Rheumatology 2002;41:114–116

Scintigraphic evidence of effect of infliximab on disease activity in ankylosing spondylitis

Sir, Disease suppression in ankylosing spondylitis (AS) has always proved difficult to achieve. Sulphasalazine has been shown to be of value in treating patients with persistent peripheral arthritis [1]. Recently, high-dose intravenous azathioprine has been used in active axial disease with some success [2] but the toxicity margin of such treatment gives cause for concern. The primary objective of treatment remains the relief of symptoms using a variety of anti-inflammatory drugs and the maintenance of spinal and peripheral joint mobility by physiotherapy.

However, the beneficial effects of anti-tumour necrosis factor α antibody (infliximab) for the treatment of AS have been reported recently in two studies [3, 4] which strongly suggest that this therapy is very effective in the short-term management of AS and holds some promise that long-term disease suppression can be achieved.

In this report we discuss a patient with active AS who demonstrated substantial objective evidence of improvement following intravenous infusions of infliximab.

A 47-yr-old man with an 11-yr history of seronegative HLA B27-positive spondylarthitis whose disease was recalcitrant to a variety of disease-modifying anti-rheumatic drugs (DMARDs), including sulphasalazine, methotrexate and systemic corticosteroids, presented to us with recurrent low back, neck and chest pain and stiffness. Characteristically, the symptoms were worse in the early morning and after rest and were relieved on activity.

Examination revealed tenderness at costochondral joints in addition to pain and tenderness over the iliac crests and ischial tuberosities. Tenderness was also elicited over the right wrist, right shoulder and left ankle joints and on sacroiliac compression. Finger–floor distance was 45 cm, tragus–wall distance 15 cm and chest expansion 5 cm. There was no history of iritis, cardiac or neurological defects, inflammatory bowel disease or psoriasis.

Laboratory data showed an erythrocyte sedimentation rate (ESR) of 91 mm/h, C-reactive protein 38 mg/l and plasma viscosity 2.04 cP. Tests for rheumatoid factor and anti-nuclear antibodies were negative. Previous X-rays showed bilateral sacroiliitis but no evidence of ascending spondylitis. 99mTc-MDP (methylenediphosphonate) bone scanning performed 1 yr previously revealed multiple areas of increased tracer uptake in the cervical, lower dorsal and lumbar spine, left ischial tuberosity, left sternoclavicular joint and a few small areas of uptake along the sternum. A current 99mTc-MDP bone scan revealed similar but more intense pathological uptake along most of the spine and the left ischial tuberosity, and peri-articular uptake in all small joints of the feet. The appearances were strongly suggestive of metastatic bone disease. However, the abnormal uptake in the sternoclavicular joints had moved to the right side and less activity was seen in the left sternoclavicular joint than in the previous scan. This change, together with the distribution of the lesions and the clinical impression, were thought to be more consistent with inflammatory lesions than with metastatic deposits (Fig. 1).

Because of the relatively widespread appearance of arthritic/enthesitic lesions on the bone scans and to further rule out the possibility of metastatic lesions, 99mTc-2-methoxyisobutylisonitril scintigraphy, a novel tumour-detecting imaging agent, was performed and showed no uptake in the lesions demonstrated on the bone scan. This method has recently been established as having a high negative predictive value of 88% in excluding musculoskeletal tumours [5].

Treatment with three infusions of infliximab at weeks 0, 2 and 6 was given at 5 mg/kg, following which the inflammatory markers showed considerable improvement (ESR 18 mm/h, C-reactive protein <10 mg/l and plasma viscosity 1.77 cP). The symptomatic improvement was less impressive. However, examination revealed no tenderness over the previously tender areas, a finger–floor distance of 35 cm and a tragus–wall distance of 12 cm, and chest expansion was unchanged at 5 cm.

The most noticeable change was in the 99mTc-MDP bone scan, which was performed 5 weeks after the last infusion and revealed remarkable improvement, with disappearance of most lesions of the spine, sacroiliac joints, iliac crest, tibial tuberosity and both feet and reduced uptake in the other areas (Fig. 2).

These findings are supportive of previous reports that infliximab is effective in ankylosing spondylitis [6] as well as being effective in other forms of inflammatory arthritides, such as rheumatoid arthritis. We feel they are a graphic demonstration of the potential role for this therapy in AS. Its anti-inflammatory and possibly disease-suppressing mode of action in AS remain to be determined, but it is interesting to note that AS is generally unresponsive to treatment with corticosteroids and other DMARDs, a feature in which it differs
clearly from RA. The pathophysiological basis of this unresponsiveness is still unclear.

Although $^{99m}$Tc-MDP bone scanning is non-specific, it has a well-established value in the evaluation and diagnosis of symptomatic AS [7] and may reveal evidence of sacroiliitis or spinal involvement many months or even years before there are any X-ray changes. To our knowledge, there are no reports of the use this diagnostic aid as a simple, reliable and cost-effective method of monitoring and evaluating the response of patients with AS to infliximab therapy and comparing its sensitivity, reliability and accuracy with those of more sophisticated methods, such as MRI scanning, in the follow-up of such patients.

The potential long-term benefits of and response to infliximab therapy in AS, and its pharmacokinetics and safety, remain to be seen.

A. HADI, P. HICKLING, M. BROWN, A. AL-NAHHAS
Departments of Rheumatology and Nuclear Medicine, Derriford Hospital, Derriford Road, Plymouth PL6 8DH, UK
Accepted 26 June 2001
Correspondence to: P. Hickling.


© 2002 British Society for Rheumatology