yielded *S. schenckii*. HPE showed histiocytes and epithelioid cells with microsuppurative foci and multinucleated giant cells. The PAS stain was negative. She was treated with itraconazole 100 mg daily. However, she developed a new lobulated lesion at the inferior palpebral conjunctiva after 2 weeks [Figure 2b]. Itraconazole dose was increased to 200 mg twice daily and continued for 8 weeks. She achieved remission with resolved lobulated lesion [Figure 2c and d].

Case 3

A 39-year-old woman presented with a history of lobulated conjunctival lesion on the left upper and lower lids for 3 weeks with minimal discharge. Ocular examination showed multiple lobulated granulomatous lesions on the inferior palpebral conjunctiva [Figure 3a] and superior palpebral conjunctiva [Figure 3b]. She had a recent history of contact with a cat diagnosed with sporotrichosis by a veterinarian. She was initially treated with antibiotic ointment for bacterial conjunctivitis. However, the lobulated lesion worsened. Conjunctival biopsy was performed, which yielded *S. schenckii*. HPE revealed mixed inflammatory cell infiltration with predominant lymphocytes and plasma cells. There were scattered foci of noncaseating granulomatous inflammation with microabscesses and foreign body-type

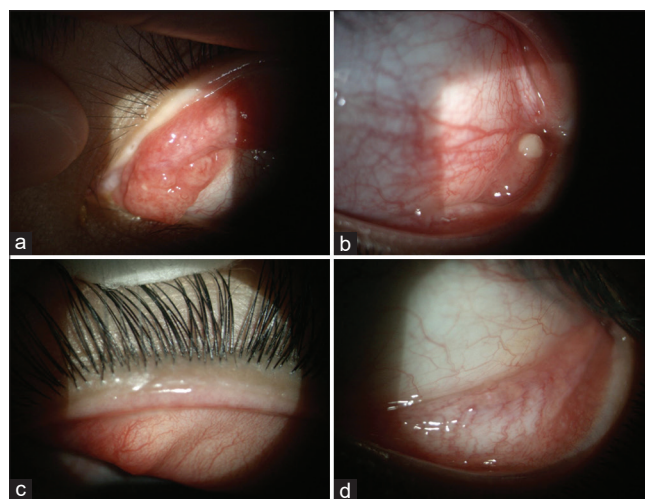


Figure 2: Multiple lobulated granulomatous nodules at the superotemporal palpebral conjunctiva (a). New yellowish conjunctival nodule at the inferior fornix after 2 weeks (b). Dose of itraconazole was increased from 100 mg daily to 200mg twice daily. Resolution of the conjunctival nodules (c and d) 8 weeks after treatment

multinucleated giant cells. The PAS and GMS stains were negative. She was started on oral itraconazole 200 mg twice daily and has completed treatment for 6 weeks without any sequelae.

Case 4

A 17-year-old man presented with left lower eyelid pain and swelling for 3 weeks, which progressively increased in size. Ocular examination showed inferior lid swelling and inflamed [Figure 4]. The examination of the lower palpebral conjunctiva revealed multiple lobulated lesions corresponding to the area of the outer skin lesion. Initial diagnosis of chalazion was made, and incision and curettage were planned. However, in the next visit, the skin lesion became ulcerated and had pus discharge. Further history taking showed that he had contact with a sick cat at home but denied a history of scratch or bite by a cat. The swab culture from the skin lesion isolated *S. schenckii*. HPE showed granulation tissue infiltrated by neutrophils forming microabscesses and aggregates of epithelioid histiocytes and Langhans multinucleated giant cells. PAS and GMS stains were negative. He was treated with oral itraconazole 200 mg twice daily for 6 months and achieved complete resolution with residual scarring on the skin.

Case 5

A 56-year-old woman presented with right eye redness and discharge for 5 days. Examination of the inferior conjunctiva revealed lobulated yellowish swelling, and treatment for the presence of concretion was started, but the swelling became larger and did not respond to treatment. On further history taking, she reported previous contact with a sick cat but denied a history of cat scratch or bite. Conjunctival biopsy sample was obtained, which was positive for *S. schenckii*. HPE showed granulomas, multinucleated giant cells, lymphocytes, plasma cell infiltration, and small foci of suppuration. Occasional fungal spores were seen after GMS staining. Treatment with oral itraconazole 200 mg twice daily was started and completed for 4 months. She achieved remission with symblepharon at the lower conjunctiva.

Case 6

A 22-year-old woman presented with a history of right eye redness and foreign body sensation for 3 weeks.

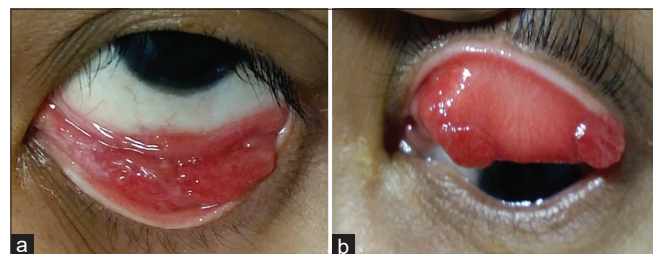


Figure 3: Multiple lobulated granulomatous nodules at the inferior palpebral conjunctiva (a) and superior palpebral conjunctiva (b)

She had a history of scratch by her cats. However, none of the cats was sick. Ocular examination showed granulomatous lesion at the right lower lateral palpebral conjunctiva involving the fornix. She was treated with chloramphenicol eye drops for conjunctivitis prior to ophthalmologist referral, but the symptoms persisted. Conjunctival biopsy sample was sent and was positive for *S. schenckii*. HPE reported moderate to marked lymphoplasmacytic cell infiltration at subepithelial stroma. The fungal stains were negative for fungal bodies. She was treated with oral itraconazole 200 mg twice daily for 5 months. She achieved remission without ocular sequelae.

