

Etanercept Therapy of Psoriatic Arthritis in a Patient with Liver Cirrhosis

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Sir,

Psoriatic arthritis (PA) represents a hyperproliferative, seronegative arthritis closely associated with psoriasis vulgaris (PV) which affects up to 5–30% of patients and is most prevalent in these with severe skin disease. PA is a chronic and relapsing inflammatory disease that usually requires systemic treatment (1). Although many effective treatment options exist, such as methotrexate (MTX), corticosteroids or cyclosporin A, there is need for alternative medications, especially in patients with liver cirrhosis. Aberrant regulation of tumour necrosis factor- α (TNF- α) seems to be involved in the development of PV and PA (2); therefore, recent intervention strategies have incorporated biological agents that specifically target TNF- α (3). Until now no data were available concerning the successful therapy of patients with PA and liver cirrhosis with etanercept.

CASE REPORT

We report here a 53-year-old man suffering from hereditary α_1 -antitrypsin-deficiency resulting in micronodular liver cirrhosis and emphysema, as well as non-insulin-dependent diabetes mellitus. The patient had a 30-year history of psoriasis and a 15-year history of painful swollen joints. PA was diagnosed by means of scintigraphy and radiological examination, affecting mainly the distal interphalangeal joints of digitus II and III of the left hand and digitus IV and V of the right hand. Five years earlier, systemic treatment with MTX and topical therapy with corticosteroids and vitamin D derivatives were initiated. Due to a considerable elevation of liver enzymes, treatment with MTX was discontinued after 3 months. Given the increasing pain and the progressive deformation and functional impairment of the affected joints, we first started with the monoclonal TNF- α antibody infliximab, 5 mg/kg body weight. The patient reached the American College of Rheumatology preliminary criteria for improvement (ACR 20), i.e. a 20% reduction in tender and swollen joint counts and fulfillment of at least three of five defined criteria concerning disablement, global assessment of the patient and physician, diminution of

pain and C-reactive protein (CRP) level. Even though the patient demonstrated a clear serological and clinical benefit after five well tolerated cycles of infliximab therapy, the therapeutic regime had to be modified due to discontinued financing by the Health Maintenance Organization (HMO). The patient thus received 25 mg etanercept by subcutaneous injection twice weekly for a period of 12 weeks. The therapy was complemented by topical treatment with urea-containing ointments. Although this treatment did not result in additional reduction of the psoriasis area severity index (PASI) score (19.2 at week 0 to 21.0 at week 12), he maintained a significant clinical improvement compared with the PASI score of 61.4 before treatment with infliximab. Moreover, subjective and objective joint affection remained cured. After 12 weeks of treatment with etanercept, transaminases, CRP and erythrocyte sedimentation rate (ESR) were not increased (Table I).

DISCUSSION

Etanercept represents a novel fusion protein consisting of the extracellular ligand-binding domain of the 75-kDa receptor for TNF- α and the constant domain of human IgG1. The central mechanism of action of etanercept lies in the competitive inhibition of soluble TNF- α . Elevated levels of TNF- α are found in psoriatic skin lesions and in synovial fluid of joints affected by PA, as well as in synovial fluid of joints of patients with rheumatoid arthritis (RA) (2, 4, 5).

TNF- α levels have been shown to correlate with disease severity and decrease after effective therapy of psoriasis (6). Physiologically, TNF- α plays a critical role in the activation of the innate and acquired immune responses, yet the sustained release of TNF- α leads to chronic inflammation, tissue damage and excessive keratinocyte proliferation (7). Consequently the employment of potent inhibitors of TNF α , such as etanercept, has been shown to be effective in the treatment of psoriasis, particularly PA (8).

Table I. Serological parameters during therapy with etanercept

Parameter	Time after start of therapy (weeks)					
	Start	2	4	8	10	12
GOT (U/l) (0–50)	55	40	47	53	49	72
GPT (U/l) (0–50)	70	54	56	70	60	76
GGT (U/l) (0–50)	158	124	132	183	155	141
CRP (mg/dl) (0–0.5)	0.9	0.7	0.8	1.0	1.0	0.8
ESR (mm/h)	16/27*	21/32	–	15/25	20/40	20/26

GOT, glutamic oxaloacetic transaminase; GPT, glutamic pyruvic transaminase; GGT, gamma glutamyl transpeptidase; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

*ESR in mm per hour for the first and second hour, respectively.

In recent investigations on patients with psoriasis or PA who received placebo or etanercept a significant benefit to patients receiving etanercept was demonstrated (9, 10). The use of etanercept has been licensed for the therapy of PA by the American Food and Drug Administration (FDA) and the European Agency for the Evaluation of Medical Products (EMA) since 2003 (3).

In our patient with PA, MTX as a therapy of first choice was contraindicated due to his liver cirrhosis. The single use of standard disease-modifying anti-rheumatic drugs resulted in rapid progression of joint destruction and increasing disablement of the patient. Therefore, treatment with TNF- α inhibitors seemed to be one favourable alternative therapy for this patient.

Etanercept can be safely combined with other systemic and topical agents to augment efficacy in severe recalcitrant psoriasis (11) and has even been found to be of therapeutic use for severe alcoholic or viral hepatitis (12, 13). Known adverse events of etanercept are infections of the upper respiratory tract. Rarely reported adverse events are injection site reactions, haematological disorders, central nervous system demyelination and an increase of discoid lupus erythematoses (14, 15). The sudden and unusually rapid development of squamous cell carcinomas in seven patients with RA within the first 2–4 months of starting etanercept therapy has also been reported (16). However, long-term experience in patients with RA treated with etanercept found malignancies in only 17 of 1197 patients analogous to age-matched controls (17). Moreover, few patients developed anti-etanercept antibodies or autoantibodies, e.g. antinuclear, anti-DNA or anticardiolipin antibodies (15).

Our patient was treated with etanercept without the incidence of any objective adverse reaction throughout therapy. Interestingly, his psoriasis skin showed a far better response to infliximab therapy than with etanercept therapy based on improvement of PASI score. However, his PA improved with both infliximab and etanercept regimes.

To the best of our knowledge, this is the first case report about the successful therapy of a patient with PA and liver cirrhosis with etanercept. The improvement of the PA without increase of transaminases was remarkable.

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