CASE REPORT

Disseminated Cutaneous Sporotrichosis with Fungal Sinusitis As An Initial Presentation of Underlying Myeloproliferative Neoplasm

Wei Hsi Chang[1], *MRCP*, Juliana Wai Theng Lee[1], *MBBS*, Soo Ching Gan[2], *MPath*, Ting Guan Ng[1], *AdvMDerm*

[1]Department of Dermatology, Hospital Tengku Ampuan Rahimah, Klang, Selangor, Malaysia
[2]Department of Pathology, Hospital Tengku Ampuan Rahimah, Klang, Selangor, Malaysia

Summary
Sporotrichosis is a rare and chronic granulomatous subcutaneous mycotic infection caused by a dimorphic fungus, *Sporothrix schenckii*. We describe a patient with disseminated cutaneous sporotrichosis who was later diagnosed with myeloproliferative neoplasm and discuss the challenges and importance in diagnosing this rare condition.

Key words: *Disseminated sporotrichosis, fungal sinusitis, myeloproliferative neoplasm*

Introduction
Sporotrichosis is a chronic granulomatous subcutaneous mycotic infection caused by *Sporothrix schenckii,* a dimorphic fungus found in soil, sphagnum moss and contaminated organic matter.[1,2] It presents as nodules, plaques, and subcutaneous swellings which often make clinical diagnosis a challenge, particularly in nonendemic areas.[1] Here, we report a case of recalcitrant disseminated cutaneous sporotrichosis with fungal rhinosinusitis in an apparent immunocompetent individual, who was later diagnosed with myeloproliferative neoplasm.

Case Report
A 49-year-old man presented with painful ulcerated nodules on his face, trunk and extremities for the past 1 month associated with low-grade fever, malaise, appetite loss and weight loss. His past medical history includes hypertension, coronary artery disease and gout. He works in a plant nursery and has a wild cat at home. On examination, there were multiple ulcerated nodules and hyperkeratotic plaques on the face, trunk, and extremities (Figure 1a&b). Lung examination was normal. Abdominal examination revealed a non-tender

Corresponding Author
Dr Chang Wei Hsi
Department of Dermatology,
Hospital Tengku Ampuan Rahimah,
Jalan Langat,
41200 Klang, Selangor, Malaysia
Email: elizzchang@gmail.com

splenomegaly. No enlarged lymph nodes were detected. Blood investigations revealed leukocytosis of 11.88 x 10^9/L, normocytic normochromic anaemia with a Hb of 11.5 g/dL, and mild thrombocytosis of 542 x 10^9/L. Liver function, renal function, blood glucose, serum cortisol, human immunodeficiency virus (HIV) test, viral hepatitis test, and chest radiograph results were normal. Histopathological examination (HPE) of the skin biopsy showed a chronic granulomatous inflammation in the dermis (Figure 2a). *Myobacterium leprae* and *Mycobacterium tuberculosis* were not detected. Fungal culture from the skin lesions grew *S. schenckii*, confirming the diagnosis of disseminated cutaneous sporotrichosis. His clinical response to 6 months of oral itraconazole and 3 months of combined oral itraconazole and terbinafine was poor. A repeated skin biopsy showed similar HPE and fungal culture findings. Abdominal ultrasonography revealed hepatomegaly and massive splenomegaly.

Bone marrow aspirate and trephine biopsy demonstrated features of myeloproliferative neoplasm (MPN). He was positive for JAK V617F, which is pathognomonic for MPN. He experienced intermittent epistaxis for the past few months. Functional Endoscopic Sinus Surgery revealed ulcerated and perforated nasal septum with crusted necrotic tissues over the middle and inferior turbinate. HPE of the nasal septum was consistent with a chronic granulomatous inflammation with fungal yeasts morphologically consistent with *S. schenckii* (Figure 2a&b). Fungal culture from nasal septum isolated *S. schenckii.* Computed tomography scan showed mucosal thickening of maxillary sinuses and hyperdense soft tissue over the right frontal sinus. He was admitted for treatment with intravenous (IV) amphotericin B, and for further workup of the newly diagnosed MPN. Regular nasal irrigation was performed by the otorhinolaryngologist. After two weeks of IV amphotericin B, he was discharged from the hospital against medical advice and opted for conservative management for his myeloproliferative disease. Unfortunately, he succumbed to severe sepsis secondary to infected cutaneous ulcers three months later.

Figure 1. (a) Disseminated sporotrichosis on left upper limb and (b) anterior trunk, demonstrating numerous erythematous nodules with occasional ulceration

