

CASE REPORT

An unsuspected and unusual case of zoonotic sporotrichosis

Ruzanna Dayanna ZAWAWI^{1,2}, Chuan Hun DING², Mohd Nizam TZAR^{2*}

¹Microbiology Unit, Department of Pathology, Hospital Kuala Lumpur, Ministry of Health Malaysia, Jalan Pahang, 50586 Kuala Lumpur, Malaysia; ²Department of Medical Microbiology and Immunology, Faculty of Medicine, UKM Medical Centre, Jalan Yaacob Latif, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur, Malaysia.

Abstract

Sporotrichosis is an infection caused by a thermally dimorphic fungus, *Sporothrix schenckii* which is commonly reported in the tropics and subtropics. Infection usually occurs as a consequence of traumatic inoculation into the skin. A previously healthy 33-year-old Malay woman presented with a scratch wound over the lateral aspect of her left thigh for 2 months after being scratched by her pet cat. Inspection of the wound revealed a granulomatous plaque measuring 3cm x 2cm with hyperkeratotic scales, fissures and multiple blackish pigments. There was a tender, palpable left inguinal lymph node measuring 1cm x 1cm but the overlying skin looked normal. She was prescribed two courses of antibiotics empirically, without any clinical improvement seen. During follow up and further history taking, the patient informed that her pet cat was diagnosed with sporotrichosis a month before the scratching incident took place, but she claimed that her pet cat had been treated and was cured. She was then empirically started with oral itraconazole 200mg twice a day for two months. Histopathological examination of a skin biopsy showed acute on chronic suppurative granulomatous inflammation but was negative for any fungal elements. However, culture of the skin biopsy isolated *Sporothrix schenckii*. A final diagnosis of localised cutaneous sporotrichosis was made and the oral itraconazole was continued for another two months. The wound improved dramatically since itraconazole started.

Keywords: *Sporothrix schenckii*, sporotrichosis, cat scratch, itraconazole

INTRODUCTION

Sporothrix schenckii is a thermally dimorphic fungus that is widely dispersed in nature. It has a worldwide distribution and can be found especially in tropical and subtropical climates.¹ Its ecology, epidemiology and clinical features vary across different geographical regions.² Most cases of sporotrichosis developed after traumatic inoculation of contaminated soil, plants and organic matter into the skin or mucosa. Alternatively, infection may occur as a result of zoonotic transmission, which has been mostly associated with scratches or bites from infected cats.³ The present case of sporotrichosis was both unsuspected as well as unusual due to its localised presentation in a patient who acquired the infection from an infected but treated pet cat.

CASE REPORT

A previously healthy 33-year-old Malay woman presented with a single wound over her left thigh that did not respond to a combination of an oral antibiotic and fusidic acid cream. Otherwise, she had no fever or any other constitutional symptoms. She was referred to a dermatology clinic at a tertiary referral hospital for further work up. Further history taking revealed that she was scratched by her pet cat, which was diagnosed with and treated for sporotrichosis one month before the incident took place. Upon inspection over the lateral aspect of her left thigh, there was a granulomatous black plaque measuring 3cm x 2cm with hyperkeratotic scales and fissures. There was a palpable left inguinal lymph node measuring 1cm x 1cm, which was tender upon palpation. Other physical examination was unremarkable.

*Address for correspondence: AP Dr. Tzar Mohd Nizam, Department of Medical Microbiology and Immunology, Faculty of Medicine UKM, UKM Medical Centre, Jalan Yaacob Latif, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur, Malaysia. Tel: +603-91459534 Fax: +603-91459524 Email: tzar@ppukm.ukm.edu.my

