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LYMPHOCUTANEOUS SPOROTRICHOSIS: CLINICAL SUSPICION WHEN LESION IS REFRACTORY TO ANTIBACTERIAL TREATMENT.

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ABSTRACT

Sporotrichosis is a fungal infection caused by *Sporothrix schenckii.* It occurs worldwide especially in tropical and subtropical areas. It manifests as lymphocutaneous skin, fixed cutaneous or disseminated lesion following exposure to contaminated source like animals, plants, or abiotic components. We report a case of a 75-year-old lady with right foot ulcerative nodule which was refractory to repeated antibacterial treatment, and cultures were all negative including mycobacterium and fungus. Skin punch biopsy was also negative for granuloma or malignancy. Based on the history, physical examination and investigation findings, a clinical suspicion of lymphocutaneous sporotrichosis was made. The patient was started on an empirical course of itraconazole 200mg od. The lesions responded well with 12 weeks of treatment. As clinicians we are occasionally faced with cases where investigations may not yield results that are helpful towards making a diagnosis and in such situations, we may need to start empirical treatment based on our best judgement.

Keywords: Clinical diagnosis, Dermatomycoses, Skin ulcer, Sporotrichosis, Sporothrix schenckii.

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ABSTRACT

Sporotrichosis is a fungal infection caused by *Sporothrix schenckii.* It occurs worldwide especially in tropical and subtropical areas. It manifests as lymphocutaneous skin, fixed cutaneous or disseminated lesion following exposure to contaminated source like animals, plants, or abiotic components. We report a case of a 75-year-old lady with right foot ulcerative nodule which was refractory to repeated antibacterial treatment, and cultures were all negative including mycobacterium and fungus. Skin punch biopsy was also negative for granuloma or malignancy. Based on the history, physical examination and investigation findings, a clinical suspicion of lymphocutaneous sporotrichosis was made. The patient was started on an empirical course of itraconazole 200mg od. The lesions responded well with 12 weeks of treatment. As clinicians we are occasionally faced with cases where investigations may not yield results that are helpful towards making a diagnosis and in such situations, we may need to start empirical treatment based on our best judgement.

Keywords: Clinical diagnosis, Dermatomycoses, Skin ulcer, Sporotrichosis, Sporothrix schenckii.

INTRODUCTION

Fungal skin infection known as sporotrichosis is caused by the dimorphic fungus *Sporothrix schenckii.*[1] It occurs worldwide especially in tropical and subtropical areas.[1] In the Southeast Asia, Malaysia (73.7%) is known to have the highest number of cases followed by Thailand (21.1%) and Laos (5.3%).[2] This involves age group ranged from 23 to 76 years and mostly affects the female gender.[2] The incidence associated with exposure to animals, plants or abiotic factor like water, soil including trauma and has very positive response with antifungal therapy.[2] Even though lymphocutaneous sporotrichosis is not life threatening condition and is treatable, it is generally chronic with few systemic manifestations, and hence frequently misdiagnosed.[3] The following case highlights a case of ulcerative nodule which was refractory to antibacterial treat-

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ment. Furthermore, both skin scraping culture and skin punch biopsy were non-diagnostic. A high index of clinical suspicion of lymphocutaneous sporotrichosis based on clinical history and examination led to initiation of an empirical course of itraconazole 200mg od orally for 12 weeks led to a successful resolution of the ulcerative lesion.

CASE REPORT

A 75-year-old woman with underlying hypertension for 10 years presented to the dermatology clinic with right foot ulcerative nodule for the past 1 month. The lesion initially started with small size clear fluid filled blister over the medial edge of right foot. The blister gradually developed into a large nodule with central necrotizing ulcer followed by upward spread of few other smaller nodules. These progressed despite treatment by her local GP with 2 courses of antibiotics and daily dressings. She denied prolonged fever, constitutional symptoms, foot trauma or tuberculosis contact. She was a housewife and her hobby included fishing at the nearby stream.

On examination, her blood pressure was 155/72mm Hg, pulse rate 72 beat per minutes and she was afebrile. There was an erythematous nodule size (3x3cm) at right medial edge of foot which had a central shallow ulcer with superficial green slough on surface. There was no undermining nor tunneling. There were few other smaller subcutaneous nodules which extended proximally following lymphatic route (Figure 1). Other systemic examination was unremarkable. Skin punch biopsy showed superficial and deep perivascular and pre adnexal inflammatory cells composed of lymphocytes and plasma cell with focal vacuolar degeneration and civatte bodies which are dead keratinocytes. However, there was no granuloma or malignancy seen. Ziehl-Neelsen stain and PAS stain were negative. Cultures for bacteria including mycobacterium and fungus were also

