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Oral mucosa sporotrichosis: Report of a rare case acquired by direct inoculation

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ABSTRACT

Sporotrichosis is a rare type of fungal infection caused by *Sporothrix* fungus. Transmissions are commonly by traumatic inoculation of the fungus through the skin and subcutaneous tissue either from environmental exposure or contact with infected animals. Due to its mode of transmission, it is commonly affecting the upper limbs. Definitive diagnosis can be obtained by fungal culture test on secretion fluids, pus, bloods or tissue biopsy. We report a rare presentation of this disease appearing as a solitary chronic ulcer of the lip which was successfully treated with itraconazole.

1. Introduction

Sporotrichosis is a mycoses caused by a dimorphic fungus, *Sporothrix schenckii*. It was first reported in 1898 in Baltimore, USA, in a 36-year-old man presented with multiple ascending, ulcerated nodules on his right limb [1]. Its transmission was initially described to spread by traumatic inoculation of the fungus through the skin and subcutaneous tissue through plant thorns, wood splinters, or contaminated organic material. Because of that, it is also known as "rosebush mycosis", or the "gardener's mycosis", given the inoculation of the fungus are mostly related to contaminated plant material [2]. The population at risk was therefore among the person involved with activities such as farming or gardening. More recently, however, zoonotic transmissions have been on the rise, especially related to cats [2,3]. A shift in the demographic of patients affected by this infection are therefore observed with more urban predilection [2,3].

Oral ulcers are a rather common presentation in dental practice. Most of these ulcers are transient, thus are considered acute ulcers. Chronic ulcers, which last for more than 2 weeks, are less common. When there are chronic multiple ulcers, the possible causes are usually related to either an autoimmune or inflammatory lesion such as linchen planus, pemphigus vulgularis, mucose membrane pemphigoid and linear IgA disease [4]. A solitary lesion meanwhile can be due to chronic trauma, infection, or neoplasia. When considering neoplastic causes, lip squamous cell carcinoma would be a common diagnosis to consider. Infective causes for chronic solitary ulcers meanwhile can be due to a variety of causes including bacterial (tuberculous or syphilitic ulceration), viruses (*cytomegalovirus*-associated ulceration) and deep fungal ulceration [4]. Ulcers caused by fungal infection are quite diverse such as aspergillosis, histoplasmosis, blastomycosis, and mucormycosis [5].

Sporotrichosis is generally an uncommon fungal infection but in a hyperendemic area the incidence can go up to 48 to 60 cases per 100,000 population [6]. When it occurs, sporotrichosis is more prevalent on the upper limbs due to the common use of unprotected hands to touch pets, soil or raw fish [7]. Sporotrichosis can also occur on the face, usually at the cheek area [7]. Oral or lip involvement sporotrichoses are rare with only a few reported cases of such occurrences [3]. We present in this report a rare case of a patient with sporotrichosis that presented as a solitary chronic oral ulcer.

2. Case presentation

A 61-year-old gentleman was first seen in our clinic with a complaint of a chronic solitary ulcer on his upper lip mucosa (Day 0). The ulcer was first noticed 3 weeks (day −21) prior to presenting to us. It started off as a small ulcer at the vermillion border. The ulcer continued to become progressively bigger and became painful especially to touch. There was also yellowish exudate from the ulcer. As the ulcer kept increasing its size, he went to seek medical care from his general practitioner 2 weeks (day −7) after the ulcer developed. He was prescribed with oral

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cefuroxime 250mg twice a day and topical fucidin cream, but after 1 week, it still did not improve the condition. Medical background check reveals that he has underlying diabetes mellitus and hypertension which was well controlled with diet modification. There were no loss of weight or appetite, fever, or other systemic symptoms over the past few months. He denies involved in any high-risk behavior in the past. There were also no history of smoking or alcohol consumption. As he is now a pensioner and previously had office-based occupations, he was infrequently exposed to the sun. There was also no family history of malignancy or any close contact with known tuberculosis infected people.

Upon further questioning, interestingly, he gave a history of being scratched by a cat at the exact area of the ulcer around 6 weeks (day −42) before presenting to us. There was initially a small scratch wound on his lip which actually had healed about a week (day −35) after the incident. Few weeks later, a small papule developed (day −25) before progressing into the ulcer he presented with. The cat responsible for the scratch is a known stray cat in his neighborhood. It has been fed by his family over the past 1 year and will on occasion be in their home. They are unsure about the cat immunization history, if any. The cat is known to be in and around his neighborhood.