A punch biopsy of the wound was taken for histopathological examination and cultures. The patient was treated empirically with oral itraconazole 200 mg twice a day for 2 months and given a follow-up appointment. Upon follow-up visit, the wound had improved dramatically to itraconazole. The histopathological examination of the skin biopsy showed presence of acute on chronic suppurative granulomatous infection (FIG. 1). However, special staining with Periodic acid Schiff (PAS) and Gomori-methenamine silver stains did not demonstrate any presence of fungal bodies. Nevertheless, cultures of the skin biopsy on Sabouraud dextrose agar at 30°C grew black fungal colonies with white periphery. The bottom side of the colonies were also black with white periphery (FIG. 2). Microscopic examination of the colonies with lactophenol cotton blue preparation showed presence of septate hyphae with conidiophores and numerous microconidia, some of which were arranged in clusters resembling a daisy flower; which were

characteristics of *Sporothrix schenckii* (FIG. 3). Culture and polymerase chain reaction of the skin biopsy for *Mycobacterium tuberculosis* were negative. Other blood tests which included full blood counts, renal profile, liver function tests and random blood sugar were within normal limits. Hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (HCV Ab) and human immunodeficiency virus (HIV) tests were non-reactive. A final diagnosis of localised sporotrichosis of the left thigh was made and oral itraconazole 200 mg twice a day was prescribed for another two months.

DISCUSSION

Sporotrichosis, which has traditionally been known as “rose gardeners’ disease”, is considered an emerging infectious disease. However, over the past two decades, the incidence of zoonotic sporotrichosis has been on the rise.^{4,5} The emergence of sporotrichosis as a major fungal

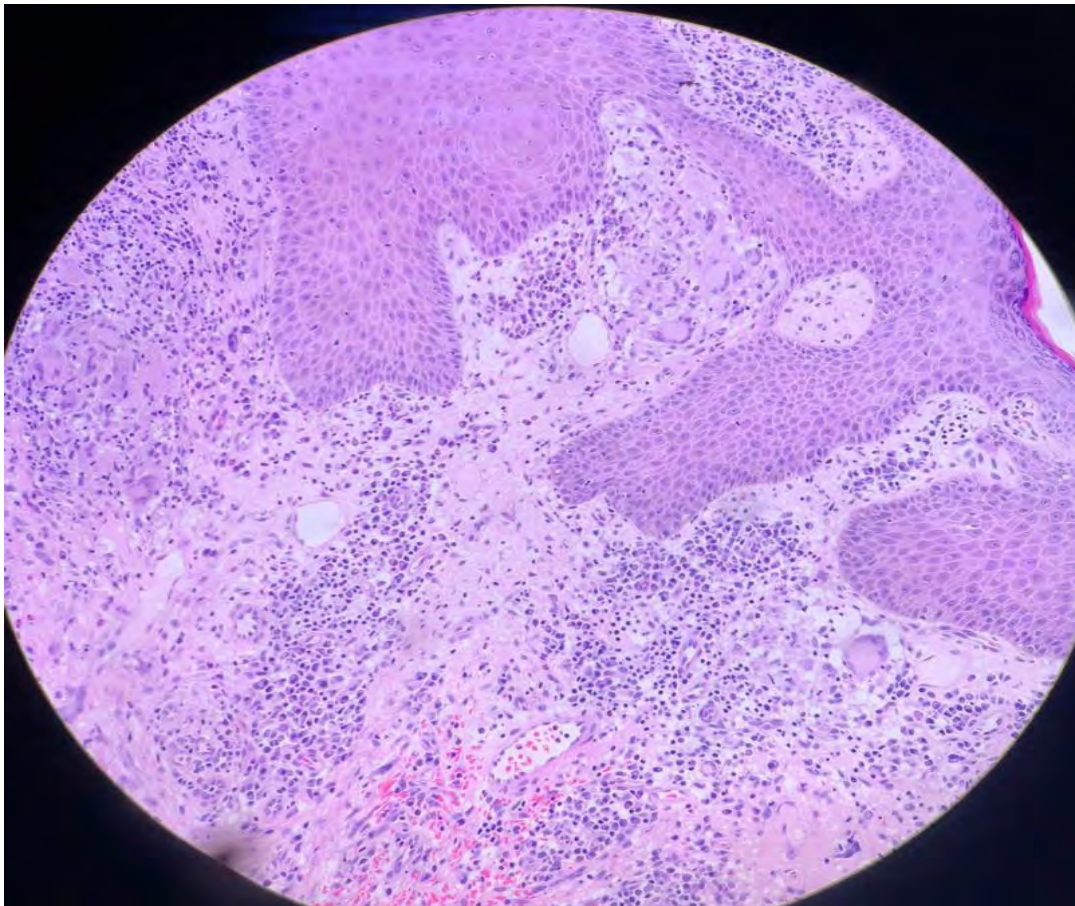


FIG. 1: Section of the skin biopsy showing infiltration by lymphocytes, plasma cells and eosinophils within the dermal layer with occasional multinucleated giant cells at the papillary dermis (H&E, 200x).

