The Effectiveness of Tumor Necrosis Factor α Antibody (Infliximab) in Treating Recalcitrant Psoriasis

A Report of 2 Cases

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Background: Psoriasis is being recognized as an autoimmune disease in which immunocyte-derived cytokines are thought to drive the development of the altered keratinocyte phenotype. Although the role of tumor necrosis factor α (TNF-α) in psoriasis is not completely understood, it may underlie many of the key steps that lead to induction and maintenance of the disease. Infliximab is an immunoglobulin monoclonal antibody that binds and inactivates TNF-α and has been successfully used in the management of TNF-α-mediated diseases, such as Crohn disease and rheumatoid arthritis.

Observations: Two patients with recalcitrant psoriasis that was unresponsive to multiple skin-directed and systemic therapies were treated with a single infusion of infliximab. The treatments resulted in rapid and complete clearing of psoriatic erythroderma and resolution of symptoms of arthritis in one case and complete clearing of widespread psoriatic plaques and improvement of symptoms of arthritis and inflammatory bowel disease in the other. The single treatments with infliximab were well tolerated with no immediate or long-term adverse effects noted.

Conclusion: A single infusion of infliximab at 5 to 10 mg/kg resulted in the rapid and complete clearing of recalcitrant psoriatic plaques and erythroderma with a disease-free interval of 3 to 4 months in these 2 patients and improved the symptoms of psoriatic arthritis.

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gual hyperkeratosis. The distal interphalangeal joints showed some edema and pain with active motion.

After informed consent was obtained, 10 mg/kg of infliximab (Remicade; Centocor, Malvern, Pa) was administered intravenously over 3 hours after premedication with acetaminophen and diphenhydramine hydrochloride. No adverse effects were associated with the infusion. Within 2 days the patient noted a decrease in pruritus and erythema of the skin and resolution of his chills and cold intolerance. A follow-up examination 10 days after the infusion showed that the plaques were noticeably thinner to palpation. Significant improvement in the erythema with persistence of scaling was noted. The patient reported resolution of pain associated in the distal interphalangeal and sacroiliac joints, and the results of the clinical examination of the fingers were clinically normal, with no pain on active motion.

A 4-week follow-up examination showed complete resolution of all psoriatic plaques, erythema, and scaling (Figure 2). The patient’s skin was clinically normal for the first time in 7 years.

A biopsy specimen of the left forearm was taken before treatment with infliximab, which showed psoriasiform acanthosis of the epidermis with parakeratosis of the stratum corneum, infiltrating neutrophils forming Munro microabscesses, thinning of the suprapapillary plates, and dilated blood vessels in the dermal papillae (Figure 3). A follow-up biopsy specimen of the left fore-

arm 10 days after treatment with infliximab revealed a resolution of psoriasiform epidermal changes. The stratum corneum showed an orthokeratotic basket weave pattern, whereas the epidermis showed spongiosis with a mild perivascular lymphocytic infiltrate and occasional eosinophils (Figure 4).

The patient noted the onset of slight pruritus beginning 4 weeks after treatment, which he thought heralded the onset of new psoriatic skin involvement. Follow-up after 8 weeks showed a few small erythematous plaques on the legs, but the patient’s trunk, arms, and scalp remained clear. Ongoing treatment with sunlight exposure and topical triamcinolone was instituted. The patient relapsed with development of psoriatic plaques 3 months following treatment.

CASE 2

A 33-year-old white woman presented with an 8-year history of psoriasis vulgaris and psoriatic arthritis. She initially presented with confluent scale over the entire scalp and generalized erythematous plaques with adherent silvery scale measuring 0.5 to 6.0 cm² over the chest, abdomen, back, buttocks, gluteal crease, and upper and lower extremities. She also had edema, warmth, and nearly incapacitating pain in the phalangeal joints. Her medical history was also notable for diarrhea, hematochezia, and crampy abdominal pain diagnosed by upper and lower
gastrointestinal tract endoscopy as unspecified inflammatory bowel disease.

Multiple therapeutic regimens were administered that ultimately failed to produce significant clearing and control of the patient’s psoriatic plaques and arthritis. A previous trial of psoralen–UV-A had been terminated because of psoralen intolerance. Treatment with high-potency topical steroids, topical calcipotriene, and methotrexate was begun. The methotrexate dose was increased up to 15 mg/wk to a total dose of 290 mg. Despite some improvement of both skin and joint disease, its use was discontinued because of the onset of diarrhea. A trial of topical tazarotene was ineffective. Broad-band UV-B for 12 treatments followed by narrow-band UV-B for 43 treatments was given. Many plaques decreased in size but were still present, and the psoriatic arthritis worsened. Treatment with cyclosporine, 4 mg/kg, showed improvement in both skin and joint symptoms, but its use was soon discontinued because of intractable headaches. Azathioprine therapy was begun concurrently with cyclosporine therapy and titrated up to 100 mg/d. After 3 months, no response was noted.

