
Successful treatment of hand and foot psoriasis with infliximab

Vito Di Lernia MD, Elisa Guareschi MD
Dermatology Online Journal 16 (7): 8

Department of Dermatology, Arcispedale Santa Maria Nuova, Reggio Emilia, Italy. vito.dilernia@asmn.re.it

Abstract

Hand and foot psoriasis is a disabling condition associated with significant quality-of-life issues. It is characterized by hyperkeratosis and/or the development of recurrent crops of sterile pustules with associated erythema, fissuring, and scaling symmetrically localized on palm and soles. Systemic conventional therapies include retinoids, psoralen-UVA (PUVA), methotrexate, and cyclosporine. So far, only limited evidence supports the use of TNF- α blockers. Because there are reports of paradoxical induction of pustular psoriasis following the use or withdrawal of infliximab as well as other TNF inhibitors, the use of these agents in palmoplantar psoriasis has been cautioned. The authors describe the clinical characteristics and evolution of 4 adult patients with severe palmoplantar psoriasis who were treated successfully with infliximab. Patient data is available for a minimum of 10 months and as many as 16. One of them with concomitant HCV infection showed no increased viral replication or progression of liver disease for a follow-up of 10 months; afterwards infliximab was stopped because of an infusion-related urticaria. All other patients displayed a good clinical response (\geq PPPASI 50) and were still receiving this regimen at last observation. This report provides preliminary evidence to support a cautious use of infliximab in patients with palmoplantar psoriasis.

Introduction

Hand and foot psoriasis (HFP) is a disabling condition that can appear in a hyperkeratotic plaque-type, pustular form or combination [1]. Palmoplantar pustular psoriasis (PPP) may be a distinct entity in epidemiology and pathophysiology because there is a lack of association with the PSOR1 gene locus [2]. In addition, it commonly affects patients lacking psoriasis elsewhere on the body [1]. However, the hyperkeratotic variant is frequently part of the general spectrum of psoriasis vulgaris and is associated with classic plaques elsewhere on the body in many cases. Palmoplantar disease severity occurs independently from the degree of body surface area involvement [1]. Although the palms and soles represent only 4 percent of the total body surface area, significant morbidity can have a debilitating effect on the patient's daily functions. Impaired mobility, pain, disability, pruritus, and embarrassment are common complaints. Hand and foot psoriasis usually represents a difficult-to-treat form of psoriasis [3]. Topical treatment with classic anti-psoriatic drugs often produces unsatisfactory results, partially because the thickened horny layer of palmar and plantar epidermis leads to a reduced bioavailability of the drugs. Systemic treatment options include systemic retinoids, psoralen-UVA (PUVA), and a combination of both [4, 5, 6], but they often fail to give convincing results. Methotrexate or cyclosporine are utilized but they often show an unsatisfactory therapeutic gain as well. Among biologics, efalizumab was found effective for treating HFP in small case series [7], single case reports, and in a 12-week, phase IV, randomized, double-blind, placebo-controlled study [8], but only modestly so. It was no more effective than it was for other areas. However, this drug is no longer available after the decision of the European Medicine Agency to recommend the suspension of the marketing authorization followed by the spontaneous withdrawal in US markets because of a potential risk to patients of developing progressive multifocal leukoencephalopathy.

Among TNF- α inhibitors, randomized studies and case reports suggest that etanercept may be successful in PPP [9, 10, 11].

Infliximab has been found effective in cases of severe pustular psoriasis von-Zumbusch type by downregulation of disease-

promoting chemokines such as IL-8, Gro-alpha, MCP-1 [11, 12, 13]. Similar positive findings were reported in localized recalcitrant PPP [14].

Here we present four case studies in which patients with recalcitrant HFP showed encouraging results with infliximab.

