Infliximab (Remicade®) for Acute, Severe Pustular and Erythrodermic Psoriasis

Steen Lisby and Robert Gniadecki
Department of Dermatology, Bispebjerg Hospital, Bispebjerg Bakke 23, DK-2400 Copenhagen NV, Denmark.
E-mail: SL05@bbh.hosp.dk
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Sir,

Pustular and erythrodermic psoriasis can run a dramatic, acute course and have a high risk of secondary complications including sepsis, oligovolaemia, electrolyte imbalance, renal failure, heart failure or amyloidosis (1, 2). Moreover, the therapeutic agents used for the treatment of psoriasis themselves carry a significant risk of side effects. Hepatotoxicity, renal toxicity and sepsis may occur in the course of treatment with methotrexate (MTX), retinoids, cyclosporin or systemic steroids.

Infliximab is a chimeric monoclonal antibody that targets tumour necrosis factor-α (TNFα), a cytokine which is thought to play a central role in the pathogenesis of psoriasis (3). Several studies showed a remarkable efficacy of infliximab in stable plaque psoriasis and psoriasis arthritis (4, 5). To date, patients with erythrodermic and pustular psoriasis have been excluded from clinical trials, and experience is limited to two case reports describing a rapid response to infliximab (6, 7). In this paper we present our preliminary experience with the use of infliximab for the treatment of hospitalized patients with acute pustular and erythrodermic psoriasis.

CASE REPORTS

Case 1

A 59-year-old woman with a 3-year history of recalcitrant relapsing generalized pustular psoriasis. The patient has previously been treated with cyclosporin and MTX in monotherapy or in combination without sufficient effect. At 5 weeks before admission this patient developed an increase in serum creatinine levels, and the cyclosporin dose was reduced by 50% resulting in an exacerbation of generalized pustular psoriasis. The disease progressed despite a brief course of systemic prednisone (15 mg/daily). On admission, the patient presented with a fever of 38.1°C, leukocytosis (21.5×10^9/l), increased ASAT (51 U/l, normal <35), basic phosphatases (638 U/l, normal range 80–275) and C-reactive protein (CRP, 333 mg/l, normal <10). Clinically the patient had generalized pustular rash affecting the trunk and the extremities. No infectious focus could be detected, and peripheral blood cultures were negative. A diagnosis of generalized pustular psoriasis of the von Zumbusch type was made. The patient received a single dose of infliximab (3 mg/kg) in combination with 25 mg MTX and a total clearing was observed during the following 4 days. Blood tests revealed normalization of the values including leukocyte count (9.5×10^9/l), ASAT (23 U/l), basic phosphatases (202 U/l) and CRP (3 mg/l). During the next week, relapse was observed and she was treated with another two courses of infliximab (3 mg/kg) at weeks 2 and 6 combined with a reduced dose of MTX (15 mg/week). The patient cleared totally following the second treatment and remained in full remission 4 weeks after the last (third) treatment.

Case 2

A 51-year-old male, with known alcohol abuse, had a 2-year history of localized pustular psoriasis classified as acrodermatitis continua Hallopeau. The patient received local treatment with potent steroids and systemic treatment with cyclosporin and MTX either as monotherapy or in combination. This treatment regimen was complicated by a gradual deterioration in kidney function and hypertension, which necessitated the reduction of the cyclosporin dose. During the following 6 months, gradual worsening of the symptoms occurred. Following this period, an acute exacerbation of the symptoms was seen, and the patient presented with a pustular affection on the volar aspects of the hands and feet (Fig. 1a). Treatment with infliximab (3 mg/kg) and MTX (20 mg/week) resulted in a total clearance of pustules (Fig. 1b). A gradual relapse was observed 2 weeks after initial treatment and the patient was treated with a second course of 3 mg/kg infliximab, after which a full remission was obtained. Unfortunately, the patient resumed his alcohol abuse and discontinued MTX treatment, which resulted in a relapse at the 14th week after the first infliximab infusion.

Case 3

A 37-year-old woman presented with a history of chronic relapsing plaque psoriasis over a period of more than 20 years. She was treated with local modalities, UVB phototherapy and MTX with only marginal effect. In 1993, cyclosporin was used with some effect, but

