

Therapy Letters

Successful treatment outcome with itraconazole and potassium iodide in disseminated sporotrichosis

Sir,

A 57-year-old man, from Rajasthan, India presented with a 6 months history of painful erythematous nodules and plaques, some of which were ulcerated and crusted over the trunk, upper, and lower limbs. Few lesions on the back were linear in shape [Figures 1 and 2]. He also complained of hoarseness of voice for 2 months. There was no preceding history of trauma, thorn pricks, or animal bites. Medical history was significant for well-controlled hypertension (on ramipril and amlodipine) and diabetes mellitus (on glimepride and metformin). Routine hematological investigations were unremarkable, whereas mantoux test and enzyme-linked immunosorbent assay (ELISA) for human immunodeficiency virus (HIV)-1 and 2 were negative. Skin biopsies from intact and ulcerated plaques showed necrotizing epithelioid cell granulomas in the dermis with neutrophilic microabscesses [Figures 3 and 4]. Special stains and culture for fungi and mycobacteria were negative. Laryngoscopy revealed a supraglottic growth, however, the patient refused for biopsy of the lesion. Contrast-enhanced computerized tomography of the chest and abdomen was unremarkable. With a provisional diagnosis of disseminated cutaneous sporotrichosis, the patient was treated with oral itraconazole 200 mg/day. Over the next 12 months, all the lesions completely healed with scarring. The patient also noticed significant improvement in his voice, and the dose of itraconazole was tapered to 100 mg/day. Within the next 3 months, few of the earlier healed lesions began to show increased nodularity. The dose of itraconazole was hiked to 200 mg/day, which led to near complete resolution of all lesions within 4 months except for one persistent lesion which was excised and showed similar histological features as the previous lesions. Subsequently, itraconazole was stopped and the patient remained well for the next 3 months. However, 1 month later, few fresh nodules appeared on the abdomen and forearms, which on histological examination showed dense mixed cell infiltrates and asteroid bodies [Figure 5] on periodic acid Schiff (PAS) staining characteristic of sporotrichosis [Figure 6]; however, the fungal culture was negative. Itraconazole was restarted at a dose of 200 mg/

day. However, this time, there was only partial flattening of the lesions, therefore, supersaturated solution of potassium iodide was added at a starting dose of 5 drops thrice daily, which was gradually increased to 40 drops thrice daily over a month. All lesions healed completely with 5 months of combination therapy, which was continued for a further 4 months with a lower dose of supersaturated solution of potassium iodide (30 drops thrice daily) as the patient complained of severe headache and rhinorrhea. After 9 months of combination therapy, biopsy from a healed lesion showed features of a scar. Subsequently, supersaturated solution of potassium iodide was stopped while itraconazole 200 mg daily was continued for 5 more months and stopped. It is now 4 years since all treatment was stopped, and presently, the only cutaneous abnormalities are scars at the sites of healed lesions, without any evidence of reactivation of older lesions [Figures 7 and 8]. The treatment course and response in our patient is summarized in Table 1.

Sporotrichosis has been reported from many parts of the world, mainly from tropical and temperate areas.¹ In India, majority of the cases have been described from the sub-Himalayan belt.^{2,3} Disseminated cutaneous sporotrichosis is usually seen in immunocompromised patients, however, it has been reported in immunocompetent patients as well.⁴⁻⁶ Diabetes mellitus, though well-controlled, could have predisposed our patient to such a widespread infection. Greater virulence of the infecting strain could be another explanation for the disseminated infection in our patient.⁷ Apart from disseminated cutaneous disease, our patient might have had laryngeal involvement, supported by the rapid improvement in hoarseness of voice with antifungal therapy. The clinical picture, as seen in our case, has a broad differential diagnosis including cutaneous tuberculosis, atypical mycobacterial infection, leishmaniasis, and other deep mycoses all of which may also share the histopathologic finding of a mixed cell infiltrate/granuloma. Though the gold standard for diagnosis of sporotrichosis is the isolation of fungus in Sabouraud's dextrose agar, a culture



Figure 1: Multiple erythematous plaques on the back. Linear configuration of some of the plaques can be noted



