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Case Report

Successful treatment of cutaneous leishmaniasis unresponsive to conventional drugs with itraconazole

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Abstract We report a young male with cutaneous leishmaniasis unresponsive to conventional drugs successfully treated with itraconazole.

Key words
Acantholytic, ATPC2, 'dilapidated brick wall appearance'.

Introduction

Leishmaniasis is a disease caused by a parasite of Leishmania Genus, transmitted by prick of an infected sand-fly. The disease presents clinically with cutaneous, mucocutaneous or visceral form, depending upon the type of infective species and the immune status of the person. Antimonial drugs are first line of treatment for all clinical forms. Amphotericin B is second choice drug.

Case report

A young male of age 16 years presented in dermatology OPD with noduloulcerative lesions on face for the last ten months. He was residence of a small village of Swat KPK. The lesion started as papule on chin then spread to involve upper lip and right side of face. The lesions became nodular, and ulcerated having purulent discharge.

He was healthy otherwise. His general physical and systemic examination was unremarkable. On cutaneous examination, there were multiple erythematous, noduloulcerative lesions present on chin, upper lip and right cheeck. There was also whitish discharge present **(Figure 1)**. His hair, mucous membrane and nails were normal. His brother had history of similar disease in the past. The diagnosis of cutaneous leishmaniais was confirmed by microscopy of the smear taken from the lesion, which demonstrated numerous intracellular parasites.

He was started on Inj. Meglumine antimoniate 1.5mg/5ml in dose of 20 mg/kg daily intramuscularly for 28 days. After 28 days there was not complete remission of the disease **(Figure 2)**. He was then given itraconazole in a dose of 100 mg bid. After one month there was remarkable improvement in the disease. At the end of second month there was complete clearance with only residual pigmentation left **(Figure 3)**. The dose of itraconazole was reduced to 100 mg per day for another month then discontinued. The drug was very well tolerated by the patient. The hematological and biochemical profile was in normal limits at the end of treatment period.

Discussion

Leishmaniasis is a parasitic disorder caused by several morphologically indistinguishable species of protozoa of the *Leishmania* genus

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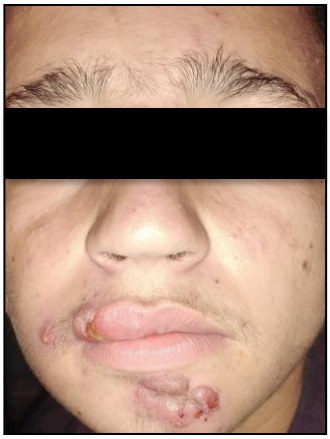

Figure 1 At the time of presentation.

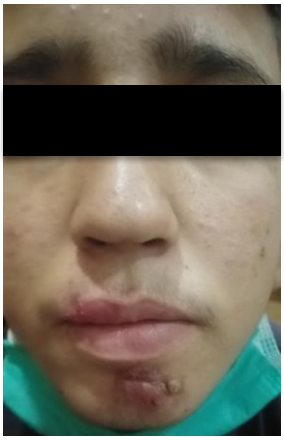

Figure 2 At the end of 1 month treatment with meglumine antimoniate.

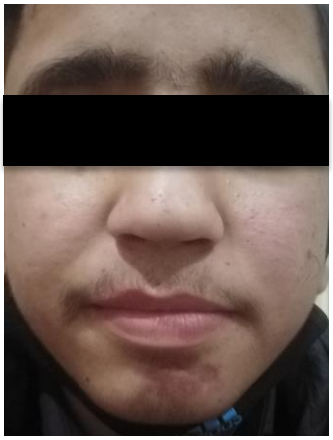

Figure 3 After completion of treatment with itraconazole.

belonging to the Trypanosomatidae family. This parasite is transmitted to humans by the prick of a sandfly of the *Lutzomia Phlebotomus* or *Psychodophygus* genus. Depending on the infectious species, the disease may be cutaneous, mucocutaneous or visceral.[1,2]

Treatment of cutaneous leishmaniasis may be difficult. There are several treatment options available **(Table 1)**.[3] Some of them are not now used, while others are in the experimental phase. Antimonial drugs (N-methylglucamine antimoniate and sodium stibogluconate) are the first lines drugs, and amphotericin B is the second choice.

Itraconazole is an antifungal agent of the triazol group that acts by inhibiting sterol 14- α desmetilase, an enzyme belonging to an enzymatic complex that depends on microsomal cytochrome p450.[4] It impairs ergosterol biosynthesis for the cytoplasmic membrane and leads to an accumulation of 14- αmethilesterols.[5] This final product breaks phospholipid chain unions, affecting the function of certain enzymes and inhibiting cell growth.[4] The absorption of itraconazole during fasting is about 30% of that measured after a meal. The maximum plasma concentration with a daily dose of 100 mg is 0.5g/ mL and is observed after 15 days of treatment. The medium half-life of elimination after 15 days of treatment is 36h.[5]

The mechanism of action leading to the destruction of the *Leishmania* parasite in humans is not known, although it is postulated that the cytoplasmic membrane of the parasite may be composed in part of ergosterol and other related lipids that are affected by itraconazole, leading to a lethal disruption of the microorganism. The satisfactory response seen with itraconazole in this patient confirms previous reports on the efficacy of this drug in the therapy of leishmaniasis, unresponsive to conventional treatment.[3]

Table 1 Treatments of leishmaniasis.

Topical	Antimonials, paramomycin, imidazolics, methylbenzethonium, ketoconazole or bleomycin.
Systemic	Antimonials , rifampicin, antimalarial, dapsone, amphotericin B, liposomal amphotericin B, cotrimoxazole, allopurinol, monomycineethyluracil, metronidazole, pentamidine, miltefosine, pentoxifiline, or itraconazole.
Physical	Radiotherapy, surgery, cryosurgery, heat or cautery.
Others	Ciclosporine, clofacimine or WR6026.
Immunotherapy	Vaccination, “Leishmanization”, levamisole or interferon-γ.

Although there are studies showing poor results with itraconazole,[6] there are studies with a significant number of patients, proving efficacy of itraconazole in the treatment of leishmaniasis.[7-11]

In a study by Momeni AZ *et al*. in Iran, out of 140 patients included in the study, 59% of patients treated with itraconazole showed complete healing with no serious side effects.[9]

In a study by Dogra J *et al*. in India, out of 15 patients treated with itraconazole, 66.6% were found to be cured.[10]

In a clinical study in Kuwait by Al-Faizan A *et al*., 15 patients were treated, an excellent clinical response was obtained in 73% of the patients, who showed either marked reduction in lesion size or complete healing. Side effects were few, and included nausea, headache and elevation in liver enzymes in one patient.[11]

The use of itraconazole with other drugs has been reported, such as N methylglucamine antimoniate,[12] terbinafine,[13] amphotericin B[14] and sodium stibogluconate,[15] which did not improve effectiveness compared with itraconazole alone.

Conclusion

This case report shows that itraconazole is effective for the treatment of cutaneous leishmaniasis in patients not responding to first-line drugs. Several reports confirming its efficacy in the treatment of leishmaniasis, its relatively low cost, its ease of administration and its few side effects suggest that this drug is a good alternative treatment. However controlled studies with a larger number of patients are required to fully evaluate its efficacy.

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