Severe Exacerbation of Psoriatic Arthritis During Treatment with Efalizumab. A Case Report

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Sir,

Efalizumab is a humanized IgG antibody, directed against CD11a, and has been approved for the treatment of plaque-type psoriasis. Psoriatic arthritis is a co-existing morbidity present in approximately 11% of patients with psoriasis (1), but clinical trials with efalizumab have not shown any beneficial effect on psoriatic arthritis. Safety data on arthropathy from over 3000 patients was presented recently and showed no increased incidence of arthropathy in patients treated with efalizumab compared with placebo (2). Here we present a case of severe exacerbation of psoriasis arthritis that developed during treatment with efalizumab.

CASE REPORT

A 38-year-old man presented with a 20-year-history of moderate to severe plaque-type psoriasis affecting the scalp, genitals, nails and predilection sites on the body and extremities. The patient had been treated previously with topical steroids, vitamin D3-analogues, phototherapy, tar and systemic retinoids, all without sufficient effect or with rapid relapse after stopping treatment. Methotrexate treatment was abandoned because of repeating incidences of elevated liver enzymes. At the time when treatment with efalizumab was initiated the patient had a psoriasis area severity index (PASI) score of 13.5 and no symptoms of arthritis.

Treatment with injections of efalizumab (Raptiva®) 100 mg (1 mg/kg body weight) subcutaneously weekly was well tolerated, with only a transient incidence of headache and a papular eruption during the first 2 weeks of treatment. The initial response was good, with reduction in PASI score from 13.5 to 6.5 after 12 weeks’ treatment.

Thirteen weeks after efalizumab treatment had been initiated the patient complained of acute onset of pain and joint stiffness in his lower back, feet, knees, left wrist and fingers. Objectively, the patient presented with synovitis in the feet, knees, left wrist and several distal interphalangeal joints of the fingers (Fig. 1). Laboratory tests showed elevated erythrocyte sedimentation rate >100 mm/h, C-reactive protein 70 mg/l and a slight mononcytotic leukocytosis of 11.5×10^9/l. All other blood samples, including rheumatoid factor, anti-nuclear antibodies screening and serum uric acid level were within normal limits. Bone scintigraphy showed increased activity in several of the distal interphalangeal joints of the hands and feet, both knees and left wrist (Fig. 1). Synovial fluid from the knees was sterile.

Efalizumab treatment was stopped and replaced with low-dose methotrexate (7.5 mg weekly) and a non-steroidal anti-inflammatory drug. The patient did not improve during the next 2 weeks and therefore treatment with oral prednisolone (50 mg daily) was initiated together with intra-articular steroid injections in both knees. The patient improved only moderately and was therefore finally treated with intravenous infliximab 500 mg (5 mg/kg body weight) i.v. at week 0, 2 and 6. The clinical response to infliximab treatment was good and prednisolone was gradually reduced and all laboratory tests returned to values within the normal limits. The patient was then finally able to return to work, after a 2-month period, during which he had been off sick due to his arthritis symptoms.

DISCUSSION

Our patient fulfilled the characteristics for the diagnosis of psoriatic arthritis according to the classic description by Moll & Wright (2) based on the findings of a rheumatoid factor negative, asymmetrical polyarthritis with involvement of the distal interphalangeal joints and the relationship to psoriasis. Psoriatic arthritis occurs in approximately 11% of patients based on self-reporting (1) but prevalences as high as 30% have been reported (3). Recently, safety data on joint complaints from nine placebo-controlled and open-label efalizumab clinical trials comprising more than 3000 patients showed that arthropathy does occur during efalizumab treatment, but not with a higher incidence than in the placebo-treated patients.

The question arises as to whether the exacerbation of psoriatic arthritis in our patient and treatment with efalizumab was a coincidence or not. Our patient had had a 20-year history of psoriasis, previously only with minimal joint symptoms, and therefore we suspect that his arthritis was severely aggravated by the efalizumab treatment. Due to the severity of the symptoms an attempt to rechallenge would be unethical. A possible association between efalizumab treatment and arthritis


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in patients with pre-existing joint symptoms is in accordance with the recently presented, safety data demonstrating a higher incidence of severe grade arthropathy in efalizumab-treated patients, with pre-existing joint symptoms, compared with placebo-treated patients. However, these data presented on posters\(^1,2\) (not in the abstracts) were non-significant, indicating that if an association exists it is a rare event.

Efalizumab is directed against CD11a on lymphocytes and targets psoriasis pathogenesis at several levels, including the prevention of T-cell binding to endothelial cells thereby blocking T-cell traffic out of the circulation and into the skin\(^4\). This increases the number of lymphocytes in the circulation, as observed in the clinical trials, and also in our patient. It is possible that this increased number of circulating T-cells, during efalizumab treatment, is directed towards another compartment, the joints, where other homing receptors mediate tissue entry and thereby could provoke worsening of psoriatic arthritis.

Even though the overall incidence of psoriatic arthritis does not seem to be increased during efalizumab treatment, preliminary data suggest that severe arthritis occurs more frequently in efalizumab-treated patients compared with placebo. In our case we were forced to discontinue efalizumab treatment because of the severity of the symptoms and instead use another biological agent with effect on psoriatic arthritis.

REFERENCES


Fig. 1. Hand with plaque-type psoriasis and joint swelling in the wrist and in the distal interphalangeal joints of the II, III and IV fingers (left). Corresponding picture from the bone scintigraphy demonstrating increased activity in the clinically involved joints (right).