Anti-tumour necrosis factor treatment in a patient with anorexia nervosa and juvenile idiopathic arthritis

J Barber, T Sheeran, D Mulherin

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Tumour necrosis factor α (TNFα) is believed to have a pivotal role in the pathogenesis of many forms of inflammatory arthritis, and anti-TNFα therapies are now licensed and recommended for the treatment of refractory rheumatoid arthritis and juvenile idiopathic arthritis (JIA).[1 2] An important role for TNFα in the pathophysiology of anorexia nervosa has also been postulated, although authors differ on the precise mechanisms underlying its role.[3] Some authors have suggested that TNFα may be mediating a stress response, whereas others have proposed that raised levels of TNFα in these patients may be secondary to anorexia rather than a cause.[4 5] Although the role of anti-TNFα therapies in the management of inflammatory arthritis is well recognised, we are not aware of experience with the use of anti-TNFα treatment in the management of anorexia nervosa. We describe the effect of such treatment prescribed to a woman with refractory JIA and anorexia nervosa.

CASE REPORT

A 28 year old woman with JIA had a disease activity score of 6.68 despite continuing treatment with weekly methotrexate, 10 mg orally.[6] She originally presented to rheumatology care at age 14 years with a nine year history of pain, swelling, and stiffness of the small joints of the hands, wrists, temporomandibular joints, and feet, leading to significant deformity and disability. At that time, her height (151 cm) was on the 50th centile and her weight (30 kg) on the 3rd centile.[7] Family habitus was described as thin. Rheumatoid factor was positive, antinuclear antibody was negative, the C reactive protein was raised (36 mg/l), and an ophthalmological review was normal. Intensive physiotherapy and non-steroidal treatment were instituted.

Her arthritis remained well controlled over the next two years. She gained 5 cm in height but only 1.8 kg in weight, and was noted to eat very little but denied drug or laxative abuse or self induced vomiting. The psychiatric service diagnosed a somewhat unusual presentation of anorexia nervosa with eating phobia and a feeling of being unattractive but at the same time a desire to be heavier. Recent stresses at home and at college were noted, but no psychotic features were identified. She received family therapy and had a spell of inpatient care for anorexia over the subsequent 18 months. Her arthritis remained inactive and her jaw malocclusion was surgically corrected, with improvement in her appearance.

At age 22 years, her arthritis flared with prolonged morning stiffness, swelling, and increasing deformity of hands, wrists, elbows, and knees. Weekly oral methotrexate treatment was instituted, but her arthritis remained problematic and she required several intra-articular injections over the ensuing years. At age 24 years her weight was 33.8 kg, and she was admitted again for treatment of her eating disorder, but with little increase in weight ensuing. At age 27 years her weight had fallen from a peak of 33.9 kg to 32 kg, with evidence of active arthritis, increased articular deformity, and functional deterioration despite increased methotrexate treatment. At age 28 years, with evidence of active disease despite methotrexate treatment, and weighing 29 kg, infliximab treatment was instituted. Within two weeks, her mood improved, as did her appetite, and improvement in her articular symptoms was also seen: five months after starting treatment, her weight had risen to 31.5 kg, an 8% increase over her pretreatment weight.

DISCUSSION

Anorexia nervosa is a severe eating behaviour disorder, characterised by weight loss below 85% of the expected body weight, amenorrhoea, and a distorted body image with associated significant morbidity and mortality.[8] It can be distinguished from the constitutional weight loss seen in inflammatory arthropathies by the associated behavioural and perceptual changes relating to food and body image. Clearly, other important causes of weight loss in these patients include occult infection and malignancy or simply the anorexia related to nauseating treatment. TNFα was originally described as "cachexin", and severe inflammatory arthritis is known to be associated with both cachexia and raised TNFα.[9 10] TNFα has also been postulated to play an important part in the development of anorexia nervosa.[3] Profound anorexia and pathological weight loss were certainly major features of this patient's disease. Although she satisfied criteria for a diagnosis of anorexia nervosa, it is clearly possible that some of her anorexia stemmed from her underlying inflammatory joint disease: it is impossible to separate these two processes. However, she exhibited abnormal eating behaviour even at times when her arthritis was clinically quiescent, suggesting that her arthropathy alone was not the exclusive cause of her arthritis. Her preliminary response to infliximab raises the intriguing possibility of a new treatment for the potentially life threatening disorder of anorexia nervosa. This clearly warrants further evaluation.

