Sequential Use of Infliximab and Etanercept in Generalized Pustular Psoriasis

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Generalized pustular psoriasis is a dramatic potentially life-threatening psoriasis variant and represents a major therapeutic challenge. Tumor necrosis factor α (TNF-α) inhibitors have been shown to be highly effective in psoriasis vulgaris and psoriasis arthritis. Currently, TNF-α can be targeted therapeutically by 2 different approaches. TNF-α antibodies show a fast onset of action and a long-lasting activity. Soluble TNF-α receptors have a slower onset and a shorter duration of activity, which allows a rapid cessation of the drug's activity in the case of adverse events. Here we report that a remission of generalized pustular psoriasis achieved by the TNF-α antibody infliximab was maintained by long-term application of the soluble TNF-α receptor etanercept. Sequential therapy with TNF-α antibodies and TNF-α receptors may represent a novel concept that combines a rapid onset of action in the initiation therapy with a lower risk for severe adverse events in the maintenance treatment of pustular psoriasis.

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Generalized pustular psoriasis of Zumbusch is a severe generalized skin disorder that may be potentially life threatening. Clinical features include disseminated pustules arising in widespread erythema, fever, and a poor general condition. Leukocytosis, neutrophilia, and elevation of cross-reacting protein and erythrocyte sedimentation rate usually are present. Infections such as pneumonia or sepsis emerging during disease progression may contribute to a fatal outcome.

Established treatment modalities include cyclosporine, methotrexate, acitretin, psoralen plus UVA therapy, or a combination of them. Quite often, however, they are insufficient to achieve disease remission. Tumor necrosis factor α (TNF-α) antagonists, which have been shown to be effective in patients with psoriasis vulgaris and psoriatic arthritis, have occasionally been used in patients with generalized pustular psoriasis of Zumbusch. Here we report that switching from the TNF-α antibody infliximab to the TNF-α receptor etanercept may represent a reasonable approach in the long-term management of generalized pustular psoriasis.

Case Report

A 54-year-old woman presented with a history of psoriasis vulgaris and psoriatic arthritis since her early childhood. The course of the skin manifestations in the past was undulating with relapsing pustular disease flares. A variety of topical and systemic antipsoriatic and antirheumatic treatment modalities including methotrexate, cyclosporine, fumaric acid esters, and acitretin had shown very little or no benefit. Systemic steroids had been administered for more than 3 decades for the treatment of psoriatic arthritis. This longtime application had resulted in arterial hypertension, diabetic metabolism, and severe osteoporosis.

At the first consultation in our department, the patient presented with a highly inflammatory generalized pustular flare of the disease (Figure, A–B). The general condition was poor and a treatment mode with a fast onset of action appeared essential. As several of the established treatment modalities had been ineffective and/or contraindicated in the past, we decided to use the TNF-α antibody infliximab for treatment. Congestive heart failure and tuberculosis were excluded. After one infusion of infliximab (3 mg/kg body weight), the skin

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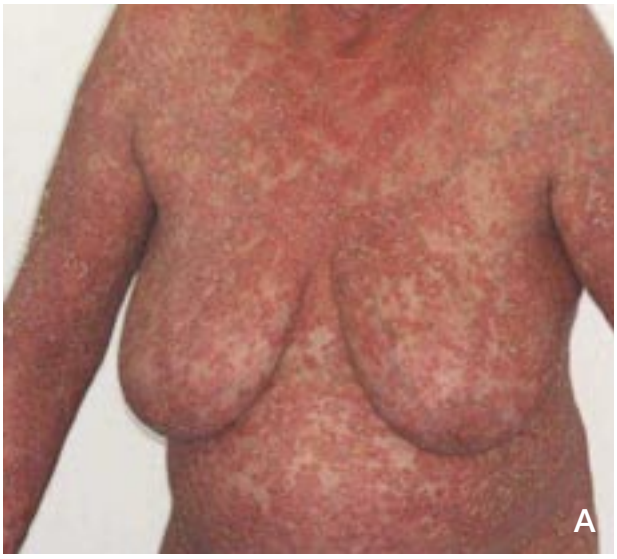

