Stress fracture in long term methotrexate treatment for psoriatic arthritis

M Wijnands, A Burgers

Case history
A 42 year old woman presented at the outpatient rheumatology department with severe, incapacitating pain of her left leg. There was no previous trauma. The patient did not recall fever or malaise.

Psoriasis had been diagnosed at age 17 years. Initially, topical drugs were prescribed. Periodically etretinate, a synthetic analogue of retinoid acid, and photochemotherapy were prescribed as additional treatment. The patient did not receive cyclosporin. Oligoarthritis of her knees and ankles first appeared at an age of 25 years. Management with non-steroidal anti-inflammatoriy drugs and sporadically an intra-articular injection of corticosteroids was adequate to control the symptoms. At age 37 a severe polyarthritis of elbows, wrists, finger joints, ankles, and metatarsophalangeal joints developed. Treatment with methotrexate (MTX) was started at an initial dose of 7.5 mg weekly, resulting in a good clinical response. Two years later the dosage was gradually increased to 20 mg weekly because of a flare.

On examination there was little pretibial oedema with tenderness of the distal tibia, especially at the lateral margin. There was an active arthritis of the left knee, wrists, metacarpophalangeal and proximal interphalangeal joints. A cardiorespiratory examination was unremarkable and the patient was afebrile. Laboratory investigations showed a slight increase in erythrocyte sedimentation rate of 20 mm/1st h. Full blood count, renal and hepatic function, creatine kinase, calcium, serum protein electrophoresis, thyroid stimulating hormone, parathyroid hormone, and vitamin D were all normal. Urine analysis was negative.

Standard anteroposterior and lateral x ray pictures showed no abnormalities on either tibia or fibula. Technetium-99m (99mTc) scintigraphy disclosed a longitudinal hot spot in the middle third of the tibia on the left (fig 1). Computed tomography showed a clear longitudinal fissure with minimal displacement and starting callus formation (fig 2). Bone mineral density (BMD) measured by dual x ray absorptiometry of the lumbar spine and femoral neck showed no manifest osteoporosis.

Treatment was started with a Sarmiento brace. As an MTX related stress fracture was considered, the MTX dosage was tapered to 7.5 mg weekly and within weeks the symptoms of the left tibia evanesced. Unfortunately, the arthritis symptoms flared and an intramuscular injection of a depot corticosteroid was given. A few months later pain on weight bearing emerged in the right foot. Repeated bone scintigraphy showed a normal left tibia, but new lesions in the right midfoot and the fifth rib at the right. An x ray examination showed a fracture of the 2nd and 3rd metatarsal bone and of

Figure 1 Technetium-99m scintigram (anterior view, delayed image) of the legs. Longitudinal hot spot in the middle third of the tibia.

Figure 2 Computed tomography of the left tibia. Fissure with minimal displacement and starting callus formation.
the rib mentioned. MTX was stopped. Thereafter the pain of the right foot diminished very slowly. Again an increase of the arthritis was noticed, and azathioprine was prescribed. This drug had to be discontinued after a few days owing to severe gastrointestinal complaints. Subsequently, hydroxychloroquine was prescribed, which was stopped because of an itching dermatitis. Then, a relaunch with a low dose MTX (7.5 mg weekly) was performed. After a follow up period of four months, no recurrence of a stress fracture has been noticed. The arthritis activity is regarded as modest, but acceptable for the patient.

Discussion
Stress fractures are a well recognised complication in arthritic patients. Osteopenia (juxta-articular or generalised, or both) caused by extensive rheumatoid involvement, corticosteroid treatment, or relative immobility is a predisposing factor. Furthermore, deformations, flexion contractures (especially valgus deformities of knees and subtalar joints) and increased mobility after arthropathies leading to increased stress on juxta-articular bone also contribute to this condition. Stress fractures in rheumatoid arthritis (RA) preferentially affect the long bones of the legs, the neck of the femur, and the pelvis.

Osteoporotic fractures associated with MTX treatment were reported for the first time in 1970 in children treated for acute leukaemia with a high dosage. This “methotrexate osteopathy” was characterised by osteoporosis, bone pain, and compression fractures, mostly occurring in the distal tibiae. When the drug was stopped the pain regressed and the fracture healed. To our knowledge Ansell et al for the first time drew attention to the occurrence of stress fractures as a possible complication of MTX treatment for non-neoplastic diseases. Since then several case reports including patients treated for psoriasis and rheumatic diseases have been published.

During MTX treatment high concentrations in arthritic patients symptoms caused by MTX on bone may be explained by di...
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