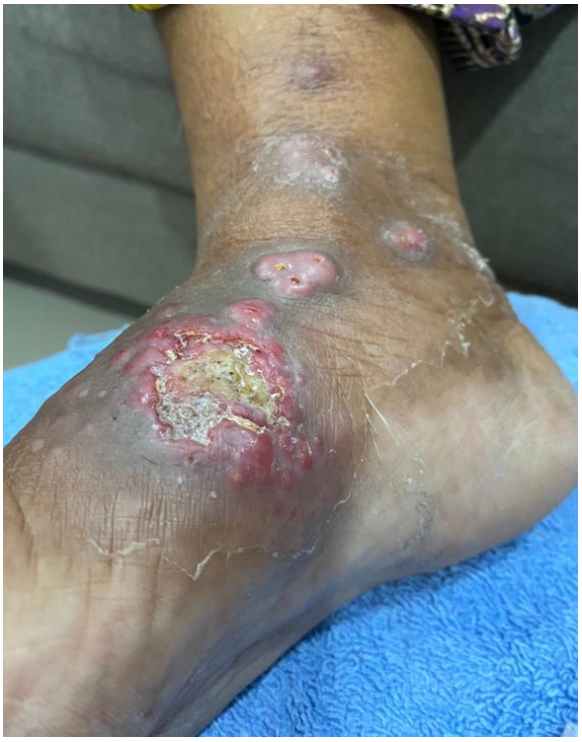

Figure 1: Right foot ulcer with nodular edge, multiple cutaneous nodular lesions in sporotrichoid spread proximally.

Negative.

A clinical diagnosis of lymphocutaneous sporotrichosis was made based on history, physical examination, and investigation finding. Therefore, an empirical course of itraconazole 200mg OD orally was initiated. The lesions responded well with resolution of the ulcer after 12 weeks of treatment (Figure 2).

DISCUSSION

Sporotrichosis is a subcutaneous or systemic fungal infection caused by the dimorphic fungus Sporothrix.[1] Commonly seen species worldwide is the *Sporothrix schenckii.*[1,3] It occurs especially in tropical and subtropical zone. The fungal spores that contaminate biotic material like animal, plants or abiotic; soil or water can penetrate skin thru cut or puncture.[1,3] The latter may be the mode of

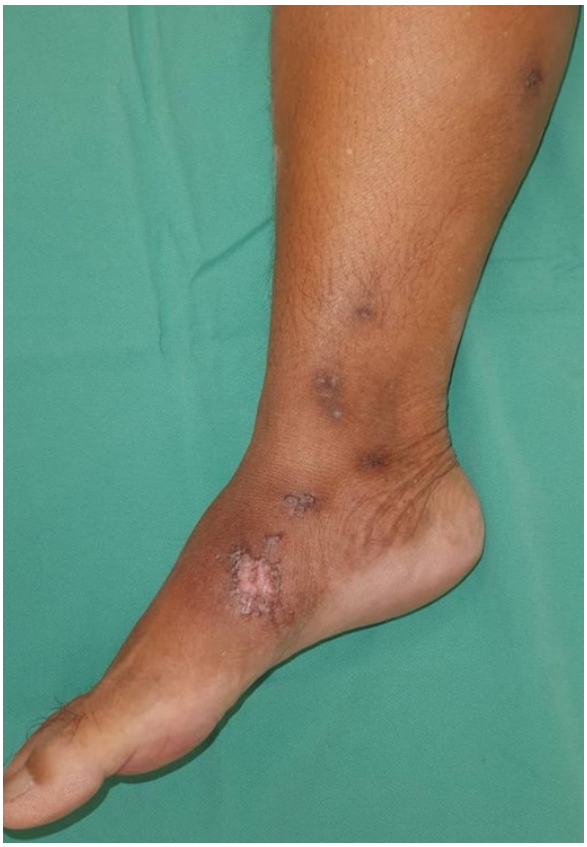

Figure 2: Healed ulcer over the right foot with post inflammatory hyperpigmentation.

transfer for our patient with frequent exposure to stream water and soil through fishing.

The lesions are usually manifested in three main clinical forms; lymphocutaneous, fixed cutaneous and disseminated cutaneous whereas hematogenous spread from primary infection can present as either extracutaneous or systemic sporotrichosis.[4] The most common presentation is lymphocutaneous and known as sporotrichoid spread.[1] Initially it appears as painless subcutaneous nodule on the skin, then progressive enlarge became pustular and ulcerated and mainly involves the upper extremities.[2] The case reported here showed identical presentation as described in literature except that the lesion was in the lower extremity. Differential diagnosis of ulcerative nodule with lymphocutaneous spread includes non-tuberculous mycobacterial infection, cutaneous nocardiosis, cat scratch disease, pyoderma gangrenosum, leishmaniasis, chromoblastomycosis, pyordermitis.[5]

