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CORRESPONDENCE

Efficacy and safety of etanercept in patients with psoriasis and hepatitis C

Patients with psoriasis and concomitant hepatitis C virus (HCV) infection present a therapeutic challenge. The treatment of choice for HCV infection, interferon-α (IFN-α), might be a precipitating or aggravating factor for psoriasis. On the other hand, the standard systemic therapies for psoriasis, cyclosporine, methotrexate and acitretin, with their hepatotoxic or immunosuppressive potentials should be avoided in these patients [1].

A 35-year-old man with psoriasis since 1990 and HCV infection, genotype 3, diagnosed in 1997, had never required antiviral therapy. He had previously been treated with topical agents and ultraviolet-B (UVB) phototherapy with inadequate control of his psoriasis. He received cyclosporine, 3 mg/kg/day, after consultation with a gastroenterologist, with a good response, but decided to stop the treatment after leaving the Hospital in 2003.

One year ago, the patient returned to our Department because the psoriasis had progressively deteriorated. He confessed self-medication with cyclosporine and clobetasol propionate ointment during the past 5 years, when the psoriasis worsened. On physical examination he presented with widespread plaque psoriasis on erythematous skin *(figure 1A)*. The Psoriasis Area and Severity Index (PASI) was 30. Etanercept 25 mg sc twice a week was started. We consulted the patient's gastroenterologist before initiating therapy. An excellent response was observed *(figure 1B)*, with a PASI of 6.6 and 3 after 12 and 24 weeks respectively. No relevant changes in liver function tests were noted but the treatment had to be stopped after 6 months due to an increase of the viral load *(table 1)*.

A 47-year-old woman with HCV infection, genotype 1b, diagnosed in 1993, was initially treated with IFN-α, which was discontinued after several months because of the appearance of typical psoriatic lesions. The psoriasis was treated with topical agents and UVB phototherapy, without a complete response.

Physical examination showed extensive erythematous hyperkeratotic plaques on the trunk, arms and legs, with

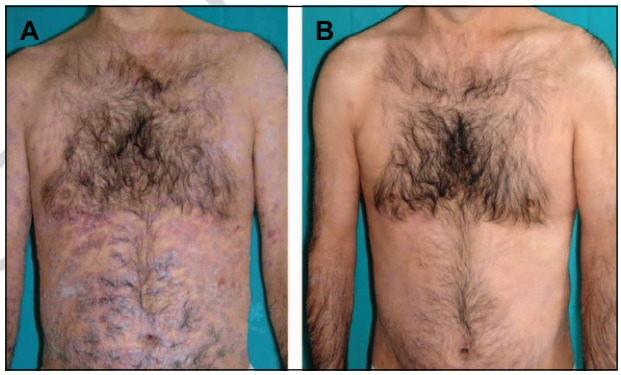

Figure 1. A) Patient 1: Extensive psoriasic lesions. **B)** Marked improvement of the lesions after 24 weeks of treatment.

Table 1. Liver parameters and viral load for 2 patients with HCV infection treated with etanercept for psoriasis

Patient 1				
	ALT (U/L)	**AST (U/L)**	**γ-GT (U/L)**	**HCV RNA (IU/mL)**
Baseline	36	47	54	1.63×10^4
1 month	40	50	53	1.50×10^4
3 months	45	68	51	1.52×10^4
6 months	44	39	45	1.94×10^6
Patient 2				
	ALT (U/L)	**AST (U/L)**	**γ-GT (U/L)**	**HCV RNA (IU/mL)**
Baseline	40	46	63	1.0×10^7
1 month	45	48	72	7.67×10^6
3 months	35	47	64	5.11×10^6
6 months	36	65	78	5.15×10^6
9 months	38	63	83	$4{,}86\times10^6$
12 months	31	51	74	3.92×10^6
15 months	35	37	67	$3{,}11\times10^6$
18 months	36	39	67	3.12×10^6

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a PASI of 17.5. She had also psoriatic arthritis mainly of the interphalangeal regions of fingers and toes. Treatment with etanercept, 50 mg/week administered as a single subcutaneous injection, was prescribed after consultation with a gastroenterologist. After 1 month her psoriasis plaques thinned, became less red and the scale disappeared. After 12 and 24 weeks of treatment her PASI was 4 and 0 respectively. The joint pains disappeared. On serologic evaluations there was no worsening of the liver function tests *(table 1)*. The patient continued the treatment with a sustained decrease in the viral load after 18 months *(table 1)*.