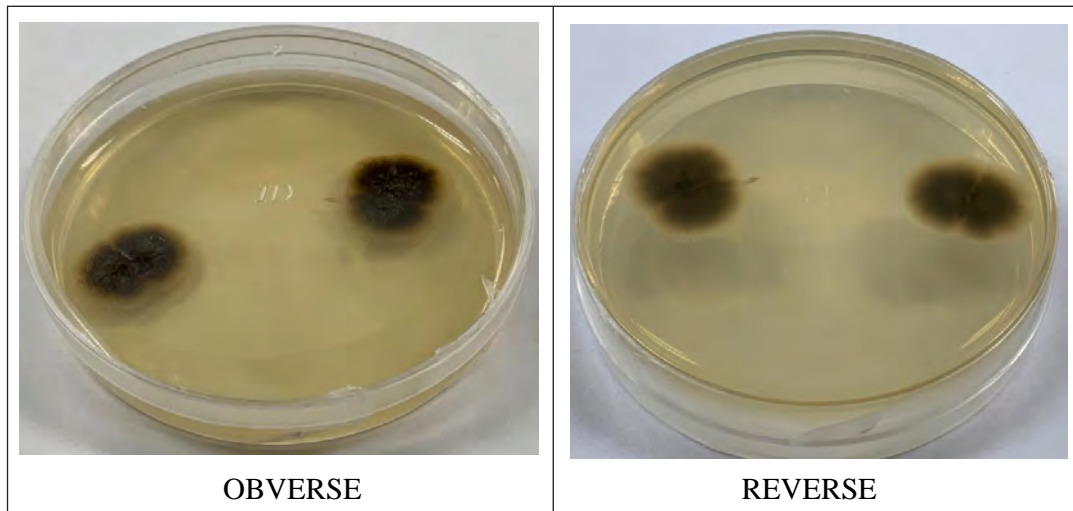


FIG. 2: Mold phase on Sabouraud dextrose agar at 30°C. The colony is wrinkled, appears black with a narrow white border on both obverse and reverse of the plate.

infection may be contributed by changes in epidemiology, distribution, taxonomic evolution and multiple outbreaks.² A retrospective study done in Malaysia has reported 19 cases of cutaneous sporotrichosis over a six-year period. Interestingly, more than half of the patients reported a history of cat scratch or bite. This

may be explained by the fact that in Malaysia, cats are considered as the most popular domestic pets.⁶ Reported cases of human sporotrichosis acquired from cats were mostly presented as localised cutaneous or lymphocutaneous forms of the disease.^{6,7}