On general examination, he looked well and had no fever on arrival to our clinic. Upon examining the lesion, there was a single painful 1.5cm × 1.5cm ulcer at the right side of his upper lip (Fig. 1). The ulcer had an irregular margin with the skin around the ulcer was erythematous and swollen. The ulcer had crusting which upon cleaning revealed a seropurulent exudate with a yellowish sloughy base and a punched-out edge. There were no other lesions intra or extra orally. There were also no palpable neck nodes. There were no other positive clinical findings. Blood investigation found mild leukocytosis (11.2 x 109/L) with lymphocyte predominance. C-reactive protein (0.25mg/dl), aminotransferase, and creatinine levels were within normal ranges.

We performed an incisional biopsy which was sent for histopathological examination together with tissue culture tests (for bacterial, fungal, tuberculosis, and non-tuberous) and tissue tuberculosis PCR (TB-PCR). The bacteriology tissue culture came back as coagulase-negative staphylococcus which could be due to contamination or superimposed infection. Tissue mycobacterial culture and TB-PCR meanwhile was negative. The fungal tissue culture meanwhile isolated *Sporothrix schenkii*. Histopathological examination finding was the tissue had focal micro-abscess formation and moderate infiltration by lymphocytes, histiocytes and some neutrophils. On special staining (PAS and GMS), occasional fungal bodies are seen, characterized by small round to oval shape yeast (Figs. 2 and 3). Based on all investigation findings, he was diagnosed to have fixed cutaneous lip sporotrichosis. Once diagnosed, he was started on tablet itraconazole 200mg twice a day. After 2 weeks (day +14) of therapy, the lesion was noticeably smaller (Fig. 4).

Fig. 1. Initial presentation of lip ulcer at the upper lip.

The ulcer completely resolves after 11 weeks (day +77). itraconazole was continued for a total of 15 weeks (day +105).

3. Discussion

Sporotrichosis infection has been reported worldwide, but its prevalence can vary from region to region. It is more commonly reported in tropical and subtropical areas with warm and humid climates. Some countries with higher reported incidence rates include Brazil, Peru, Colombia, China, Japan, South Africa, Mexico, and the United States [3]. In each of the different localities, there are also differences in the predominant mode of transmission and its epidemiology [3]. *S. schenckii* and *S. globosa* species generally follow an environmental route of transmission, while *S. brasiliensis* is commonly associated with zoonotic transmission. Due to the differences in transmission, also observed are the different geographical territory and distribution of the species. For example, *S. schenckii* can be found worldwide while *S. brasiliensis* are predominantly in Brazil [3,8]. In Southeast Asian region, most of the reported cases that were reported are caused by *S. schenckii* even in cases where the inoculation reported was due to scratch or bites from cats [7,9]. The predominance of *S. schenkii* in this region is further supported by the finding of this presented case where *S. schenckii* was isolated from the tissue fungal culture following a cat scratch incident.

The presentation of solitary chronic oral ulcers could be due to several potential causes. The most common oral ulcer would be aphthous ulcers, but this is not usually seen at the lip vermillion border as presented in this case. Neoplastic causes such as lip squamous cell carcinoma, while worthwhile to consider, is an uncommon presentation in our population. For an infective cause for chronic solitary ulcers to be considered, an exposure to a potential pathogen could be elicited by proper history taking. Definitive diagnosis of the infective cause of an ulcer can only be made with a microbiological culture. Infective cutaneous ulcers are clinically indistinguishable, with possible causes being leishmaniasis, paracoccidioidomycosis, rosacea, chromoblastomycosis, blastomycosis, tuberculosis, bacterial pyoderma, subcutaneous abscesses of tularaemia, primary syphilis and cat-scratch disease [2,10]. As tuberculosis is endemic in our region, we did consider it as a potential cause and performed mycobacterium screening which turned out to be negative. Sporotrichosis is uncommon and are exceedingly rare to occur in the oral or perioral mucosal area, thus was only considered due to the positive cat scratch history. Finally, although presented with a possible rare disease, the history, clinical presentation, and consideration of endemicity locations should guide the clinician on a further investigative course. The confirmation of an inoculation incidence, however, can be difficult as the sporotrichosis lesion typically starts as an indurated papule that develops after a significant delay around 1–4 weeks after inoculation of the fungus into the skin [10]. Ulceration would only develop later on, as seen in this reported case. In fact, with activities such as floriculture, horticulture, gardening, fishing, hunting, and farming, a history of trauma can be absent or unnoticed. An incident of a cat scratch on the face, however, would not be forgotten easily and should be easily elicited by proper history taking compared to an innocuous incident while gardening. With the increasing incidence of zoonotic transmission, especially involving cats, specific questions on any animal contact would be very helpful in diagnosis, as seen in this case.