Authors' affiliations
J Barber, T Sheeran, D Mulherin, Department of Rheumatology, Cannock Chase Hospital, Brunswick Road, Cannock, WS11 2XY, UK

Correspondence to: Dr D Mulherin;
diarmuid.mulherin@msgh-tr.wmids.nhs.uk

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Transient joint effusion: a forgotten side effect of high dose corticosteroid treatment

F Schiavon

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Pulse therapy with high doses of corticosteroids, although generally well tolerated, is associated with a variety of side effects, sometimes life threatening but, more often, mild. Among these, joint manifestations are only rarely encountered. Patients sometimes feel transient arthralgias, but the development of synovial effusion is exceptionally reported.

We described the case of a woman with systemic lupus erythematosus (SLE) and nephritis who developed a transient bilateral knee synovial effusion during pulse therapy with a high dose of corticosteroids.

CASE REPORT

A 62 year old woman was admitted to our division because of SLE with nephritis. Eight months before the admission, in April 2000, she developed arthritis in the last four toes of the left foot. She was treated with non-steroidal anti-inflammatory drugs, with complete remission. Serological findings showed a raised erythrocyte sedimentation rate (ESR) of 52 mm/1st h, normal C reactive protein, and a decrease in total protein and albumin. Three months later laboratory features showed an increase in ESR (62 mm/1st h), fibrinogen (4.4 g/l), proteinuria (5 g/24 h), and haematuria (>5 red blood cells (RBC)/high power field), with normal renal function and a decrease in total protein and albumin and the presence of antinuclear (ANA) and anti-Sm antibodies. Therefore she was admitted to our division where she had a kidney biopsy, which showed a mesangioproliferative glomerulonephritis (WHO class III). After four months of inadequate response to traditional treatment, she started monthly pulse corticosteroid therapy (1 g methylprednisolone for three days) before immunosuppressive drugs.

At admission we did not observe any arthritis. On the evening of the second day of pulse steroid therapy, after a short walk, she complained of pain and flexion discomfort to both knees, which a physical examination showed were swollen. Thus, an arthrocentesis was performed with aspiration of synovial fluid (5 ml from the right and 6 ml from the left knee). Synovial fluid analysis showed a colourless fluid, with high viscosity and excellent mucin clot formation (fig 1). A leucocyte count disclosed only 1 mononucleate cell/mm^3 in the right knee synovial fluid and no cells in the left. No crystals were identified by light or compensated polarised microscopy. Inflammatory laboratory measurements carried out simultaneously were unchanged. Radiographs of the affected joints showed normal aspects. Effusion resolved with arthrocentesis and did not recur during admission to hospital.

Figure 1 Synovial fluid analysis showing mucin clot formation.

DISCUSSION

A transient non-inflammatory joint effusion was described for the first time by Woods *et al*[1] in a patient treated with high dose corticosteroids for the management of renal transplantation, but the characteristics of this effusion were not reported. In other cases of patients treated for renal transplant rejection or lupus nephritis in whom analysis was performed, the synovial fluid was a light yellow or colourless fluid with normal viscosity, low leucocyte count, and lymphocyte or monocyte predominance.[2 3] MacFarlane *et al* studied the relation between corticosteroid treatment and effusion in patients treated for renal transplantation, by joint radiography, bone scan, and synovial biopsy.[4] Because these examinations were always normal, it was postulated that the effusion might result from steroid induced transudation of fluid across synovial capillary walls. A transient synovial fluid knee effusion with the same characteristics was also noted by Lally in 28.3% of patients with chronic obstructive pulmonary disease treated with high dose corticosteroids or during withdrawal from such treatment.[5]