

Case report

Unresolved chronic ulcerated nodules: Disseminated Cutaneous Sporotrichosis

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Abstract

We present a case of disseminated cutaneous sporotrichosis in a 72-year-old male patient who has multiple ulcerated painless nodules over the left side of his chest and on his upper and lower left limbs for three years. He was initially diagnosed to have nodular vasculitis based on early repeated biopsies. Despite the patient's good compliance with his prednisolone medication, no significant clinical improvement was observed. Another biopsy, which was arranged after two years of treatment for nodular vasculitis, supported the diagnosis of sporotrichosis. Itraconazole was initiated, and all the lesions showed a remarkable response toward the treatment. The delay in finding the correct diagnosis unnecessarily exposed the patient to the side effects of steroid and caused the disease to worsen.

Keywords: cutaneous sporotrichosis; nodular vasculitis; sporotrichosis; *Sporothrixschenckii*; ulcerated nodules.

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Introduction

Sporotrichosis is a chronic granulomatous infection caused by dimorphic fungus *Sporothrixschenckii*. The organism exists saprophytically in soil; it decays wood, hay, and sphagnum moss, and it is most commonly seen in tropical and sub-tropical areas¹. Sporotrichosis characteristically involves only the skin and subcutaneous tissue following the traumatic inoculation of the causative organism. In rare cases, it may disseminate and affect the neighbouring joints and other multiple visceral organs and systems, such as respiratory, genitourinary, and central nervous system, especially in immunocompromised patients^{1,2}.

Cutaneous sporotrichosis infection can be classified into fixed cutaneous, lymphocutaneous and disseminated cutaneous infection. Disseminated cutaneous sporotrichosis infection usually presents as small and indurated papulonodular lesions. These lesions then progressively enlarge which eventually ulcerate (sporotrichotic chancre) and spread to other skin areas, causing multiple lesions¹.

Clinical suspicion is the key for early diagnosis,

and cutaneous lesions must be differentiated from cutaneous tuberculosis, cutaneous leishmaniasis, nocardiosis, blastomycosis, chromoblastomycosis, paracoccidioidomycosis, atypical mycobacteriosis, pyoderma gangrenosum, and nodular vasculitis. Culture of the causative organism remains as a diagnostic tool given that a direct smear of pus and biopsy specimen barely catches the causative organism due to paucity of the fungal cells¹.

Itraconazole is the first line anti-fungal agent for the treatment of sporotrichosis¹⁻⁵. It is a first generation triazole-derivative antifungal agent with a broad-spectrum antifungal activity. It demonstrates less toxicity, making it a first-choice treatment especially in immunocompromised patients^{2,5}.

Case Report

A 72-year-old pensioner who has been suffering from multiple ulcerated painless non-itchy nodules over the left side of his chest and on his upper and lower left limbs for 3 years presented to our dermatology clinic in early 2019. He spent most of his time with gardening. Moreover, he always provides food to stray cats but denies a history of cat bite or scratch. He

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has no known history of food or drug allergy.

His medical history revealed that he has underlying primary myelofibrosis since February 2016 and has been under follow up at a general hospital. For that, he has been taking 15 mg ruxolitinib tablet (jakavi) twice daily. Additionally, he has gastroesophageal reflux disease (GERD) and has been put on 40 mg pantoprazole tablet daily.

He was first noted to have multiple painless non-itchy nodules over his left chest (figure 1) and upper and lower left limbs (figure 2 & 3) during his routine follow up for his myelofibrosis in 2016. No fever or any systemic manifestations were noted.



Figure 3: Nodule over left lower limb (2016)



Figure 1: Nodule over chest (2016)



Figure 2: Nodule/induration over left upper limb (2016)

He was then referred to the dermatology clinic in the same hospital for further assessment. A biopsy was arranged which came back as nodular vasculitis. Thus, he was diagnosed with nodular vasculitis secondary to ruxolitinib. He was started with a daily dose of 10 mg prednisolone tablet. However, despite the treatment, the nodules did not show much improvement. From 2016 to 2019, there were a few episodes of flare during which the nodules became more prominent and ulcerated. The subsequent repeated biopsies still showed the same result. Mycobacterium tuberculosis (MTB) and fungal culture test were also performed, and they came back negative. The prednisolone was continued wherein the dose was increased up to 30mg daily during a flare and then tapered to the maintenance dose of 5mg daily once the lesion improved.

In February 2019, he moved to his hometown where he came to see us in our dermatology clinic. His prednisolone was continued. After a few months of follow up, the lesions over his upper and lower left limbs worsened with purulent discharge (Figure 4).



Figure 4: Multiple ulcerated nodules with pus discharge (2019)

Thus, another skin biopsy was arranged in our clinic. This time, the result showed presence of suppurative granulomatous inflammation secondary to fungal infection in yeast form. The skin biopsy result was further supported by fungal culture and polymerase chain reaction (PCR) which came back as *Sporothrixschenkii*. As the disease may disseminate to the lungs and joints, a radiograph of the chest and underlying bones and of the joints adjacent to the lesions were taken. Fortunately, all the radiographs were clear wherein no lytic lesions or erosions of articular surfaces were seen. His liver function test also showed normal results. Finally, he was diagnosed to have disseminated cutaneous sporotrichosis, and treatment with 200mg itraconazole capsule twice daily was commenced.