Case reports

The four patients included in this small case series were all patients with HFP treated with infliximab. The main characteristics of our four patients with HFP are summarized in Table 1. In all cases the physical examination showed hyperkeratosis with fissures over at least 50 percent of a single palmar or plantar surface involved, significantly limiting their daily activities. In one case there were additional recurrent pustules. Additional body involvement was present in all cases. No patient suffered from psoriatic arthritis. Bacteriological and mycological tests of the skin lesions were negative in all cases. All patients failed to respond to different topical preparations, ultraviolet-B, and PUVA phototherapy. Acitretin gave a moderate and transient improvement only in patient 3, followed by relapse. Acitretin had never been considered for patient 1 because she was a female of childbearing potential. After therapy with methotrexate 15 mg/weekly, patients 3 and 4 experienced only partial control of their disease. Methotrexate had never been considered because of a moderate alcoholic hepatopathy in patient 1 and a concurrent chronic HCV infection in patient 2. In all cases cyclosporine gave a significant improvement, but skin lesions deteriorated during the following months of treatment. For the evident therapeutic difficulties (lack of efficacy, intolerance or contraindication with systemic conventional therapies) the patients were considered as “High Need” for biological therapy with TNF-alfa antagonists.



Figure 1

Figure 1. Patient 1, clinical appearance of the hands before initiation of treatment



Figure 2

Figure 2. Patient 1, hands after 12 months of treatment with infliximab monotherapy



Figure 3

Figure 3. Patient 1, severe erythema and scaling of feet before treatment



Figure 4

Figure 4. Patient 1, clearing of foot psoriasis after treatment with infliximab

Before starting treatment, complete laboratory and additional tests were performed, including chest x-rays, complete blood count, creatinine, transaminases, cholesterol, triglycerides, antinuclear antibodies, and urinalyses. No significant alterations were found. The severity of psoriasis was assessed by the Palmoplantar Pustular Psoriasis Area and Severity Index (PPPASI). Therapeutic response was assessed by 75 percent improvement on PPPASI (PPPASI 75). Initiation of treatment (at weeks 0, 2, and 6) with infliximab at a dose of 5 mg/kg was started and then maintained every 8 weeks. The clinical appearance of the hands and feet of patient 1 before initiation of monotherapy with infliximab and after 12 months of treatment is shown in Figures 1 through 4. Blood tests were repeated after the first 4 weeks and every 8 weeks thereafter. A considerable improvement of their skin lesions was already obtained within 8 weeks after the first infusion of infliximab in all cases. At week 16, 1 out of 4 patients had achieved 100 percent reduction in her PPPASI score, 2 patients had reached PPASI 75, and 1 patient PPPASI 50. In case 2 the treatment of infliximab was discontinued due to an infusion-related

reaction characterized by urticaria after 46 weeks of treatment; at this point, an increase of PPPASI score and a relapse of HFP was also documented in this patient.

Discussion

Despite the full range of therapeutic approaches, treatment of a patient with HFP can be challenging. Systemic therapies sometimes show initial efficacy in only a certain proportion of patients, whereas other patients are resistant to any kind of therapy.

TNF- α is a cytokine involved in the regulation of leukocyte recruitment to sites of evolving or ongoing inflammation. It induces expression and secretion of multiple chemokines that guide leukocytes to sites of evolving inflammation. A key role of TNF- α in the pathogenesis of pustular psoriasis has been hypothesized [1]. Skin biopsies obtained from pustular psoriatic lesions (von Zumbusch type) following administration of infliximab showed an immediate and effective downregulation of the neutrophil-attractant chemokine interleukin (IL)-8 and growth-related oncogene (Gro)- α as well as monocyte chemoattractant protein (MCP)-1. At the histologic level, no further formation of micropustules and a strongly reduced inflammatory infiltrate were observed 5 days after the first infusion of infliximab [1]. However, infliximab caused only transient improvement when applied as monotherapy or in combination with methotrexate in some patients affected by PPP reported in the literature who responded later to efalizumab [14]. In addition, the development of paradoxical induction of pustular psoriasis following the use or withdrawal of infliximab or other TNF- α inhibitors has been described [15]. Thus, the use of these agents in PPP has been cautioned.