When an infection is unresponsive to treatment, a high index of clinical suspicion is warranted, thus a comprehensive history and physical examination were vital to minimize treatment delays. Sporortrichosis is usually diagnosed by identification of Sporothrix species from the clinical sampling like skin biopsy, abscess, aspirate and other.[5] Diagnosis of sporotrichosis can be made through a correlation of clinical, epidemiology and laboratory investigation. [1] In our case, we were unable to culture the organism and skin biopsy was inconclusive. However clinical diagnosis was made based on feature of ulcerative nodule with surrounding subcutaneous nodules in sporotrichoid spread and cultures ruling out other common organisms such as nocardia and non-tuberculous mycobacterium. False-negative results may occur either due to poor tissue selection for biopsy, lack of fungal growth at the tissue itself and histological method used for detection.[6] Histological features of *S.schenckii* show suppurative granulomas, neutrophils and liquefaction.[6] However it has been reported to present as non-specific inflammation.[7] Sporotrichosis can be diagnosed using enzyme linked immunosorbent assays (ELISA) detection of IgG and via detection *S. schenckii* DNA molecular.[8],[9] Most centres rely heavily on fungal cultures due to costs, however this can also be negative.[5] ELISA and PCR methods may be of assistance in such cases. Unfortunately these specialized molecular testings were unavailable at our centre. We could have sent off the skin biopsy for ELISA and PCR at outside centres but this would have taken time and delay initiation of treatment.

Spontaneous resolution is extremely rare and most of the patients require antifungal therapy. The first line is tablet itraconazole for eradication of *Sporothrix schenckii* for 3–6 month duration.[4] The recommended dose

for cutaneous sporotrichosis ranges from 100 to 200 mg/day of oral itraconazole.[1] This present patient responded well to oral itraconazole 200 mg / day with no adverse effects and upon review at week 12 the lesion had healed. We advised the patient to wear protective gears such as thick waterproof gloves and boots during outdoor activity in the future to prevent re-exposure to the fungus.

CONCLUSION

This case highlights the importance of taking a focused history taking with careful observation of skin lesion in managing skin conditions in primary care settings when all investigations such as skin biopsy and culture are unfruitful in deriving a diagnosis. A possibility of Sporortrichosis should be considered especially when a patient presents with subcutaneous nodule with lymphocutaneous spread which is refractory to antibacterial treatment.

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CONFLICT OF INTEREST

None to declare.

REFERENCES

1: de Lima Barros MB, de Almeida Paes R, Schubach AO. Sporothrix schenckii and sporotrichosis. Clin Microbiol Rev. 2011;24:354–633. [Accessed on 2022 June 18].
2: Tovikkai D, Maitrisathit W, Srisuttiyakorn C, Vanichanan J, Thammahong A, Suankratay C. Sporotrichosis: The case series in Thailand and literature review in Southeast Asia. Med Mycol Case Rep [Internet]. 2020;27:59–63. [Accessed on 2022 June 18].
3: Chakrabarti A, Bonifaz A, Gutierrez-Galhardo MC, Mochizuki T, Li S. Global epidemiology of sporotrichosis. Med Mycol. 2014;53:3–14. [Accessed on 2022 June 18].
4: Mahajan VK. Sporotrichosis: An overview and therapeutic options. Dermatol Res Pract. 2014;2014. [Accessed on 2022 June 18].
5: Orofino-Costa R, Rodrigues AM, de Macedo PM, Bernardes-Engemann AR. Sporotrichosis: An update on epidemiology, etiopathogenesis, laboratory and clinical therapeutics. An Bras Dermatol. 2017;92:606–20. [Accessed on 2022 June 18].
6: Quintella LP, Lambert Passos SR, Francesconi Do Vale AC, Gutierrez Galhardo MC, De Lima Barros MB, Cuzzi T, et al. Histopathology of cutaneous sporotrichosis in Rio de Janeiro: A series of 119 consecutive cases. J Cutan Pathol. 2011;38:25–32. [Accessed on 2022 June 18].
7: Mahajan VK, Sharma NL, Sharma RC, Gupta ML, Garg G, Kanga AK. Cutaneous sporotrichosis in Himachal Pradesh, India. Mycoses. 2005;48:25–31.
8: Almeida-Paes R, Pimenta MA, Monteiro PCF, Nosanchuk JD, Zancopé-Oliveira RM. Immunoglobulins G, M, and A against Sporothrix schenckii exoantigens in patients with sporotrichosis before and during treatment with itraconazole. Clin Vaccine Immunol. 2007;14:1149–57. [Accessed on 2022 June 18].
9: Hu S, Chung WH, Hung SI, Ho HC, Wang ZW, Chen CH, et al. Detection of Sporothrix schenckii in clinical samples by a nested PCR assay. J Clin Microbiol. 2003;41:1414–8. [Accessed on 2022 June 18].