After two months, the lesions dried up and the purulent discharge was gone. However, new ulcers emerged in the neighbouring area despite his good compliance with the medication. Considering his poor appetite and dependence on pantoprazole tablet for the frequent episodes of GERD symptoms, the formulation of itraconazole was changed from capsule to syrup, and he was advised to take the syrup in fasting state to improve its absorption. The syrup was started at 200mg three times daily and was tapered to 200mg twice daily after three days. The therapeutic drug monitoring (TDM) level was regularly monitored to ensure it was within the targeted level for disseminated cutaneous sporotrichosis treatment. The liver function tests results were always within the normal range.

Three months after the initiation of itraconazole syrup, a marked clinical improvement of the lesions was observed (figure 5). Also, no new lesion or



Figure 5: Lesions dried up and no more pus discharge. (2019, after 3 months course of Syrup Itraconazole)

ulcer was seen. The TDM level was also within the target. The patient was intended to continue with itraconazole syrup for six months after all of the lesions were fully resolved.

Discussion

Sporotrichosis is a rare infection in certain countries but not in tropical and subtropical countries, such as Mexico, Central America, South America and Africa, where the highest numbers of cases have been reported⁶. With the emergence of a vast variety of diseases, medical practitioners should have a high index of suspicion towards certain diseases that are common in their locality. When dealing with multiple nodular painless lesions that occur with risk factors such as exposure to thorns while gardening and cat bites or scratches, fungal infection must not be discounted. However, other common diagnoses, such as cutaneous tuberculosis and basal cell carcinoma, should also be considered when dealing with immunocompromised patients, similar to the present case.

Nodular vasculitis is an uncommon inflammatory disorder characterized by erythematous, warm, tender subcutaneous nodules classically present on the calf, which eventually ulcerate. It appears to be a disease of various aetiologies, such as infections, inflammations, and hypersensitivity effects⁷. The clinical and histological presentations of nodular vasculitis are nearly identical to those of various infections, such as sporotrichosis and tuberculosis. Histologically, nodular vasculitis is characterized by panniculitis, along with the combination of vasculitis, focal necrosis and granulomatous lesions⁷. By contrast, sporotrichosis and tuberculosis involve a combination of granulomatous and pyogenic processes caused by organisms that are rarely visualized due to their small number and scattered distribution¹. Thus, culture of the organism remains the appropriate discriminative diagnostic tool. Unfortunately for this patient, MTB and fungal C&S were negative in the earlier cultures, limiting the diagnosis to nodular vasculitis.

Due to the unknown cause of infection, the patient was treated with steroid to reduce inflammation. The chronic use of steroid and late detection of the disease could be the reason for the worsened and disseminated lesions caused by the fungal infection. The chronic use of steroid also induced the multiple flare episodes, which indicate a reduction in the patient's immune system, as well as spreading and

worsening of the infection.

Among other treatments available for sporotrichosis, such as saturated solution of potassium iodide, ketoconazole and amphotericin B, itraconazole is the most commonly available in a primary care setting. Furthermore, itraconazole has 90-100% efficacy in cutaneous as well as extracutaneous sporotrichosis, and it demonstrates less toxicity^{1,2}. Improvement of lesions is seen one to two weeks after itraconazole initiation, and this medication is continued for three to six months after all of the lesions resolved¹. In our patient, despite the two-month-long therapy of itraconazole, the lesions did not show much improvement, and new lesions even developed, thus, the formulation of the medication was changed from capsule to syrup to achieve a better effect. The bioavailability of itraconazole syrup is 30-33% greater than that of the capsule formulation when taken in a fasted state⁸. Moreover, treatment with pantoprazole tablet has been shown to increase gastric pH, thereby reducing the absorption of itraconazole in the capsule form².

According to the Infectious Disease Society of America (IDSA), the medication response following initiation of treatment with itraconazole syrup is best reviewed after three months of follow-up¹. Also, itraconazole exhibits a non-linear pharmacokinetics activity, which makes the regular monitoring of the TDM level of itraconazole crucial in all patients⁹. For our patient, the TDM level taken after three months were within the therapeutic range.

Overall, the diagnosis of sporotrichosis can be made by having a high index of suspicion in patients presenting with nodular-ulcerative lesions. However,

skin biopsy for culture and sensitivity remains the definitive diagnostic tool in diagnosing any skin lesions. A correct early diagnosis is mandatory to avoid unnecessarily causing unwanted side effects in patients. Itraconazole is believed to be the most effective and well-tolerated drug for the treatment of disseminated cutaneous sporotrichosis.

Having a high index of suspicion towards sporotrichosis in patients who present with unresolved chronic skin nodules or ulcers despite first-line treatment help the primary healthcare providers to detect the disease at early stage, preventing it from disseminating into other body systems. Education regarding the risk factors, disease spread, and disease manifestation should be given to the public as preventive measures.

Ethical approval about publication

Ethical approval not required. The patient's permission was obtained.

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Conflict of interest

There is no potential conflict of interest relevant to this case report.

Authors contribution

Data gathering: Nurkhaniza Kaman.

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