To obtain the diagnosis of sporotrichosis, fungal culture is the most common and definitive method [7,11]. Specimens in any form including lesion secretion fluids, pus, bloods, or tissue biopsy could all be used to inoculate Sabouraud dextrose agar or potato dextrose agar and incubated at room temperature. Occasionally, the cultures might be negative [7]. Colonies usually appear after a few days and present initially as a creamy white colour that progresses into brown to black coloured fungal colonies [7,8,10,11]. Other supportive investigative methods such as histopathology infrequently provide definitive features of sporotrichosis infection [2,7,10]. Histopathology examinations seldomly detects

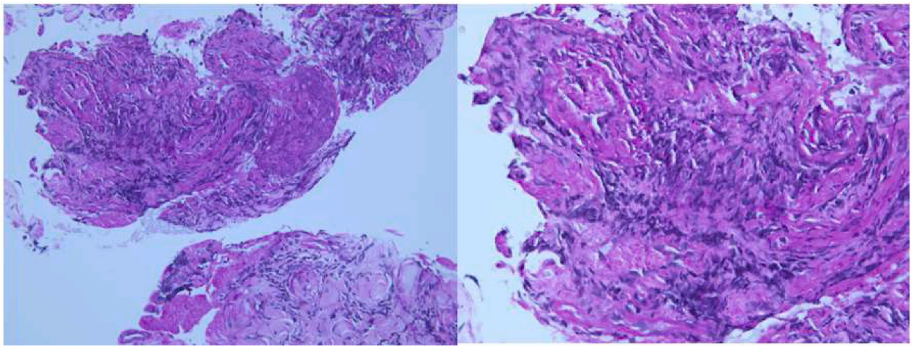

Fig. 2. PAS staining histology at magnifications of 200× and 400x revealed highly inflammatory cell infiltration and the presence of a fungus body.

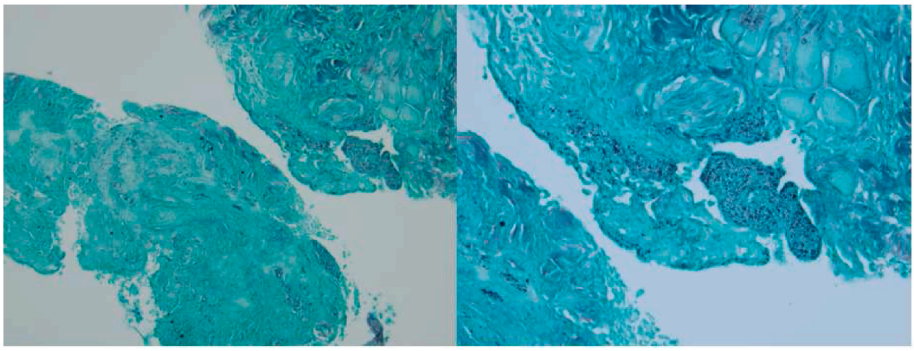

Fig. 3. GMS staining histology at magnifications of 200× and 400x GMS showed abundant fungal bodies are seen characterized by small round to oval shape yeast.

Fig. 4. Clinical picture of the lesion at day +14 (A), day +42 (B), day +77 (C), and day +180 (D).

fungal structures even when using fungal specific stains such as PAS or methenamine silver [2,7]. The non-specific inflammatory infiltrate can be seen with haematoxylin-eosin stain [2,7,10]. A previous study detected fungal structures in only 16 % of the histopathological examinations, illustrating the limited ability of this type of examination to consistently establish a diagnosis [7]. A more recent diagnostic tool is using molecular detection such as nested polymerase chain reaction (PCR) technique. PCR test offers a swifter diagnosis and is highly sensitive which is beneficial in instances of negative cultures due to a low fungal burden [11]. Nevertheless, the utilization of PCR for the

diagnosis of sporotrichosis is still limited, particularly in settings with limited resources, due to its associated costs and technical complexity. In this reported case, fungal bodies were seen with an inflammatory infiltrate in the HPE, thus in combination with the fungal culture results, providing a definitive diagnosis of the disease.