In January 2000, the patient presented with low-grade fever (temperature, 37.8°C) and complaints of worsening joint pain and swelling, increased numbers of psoriatic plaques, and bloody diarrhea accompanied by crampy abdominal pain. Physical examination findings were notable for erythematous, thin, guttate plaques and papules over the arms, legs, back, chest, and abdomen. There were scaling patches on the scalp. The distal and proximal interphalangeal joints were erythematous, edematous, and tender. The patient, although motivated and compliant with therapy, had had a poor response to conventional topical treatment, phototherapy, and systemic immunosuppressive agents. In addition, intolerance to multiple agents and the potential to exacerbate the inflammatory bowel disease limited treatment options. An alternate treatment to address both the refractory psoriasis and inflammatory bowel disease was needed.

After informed consent was obtained, infliximab was administered intravenously at a dosage of 5 mg/kg for 3 hours. The patient was premedicated with acetaminophen and diphenhydramine, and the infusion was tolerated well. The patient reported decreased erythema in the psoriatic plaques within 24 hours. She also noted a rapid resolution of diarrhea and abdominal symptoms. Complete clearing of the plaques occurred within 2 weeks, and arthritis symptoms improved significantly. A follow-up examination after 2 weeks was remarkable for complete clearing of all plaques with residual macules and patches of hyperpigmentation with minimal overlying scale (Figure 5). Examination of the interphalangeal joints showed no erythema and minimal discomfort on active motion. Biweekly etanercept, 25 mg subcutaneously, was initiated. The patient discontinued the etanercept therapy after 2 weeks. She maintained a 4-month disease-free interval before relapsing with psoriatic plaques and arthritis.

Figure 5. Patient 2 one month after a single dose of infliximab. Note flat, mostly hyperpigmented lesions.
receptors. It has been shown in vitro that infliximab also interacts with membrane-bound TNF-α, leading to lysis of the cell.20

Infliximab has been used with success in multiple trials in the treatment of Crohn disease and rheumatoid arthritis; both are diseases in which TNF-α plays a central role in the pathogenesis.21-23 Treatment with infliximab has led to observations of profound down-regulation of inflammation in Crohn disease and rheumatoid arthritis. In Crohn disease, a regression of the inflammatory infiltrate, especially neutrophils, is noted, as well as a reduction or disappearance of activation markers and adhesion molecules such as aberrant HLA-DR expression, intercellular adhesion molecule 1, and leukocyte function–associated antigen 1.24 Similar findings have been observed in patients with rheumatoid arthritis treated with the antibody.25,26 Infliximab also suppresses serum markers of inflammation, such as C-reactive protein and the erythrocyte sedimentation rate, and down-regulates the production of numerous cytokines in vivo.26,27 In addition, some actions of infliximab may be due to an inhibition of angiogenesis that has been observed with its use.26

Infliximab has a half-life of approximately 10 days when administered as a single 5-mg/kg dose.26 Its metabolism and excretion are not known, but as a protein, infliximab is not metabolized by cytochrome P-450 enzymes, decreasing the concern for complex drug interactions. The most commonly reported adverse effects are headache, diarrhea, rash, rhinitis, and coughing. The incidence of mild infections is increased, with upper respiratory tract infection occurring in 4.6% and urinary tract infection occurring in 4.6%, and serious infections resulting in death, although rare, have been reported.29 Chimeric antibodies are less immunogenic than murine antibodies, but immediate hypersensitivity reactions have been reported with the administration of infliximab, similar to those seen with other immunoglobulin preparations.30 For this reason, it is recommended that antiestimases, corticosteroids, and epinephrine should be available during the infusion.31 The development of lymphomas in patients treated with infliximab has been a theoretical concern. In several trials, 3 of 555 patients with rheumatoid arthritis treated with infliximab developed lymphoma during 3 years of follow-up.23 Cause and effect have been difficult to determine because patients with rheumatoid arthritis and other autoimmune diseases, especially when treated with immunosuppressive medications, have higher incidences of lymphoma.32

Because of the concern for potential exacerbation of a concurrent infection secondary to infliximab use, both of our patients underwent complete physical examinations and chest radiography before administration.

Infliximab has been observed to improve psoriatic skin lesions in a single case of a patient undergoing treatment for Crohn disease.33 We present a case significant for complete clearing of psoriatic erythroderma and another in which the plaques of psoriasis vulgaris, arthritis, and inflammatory bowel disease cleared rapidly after treatment with anti–TNF-α antibodies. Psoriasis has been shown to be more prevalent in patients with inflammatory bowel disease and may be of use in patients in whom these diseases coexist.34 Use of infliximab should be reserved for those patients who are acutely ill and in whom more conventional therapies have failed. It may be a useful agent in such patients to rapidly clear widespread psoriasis before other systemic and skin-directed therapies begin to mediate their effects. The role of infliximab in TNF-α–mediated diseases seems very promising. The efficacy of a treatment suggested by a single report may serve to provide clues about the pathogenesis of a disease, but will need to be subjected to trials before its widespread use.

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News and Notes

A symposium will be held on the clinical management of epidermolysis bullosa (EB) in children and adults on November 7-8, 2002, at The Institute of Child Health, 30 Guilford St, London WC1N 1EH, England. All individuals and multidisciplinary teams who care for patients with EB are invited. The meeting is sponsored by DEBRA UK. Those interested in participating should contact DEBRA UK, DEBRA House, 13 Wellington Business Park, Dukes Ride, Crowthorne, Berks RG14 6LS, England; phone: 0044-7779-221909; fax 0044-1344-762777 (e-mail: sue.glazier@btinternet.com).