Successful treatment of cutaneous leishmaniasis with nitazoxanide

Sir,

An 18-year-old man presented to the dermatology outpatient department with complaints of a raised skin lesion for 4 months. He had history of an insect bite over the left side of the neck two and a half months previously, followed by development of a papule which gradually increased in size and was slightly painful. On examination, the patient was found to have a single erythematous plaque on the right side of his neck, measuring 3 × 2 cm with ulceration and crusting at a few areas [Figure 1]. He also had a single significantly enlarged mobile left upper cervical lymph node measuring 2 × 1.5 cm. Other cutaneous and systemic examination was negative and hematological and biochemical investigations were normal.

Histopathological examination showed dense granulomatous inflammation comprising of lymphocytes, plasma cells, a few neutrophils involving the entire depth of the dermis and Leishman-Donovan (LD) bodies inside the macrophages [Figure 2]. Cytological examination of the enlarged lymph node demonstrated a pattern of reactive lymphadenopathy. Both tissue imprints and culture for leishmania species on Tobie's medium were negative. Polymerase chain reaction (PCR) examination of the skin biopsy sample was strongly positive for *Leishmania donovani* species using a highly sensitive and specific PCR (minicircle of kinetoplast DNA) assay. Since the lesion was present on a cosmetically important site (neck) and did not show any signs of spontaneous resolution for 4 months, the patient was treated with tablet nitazoxanide (NTZ), 500 mg twice daily. The patient showed a clinical response but complained of dyspepsia. Subsequently, he was started on oral pantoprazole 40 mg before breakfast, with only slight improvement in dyspepsia. In view of his gastric complaints, his dose was reduced to 500 mg daily following which these complaints markedly reduced and the same dosage was then continued for 3 months. There was complete resolution of the lesion at the end of the treatment [Figure 3] with no relapse up to the last follow up at 6 months.

Leishmaniasis is a vector-borne disease caused by obligate, protozoan parasites of the genus *Leishmania*.[1] The Leishmania species cause a variety of diseases ranging from self-healing cutaneous lesions to life-threatening visceral infections. Cutaneous leishmaniasis (CL) is the most common form of leishmaniasis worldwide, representing 50–75% of all new cases. In India, the condition is endemic in some pockets of Thar Desert of Rajasthan, Punjab and Himachal Pradesh. Recently, cases of cutaneous leishmaniasis caused by *L. donovani* have been reported from Agasthyamala biosphere forest reserve from Western Ghats, Kerala.[2] The gold standard for diagnosis includes demonstration and isolation of the parasite from tissues (biopsy sample or tissue aspirate) by culture or by animal inoculation.[3] Newer and specific methods include indirect hemagglutination (IHA), counter-current immunoelectrophoresis

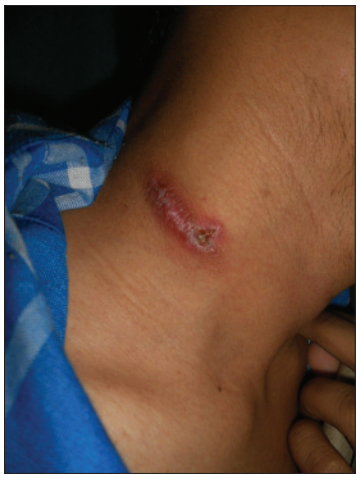

Figure 1: An erythematous plaque (3 × 2 cm) on the right cervical region with areas of ulceration and crusting

