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CASE REPORT

Osteonecrosis and monoarticular rheumatoid arthritis treated with intra-articular adalimumab

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Abstract We report a 54-year-old patient with RA presented with osteonecrosis (ON) and monoarthritis of left knee remitting in the last 2 years. Monoarthritis was resistant to disease-modifying antirheumatic drugs (DMARDs) and intra-articular corticosteroids. Intra-articular administration of adalimumab provided a good clinical and radiographic response. Synovitis resolved and osteonecrosis disappeared almost totally.

Keywords Monoarticular rheumatoid arthritis · Osteonecrosis · Adalimumab

Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory disorder that may cause destructive joint disease related with significant disability and increased mortality. The pathogenesis of the disease is multifactorial. In vitro studies have confirmed the critical and potent role of several inflammatory cytokines in the rheumatoid synovium. These inflammatory mediators promote bone and cartilage destruction and provide important therapeutic targets for intervention in RA. Tumor necrosis factor alpha (TNFA) is an important cytokine in the pathogenesis of RA. Interleukine-1 (IL-1) and TNFA are both present in synovial fluid of patients with RA and provide an inflammatory signal to the synovium [1]. Many studies indicate that TNFA is primarily responsible for the proliferative phase of the disease [2]. The efficacy of the anti-TNFA agents in RA is well established [3]. The efficacy and safety of intra-articular administration of anti-TNFA agents in patients with RA have been reported [4, 5]. We report a case with persistent monoarticular RA and osteonecrosis (ON) in whom a significant clinically and radiologically regression has been achieved after administration of two doses of intra-articular adalimumab.

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Case report

The patient, a 54-year-old male, was diagnosed as having RA according to ACR criteria in 1992. In January 2006, he presented with monoarthritis of the left knee remitting in the last 2 years. He had been treated with methylprednisolone 4 mg/day and methotrexate 15 mg/week since 1998 and leflunomide 20 mg/day has been added to therapy 2 years ago. On physical examination, he had chronic non-erythematous arthritis of the left knee. Aspiration of the joint fluid showed a white blood cell (WBC) count of 20,000 without any evidence of crystals or infection. Laboratory investigation was performed; erythrocyte sedimentation rate (ESR) was 54 mm/h, C-reactive protein (CRP) was 12 mg/dl, and rheumatoid factor (RF) was positive. PPD was negative and direct radiography of the lungs was normal. Radiographic imaging of both knees showed the presence of narrowing, cysts, and erosion of the left knee. Magnetic resonance imaging (MRI) was performed and large effusion, synovial proliferation and evidence of avascular necrosis of the left knee was confirmed (Fig. 1).

High-resolution ultrasonography of the left knee and suprapatellar bursa revealed a large effusion and synovial

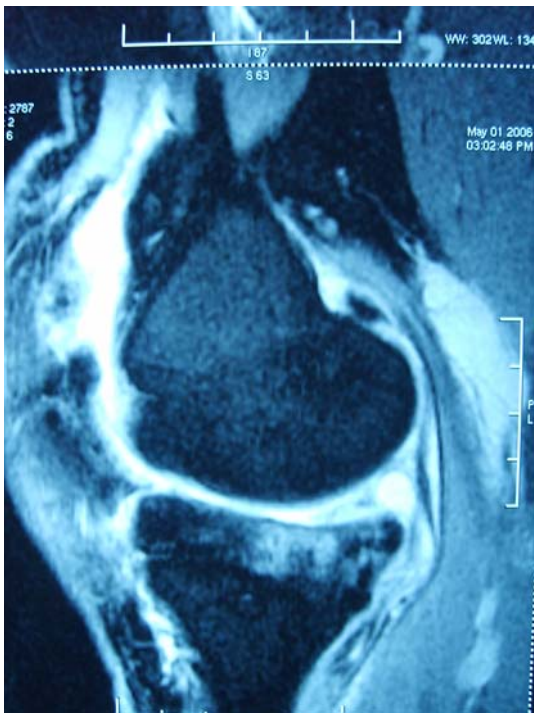

Fig. 1 MRI of the left knee showed effusion, synovial proliferation, and avascular necrosis before intra-articular adalimumab therapy

