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DOI: [10.1159/000156087](https://doi.org/10.1159/000156087)**Visceral Leishmaniasis Infection in a Patient with Psoriasis Treated with Efalizumab**Anna Balato^a, Nicola Balato^a, Cataldo Patruno^b, Lucia Gallo^a, Fabio Ayala^a^aDepartment of Dermatology, University of Naples Federico II, and ^bDermatology Clinic, Azienda Sanitaria Locale Napoli 1, Napoli, Italy**Key Words**

Efalizumab · Leishmaniasis · Psoriasis

We describe the case of a 42-year-old man with generalized plaque psoriasis, refractory to other systemic treatments, namely cyclosporine A and acitretin, that responded to efalizumab. After 12 weeks, the treatment was discontinued following an episode of intermittent daily fever and severe asthenia. The diagnosis was visceral leishmaniasis (VL).

In January 2007, a 42-year-old white male with a history of 2 years of psoriasis non-responding to standard systemic treatments was admitted to our Department. He had no other relevant diseases, except for essential hypertension. He did not suffer of concurrent psoriatic arthritis. He presented a psoriasis area severity index (PASI) score of 44. All routine laboratory tests (serum chemistry, haematology and urinalysis) were normal. Auto-antibody status (anti-dsDNA) was within normal range. Antibodies for hepatitis A, B and C viruses were negative. We also performed chest X-ray with no evidence of abnormalities and a tuberculin skin test with negative results.

He was started on a course of treatment with efalizumab (1 mg/kg per week, subcutaneous injection). After 12 weeks of consecutive therapy with efalizumab, the patient showed intermittent daily fever (maximum 40°C) for a week and severe asthenia. Efalizumab administration was promptly stopped. He did not present any cutaneous manifestations, except for his psoriasis. He presented a PASI score of 12. He reported that his dog had died of leishmaniasis 2 weeks before.

Laboratory test analysis showed a C-reactive protein of 41.8 mg/l, an erythrocyte sedimentation rate of 50 and pancytopenia (haemoglobin 9 g/dl, white blood cells $3.2 \times 10^3/\mu\text{l}$ and platelets $80 \times 10^3/\mu\text{l}$).

A lymphocyte stimulation TBNK assay was performed showing the following results: CD3+ lymphocytes 83.12%, CD4+ lymphocytes 51.66%, CD8+ lymphocytes 28.45%, CD3-/CD56+ lymphocytes (NK cells) 7.30%, CD19+ lymphocytes (B lymphocytes) 10.46%. At the bone marrow level, the analysis through CD45/

LDS751/SSC revealed: 4% lymphocytes, 2% monocytes, 66% granulocytes, 6% immature blast cells, 18% erythroblasts and other CD45- cells, confirming the diagnosis of pancytopenia.

Physical examination revealed splenomegaly and hepatomegaly, confirmed by ultrasonography too. Serology for typhoid fever and brucellosis was negative. The examination of a Giemsa-stained smear from a bone marrow aspirate detected *Leishmania* amastigotes, and indirect immunofluorescence antibody test (ELISA) serology was positive at the titre of 1/640. The IgM + IgG ELISA test detected an IgM anti-*Leishmania* concentration of 1.6×10^{-7} M, indicating a primary infection. A polymerase chain reaction for the amplification of *Leishmania* genomic sequences in peripheral blood and in bone marrow samples confirmed the diagnosis.

The patient was treated intravenously with teicoplanin, ciprofloxacin, furosemide, albumin and folic acid and intramuscularly with vitamin B₁₂. Despite the initial treatment, the patient remained febrile in a markedly fluctuant manner so that a combination of piperacillin sodium and tazobactam was added to his intravenous treatment. He was not started on a course of any antiparasitic treatments. After 6 weeks, the bone marrow examination did not detect any *Leishmania* parasites.