There are some small-scale studies involving the use of etanercept on patients with HCV infection [2, 3], as well as case reports of a limited number of patients being treated for rheumatoid arthritis, psoriasis and ankylosing spondylitis [1, 4, 5]. The safety profile of TNF-α blockers in patients with HCV infection remains a concern because of risks associated with immune suppression. However they are not directly hepatotoxic, so seem to be a good alternative in individuals with liver disease.

Potentially relevant is the fact that high levels of TNF-α have been documented in patients with HCV infection and associated with a worse prognosis regarding hepatic fibrosis. Zein showed that etanercept may also be safe and effective as an adjuvant therapy to IFN-α and ribavirin for HCV infection [6].

We report two more patients with psoriasis and HCV infection treated with etanercept, without worsening of their liver function tests. However, one patient showed an increase in viral load after 6 months of treatment, so it was stopped. The other patient continued the treatment with a sustained decrease in viral load after 18 months. ■

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Buruli ulcer caused by "*Mycobacterium ulcerans* subsp. *shinshuense*"

Buruli ulcer (BU) is a necrotizing disease of the skin caused by *Mycobacterium ulcerans* (*M. ulcerans*), occurring mainly in tropical areas [1]. In Japan, BU is extremely rare and there have only been 8 reports so far [2-4].

A 46-year-old-man presented with a 9-day history of swelling on the right dorsal foot. Physical examination revealed a painless swelling with flare and a vesicle on his right dorsal foot *(figure 1A)*. We suspected an insect bite and treated the lesion with oral administration of predonisolone (30 mg/day). The symptoms improved immediately but worsened with a reduction in the dose of predonisolone. Results of routine laboratory investigations were within normal limits. A skin biopsy at day 20 revealed papillary dermal edema and necrobiosis of the dermis *(figure 1B)*. Based on these findings, we suspected a persistent insect bite and continued oral predonisolone. However, the response was poor and we took another biopsy at day 51.

Histopathological examination revealed dense neutrophilic infiltration without vasculitis, from the upper dermis to subcutaneous tissue. Cultures of microorganisms were all negative. Based on these results, we suspected neutrophilic dermatosis and treated with oral prednisolone (5-30 mg/day). The lesions gradually formed a painless ulceration with necrotic masses *(figure 1C)*. A smear from the ulcer at day 185 revealed acid-fast reddish rods by Ziehl-Neelsen staining, but we detected no organism by culture. At this time, we retrospectively performed Ziehl-Neelsen staining on the histological section of the first biopsy specimen and detected many acid-fast bacilli *(figure 1D)*. Polymerase chain reaction (PCR) of necrotic tissue revealed positive reactions to genes, suggesting *M. ulcerans* subsp. *Shinshuense* infection. A chest X-ray and computed tomography scan of the whole body revealed no abnormalities. Based on these results, a diagnosis of Buruli ulcer caused by *M. ulcerans* subsp. *Shinshuense* was made.

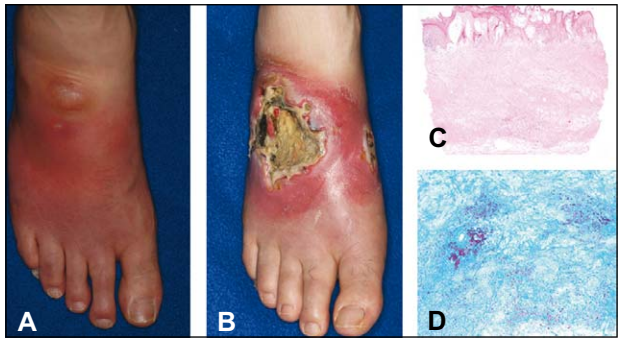

Figure 1. A) Swelling with flare and vesicle on the right dorsal foot. **B)** Ulceration with necrotic masses. **C)** Papillary edema and necrosis of dermis (H and E staining; original magnification ×40). **D)** Ziehl-Neelsen staining revealed many acid-fast bacilli in the dermis (original magnification ×100).