Palmoplantar pustular psoriasis: successful therapy with efalizumab after non-response to infliximab

G. Wozel, L. Vitéz, and M. Meurer

SUMMARY

Palmoplantar pustular psoriasis (PPP) is a chronic inflammatory skin condition mainly characterized by recurrent eruptions of sterile pustules on erythematous skin; hyperkeratosis and fissures on the palms and soles are additional clinical features. Treatment options for PPP are unsatisfactory. We present a patient with a typical course of PPP that had previously received a broad range of topical and systemic antipsoriatic therapies. They all had to be discontinued due to ineffectiveness or side effects. Being aware of the high efficacy of infliximab in generalized pustular psoriasis, we initiated this therapy. An initial improvement was followed by a substantial flare after 7 months, during which a combination treatment of infliximab with methotrexate was administered. Only subsequent monotherapy with efalizumab led to complete clearing up of PPP after 10 to 12 weeks of treatment without any adverse effects. This indicates that efalizumab is potentially effective in PPP.

KEY WORDS

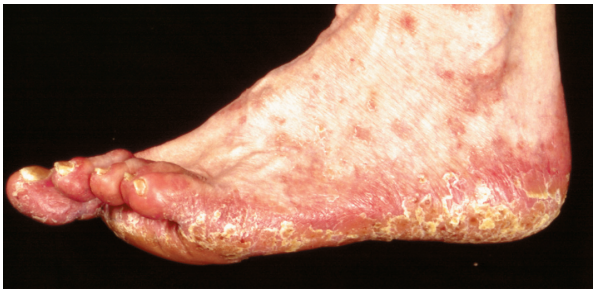
efalizumab, palmoplantar, pustular psoriasis

Introduction

Despite the full range of therapeutic modalities now available, PPP remains one of the most resistant entities to control (1–6). The response to treatment with topical antipsoriatic drugs often proves to be unsatisfactory. One reason for this is attributed to the thickened horny layer of palmar or plantar epidermis leading to reduced bioavailability. Occlusive dressings were applied to facilitate penetration of active ingredients. Many systemic treatments are effective in certain patients only initially, and some patients are resistant to all therapies. In others, adverse events require dose reduction or discontinuation of therapy (3). Because the new biologics have been shown to represent an improvement in the therapy of moderate to severe chronic stable psoriasis (7, 8), it was reasonable to apply them in treatment of PPP as well.

Case report

A currently 61-year-old female with a completely negative familial history of psoriasis has suffered from PPP since January 2000. Initially she developed pustules on erythematous skin on both palms, and about 4



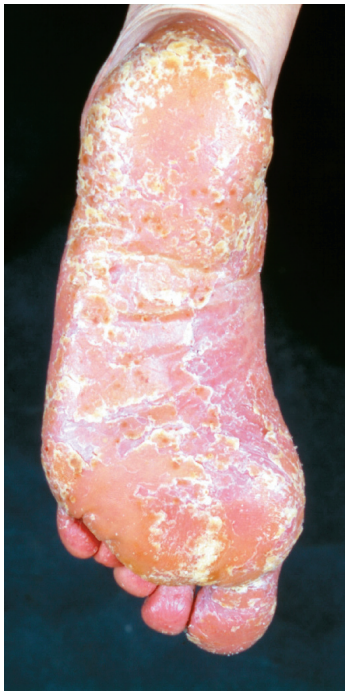
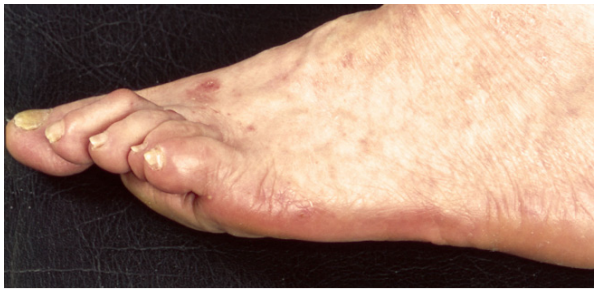


Figure 1a and b. Clinical picture of the left foot of the PPP patient before efalizumab treatment.