Figure 2: Plaque with overlying ulceration on the left arm

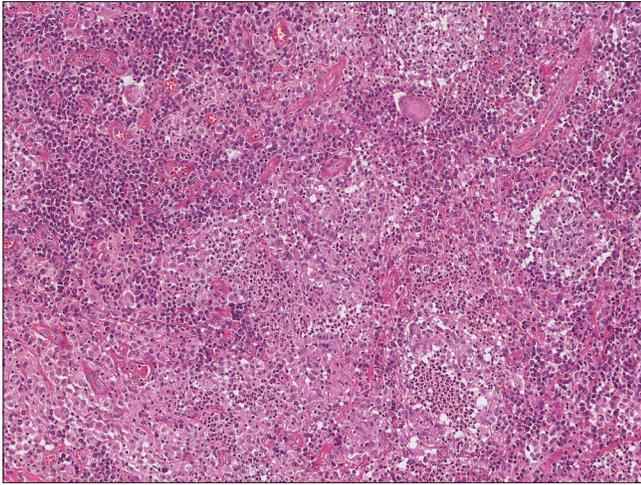


Figure 3: Biopsy from one of the plaques showing dense dermal infiltrate composed of lymphocytes, histiocytes, plasma cells with collection of epithelioid cells and an occasional giant cell admixed with polymorphs (hematoxylin and eosin, ×100)

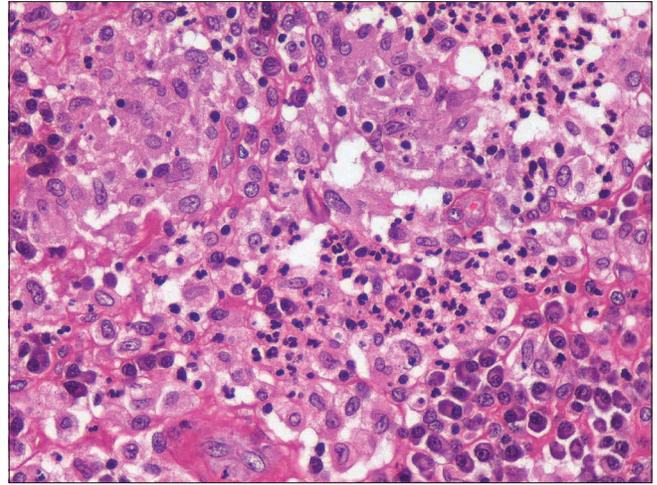


Figure 4: Higher magnification showing collection of neutrophils (neutrophilic microabscess) along with epithelioid cells and plasma cells (hematoxylin and eosin, ×400)

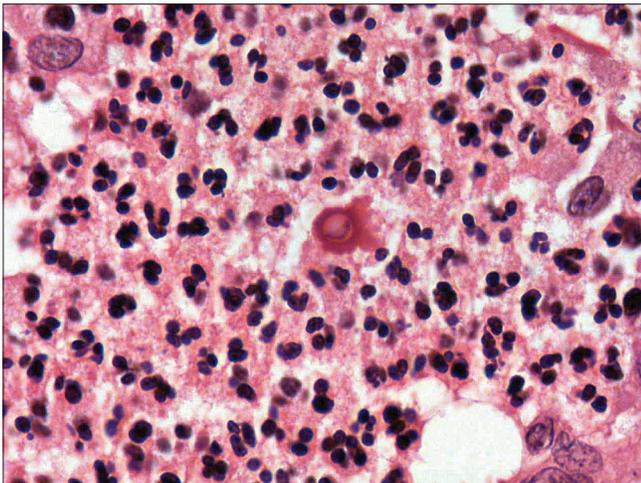


Figure 5: Central yeast with surrounding radiating eosinophilic material (asteroid body) seen in the subsequent biopsy (hematoxylin and eosin, ×400)

