

## Palmoplantar Pustular Psoriasis: Successful Therapy with Efalizumab after Non-response to Infliximab

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Sir,

Treatment of palmoplantar pustular psoriasis (PPP) is difficult (1). Topical treatment with anti-psoriatic drugs often gives unconvincing results. Even systemic treatments show initial efficacy in only a certain proportion of patients. Other patients are resistant to any kind of therapy. And in other patients, again, adverse events lead to dose reduction or, imperatively, to discontinuation of therapy.

The patient described here had a long history of PPP. Even tumour necrosis factor (TNF)- $\alpha$  antibody infliximab, given a short time before caused only transient improvement when applied as monotherapy or in combination with methotrexate. We finally initiated treatment with efalizumab, whereby the condition cleared within 10–12 weeks.

### CASE REPORT

A 55-year-old female patient developed PPP in January 2000. Histopathological investigation confirmed a characteristic pattern. In October that year the patient additionally developed extensive psoriasis plaques on the trunk, extremities and scalp. Topical treatment and selective ultraviolet phototherapy (SUP) in an outpatient dermatology department did not lead to an improvement. The patient underwent subsequent climatotherapy at Norderney (North Sea) with no success. Finally, systemic therapy with prednisolone (initial dose 30 mg/day) was administered in the last week of her stay. In the 2–3 weeks of systemic steroid treatment, the patient noticed partial relief of her discomfort. Overlapping therapy with fumaric acid esters (Fumaderm® initial, Fumedica GmbH, Herne, Germany) was initiated, which had been discontinued previously. In May 2002 the patient was treated with acitretin (initial dose 20 mg/day and later on 30 mg/day) (Neotigason®, Hoffmann-La Roche AG, Grenzach-Wyhlen, Germany). Because the patient developed marked hypertriglyceridaemia (19 mmol/l), retinoid therapy was discontinued. The following administration of methotrexate (15 mg weekly) was discontinued due to obvious ineffectiveness after 6 weeks. Treatment with doxycycline 200 mg/day for a few weeks also proved inefficient. Therefore, cyclosporine treatment (initial dose 200 mg/day) was initiated in February 2003. The patient experienced a marked amelioration

of her discomfort for the first time. Due to concomitant persistent hypertension, cyclosporine treatment was discontinued in April 2003. Ten days after discontinuation, a substantial flare occurred. A renewed therapy with fumaric acid esters was discontinued because of severe adverse events in July 2003.

On referral to our hospital we recommended therapy with a TNF- $\alpha$  antagonist (Fig. 1). The preliminary investigation was protracted due to a persistent erythrocyturia, and in particular renal tuberculosis had to be excluded before starting infliximab. Therapy with



Fig. 1. The left foot in the patient with palmoplantar pustular psoriasis before treatment (a, c) and after 43 weeks' therapy with efalizumab (b, d).

infliximab (5 mg/kg) was administered on 17 August 2004, followed by infusions on 31 August and 28 September 2004. After only 4 days a marked improvement in the condition was observed, but no complete clearance was noted. Since the initial good response could not be maintained, additional low-dose methotrexate therapy was initiated (7.5 mg weekly), which was continued over 4 months in combination with infliximab (infusions every 8 weeks). At the beginning of April 2005 a major relapse affecting other parts of the body was noted, despite the combination therapy with infliximab and methotrexate.

Due to our observation in plaque psoriasis that palmoplantar lesions first responded to efalizumab, we commenced efalizumab therapy on 27 April 2005 (Raptiva®, SERONO GmbH, Unterschleißheim, Germany). After approximately 10 weeks of efalizumab therapy marked improvement was seen. By the 11th week of treatment her palms were clinically free and her soles showed only slight erythema and scaling. For the first time in years, the patient was now able to use her hands without restriction and to walk on her soles without pain. Her palms are currently clinically free after 68 weeks of efalizumab administration.

## DISCUSSION

Current treatment modalities for PPP include the use of topical and systemic drugs (e.g. retinoids, methotrexate, cyclosporine, phototherapy) (1). None of these is curative, and in most cases none can reliably maintain remission. While topical therapy may provide transient relief, it tends to be ineffective when applied as a monotherapy. Systemic therapeutic options and photochemotherapy are limited by lack of long-term efficacy, incompatibility, contraindications, or the risk of cumulative toxicity (2, 3).