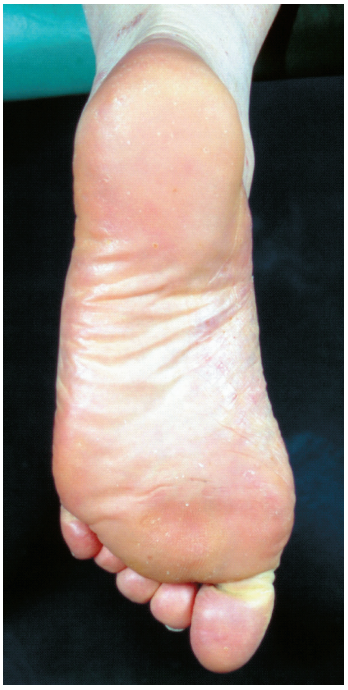


Figure 2a and b. Clinical picture of the left foot of the PPP patient after 43 weeks of efalizumab therapy.

months later multiple pustules on both soles. Histopathological analysis showed a characteristic pattern with sporadic Munro microabscesses. In October of the same year widespread psoriatic plaques appeared on the trunk, extremities, and scalp, affecting about 10% of her body surface. The patient was unsuccessfully treated over 7 weeks with a combination therapy including topical glucocorticosteroids, vitamin D analogues, coal tar, and phototherapy (SUP). This treatment, however, did not lead to an improvement in either the PPP or the plaque psoriasis. She also underwent climatotherapy on an island in the North Sea for 4 weeks, again without success. Thereafter, systemic glucocorticosteroids (initial dose: 30 mg prednisolone/day) with subsequent tapering were introduced resulting in partial improvement. Additional therapy with fumaric acid esters (Fumaderm®) was initiated, which unfortunately was discontinued because "the drug was too expensive." In May 2002 she received oral acitretin (Neotigason®) in alternating daily doses of 20 and 30 mg. One month later she developed marked hypertriglyceridemia (19 mmol/l) and the retinoids had to be discontinued. Oral treatment with methotrexate (15 mg weekly) was discontinued after 6 weeks because it was ineffective.

Systemic tetracyclines over a period of a few weeks (doxycycline 200 mg/d) proved to be ineffective. Systemic treatment with cyclosporine, although beneficial, had to be stopped due to persistent hypertension and increasing arthralgia. Ten days after discontinuation, a substantial flare occurred with extensive pustulation on both soles.

After referral to our hospital, treatment with the TNFα monoclonal antibody infliximab (Remicade®) (5 mg/kg) was started on 17 August 2004, followed by infusions on 31 August 2004 and 28 September 2004. After only 4 days a marked improvement of the pustular eruptions was noted. The initial good response, however, could not be maintained, despite additional topical antipsoriatic treatment with Daivonex® and Daivobet® ointments. A low-dose therapy with methotrexate was initiated (7.5 mg per week), which was combined with infliximab (one infusion every 8 weeks) over 4 months. Even during this combination treatment, extensive use of topical preparations was still necessary (e.g., Daivobet® under occlusion). In April 2005 a severe relapse involving not only the palms and soles but other body areas as well was noted, despite continuous therapy with infliximab and methotrexate. Figure 1a and b.

We decided to switch to a monotherapy with efalizumab (Raptiva®); the initial dose was 0.7 mg/kg in the first week, followed by doses of 1 mg/kg once weekly. The treatment is recorded in Figure 1a. During