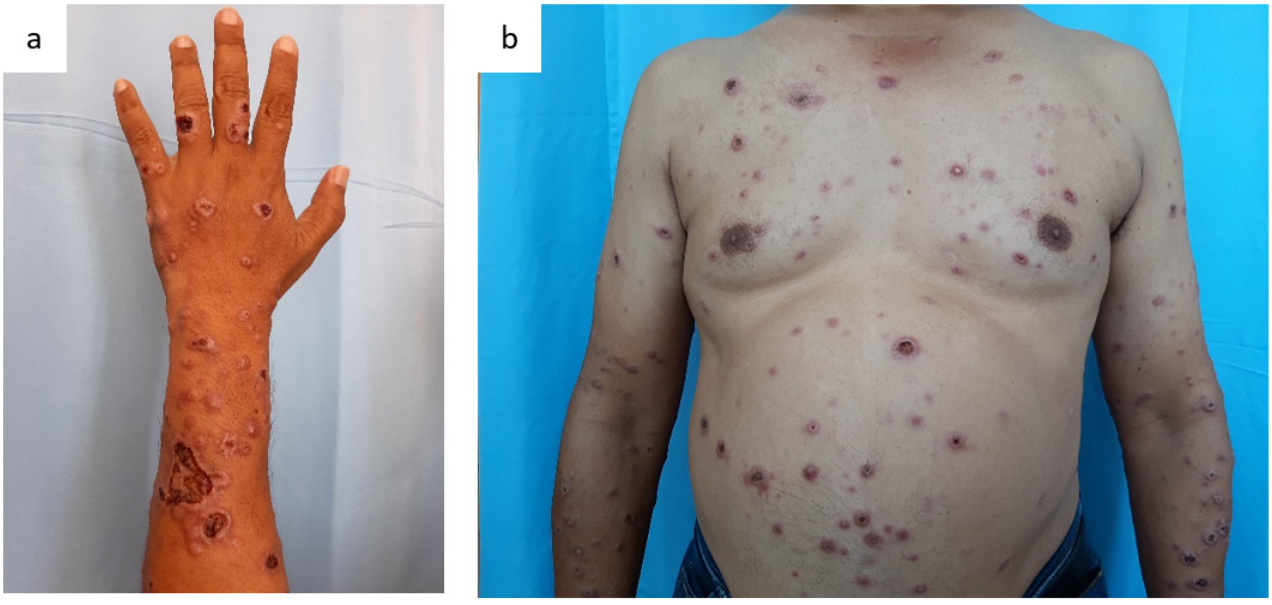
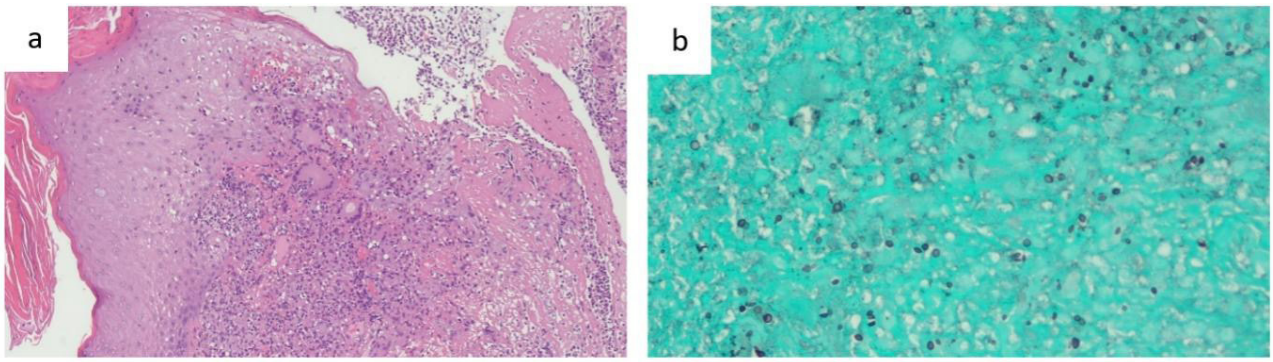


Figure 2. (a) Left arm skin biopsy, haematoxylin and eosin stain (20X) showing chronic granulomatous inflammation in the dermis; (b) Nasal septum biopsy, Gomori methenamine stain (40X) demonstrating ovoid and elongated fungal spores



Discussion

Sporotrichosis is a cutaneous fungal infection reported worldwide.[2,3] Its clinical manifestations depend on the route of infection, burden of inoculum and immune status of the host.[4,5] Dissemination may occur in immunocompromised individuals.[4] Infection with HIV, iatrogenic immune suppression, and haematological malignancies are some of the reported predisposing conditions.[4] Myeloproliferative conditions like myelofibrosis are also associated with extracutaneous sporotrichosis.[1] The newly diagnosed MPN in this case may have contributed to the progression of disseminated disease.

Cutaneous infection is commonly associated with trauma during outdoor activities.[3] *S. schenckii* may enter the body directly through a thorn prick, abrasion or blunt injury, or indirectly through animal bites or scratches.[6] Our case does significant outdoor work and is thought to have contracted the infection through skin inoculation, from traumatic implantation of thorns and splinters, or inhalation. The activation and proliferation of macrophages and T lymphocytes are involved in controlling fungal infection.[7] The immune response against *S. schenckii* infections is most likely a combination of humoral, cellular and innate immune responses.[2]

Treatment with amphotericin B was initiated according to the current guideline recommendations in Malaysia.[8] Several studies have reported the *in vitro* efficacy of other agents such as amphotericin B and posaconazole against disseminated sporotrichosis.[4,9] In a similar case report, Bunce *et al*. (2012) reported a significant improvement using a combined antifungal treatment of amphotericin B and posaconazole in a patient with disseminated sporotrichosis who had underlying hairy cell leukemia that was refractory to initial therapy with liposomal amphotericin B and oral itraconazole.[4] The patient, who worked as an outdoor contractor, achieved resolution of symptoms after 8 months of treatment with amphotericin B, and remains stable on posaconazole after 5 months.[4] Thus, this supported the use of amphotericin B in our patient.

Conclusion

In summary, we have reported a case of disseminated *S. schenckii* infection in a patient with newly diagnosed MPN initially refractory to oral itraconazole and terbinafine, and eventually required IV amphotericin B. A high index of clinical suspicion is important for early diagnosis to prevent further complications of this disease.

Conflict of Interest Declaration

The authors declare that there is no conflict of interest in this work.

Acknowledgement

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