The aetiology of PPP is still unclear. Eriksson et al. (2) hypothesized that the acrosyringium might be the target for the inflammation. Smoking also has been suggested as a causative factor (4, 5). In psoriasis there is substantial evidence of the crucial role of activated T-cells and pro-inflammatory cytokines. Considering published case reports with infliximab indicating a high efficacy in *generalized* pustular psoriasis (6, 7), we assumed it to be effective in PPP. Initially the treatment indicated high efficacy, but after the induction treatment phase of infliximab, the amelioration began to stagnate and a combination therapy with methotrexate in addition to an intensive topical treatment became necessary. The patient eventually developed a distinct flare-up, involving not only hands and feet, but also other regions of her body, which led to discontinuation of infliximab

therapy. A theoretical explanation for this phenomenon is provided by Michaëlsson et al. (8).

In the literature there is no clear distinction between PPP and palmoplantar pustulosis. However, difficulties on the therapeutic level in both diseases reveal similarities. Despite this limitation, anecdotal case reports about successful treatment of PPP or palmoplantar pustulosis with biologics, for example with alefacept and efalizumab, can be found in the literature (9–11).

Efalizumab as humanized monoclonal CD11a-antibody has demonstrated efficacy, safety and health-related quality of life in chronic plaque psoriasis. According to our observation with a representative course of PPP, efalizumab appears to be efficient in the treatment of PPP. Further randomized clinical trials are needed to confirm these findings.

*Conflict of interest:* G. W. has been an investigator of clinical trials with biologics and has received speaker's fees from Abbott, Biogen-Idec, Centocor, Essex, Serono and Wyeth.

## REFERENCES

1. Marsland AM, Chalmers RJG, Hollis S, Leonardi-Bee J, Griffiths CEM. Interventions for chronic palmoplantar pustulosis. *Cochrane Database Syst Rev* 2006; 25: CD001433.
2. Eriksson MO, Hagforsen E, Lundin PI, Michaëlsson G. Palmoplantar pustulosis: a clinical and immunohistological study. *Br J Dermatol* 1998; 138: 390–398.
3. Hellgren L, Mobacken H. Pustulosis palmoplantaris et plantaris. Prevalence, clinical observations and prognosis. *Acta Derm Venereol* 1971; 51: 284–288.
4. Hagforsen E, Awder M, Lefvert AK, Nordlind K, Michaëlsson G. Palmoplantar pustulosis: an autoimmune disease precipitated by smoking? *Acta Derm Venereol* 2002; 82: 341–346.
5. Hagforsen E, Edvinsson M, Nordlind K, Michaëlsson G. Expression of nicotinic receptors in the skin of patients with palmoplantar pustulosis. *Br J Dermatol* 2002; 146: 383–391.
6. Schmick K, Grabbe J. Recalcitrant, generalized pustular psoriasis: rapid and lasting therapeutic response to anti-tumour necrosis factor alpha antibody (infliximab). *Br J Dermatol* 2004; 150: 367.
7. Newland MR, Weinstein A, Kerdel F. Rapid response to infliximab in severe pustular psoriasis von Zumbusch type. *Int J Dermatol* 2002; 41: 449–452.
8. Michaëlsson G, Kajermo U, Michaëlsson A, Hagforsen E. Infliximab can precipitate as well as worsen palmoplantar pustulosis: possible linkage to the expression of tumour necrosis factor-alpha in the normal palmar eccrine sweat duct? *Br J Dermatol* 2005; 153: 1243–1244.
9. Yeung-Yue K, Aronson PJ, Murakawa GJ. Clinical improvement of palmoplantar pustular psoriasis with alefacept. *J Am Acad Dermatol* 2005 (suppl); 52: P2730.
10. Fretzin SA, Dawes KW. Efficacy and safety of efalizumab for patients with palmoplantar pustulosis. *J Am Acad Dermatol* 2005; Suppl 52: P2745.
11. Sobell J, Fretzin S. Case studies of efalizumab in hand and foot psoriasis. *American Academy of Dermatology*, March 3–7, 2006, San Francisco: P2864.