Discussion

In Malaysia, sporotrichosis is rare. The first report of sporotrichosis in human patients was made by Zamri-Saad *et al.*^[8] Majority revealed a history of skin trauma, and half of these proportion had cat bite or scratch.^[9] Lymphocutaneous is the most common presentation of sporotrichosis.^[1] Extracutaneous, mucosal, and disseminated infections are the other variants with less reported cases.^[1] Ocular sporotrichosis is uncommon in Asia. The published data with the highest number of cases reported were in China.^[3] Zhang *et al.* reported endemic sporotrichosis situation with 72 cases of eyelid sporotrichosis in Jilin province in Northeast China.^[3] There were other scattered reported cases from the similar area, and all showed eyelid involvement.^[10-12] The humidity, regional farmer activity, and employment of various methods in the diagnosis are the contributory factors for the highest identification of the ocular sporotrichosis cases.^[3] In Japan, Malaysia and Thailand, to date, only one case of ocular sporotrichosis had been reported, respectively, and conjunctiva is the primary site.^[5-7]

The findings in our case series of six patients showed granulomatous conjunctivitis in all cases and one case present with eyelid granuloma [Table 1]. Our series showed similarity with the study of Yamagata *et al.*, in which all cases were mistakenly diagnosed as bacterial conjunctivitis, and Arinelli *et al.* collected 26 cases of ocular sporotrichosis, with 21 of them having granulomatous



Figure 4: Left lower lid swelling and erythematous nodules with overlying crusted skin, mistakenly diagnosed as chalazion

Table 1: Demographic, clinical presentation, and treatment of 6 patients with positive culture of *Sporothrix schenckii*

Demographic		Clinical presentation				Treatment				
Patient	Age (year)/sex	Symptoms	Ocular presentation	Site of lesion	Duration (d)	Predisposing factors	HPE results	Treatment (oral)	Duration (months)	Outcome
			Signs			Exposure to cats	Others			
Case 1	61/male	RE purulent discharge, eyelid swelling	Granulomatous conjunctivitis	Conjunctiva	7	No	Gardener	Itraconazole 200 mg bd	6	Resolved with symblepharon
Case 2	24/female	LE lobulated lesions at palpebral conjunctiva	Granulomatous conjunctivitis	Conjunctiva	2	Yes		Itraconazole 100 mg od for 2 weeks then increased to 200 mg bd for 2 months	2	New lesion at lower palpebral conjunctiva when on lower dose and resolved with higher dose
Case 3	39/female	LE lobulated lesions at palpebral conjunctiva	Granulomatous conjunctivitis	Conjunctiva	21	Yes		Itraconazole 200 mg bd	2	Resolved
Case 4	17/male	LE lower eyelid skin swelling	Lid and granulomatous conjunctivitis	Eyelid and conjunctiva	21	Yes		Itraconazole 200 mg bd	6	Resolved with skin scarring
Case 5	56/female	RE discomfort, discharge	Lower palpebral conjunctiva nodules mimicking concretion	Conjunctiva	5	Yes		Itraconazole 200 mg bd	4	Resolved with symblepharon
Case 6	22/female	RE redness, foreign body sensation	Granulomatous conjunctivitis	Conjunctiva	21	Yes		Itraconazole 200 mg bd	5	Resolved

RE=Right eye, LE=Left eye, HPE=Histopathological examination, bd=Twice daily

conjunctivitis and regional lymphadenopathy.^[2,13] In contrast to a reported case series from an endemic area in Brazil and Peru, 19 patients had eyelid lesions and 2 in the eyebrows.^[4] Variability of the clinical manifestations reported in different regions leading to diagnostic challenges.

The gold standard in establishing the definitive diagnosis of sporotrichosis is by culture of the lesions.^[14] Tissue biopsy for culture in Sabouraud dextrose agar medium will grow cream-colored moist colonies within a week that may develop a dark color in the center after some time.^[14]

Sporotrichosis in ocular adnexa is treated with oral itraconazole in the same dose as the cutaneous form.^[15] Itraconazole (200 mg/day administered for 3–6 months) is the drug of choice in sporotrichosis cases. Besides its efficacy profile of almost 100%, it has low relapse rate and few side effects, such as hepatotoxicity.^[15]

Ocular sporotrichosis involving the ocular adnexa is rare and may mimic other common ocular diseases, making diagnosis difficult for the ophthalmologist. The invasiveness of obtaining ocular tissue samples and longer waiting time of obtaining positive cultures are also some limitations. Therefore, we should suspect this condition in a patient who came with suggestive clinical presentations, especially related to close contact with cats and/or associated cutaneous lesion. Early initiation of systemic antifungal therapy may lead to complete disappearance of the lesion.

Declaration of patient consent

We certify that we have obtained all appropriate patient consent forms. In the form, the patients have provided their consent on the publication of their images and other clinical information in the journal. The patients understand that their names and initials will not be published and that due efforts will be made to conceal their identity, but anonymity cannot be guaranteed. Ethical approval was obtained from the National Institute of Health, Ministry of Health Malaysia (NIH.800-4/4/1 Jld. 89[22]).

Acknowledgement

I would like to thank Enago (www.enago.com) for the English language review.

Financial support and sponsorship

Nil.

Conflicts of interest

The authors declare that there are no conflicts of interests of this paper.

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