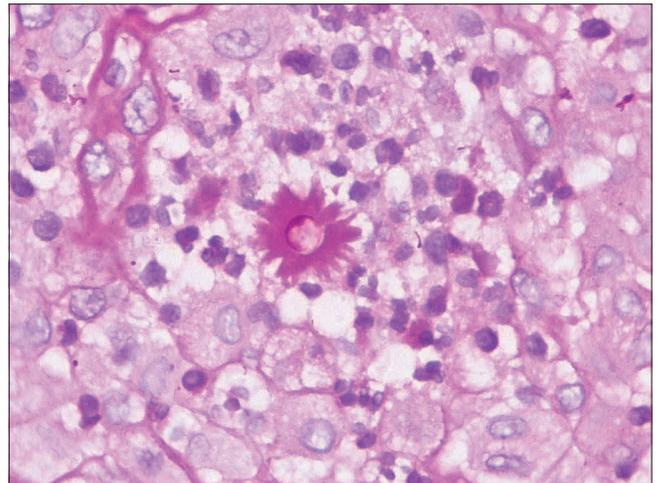


Figure 6: Central yeast with surrounding radiating eosinophilic material (asteroid body) seen in the subsequent biopsy (periodic-acid Schiff, ×400)



Figure 7: Post-treatment photograph showing healed scars on the back



Figure 8: Post-treatment photograph showing healed scars on the left arm

Table 1: Summary of treatment received and response

Time period	Duration (months)	Treatment	Response
April 2008 to April 2009	13	Itraconazole 100 mg BD	All except two lesions healed
May 2009 to July 2009	3	Itraconazole 100 mg OD	Few lesions showed increased nodularity
August 2009 to November 2009	4	Itraconazole 100 mg BD	All lesions resolved except one-excision biopsy showed granulomas with background mixed cell infiltrate
December 2009 to March 2010	4	No treatment	Remained well for next 3 months. Then few fresh nodules appeared. Biopsy showed granulomas, microabscesses, asteroid bodies
April 2010 to September 2010	6	Itraconazole 100 mg BD	Partial response. Few lesions ulcerated while on treatment
October 2010 to February 2011	1	Itraconazole 100 mg BD + Supersaturated solution of potassium iodide 5 drops TDS, gradually increased to 40 drops TDS	Ulcerated lesions started drying up, began to heal
November 2010 to February 2011	4	Itraconazole 100 mg BD + Supersaturated solution of potassium iodide 40 drops TDS	Complete healing of all lesions by January 2011. Complained of severe headache, rhinorrhea due to supersaturated solution of potassium iodide
March 2011 to July 2011	5	Itraconazole 100 mg BD + Supersaturated solution of potassium iodide 30 drops BD	No activity in lesions. Biopsy showed features of scar
August 2011 to December 2011	5	Itraconazole 100 mg BD	Only scars
January 2012 to August 2015	50	No treatment	Only scars

BD: Twice a day, TDS: Three times a day

may not always be positive. Molecular tests such as polymerase chain reaction can also be used to establish the diagnosis, but are not available widely. In such a scenario, a therapeutic trial may help in settling the diagnosis. Though there was an initial good response to itraconazole, lesions relapsed soon after tapering or stopping treatment. It was only on repeated biopsies that the asteroid bodies were visualized, thus confirming the diagnosis. The recommended treatment for disseminated/systemic sporotrichosis, is Amphotericin B followed by oral itraconazole 400 mg/day (for a total of 12 months).⁸ Successful treatment of disseminated sporotrichosis with oral itraconazole⁹ as well as supersaturated solution of potassium iodide¹⁰ has also been reported previously. As our patient refused amphotericin B citing the high cost of therapy and the need for inpatient treatment, we decided to continue oral itraconazole in view of the initial improvement with this agent. We could not increase the itraconazole dose considering the financial constraints of the patient, and added supersaturated solution of potassium iodide when the clinical response was less than satisfactory. Our patient benefited from the combination of itraconazole and potassium iodide.

To conclude, we wish to emphasize the utility of a therapeutic trial in sporotrichosis and the need for multiple biopsies in arriving at the correct diagnosis, where a definitive diagnosis maybe difficult at the outset. Prolonged combination treatment with itraconazole and potassium iodide may be an alternative treatment strategy in patients with disseminated sporotrichosis who cannot be treated with amphotericin B for any reason.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for her images and other clinical information to be reported in the journal. The patient understands that his name and initial will not be published and due efforts will be made to conceal his entity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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