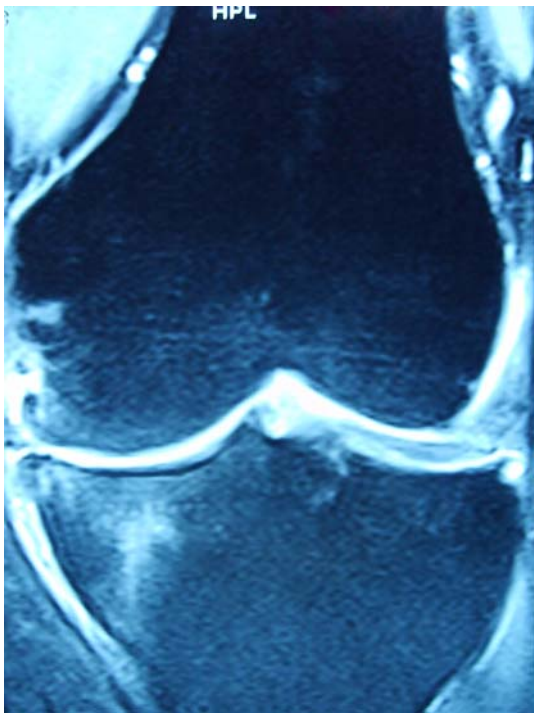

Fig. 2 MRI of the left knee after intra-articular adalimumab therapy showed regression of effusion and osteonecrosis. Synovial proliferation remained

proliferation. Despite intra-articular corticosteroid injection and systemic treatment, our patient had active monoarticular disease with increased acute phase reactants and avascular necrosis of the same knee. Intra-articular adalimumab (40 mg) was administered under ultrasound guidance. Within 1 week of intra-articular injection of adalimumab, the patient experienced complete and total relief of pain and stiffness. Physical examination revealed decreased left knee effusion and normal range of motion. ESR and CRP decreased to normal value. The physical disability associated with synovitis also resolved. After 15 days, second intra-articular adalimumab injection was administered. One month later, control MRI was performed and suprisingly healing of osteonecrosis was seen (Fig. 2). There were no complications or adverse events reported, although the synovial thickening persisted. He had now been symptom-free for 3 months since receiving the second injection.

Discussion

We report a case with remitting monoarticular RA and ON who responded well to intra-articular injection of adalimumab. Within a week, all symptoms and following parameters returned to normal. Interestingly, avascular necrosis also disappeared on control MRI. To our knowledge, this is the first report of intra-articular adalimumab administration for remitting monoarticular RA and avascular necrosis in literature. Treatment of remitting monoarticular RA, resistant to disease modifying antirheumatic drugs (DMARDs) and glucocorticoids, with intra-articular anti-TNFA appears to be a promising and alternative option. The efficacy and safety of intra-articular administration of infliximab and etanercept in patients with RA have been reported. Arnold et al. showed the efficacy of intra-articular etanercept injection in a patient with persistent monoarticular RA [6]. Bliddal et al. showed the efficacy and safety of etanercept injection into arthritic joints in a randomised, controlled study [4, 5].

ON frequently develops in patients with RA and closely related with long-time cortcosteroid treatment. The pathogenesis of ON is multifactorial. Corticosteroids decrease bone blood flow, thereby enhancing ischemia owing to increased bone marrow pressure produced by intra-medullary lipocytes hypertrophy [7]. The role of the cytokines including TNFA in the pathogenesis of ON is not fully understood. TNFA may act to increase the recruitment, proliferation and differentiation of osteoclast progenitors [8, 9]. The mechanism of action of adalimumab on necrotic tissue in osteonecrosis is unknown. The possible theory is local effect of drug. Adalimumab may penetrate to cartilage tissue through pumping mechanism. The other possible way is through blood stream after resorbtion in

synovium. If the latter is the case, systemic administration of adalimumab may also be effective in the treatment. In our patient, ON responded well to intra-articular adalimumab administration showed with control MRI. The application of anti-TNFA in the treatment of osteonecrosis is promising, however further clinical studies on efficacy and safety are needed.

In conclusion, intra-articular adalimumab administration provided a dramatic clinical and radiographic regression in our patient with ON and remitting monoarthritis due to RA. Adalimumab given as intra-articular injection might be a good alternative to steroids in monoarthritis resistant to DMARDs.

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