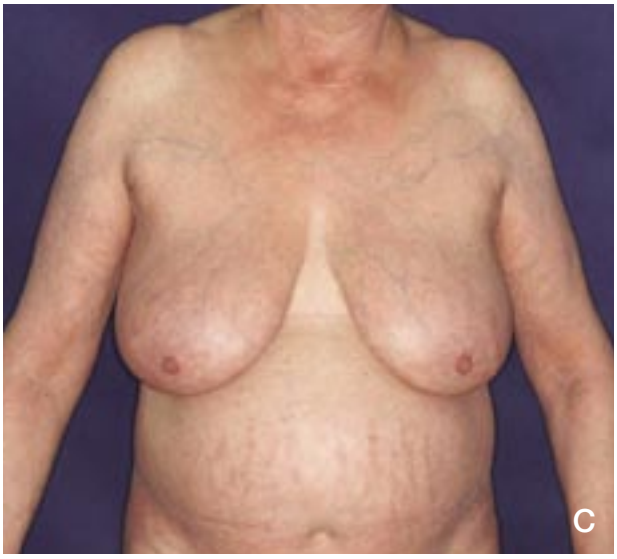

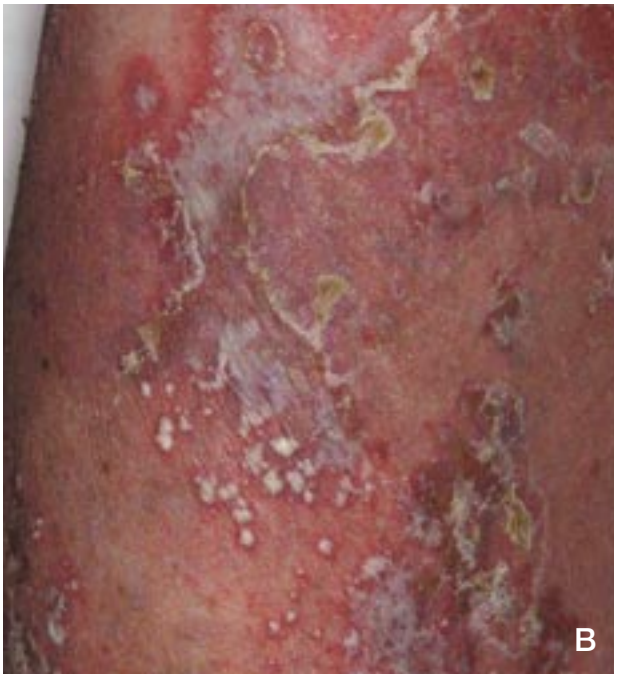

A 54-year-old woman with generalized pustular psoriasis of Zumbusch at presentation to the dermatology department (A). Detail of left thigh (B). Same patient 2 weeks after one infusion of infliximab (3 mg/kg body weight) (C).

manifestations immensely improved within the first 24 hours and kept improving within the next 2 weeks (Figure, C). Concurrently, systemic steroids were tapered. Topical treatment included only moisturizing creams. At week 3, a subsequent treatment with the soluble TNF-α receptor etanercept was initiated (25 mg administered subcutaneously twice weekly). The skin manifestations completely cleared at week 5 and the joint manifestations were reduced to a minimum. After 8 weeks, the etanercept dose was reduced from 8 to 6 injections of 25-mg etanercept monthly without a disease relapse so far.

Comment

The high therapeutic efficacy of TNF-α antagonists has revealed that TNF-α plays a crucial role in the inflammatory cascade in psoriasis vulgaris and psoriatic arthritis.[1-3] TNF-α blocking agents are employed as antibodies or soluble receptors. The main clinically relevant differences between the agents are efficacy, pharmacodynamics, and safety. Measured by the Psoriasis Area and Severity Index 75 after 10 to 12 weeks of treatment, the overall efficacy of soluble TNF-α receptors is lower compared with TNF-α antibodies.[2,3] TNF-α antibodies like infliximab show a rapid onset of action and are highly effective. The

serum half-life of approximately 9 days results in a low administration frequency. Full elimination of infliximab requires up to 6 months. The prolonged elimination may result in a reduced controllability of drug activity and patient condition in the event of adverse events.

Soluble TNF-α receptors like etanercept have a shorter serum half-life. It is 68±19 hours after a standard 25-mg dose of etanercept.[4] Consequently, soluble TNF-α receptors require shorter application intervals. The faster decrease in activity as compared with that of the monoclonal antibodies may prove to be an advantage when adverse events occur.

Combining the rapid onset of action of antibodies and the better controllability of soluble receptors might prove beneficial in particular patients. Both drugs have been shown to be effective as monotherapy in generalized pustular psoriasis.[5,6]

In such a concept, initial administration of a TNF-α antibody may be used to rapidly improve the disease. After a sufficient improvement has been achieved, soluble TNF-α receptors may be administered to stabilize the skin condition and maintain the remission. Switching from a TNF-α antibody to a soluble receptor after improvement of severe psoriasis manifestations appears reasonable based on controllability and safety factors. The incidence of severe infections is substantially higher in patients treated with infliximab compared with those treated with etanercept.[7] This case demonstrates that the successive administration of a TNF-α antibody and a soluble TNF-α receptor may combine the advantage of a rapid and efficient onset of action with the benefits of a somewhat safer maintenance treatment in generalized pustular psoriasis. Furthermore, the results suggest that the essential maintenance dosage of etanercept to prevent relapses might be lower in select cases than the generally recommended dose of 25 mg twice weekly. This is an intriguing side aspect that could help to lower the extensive costs of antipsoriatic biologics in certain patients.

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