Infliximab-Induced Remission of Extensive Plaque Psoriasis

Howard Amital MD[1], Arieh Ingber MD[2] and Alan Rubinow MD[1]

[1]Rheumatology Unit, Division of Internal Medicine, and [2]Department of Dermatology, Hadassah University hospital and Hebrew University-Hadassah Medical School, Jerusalem, Israel

Key words: psoriasis, tumor necrosis factor-alpha, infliximab, cytokines

IMAJ 2003;5:827–828

For Editorial see page 817

Psoriasis is a relatively common disease, affecting 1–3% of the general population of whom many will experience prolonged annual hospital stays. In addition, many patients need psychological assistance particularly when the cutaneous involvement causes cosmetic impairment and social avoidance.

Tumor necrosis factor-alpha plays a seminal role in the pathogenesis of many inflammatory disorders [1]. Recent data on skin and synovial biopsies from patients with psoriasis indicate that TNFα has a major role in the pathogenesis of this disease as well [1,2]. Consequently, this cytokine has become a key therapeutic target of many new biological anti-rheumatic drugs. The two most marketed anti-TNFα agents worldwide are etanercept, a genetically engineered dimer of an extracellular domain of the p75 receptor to TNFα that has been fused to the constant region of human immunoglobulin G; and infliximab, which is a chimeric anti-TNFα monoclonal antibody composed of a murine variable region covalently linked to a human immunoglobulin G constant region [1].

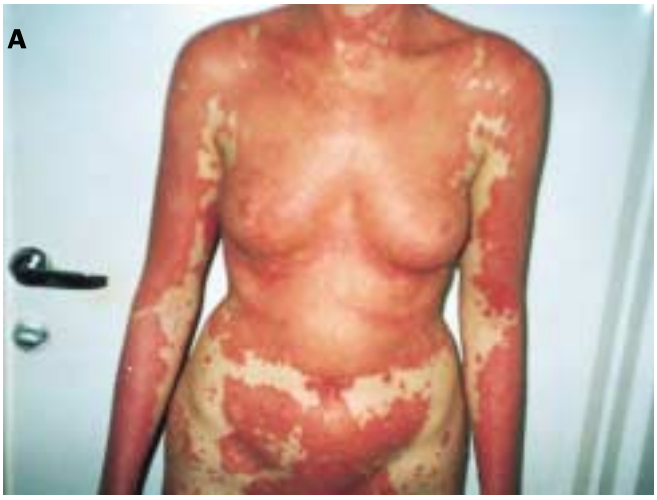
We report a young woman with plaque psoriasis covering almost her entire skin surface. Treatment with infliximab markedly changed the course of her disease and her daily life.

Patient Description

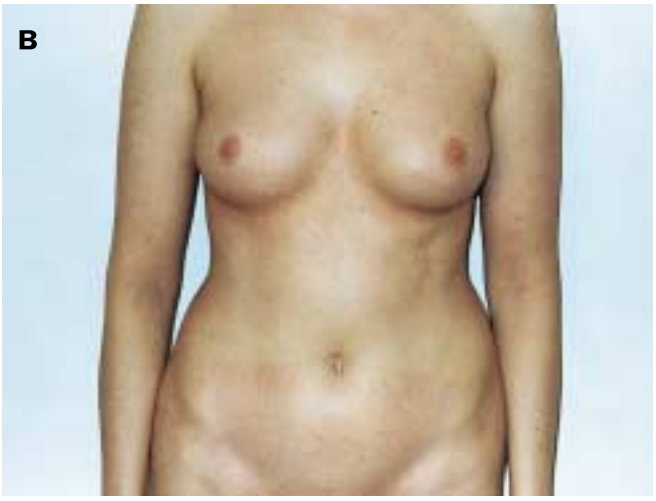
A 25 year old woman with a 12 year history of extensive psoriasis vulgaris, the large plaque-forming type, was admitted following a 2 week deterioration in her disease despite 25 mg of weekly methotrexate therapy. In the past, she gained temporary relief with topical steroids, systemic agents, and several weeks each year of climatotherapy at the Dead Sea. At the present admission, she received methotrexate, psoralen-ultraviolet A, UVB and cyclosporine A, without benefit. A trial with etretinate resulted in severe alopecia and concomitant dryness of her skin and ulcerations of her lips. She exhibited severe extensive large psoriatic plaques with thick scaling that involved 90% of her skin surface [Figure A]. During this period, she withdrew from her regular academic and social activities and developed a reactive depression. No significant benefit was achieved with the topical agents. The extensive and refractory nature of her illness prompted the initiation of intravenous infliximab at a dose of 5 mg/kg together with 10 mg of weekly oral methotrexate [5]. She received subsequent courses on weeks 2 and 6 and thereafter at bimonthly intervals.