This retrospective study shows preliminary evidence to support a cautious use of infliximab in patients with refractory HFP psoriasis. Because 3 out of our 4 patients showed a hyperkeratotic subtype of HFP and only 1 patient showed a combined hyperkeratotic/pustular form, we cannot exclude that the hyperkeratotic form can be more responsive to infliximab than the pustular type. Indeed, the latter type, as a distinct genetic entity, could show a different response to the therapy. Therefore, the assessment of psoriatic lesion morphology on the hands and feet could be important, as suggested by Farley et al. [1], because different subtypes of psoriasis could influence responses to different treatment modalities. Because the duration of the treatment in our small case series lasted from 10 to 16 months, we cannot exclude the possibility of loss of response over time. Further clinical experience will help to elucidate the helpfulness of infliximab in HFP and the different responses relatively to the phenotypical subtypes.

References

1. Farley E, Masrour S, McKey J, Menter A. Palmoplantar psoriasis: a phenotypical and clinical review with introduction of a new quality-of-life assessment tool. *J Am Acad Dermatol* 2009 Jun;60(6):1024-31. [[PubMed](#)]
2. Asumalahti K, Ameen M, Suomela S et al. Genetic analysis of PSOR1 distinguishes guttate psoriasis and palmoplantar pustulosis. *J Invest Dermatol* 2003 Apr;120(4):627-32. [[PubMed](#)]
3. Marsland AM, Chalmers RJ, Hollis S et al. Interventions for chronic palmoplantar pustulosis. *Cochrane Database Syst Rev* 2006 Jan 25;(1):CD001433. [[PubMed](#)]
4. Lassus A, Geiger JM. Acitetin and etretinate in the treatment of palmoplantar pustulosis: a double-blind comparative trial. *Br J Dermatol* 1988 Dec; 119 (6) :755-9. [[PubMed](#)]
5. Layton AM, Sheehan-Dare R, Cunliffe WJ. A double-blind, placebo-controlled trial of topical PUVA in persistent palmoplantar pustulosis. *Br J Dermatol* 1991 Jun;124(6):581-4. [[PubMed](#)]
6. Matsunami E, Takashima A, Mizuno N et al. Topical PUVA, etretinate, and combined PUVA and etretinate for palmoplantar pustulosis: comparison of therapeutic efficacy and the influences of tonsillar and dental focal infections. *J Dermatol* 1990; Feb;17 (2):92-6. [[PubMed](#)]
7. Fretzin S, Crowley J, Jones L et al. Successful treatment of hand and foot psoriasis with efalizumab therapy. *J Drugs Dermatol* 2006 Oct; 5(9): 838-46. [[PubMed](#)]
8. Leonardi C, Sobell J, Sofen H et al. Phase IV study to evaluate

the safety and efficacy of efalizumab for treatment of hand and foot psoriasis. *J Am Acad Dermatol* 2007; 56 (2): AB48.

9. Bissonnette R, Poulin Y, Bolduc C, Maari C, Provost N, Syrotuik J, Poulin-Costello CM, Nigen S. Etanercept in the treatment of pustolosis palmoplantaris. *J Drugs Dermatol* 2008 Oct; 7 (10): 940-6. [[PubMed](#)]

10. Weinberg JM. Successful treatment of recalcitrant palmoplantar psoriasis with etanercept. *Cutis* 2003 Nov;72(5):396-8. [[PubMed](#)]

11. Benoit S, Toksoy A, Brocker EB, Gillitzer R, Goebeler M. Treatment of recalcitrant pustular psoriasis with infliximab: effective reduction of chemokine expression. *Br J Dermatol* 2004; 150:1009-12.

12. Schmick K, Grabbe J. Recalcitrant, generalized pustular psoriasis: rapid and lasting therapeutic response to anti-tumor necrosis factor alpha antibody (infliximab). *Br J Dermatol* 2004; 150: 367.

13. Newland MR, Weinstein A, Kerdel F. Rapid response to infliximab in severe pustular psoriasis von Zumbusch type. *Int J Dermatol* 2002; 41:449-52.

14. Wozel G, Vitéz L. Palmoplantar pustular psoriasis: successful therapy with efalizumab after non-response to infliximab. *Acta Derm Venereol* 2008; 88: 169-70.

15. Thurber M, Feasel A, Stroehlein J, Hymes SR. Pustular psoriasis induced by infliximab. *J Drugs Dermatol* 2004; 3: 77-9.