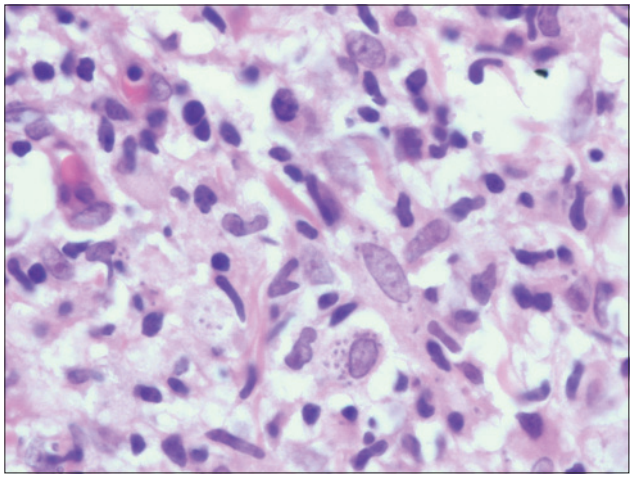

Figure 2: Biopsy showing plasma cells, macrophages and Leishman-Donovan bodies in mononuclear cells. (inset, H and E, ×400)

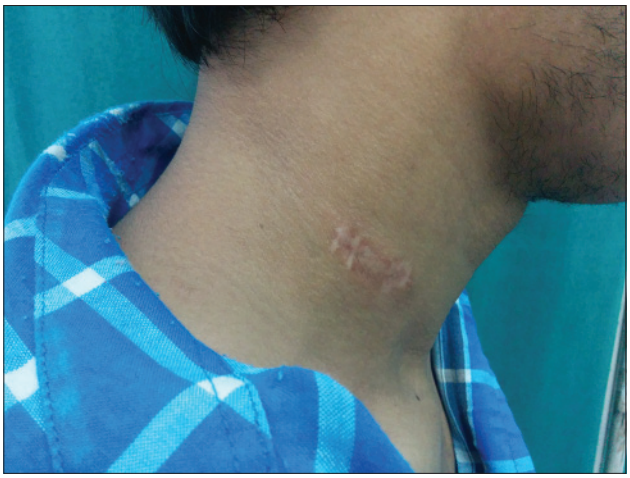

Figure 3: Complete resolution of lesion after 3 months of nitazoxanide 500 mg once daily

(CCIEP), immunodiffusion (ID) and nucleic acid detection methods.[3]

Despite being self-healing, treatment for the disease may be indicated to accelerate healing, to reduce morbidity associated with large or persistent skin lesions particularly on the face or near joints and to decrease risk of dissemination, relapse (clinical reactivation) and eliminate a reservoir of infection. Local therapies include cryotherapy, radiofrequency, intralesional sodium stibogluconate and topical paromomycin. Systemic treatment includes pentavalent antimonial therapy (sodium stibogluconate), amphotericin B and miltefosine.[4] Other drugs like pentamidine and oral azoles have also been used with mixed results. However, these chemotherapeutic agents are often inadequate since they require long courses of parenteral administration, have toxic side effects or have become less effective due to resistance.

Nitazoxanide [2-(5-nitrothiazol-2-ylcarbamoyl) phenyl acetate] is a broad-spectrum anti-parasitic compound belonging to a nitroheterocyclic class named thiazolides with activity against protozoa, nematodes, cestodes and trematodes. In humans, nitazoxanide is rapidly metabolized to tizoxanide, a compound as effective as the parent drug.[5] A total of 200 μg/mL nitazoxanide inhibits the growth of >90% of promastigotes showing activity similar to that of the reference drug amphotericin B ($P > 0.05$).[6] It is approved for the treatment of diseases caused by *Giardia intestinalis* and *Cryptosporidium* species and has been used in liver diseases.[6] It is well tolerated, has few side effects and requires a short course of treatment. There are no major contraindications, except previous hypersensitivity.[7] However, it requires monitoring when concurrently administered with drugs like warfarin or phenytoin and there are no data on cutaneous bioavailability.[6]

We found only a single previously published report of nitazoxanide in the treatment of sodium stibogluconate resistant leishmaniasis. The patient showed 90% clinical and histological improvement at 8 weeks and complete clearance of the lesion at 16 weeks without any adverse effects.[7] Nitazoxanide is an effective drug in the treatment of leishmaniasis with fewer side effects than other treatment options. However, additional studies are required to validate the efficacy and the potential adverse effects.

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