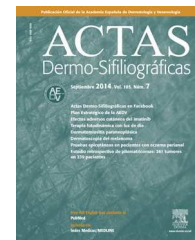




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CASE AND RESEARCH LETTERS

Cutaneous Leishmaniasis in a Patient Receiving Infliximab for Psoriatic Arthritis: Treatment with Cryotherapy and Intralesional Meglumine Antimonate[☆]



Leishmaniasis cutánea en un paciente con artritis psoriásica tratado con infliximab: tratamiento con crioterapia y Glucantime[®] intralesional

To the Editor:

We report the case of a 33-year-old man referred to our department with a skin ulcer that had appeared 1 year earlier on the left posterior axillary fold. His medical history was remarkable for chronic hepatitis B infection being treated with adefovir and for psoriatic arthritis, under treatment with leflunomide 20 mg/d, prednisone 5 mg/d, and infliximab 5 mg/kg every 8 weeks for the past 2 years. Physical examination revealed an ulcerated plaque measuring 9 × 6 cm and several erythematous-scaling papules measuring 1 to 2 cm on and around the plaque (Fig. 1A). There was no evidence of enlarged lymph nodes, liver, or spleen on palpation. Histologic examination showed a mixed inflammatory infiltrate with lymphocytes, histiocytes, and some macrophages with intracellular and extracellular *Leishmania* amastigotes (Fig. 2). Two additional biopsies were performed to complete the study. Giemsa staining of one of the biopsy specimens showed scarce amastigotes and culture of the other specimen was positive for *Leishmania* species. The subtype could not be identified. Mycobacterial culture was negative and the fungal culture was positive for *Candida albicans*. Serology showed a *Leishmania* antibody titer of 1:80. No parasite material was detected by Giemsa stains or culture of bone marrow aspirate smears. The organs did not appear enlarged on abdominal ultrasound and the blood workup showed mild neutropenia ($1.64 \times 10^9/L$) and thrombocytopenia ($127 \times 10^9/L$); the results of the liver and kidney function tests were normal.

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Following confirmation of the diagnosis of cutaneous leishmaniasis, infliximab therapy was discontinued and treatment was started with intralesional pentavalent antimonial injections and superficial cryotherapy (9 sessions over 2.5 months). Intralesional meglumine antimoniate (MA) injections (4–8 mL) were administered every 1 or 2 weeks depending on the patient's tolerance. The total dose administered on completion of treatment was 44 mL. The patient was also prescribed itraconazole 100 mg/d for a month to treat the *Calbicans* infection identified by culture. The ulcer healed completely after 3 months of treatment. To achieve better control of the patient's arthritis, he was prescribed etanercept 50 mg/wk, abatacept 750 mg/mo, and golimumab 50 mg/mo. He has been taking this medication for 2.5 years and there has been no recurrence of the cutaneous leishmaniasis (Fig. 1B).

Tumor necrosis factor is a proinflammatory cytokine that has been implicated in the pathogenesis of inflammatory disorders and immune responses to various infections, particularly those caused by intracellular pathogens.¹ *Leishmania* species are obligate intracellular parasites of macrophages and to control infection, it is necessary to activate these cells and induce the formation of granulomas. Opportunistic *Leishmania* infections can occur following the reactivation of a latent, previously undetected, infection or they can develop as a primary infection during immunosuppressive treatment. Of the cases reported in the literature of cutaneous or mucocutaneous leishmaniasis associated with anti-TNF drugs (Table 1),^{1–9} infliximab was being used at the time of diagnosis in 5 cases. All of the other patients were receiving adalimumab. We did not identify any cases of treatment with etanercept. Furthermore, all the patients described in the above reports either lived in areas where *Leishmania* species are very common or had travelled to *Leishmania*-endemic areas. Pentavalent antimonials at a dosage of 20 mg/kg/d for 20 days are recommended by the World Health Organization as the first-line treatment of localized cutaneous leishmaniasis (1–10 skin lesions with no evidence of systemic involvement).¹⁰ However, many patients do not complete treatment because of the need for daily intramuscular injections, the duration of treatment, and its adverse effects. Several alternatives have been proposed, including liposomal amphotericin B, miltefosine, allopurinol, azoles, paromomycin, dapsone, and azithromycin.

Asilian et al.¹¹ reported good results for cryotherapy combined with intralesional MA, with higher cure rates observed for the combined regimen (90.9%) than for cryotherapy



Figure 1 Cutaneous lesions before (A) and after (B) treatment.

Table 1 Cases of Cutaneous and Mucocutaneous Leishmaniasis Associated With Anti-Tumor Necrosis Factor Drugs.