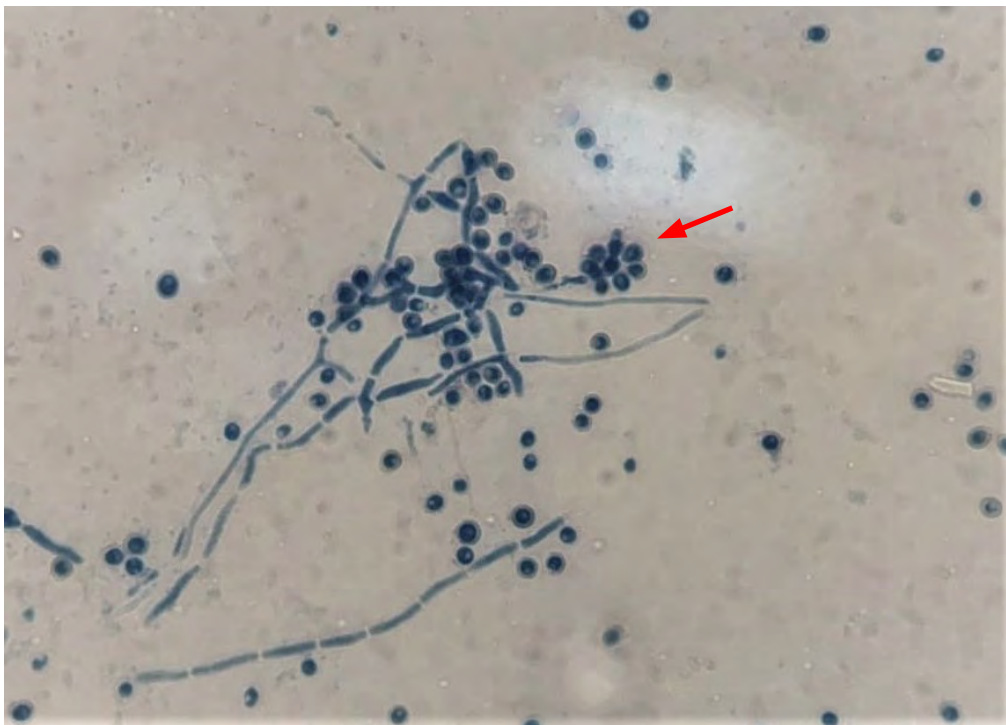


FIG. 3: *Sporothrix schenckii* in mold phase showing conidiophores and clustering of microconidia, forming daisy-like appearance [red arrow] (Lactophenol cotton blue, 400x).

Sporotrichosis has a wide spectrum of clinical manifestations and can be classified into fixed cutaneous, lymphocutaneous, disseminated cutaneous and extracutaneous sporotrichosis.^{1,8} The commonest form of human sporotrichosis is cutaneous, where cutaneous-lymphatic form is reported in up to 95% of cases. Another type is cutaneous-fixed sporotrichosis, reported in up to 30% of cases. Complications of these cutaneous types may occur in immunocompromised individuals (e.g. HIV-AIDS, chronic alcoholism, haematologic malignancy) where the sporotrichosis becomes disseminated. These extracutaneous forms are less commonly seen, and may include pulmonary, osteoarticular, ocular and central nervous system sporotrichosis.⁹ In terms of differences, cutaneous types have a balanced gender proportion, whereas disseminated types are more inclined to involve male individuals (4:1 male preponderance). This is probably due to more males are affected by immunosuppressive states such as HIV-AIDS and chronic alcoholism. Cutaneous types occur primarily in immunocompetent individuals. Yeast forms in cases of disseminated sporotrichosis are also more easily detected in the laboratory than in cases of cutaneous sporotrichosis. Treatment of disseminated types is also more invasive and prolonged than for cutaneous types. Finally, the prognosis of disseminated sporotrichosis is much worse than cutaneous sporotrichosis, where the mortality rate may approach 30% in cases of HIV/AIDS.⁹

The diagnosis of sporotrichosis can be easily overlooked especially in cases of atypical presentation of sporotrichosis or in patients without classical nodular lymphangitis lesion.^{10,11} In this patient, sporotrichosis was not initially suspected because the lesion did not manifest as classical nodular lymphangitis but rather a single wound which worsened, forming a granulomatous plaque. The diagnosis of sporotrichosis was only suspected when there was no clinical improvement of the wound after completion of antibiotics and when further questioning revealed a history of cat scratch. The gold standard for definitive diagnosis of cutaneous sporotrichosis is fungal culture from tissue specimen.⁶ However, in cases of disseminated infection, specimens such as sputum, blood, cerebrospinal or synovial fluid can be sent for fungal culture.¹ It is important to note that the yield of fungal culture is variable and dependent on various factors, including proper sampling method, prompt and

appropriate transport of specimen, as well as laboratory technique in culture. Tissue biopsy or pus collected from deep tissue or lesion is recommended for successful fungus isolation. The sample should be kept in a sterile container and sent immediately to the microbiology laboratory for prompt processing of the specimen. The fungus grows well on Sabouraud dextrose plus cycloheximide and chloramphenicol agar after 4-5 days of incubation. Dimorphic conversion test of the mycelial phase to yeast phase can be performed by subculturing the fungus onto an enriched medium such as brain heart infusion agar or blood agar or chocolate agar and incubating at 35 to 37°C.¹² Omitting culture of tissue biopsy is a common mistake that may lead to misdiagnosis because fungal elements of *Sporothrix* spp. are rarely seen in histopathology sections, even with the use of special fungal stains.¹³ On the other hand, tissue or pus cultures may turn out negative if empirical antifungal therapy was prescribed before fungal culture was obtained.^{6,11}

