LETTER TO EDITOR
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EUMYCETOMA FOOT – SUCCESSFUL TREATMENT WITH COMBINATION OF ITRACONAZOLE AND POTASSIUM IODIDE

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Sir,

Mycetoma is a chronic progressive granulomatous infection presenting with triad of localized swelling, underlying sinus tracts and production of grains or granules within the sinus tracts. It is caused by either eumycetes fungi or actinomycetes bacteria, giving rise to eumycetoma or actinomycetoma, respectively. Differentiaton between these two is important as treatment protocol and outcome are entirely different. Actinomycetoma responds to a number of antibacterial drugs including modified Welsh regimen with our modification [1] with good outcome whereas response of eumycetoma to medical treatment alone is disappointing. Mostly eumycetoma patients have to undergo repeated surgeries including amputation of affected part. In this article, we report the outcome of treatment with combination of itraconazole and saturated solution of potassium iodide used in five patients of eumycetoma.

A baseline skin biopsy, KOH mount, liver function test, thyroid function test, digital X-ray and MRI were done in all cases. Fungal and bacterial cultures were not done as all cases had classical black granules and showed thick septate hyphae on KOH mount. The criterion for diagnosis of eumycetoma was taken as presence of black granules and was confirmed by presence of PAS & GMS positive fungal colonies in histopathology. Patients were treated with combination of itraconazole and saturated solution of potassium iodide (KI). Itraconazole was given at doses of 400 mg daily in two divided doses. KI was administered as a saturated solution of potassium iodide (SSKI) which contains approximately 14 gms in 20 ml. Initially 5 drops of SSKI was administered three times a day. Gradually the dosage was increased as tolerated to a maximum of approximately 30-40 drops three times daily. Surgical debridement of the lesion was also done if required. Patients were evaluated clinically and radiologically. Liver function test, thyroid function test were done monthly to monitor any adverse effects. Digital X-ray was done monthly and MRI six monthly to monitor treatment response.

Figure 1: Pretreatment photograph of case 2 showing nodules and discharging sinuses

Figure 2: Photograph of case 2 twelve month after treatment showing healed nodule and sinuses

Five patients (4 males, 1 female), age ranging from 13 to 42 years (mean 23.8 years), were included in this case series. Disease duration ranged from 1 year to 15 years (mean 8 years) at the time of presentation. There clinical and histopathological details have been summarized in Table 1.

After ten months of treatment in case 1 the sinuses healed completely with no new lesions. Treatment was continued for another two months during which no activity, clinical or radiological, was seen. No new lesions were seen in next six months of followup without treatment. In case 2, complete healing was seen after twelve months of treatment. The lesion had to be surgically debrided twice. The treatment was continued for next two months and was followed for six months without treatment during which no new activity was seen (Fig. 1-4). In case 3 the lesions healed in eight months of treatment. The patient is still on treatment and no new lesions have evolved. Case 4 is on treatment for six months. There is no discharge of granules and sinuses have healed but there is occasional serous discharge from sinuses, although the lesion is not spreading radiologically. Similarly in case 5 after eight months of treatment there are no new lesion and granules but occasional serous

Case No.	Age/Sex	Location and clinical presentation	Histopathology	Bone Involvement	Previous Treatment
1	32/F	Plantar aspect of left foot-discharging ulcer with black grains present	multiple abscesses with centrally lying fungal colonies; positive with GMS & PAS stain	No	Surgically excised 3 months back, 2 month later recurrence occurred with discharge of black granule
2	14/M	At knee of left Leg – swelling, discharging sinuses and black grains (Fig. 1-4)	Multiple colonies with septate hyphae which stain positively with GMS &PAS stain	Yes	Surgically excised four times previously
3	18/M	Dorsal aspect of left foot extending to ankle- swelling, discharging sinuses with ulceration and black grains	GMS & PAS positive fungal colonies seen	Yes	No
4	13/M	Dorsal aspect of left Foot– single nodule on dorsal aspect, black grains	GMS & PAS positive fungal colonies seen	Yes	No
5	42/M	Palmar aspect of left foot-swelling & discharging sinuses with black grains	dense chronic inflammatory infiltrate; definitive evidence of mycetoma not seen	Yes	Surgically excised thrice previously

Table 1: Clinical and histopathological findings of patients

discharge is seen and is on treatment. No adverse effect of treatment was seen in any patient.

Various antifungal agents have been tried in eumycetoma with little success. Fluconazole and griseofulvin have been found to be ineffective. Ketoconazole, itraconazole and terbinafine have shown variable efficacy at higher doses after long duration of treatment.[2,3] Drawback of amphotericin B is cost, toxicity and parenteral route of administration. Voriconazole and posaconazole are newer drugs which have shown good efficacy and broader spectrum of action than older azoles.[4,5]

Potassium iodide (KI) has been used in various deep fungal infections such as cutaneous sporotrichosis and subcutaneous phycomycosis[6]. There are not enough data in literature supporting its use in eumycetoma. There is a single case report of multiple subcutaneous mycetomas caused by Pseudallescheria boydii treated with oral potassium iodide solution[7]. KI gets concentrated in infected granuloma and necrotic tissue and has

Figure 3: Pretreatment CT scan of case 2 showing multiple lytic areas in proximal end of tibia along with sinus tract

Figure 3: CT scan of case 2 twelve month after treatment showing absence of sinuses

been shown to inhibit granuloma formation[8]. Other postulated mechanisms of actions are immunosuppressive effect mediated through heparin and suppression of inflammatory oxygen intermediates generation from activated neutrophils. It is a safe drug to use with very few side effects and combining it with itraconazole leads to enhance therapeutic effect in eumycetoma. Our study has less number of cases, due to rare incidence of disease, to draw any definite conclusion. But as all five patients of our series have responded well to this combination therapy, it seems to be an effective therapy for eumycetoma and can prevent a patient from recurrent surgeries and amputation. However, further studies are needed to support this observation.

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