Case No.	Age, y/Sex	Primary Disease	Type of Leishmaniasis	Anti-TNF Drug (Treatment Duration)	Other Immunosuppressants	Treatment	Authors (Year)
1	55/F	AS	CL	Infliximab (12 mo)	Methotrexate	Liposomal amphotericin B	Xynos et al. ¹ (2009)
2	51/F	AS	CL	Adalimumab (24 mo)	Methotrexate	Liposomal amphotericin B	Schneider et al. ² (2009)
3	56/F	RA	MCL	Adalimumab (2 mo)	Methotrexate, corticosteroids, infliximab	Meglumine antimoniate	Baltà-Cruz et al. ³ (2009)
4	31/M	AS	CL	Infliximab (48 mo)	Not reported	1. Miltefosine 2. Meglumine antimoniate	Mueller et al. ⁴ (2009)
5	42/F	RA	MCL	Adalimumab (2 mo)	Corticosteroids, methotrexate	Liposomal amphotericin B	Franklin et al. ⁵ (2009)
6	50/M	AS	CL	Infliximab (13 mo)	Corticosteroids	Meglumine antimoniate	Hakimi et al. ⁶ (2010)
7	38/M	RA	CL	Infliximab (0.25 mo)	Corticosteroids, methotrexate	Liposomal amphotericin B	Zanger et al. ⁷ (2011)
8	36/F	AS	CL	Adalimumab (12 mo)	Methotrexate	Meglumine antimoniate	Gomes et al. ⁸ (2012)
9	66/F	RA	CL	Infliximab (25 mo)	Methotrexate, corticosteroids	Meglumine antimoniate	Garcia-Castro et al. ⁹ (2012)
10	33/M	PA	CL	Infliximab (48 mo)	Leflunomide, corticosteroids	Meglumine antimoniate + cryotherapy + itraconazole	Current case

Abbreviations: AS, ankylosing spondylitis; CL, cutaneous leishmaniasis; MCL, mucocutaneous leishmaniasis; PA, psoriatic arthritis; RA, rheumatoid arthritis; TNF, tumor necrosis factor.

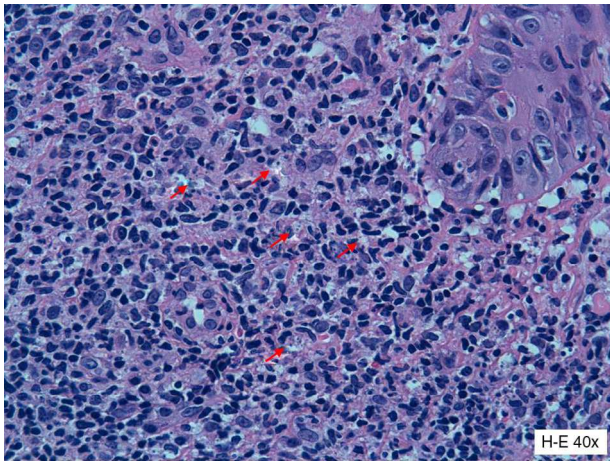


Figure 2 Histologic examination of a biopsy specimen from the edge of the ulcer showed a mixed inflammatory infiltrate with lymphocytes, histiocytes, and several macrophages with intracellular and extracellular amastigotes (red arrows) (hematoxylin-eosin, original magnification $\times 4$).

(57.15%) or MA (55.63%) alone. The use of intralesional MA allows the total dose—and consequently the adverse effects—to be reduced. This treatment option yielded good results in our patient, although it should be noted that even though we used lower doses that would have been required with intramuscular MA, our patient still experienced adverse effects in the form of tachycardia, headache, and chest pain. The effects of treatment with itraconazole must also be taken into account. In conclusion, we highlight the importance of considering the possibility of cutaneous or visceral leishmaniasis in patients treated with anti-TNF drugs in *Leishmania*-endemic areas. We also recommend considering MA combined with cryotherapy as a more effective and less toxic option than intramuscular MA.

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Aprepitant in the Treatment of Refractory Pruritus Secondary to Cutaneous T-Cell Lymphoma[☆]



Tratamiento con aprepitant del prurito refractario secundario a linfoma cutáneo de células T

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Patients with cutaneous T-cell lymphoma frequently develop intense pruritus, which can often be refractory to anticancer and symptomatic treatments and can affect quality of life to a significant degree.¹ Aprepitant, an antiemetic that is a substance P antagonist, has been used successfully to manage refractory pruritus.^{2,3}

We present the case of a 61-year-old woman who was a smoker with a history of chronic obstructive pulmonary disease and who required home oxygen. In August 2011 she was seen for a 5-month history of skin lesions that she described as very itchy. The lesions, which were present on the head, trunk, and limbs, consisted of plaques and nodules with areas of necrosis (Fig. 1). Biopsy revealed acanthosis and partial necrosis of the epidermis, which