In cases whereby fungal culture results were negative, a clinical diagnosis of cutaneous sporotrichosis was made in patients with 'sporotrichoid' lesions together with negative tuberculosis, bacterial and mycobacterial workup.⁶ Clinically, cutaneous tuberculosis (particularly those known as sporotrichoid cutaneous tuberculosis) mimics the lymphangitic form of cutaneous sporotrichosis. Even when a highly suggestive exposure history is present (such as a thorn prick), cutaneous tuberculosis should not be discounted straight away.¹⁴ Histologically, both clinical entities can display epithelioid granulomata with Langhans giant cells in tissue biopsies.¹⁵ In cutaneous tuberculosis, fungal stains such as Periodic acid-Schiff (PAS) will be negative for fungal elements while acid-fast stains such as Ziehl-Neelsen (ZN) are likely to be positive. However, relying on special histological stains alone to correctly diagnose sporotrichosis is imprudent because the oval to round, single budding forms of the yeast phase of *S. schenckii* is, although diagnostic, rarely observed in biopsies. Out of 63 biopsy specimens from patients with cutaneous sporotrichosis, the PAS stain could only reveal fungal elements in 2 (3%).¹³ Cultures appear to be more beneficial than histopathological examination, with a pickup rate of approximately 32% with the former. A favourable response to either anti-tuberculous therapy or antifungal therapy (namely itraconazole or potassium

iodide) will also help validate the diagnosis retrospectively. In cutaneous sporotrichosis, patients will show significant improvement once antifungal agent was started.^{6,11} A good clinical judgement and experience is necessary in diagnosing fungal infections in this group of patients.¹⁶ Recently, the development of DNA amplification procedures, such as polymerase chain reaction to identify fungal isolates has led to rapid and precise diagnosis.¹⁷ Molecular detection of *Sporothrix schenckii* is also valuable in cases of negative cultures due to low fungal burden.¹ However, fungal culture remains the gold standard and correlation with phenotypic characteristics and molecular data is essential in the diagnosis of sporotrichosis.¹⁷ Matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) is another laboratory method which is simple, reliable, rapid and suitable for routine identification of fungal isolate. Recent study has shown that MALDI-TOF MS was able to correctly identify all clinical and environmental *Sporothrix* isolates at the species level and has shown 100% agreement with DNA-based method by using partial sequencing of the CAL gene.¹⁸

In patients with fixed cutaneous and lymphocutaneous sporotrichosis, itraconazole is considered as the first line therapy. A dose of 100-400 mg daily was given until the lesions resolved with an additional extended treatment duration of four weeks. On average, the duration of treatment in patients who received itraconazole as monotherapy was 15.6 weeks. Oral itraconazole was well tolerated by most patients with no documented incidence of itraconazole-induced hepatitis.⁶ As described in this case report, the patient's wound has shown significant improvement after itraconazole was prescribed. This finding is concurrent with other studies which have proven the effectiveness of oral itraconazole in cases of localised sporotrichosis.^{5,6,19} Alternatively, other treatment that can be considered include fluconazole, potassium iodide solution, terbinafine and local hyperthermia.¹⁹

CONCLUSION

Sporotrichosis is commonly diagnosed among people who were exposed to soil and plant matter. However, it should be considered as a differential diagnosis in patients with chronic skin lesions that do not respond to antibiotics, especially with a history of cat scratch or bite. To prevent

the possibility of zoonotic transmission, pet cat owners should handle infected pets, even those already treated for sporotrichosis, with proper care and practice precautionary measures. Even though fungal culture is regarded as the gold standard in diagnosing sporotrichosis, the use of PCR and MALDI-TOF MS has been proven to yield a reliable and accurate result, permitting a faster diagnosis to be established. As for treatment, monotherapy with oral itraconazole was proven to be highly effective in patients with localised subtypes of sporotrichosis.

ACKNOWLEDGEMENTS: The authors would like to thank the Director General of Health Malaysia for his permission to publish this article.

Authors' contribution: RDZ identified the case and was responsible for writing up the case report and provided the figures. CHD and MNT were responsible for writing up the discussion and conclusion. All authors have reviewed the final manuscript and approved it to be published.