Sporotrichosis can clinically be classified in four different presentations, namely, lymphocutaneous, fixed cutaneous, disseminated, and the extracutaneous type [12]. The lymphocutaneous type is reported to be the most common presentation [7]. Commonly seen in the extremities, there is formation of a papule or pustule is followed by the formation of a subcutaneous nodule. As the infection progresses, secondary lesions emerge along the course of regional lymphatics, demonstrating suppurative inflammatory nodule along the lymphatic vessels. The fixed cutaneous form meanwhile is characterized by a single or a few lesions at the inoculation site which are typically ulcerated with erythematous borders and without lymphatic involvement, as in the current case. Based on previous studies, the most common affected area for cutaneous and lymphocutaneous form is upper extremities [9]. Interestingly, in a series of reported cases by Tang et al. all cases where the lesion involved the face had fixed cutaneous type [7]. The reasons for the predilection of fixed cutaneous type when involving the face in not clear [13]. Fixed cutaneous type is the least severe form of infection and is said to responds better to treatment [13]. Clinical presentation of sporotrichosis may vary according to several factors including the immunological status of the host, the load and depth of the inoculum, the pathogenicity, virulence and thermal tolerance of the strain [11,13].

Some authors classify mucosal sporotrichosis as a separate classification than that of the cutaneous form, while others accept it as a variant of it [11]. Mucosa involvement of sporotrichosis can be involving the nasal mucosa, oral mucosa or the conjunctiva [11]. Previous reported cases mostly involve nasal or conjunctiva [14]. Lip or oral mucosa sporotrichosis lesions are rare, but when it occurs, it is mostly feline-related [3,15]. Reported cases of oral mucosal involvement were among children with lip lesions after kissing an infected cat [3,15]. Oral mucosa involvement can also be part of the presentation of the disseminated type [16–18]. In such cases, the host immunes were compromised and oral mucosa involvement was not related to any contact or traumatic inoculation to the oral mucosa region [16–18]. Thus, in an isolated lesion involving the labial mucosa, it is important to explore the history of feline-related traumatic inoculation.

Antifungal therapy, namely, itraconazole, is the first-choice treatment for sporotrichosis infection [19]. Itraconazole has an excellent outcome with a response rate of more than 90 % [20]. The recommended regime for itraconazole is with doses of 200mg once or twice daily given and continued for another 2–4 weeks after all lesions disappear [19]. It is the 1st choice due to its good tolerability and low relapse rate [20]. In the presented case, itraconazole was prescribed following diagnosis and the lesions could disappear completely after 11 weeks of therapy. Itraconazole was then continued for another 4 weeks as per the recommended guideline. A study by de Lima Barros et al. found that the median length of therapy was shorter with the fixed form (10.5 weeks) compared to lymphocutaneous forms (12 weeks) [20]. Specifically, for the fixed cutaneous form, 52 % of the cases had a treatment period between 9 and 16 weeks, which is comparable to the duration of therapy administered to the case presented herein [20]. Other antifungals that has a good therapeutic outcome for Sporotrichosis infection include potassium iodide, terbinafine, amphotericin B, and fluconazole. Potassium iodide is a particularly popular option as it is considerably cheaper with comparable response rate to itraconazole [19]. It is however associated with some common adverse effects, such as metallic taste, nausea, abdominal pain, salivary gland enlargement and rash [19].

In conclusion, an infective cause should always be considered when there is a presentation of a chronic solitary lip ulcer. A thorough history taken to explore possible exposure to a potential pathogen is key in guiding the investigative diagnostic steps. Culture test is the standard diagnostic procedure, but histopathology with specific staining may aid in the detection of fungal bodies. Itraconazole is the therapy of choice for sporotrichosis, and it should be continued until clinical cure is achieved.

CRediT authorship contribution statement

Syed Nabil: Conceptualization, Writing – review & editing, Visualization. **Mohd Ferdaus Isa:** Writing – original draft, Visualization. **Badrul Iskandar Abdul Wahab:** Investigation, Resources. **Nurismah Md Isa:** Investigation, Resources, Validation, Supervision.

Declaration of competing interest

The authors declare that they have no conflicts of interest.

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