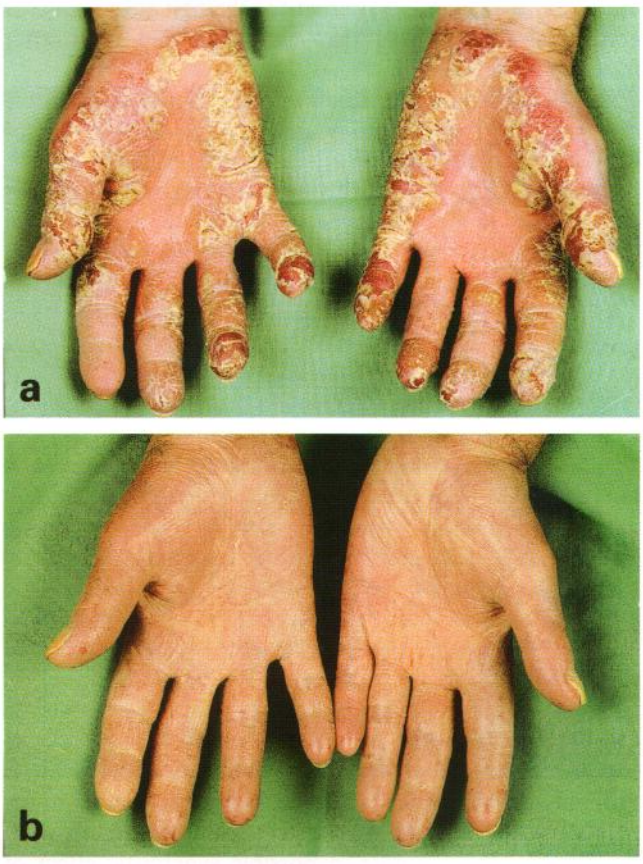

Fig. 1. Volar aspect of hands (a) before treatment, showing erythema, scaling and pustulosis; (b) 1 week after initial treatment with infliximab 3 mg/kg, demonstrating total remission of pustulosis.

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the treatment had to be stopped due to renal side effects. A month before admission, the disease progressed rapidly and the patient experienced erythrodermic psoriasis affecting more than 90% of the body surface. She was treated with 3 mg/kg infliximab in combination with MTX (5 mg/week), and an almost complete clearance of psoriasis was experienced within a week. Infliximab treatment was repeated after 2 weeks. Eight weeks following the second treatment, the patient remained in remission. However, 14 weeks after the second treatment, relapse was observed in the form of guttate psoriasis and a third treatment with infliximab was administered.

DISCUSSION

Only two case reports are available in the literature describing the effect of infliximab in acute pustular psoriasis. Newland et al. (7) treated a 44-year-old Caucasian woman with the von Zumbusch type pustular psoriasis with 5 mg/kg infliximab, 100 mg cyclosporin and 150 mg bexarotene and observed a rapid clearing of pustules and erythema, normalization of fever, leukocytosis, erythrocyte sedimentation rate and CRP levels within 24 h. Elewski (6) described a 39-year-old Caucasian man with generalized pustular psoriasis who cleared rapidly after treatment with 5 mg/kg infliximab, 25 mg/week MTX, 75 mg/day acitretin and 20 mg/day prednisolone. An additional case report describes favourable responses to infliximab in pustulosis palmo-plantaris (8). Our data further support the conclusion that infliximab produces a rapid amelioration of pustular psoriasis (cases 1 and 2). Moreover, we present for the first time a case of erythrodermic psoriasis that cleared within days after injection of infliximab.

TNFα is a proinflammatory and immunomodulating cytokine, the concentration and biological activity of which is increased in skin and serum of patients with psoriasis (9). Moreover, TNFα induces other cytokines responsible for the pathogenesis of psoriasis: interleukin-6 (IL-6) and IL-8. A rapid systemic release of these circulating proinflammatory cytokines, in particular TNFα, is thought to be responsible for the onset of pustular psoriasis and possibly psoriatic erythroderma (10). Administration of TNFα blocking agents, such as infliximab or etanercept, would lead to an almost instantaneous neutralization of this cytokine.

Side effects to infliximab are only rarely encountered, but this drug is potentially capable of producing severe immunosuppression with the risk of life-threatening bacterial infections, such as sepsis or tuberculosis (11). The patients should be carefully evaluated for possible infection, especially the patients with von Zumbusch-type psoriasis, the course of which is sometimes complicated with septicaemia. Infliximab is also contraindicated in patients with heart failure (12) and pre-existing neoplastic diseases. Combination with other treatment modalities is also an issue. Simultaneous administration of MTX is probably advantageous (13), most probably due to its ability to prevent the synthesis of anti-infliximab antibodies (14). Furthermore, a possible synergistic effect of MTX in combination with infliximab has been described (15). Conversely, combination with potent immunosuppressives such as cyclosporin may lead to an increased risk of complications. The effect of infliximab on pustular/erythrodermic psoriasis occurred early following treatment; however, a single infusion is insufficient to yield long-term clinical response. To date no fixed regimen for the treatment of pustular psoriasis with infliximab has been enforced, but we recommend that at least three treatments should be given (weeks 0, 2 and 6). In the future, the TNFα-blocking agents are likely to constitute the first line of treatment of severe acute forms of psoriasis if the abovementioned safety issues are resolved and therapeutic efficacy is confirmed in larger trials.

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