Conflict of interest: The authors declare no conflict of interest.

REFERENCES

1. Barros MB, de Almeida Paes R, Schubach AO. *Sporothrix schenckii* and sporotrichosis. Clin Microbiol Rev. 2011; 24(4): 633-54.
2. Chakrabarti A, Bonifaz A, Gutierrez-Galhardo MC, Mochizuki T, Li S. Global epidemiology of sporotrichosis. Med Mycol. 2015; 53: 3-14.
3. Rodrigues AM, de Hoog GS, de Camargo ZP. *Sporothrix* species causing outbreaks in animals and humans driven by animal-animal transmission. PLoS Pathog. 2016; 12(7): e1005638.
4. Gremião IDF, Miranda LHM, Reis EG, Rodrigues AM, Pereira SA. Zoonotic epidemic of sporotrichosis: cat to human transmission. PLoS Pathog. 2017; 13(1): e1006077.
5. Kaadan MI, Dennis M, Desai N, Yadavalli G, Lederer P. One health education for future physicians: a case report of cat-transmitted sporotrichosis. Open Forum Infect Dis. 2020; 7(3): ofaa049.
6. Tang MM, Tang JJ, Gill P, Chang CC, Baba R. Cutaneous sporotrichosis: A six-year review of 19 cases in a tertiary referral center in Malaysia. Int J Dermatol. 2012; 51(6): 702-8.
7. Reed KD, Moore FM, Geiger GE, Stemper ME. Zoonotic transmission of sporotrichosis: case report and review. Clin Infect Dis. 1993; 16: 384-7.
8. Ramli R, Abd Rashid AH, Phang KS, Khaithir TM. Sporotrichosis atypical presentation as a soft tissue tumour. Malays J Pathol. 2009; 31(2): 143-5.
9. Bonifaz A, Tirado-Sánchez A. Cutaneous dissemi-

- nated and extracutaneous sporotrichosis: current status of a complex disease. *Journal of Fungi*. 2017 Mar;3(1):6.
10. Falqueto A, Bravim Maifrede S, Araujo Ribeiro M. Unusual clinical presentation of sporotrichosis in three members of one family. *Int J Dermatol*. 2012; 51(4): 434–8.
 11. Xavier MO, Riffel Bittencourt L, da Silva CM, Stone Vieira R, Pacheco Pereira HC. Atypical presentation of sporotrichosis: report of three cases. *Rev Soc Bras Med Trop*. 2013; 46(1): 116–8.
 12. Rudramurthy SM, Chakrabarti A. Sporotrichosis: Update on diagnostic techniques. *Current Fungal Infection Reports*. 2017; 11(3): 134–40.
 13. Mahajan VK, Sharma NL, Sharma RC, Gupta ML, Garg G, Kanga AK. Cutaneous sporotrichosis in Himachal Pradesh, India. *Mycoses*. 2005 Jan;48(1):25–31.
 14. Nagesh TS, Akhilesh A. Sporotrichoid cutaneous tuberculosis. *Indian J Dermatol Venereol Leprol*. 2014; 80: 279.
 15. Mahajan V, Sharma N, Shanker V, Gupta P, Mardik K. Cutaneous sporotrichosis: unusual clinical presentations. *Indian journal of dermatology, venereology and leprology*. 2010 May 1;76(3):276.
 16. Hassan K, Turker T, Zangeneh T. Disseminated sporotrichosis in an immunocompetent patient. *Case Reports Plast Surg Hand Surg*. 2016; 3(1): 44–7.
 17. Oliveira MME, Almeida-Paes R, Gutierrez-Galhardo MC, Zancoppe-Oliveira RM. Molecular identification of the *Sporothrix schenckii* complex. *Rev Iberoam Micol*. 2014; 31(1): 2–6.
 18. Oliveira MME, Santos C, Sampaio P, *et al*. Development and optimization of a new MALDI-TOF protocol for identification of the *Sporothrix* species complex. *Res Microbiol*. 2015; 166(2): 102–10.
 19. Kauffman CA, Hajjeh R, Chapman SW. Practice guidelines for the management of patients with sporotrichosis. *Clin Infect Dis*. 2000; 30(4): 684–7.