TNF = tumor necrosis factor-alpha

UVB = ultraviolet B



[A] Large plaque-forming type of psoriasis vulgaris covering an extensive surface of the skin before treatment with infliximab.



[B] Complete resolution of the psoriatic lesions following three cycles of infliximab therapy.

Two weeks following the initial infusion of infliximab there was a remarkable improvement, with almost complete resolution of her skin lesions by the sixth week [Figure B]. She resumed her normal daily activities, reestablished social contacts, returned to her academic life as a university student, and recovered her self-esteem. After 1.5 years of infliximab therapy, the improvement in her skin and psychological status was such that she has not had to spend a single day indoors. Since the initiation of therapy she enjoys a complete clinical remission.

Comment

Over the last two decades a large body of evidence has accumulated showing that the pathogenesis of psoriasis is T cell-driven, primarily of the Th1 subtype [1,2]. Studies have shown elevated levels of interferon-gamma as well as TNFα in keratinocytes of psoriatic cutaneous lesions [1,2].

Anti-TNFα agents have the propensity to halt the progressive destructive course of rheumatoid arthritis and Crohn's disease. These agents considerably alleviate the symptoms and modify the outcome of other inflammatory rheumatic disorders, such as juvenile idiopathic arthritis, ankylosing spondylitis, psoriatic arthritis, adult-onset Still's, etc [1].

Recently, Chaduri et al. [3] reported on the pivotal role of infliximab in alleviating psoriasis. Nine of 11 patients (82%) and 10 of 11 patients (91%) who were randomly assigned to receive infliximab at dosages of 5 mg/kg and 10 mg/kg respectively (given at weeks 0, 2 and 6) showed significant improvement of the psoriatic skin lesions in comparison to only 2 patients (18%) who received placebo. Interestingly, extension of this study for 6 months on an open-label basis demonstrated that 16 of the 29 patients who received infliximab maintained a 50% improvement of their Psoriasis Severity Index score. No serious adverse reactions among the treated patients were recorded. Mease et al. [4] reported that 73% of patients treated with etanercept achieved a clinical and laboratory improvement (measured by ACR20 criteria) compared to 13% of non-treated patients. In addition to the improvement in the articular involvement, the extent of the area involved by psoriatic lesions as well as the PASI score also improved by 75% in 6 of 30 etanercept-treated patients (21%) compared to 0 of 30 of placebo-treated patients (0%). Similar results were also obtained using 5 mg/kg of infliximab (with maintenance doses of 3 mg/kg). After 10 weeks of therapy 8 patients improved by 70% (ACR70), and magnetic resonance imaging revealed an 82.5% mean reduction in inflammation from baseline with a remarkable concomitant reduction in the psoriasis area and PASI score [5].

Every year in Israel, the medical community and the public deliberate on which medications and medical services the Ministry of Health will allocate to the basket of services for the country's health providers. Unfortunately, the entitlement of patients with severe cutaneous or articular psoriasis to receive anti-TNFα therapy has not been approved. The excessive direct and indirect costs required to treat patients suffering from refractory psoriasis in the hospitals and in the community affirm the need to modify the current policy. The inclusion of anti-TNFα therapy as part of the national "health basket" is mandatory for patients such as the one described in this report. Treating this select group with anti-TNFα therapy will give many of them an opportunity to return to a normal and productive life

PASI = Psoriasis Severity Index

References

1. Criscione LG, St. Clair WE. Tumor necrosis factor-α antagonists for the treatment of rheumatic diseases. *Curr Opin Rheumatol* 2002;14:204–11.
2. Ritchlin C, Haas-Smith SA, Hicks D. Patterns of cytokine production in psoriatic synovium. *J Rheumatol* 1998;25:1544–52.
3. Chaudhari U, Romano P, Mulcahy LD, et al. Efficacy and safety of infliximab monotherapy for plaque-type psoriasis: a randomised trial. *Lancet* 2001;357:1842–7.
4. Mease PJ, Goffe BS, Metz J, et al. Etanercept in the treatment of psoriatic arthritis and psoriasis: a randomised trial. *Lancet* 2000; 356:385–90.
5. Antoni C, Dechant C, Lorenz HM, et al. Open-label study of infliximab treatment for psoriatic arthritis: clinical and magnetic resonance imaging measurements of reduction of inflammation. *Arthritis Rheum* 2002; 47:506–12.

Correspondence: Dr. A. Rubinow, Chief of Rheumatology Unit, Hadassah University Hospital, P.O. Box 12000, Jerusalem 91120, Israel.
Phone: (972-2) 677-7317
Fax: (972-2) 643-9080
email: arubinow@hotmail.com