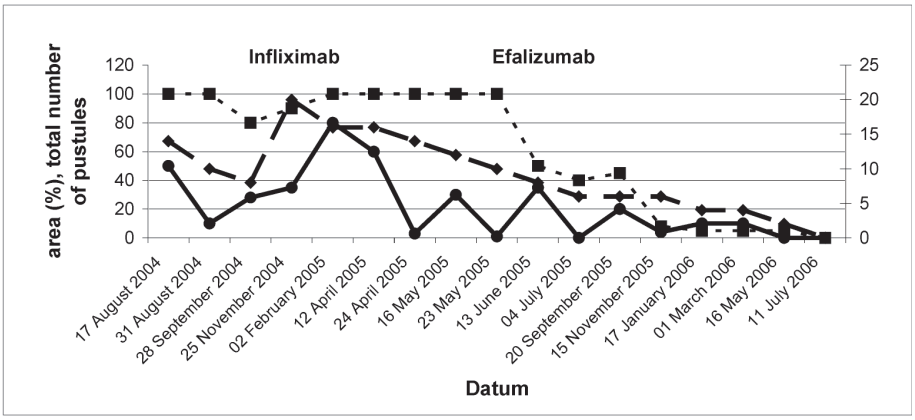


Figure 3. Clinical course under therapy with Infliximab (gray background) and efalizumab (white background).

Comment: We examined the patient's soles and plotted the total number of pustules, expressed the affected area as a percentage of the total area of her soles, and the severity of the disease. Severity was then calculated by adding scores (slight = 1, moderate = 2, severe = 3) for the following parameters: erythema, infiltration, and desquamation.

the first 10 weeks of treatment the patient noticed only moderate relief and pustular eruptions continued to occur even under additional topical therapy with mometasone furoate (Ecural® ointment) and calcipotriol (Daivonex® ointment). However, after 10 weeks of therapy with efalizumab, a sudden and marked improvement was noticed and topical treatment could be discontinued. As of the 11th week of treatment, her palms were clear 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 restrictions and to walk without pain. In addition the patient showed marked improvement of the affected nails on hands and feet resulting in complete healing. To date the palms still are free of pustules and erythema under efalizumab administration (Figure 1b). No side effects were observed during this treatment. Figure 2 shows the clinical course during therapy with infliximab and efalizumab.

For about 15 years the patient had suffered from continuous pain in her hips, diagnosed as osteoarthritis of the hip joint and ineffectively treated with non-steroid antirheumatic drugs. Only after about 1 week of treatment with efalizumab, the patient noticed substantial relief and is now free of any pain, even without additional medication being administered.

Discussion

The etiology of PPP is still unclear. Some authors hypothesize that the acrosyringium might be a target of inflammation (4). Smoking also has been suggested as causative factor because 95% of the patients are smokers at onset of the disease (4, 5, 9, 10). Moreover, in the literature there is no clear distinction between PPP and palmoplantar pustulosis, although the difficulties of treating both diseases are similar. The exact mechanism of action of the drugs used in PPP has not been fully elucidated.

Based on the crucial role of activated T-cells and pro-inflammatory cytokines (7, 8, 11, 12) in the pathophysiology of psoriasis, the biologics have proven to be a safe and highly effective treatment (13). Infliximab, a chimerical monoclonal antibody directed against TNFá, has demonstrated high efficacy in the treatment of chronic plaque psoriasis and other inflammatory immune-mediated diseases. Reports have indicated a rapid onset of action and high efficacy in generalized pustular psoriasis (14, 15). Eventually our patient developed a distinct flare, which led to discontinuation of infliximab therapy.

In the literature there are anecdotal case reports on successful treatments, such as treatment with alefacept as published by Yeung Yue et al., which resulted in an improvement after 7 to 9 weeks (16). Fretzin and Dawes reported on three patients with PPP, who responded to monotherapy with efalizumab with "rapid and significant improvement" (17); this report is in accordance with a case report of PPP recently published by Sobell and Fretzin (18).

Efalizumab is a humanized monoclonal CD11a-antibody. It selectively and reversibly inhibits T-cell activation, reactivation, and migration, which are essential in the pathogenesis of psoriasis (12). Several clinical trials have demonstrated its efficacy in patients with moderate to severe chronic plaque psoriasis (12). Further and larger randomized clinical trials are now needed to confirm these observations. The fact that our patient, after being ineffectively treated with non-steroid antirheumatic drugs over 12 years for osteoarthritis of the hip joint, experienced complete pain relief under treatment of efalizumab, is noteworthy and, to our knowledge, has not yet been published.