Leishmaniasis is a parasitic (protozoan) disease, caused by various species of *Leishmania*. Humans, wild animals and domestic animals are known to act as reservoir hosts. In Italy the domestic and wild canines are the reservoir of the parasite *Leishmania infantum*. Our patient was living in Campania, southwest Italy, which has long been known to be endemic for VL [1]. A consistent principle is that healing and resistance to reinfection are associated with expanding numbers of *Leishmania*-specific Th1 cells, production of γ -interferon and activation of macrophages to kill intracellular amastigotes.

Efalizumab (Raptiva®) is a humanized monoclonal immunoglobulin G1 antibody that binds with high specificity and affinity to the α -subunit of leucocyte function-associated antigen 1 on the surface of T cells. Efalizumab is one of several biological therapies used for the treatment of psoriasis. Its efficacy in clinical trials has ranged from 24 to 38% of patients achieving a 75% or better improvement from baseline in PASI score at 12 weeks, increasing to 44% at 24 weeks in one trial [2, 3]. The most common adverse events seen are fever, chills, headache, nausea and myalgias, usually occurring within 48 h of the initial conditioning dose [4]. More serious adverse effects are rare but include reports of psoriasis flares during and after discontinuation of treatment, infection and malignancy [5].

Malignancies occur more frequently in populations that are immunosuppressed or immunodeficient, and the development of biological therapies for psoriasis that target the immune system has focused attention on the risk. From an analysis of 2,980 psoriasis patients treated with efalizumab, the incidence of malignancy over the relatively short duration of the clinical trials (aver-

age 10 months) was similar to placebo, generally low, and consistent with the rates reported for the US general population and those observed in external cohorts of patients with moderate to severe psoriasis [6].

There is a report on multiple eruptive dermatofibromas (MED) during efalizumab treatment for psoriasis. The pathogenesis of MED is poorly understood, but it has recently been proposed that this should be regarded as an immunoreactive process; according to this hypothesis, the development of MED in immunodeficient states could be facilitated by the inhibition of down-regulatory T cells; alternatively, MED could develop as an exaggerated response to a putative pathogen that could not be cleared by the suppressed immune system [7].

Clinical trials suggest that efalizumab is not associated with an increased risk for infection in patients receiving initial or long-term (27-month) treatment for moderate to severe chronic plaque psoriasis [8]. There are few reports of VL in patients with a diagnosis of rheumatoid arthritis and just one with a diagnosis of psoriasis arthritis treated with biologicals [9–12]; our case is the first, to our knowledge, after efalizumab treatment in a patient with a diagnosis of psoriasis. All these patients, either with rheumatoid arthritis or psoriasis arthritis, had received several immunosuppressive drugs during the course of their disease and had been treated with biologicals for several months. This fact could be a bias in relating the development of VL and the specific biological therapy at that time.

In our case the patient had taken only cyclosporine and retinoids, as systemic treatment for his psoriasis, and for a period of 1 month each; he had to stop cyclosporine for causing hypertension and retinoids for no efficacy. Efalizumab was his first and only biological drug. In no cases was the biotherapy resumed after treatment of VL, so we chose to stop the drug, wait until the patient had recovered, supporting him with topical therapy, and after that to start with phototherapy (UVB narrow band). He did not experience any adverse effects.

Cutaneous leishmaniasis is also associated with a suppressed immune system; so we should be alert to the appearance of cutaneous leishmaniasis in patients treated with biological drugs. A diagnosis of lupoid leishmaniasis should be suspected in all patients from endemic areas of leishmaniasis presenting with facial granulomas and confirmed by molecular techniques to avoid the associated sequelae [13].

We think that in the presence of fever and cytopenia in a patient undergoing treatment with biologicals, the clinician has to investigate the immune status because of the risk of opportunistic infections.

We present this case to point out that VL is a rare event which may occur during biological treatments of psoriasis. Leishmaniasis screening is not recommended in patients undergoing therapy with biologicals, because of the low incidence rate, although the possibility of VL should be taken into account, at least for patients living in endemic areas.

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