REFERENCES

1. Weinstein GD, Menter MA. An overview of psoriasis. In: Weinstein GD, Gottlieb AB, editors. Therapy of moderate to severe psoriasis. 2nd ed. New York, Basel: Marcel Dekker; 2003. p. 1–28.

2. Wright S, Baker H. Localized pustular psoriasis. In: Roenigh HH, Maibach HI, editors. Psoriasis. New York, Basel: Marcel Dekker; 1985. p. 45–57.

3. Marsland AM, Chalmers RJG, Hollis S, Leonardi-Bee J, Griffiths CEM. Interventions for chronic palmoplantar pustulosis. Cochrane Database Syst Rev. 2006; 25: CD001433.

4. Eriksson MO, Hagforsen E, Lundin PI, Michaelsson G. Palmoplantar pustulosis: a clinical and immunohistological study. Brit J Dermatol. 1998;138:390–8.

5. O'Doherty CJ, Macintyre C. Palmoplantar pustulosis and smoking. Brit Med J. 1985;291:861–4.

6. Hellgren L, Mobacken H. Pustulosis palmoplantaris et plantaris. Prevalence, clinical observations and prognosis. Acta Derm Venereol. 1971;51:284–8.

7. Sterry W, Barker J, Boehncke WH et al. Biological therapies in the systemic management of psoriasis: International consensus conference. Brit J Dermatol. 2004;151 (suppl.):3–17.

8. Wozel G. Clinical review: Biological agents in the treatment of psoriasis. Hosp Pharm Eur. 2005;23:59–61.

9. Hagforsen E, Awder M, Lefvert AK et al. Palmoplantar pustulosis: an autoimmune disease precipitated by smoking? Acta Derm Venereol. 2002;82:341–6.

10. Hagforsen E, Edvinsson M, Nordlind K, Michaelsson G. Expression of nicotinic receptors in the skin of patients with palmoplantar pustulosis. Brit J Dermatol. 2002;146:383–91.

11. Christophers E. Targeting T-cell subsets to achieve remission. J Eur Acad Dermatol Venereol. 2003;17 (suppl.):6–11.

12. Gottlieb AB, Hamilton T, Caro I et al. Long-term continuous efalizumab therapy in patients with moderate to severe chronic plaque psoriasis: updated results from an ongoing trial. J Am Acad Dermatol. 2006;54:154–63.

13. Reich K, Nestle FO, Papp K, Ortonne JP, Evans R, Guzzo C, Li S, Dooley LT, Griffiths CEM. Infliximab induction and maintenance therapy for moderate to severe psoriasis: a phase III, multicentre, double-blind trial. Lancet. 2005;366:1367–74.

14. Schmick K, Grabbe J. Recalcitrant, generalized pustular psoriasis: rapid and lasting therapeutic response to antitumor necrosis factor alpha antibody (infliximab). Brit J Dermatol. 2004;150:367.

15. Newland MR, Weinstein A, Kerdel F. Rapid response to Infliximab in severe pustular psoriasis, von Zumbusch type. Int J Dermatol. 2002;41:449–52.

16. Yeung-Yue K, Aronson PJ, Murakawa GJ. Clinical improvement of palmoplantar pustular psoriasis with alefacept. J Am Acad Dermatol. 2005;Suppl. 3:52:P 2730.

17. Fretzin SA, Dawes KW. Efficacy and safety of efalizumab for patients with palmoplantar pustulosis. J Am Acad Dermatol. 2005;52;Suppl. 3:P2745.

18. Sobell J, Fretzin S. Case studies of efalizumab in hand and foot psoriasis. J Am Acad Dermatol. 2006;54;Suppl. 3:P2864.

AUTHORS' ADDRESSES

Gottfried Wozel MD, Professor of Dermatology, Department of Dermatology, Carl Gustav Carus University Hospital, Technical University of Dresden, Fetscherstrasse 74, 01307 Dresden, Germany, E-mail: anja.thuselt@uniklinikum-dresden.de
Lilla Vitez, MD, same address
Michael Meurer, MD, Professor of Dermatology and Chairman, same address