Mod Rheumatol (2005) 15:358–360
DOI 10.1007/s10165-005-0415-9

CASE REPORT

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An unusual complication of familial Mediterranean fever: protracted arthritis with bilateral coxarthrosis and intraosseous amyloidosis of femoral head

Received: March 11, 2005 / Accepted: May 30, 2005

Abstract Protracted arthritis is uncommon in familial Mediterranean fever (FMF) and rarely may result in degenerative joint damage, a well-known complication of FMF, usually affecting kidneys. We present an unusual case of FMF involving severe bilateral coxarthrosis leading to residual incapacity that was treated by total hip arthroplasty, and an unusual presentation of amyloidosis – intraosseous amyloidosis of the femoral head.

Key words Arthroplasty · Familial Mediterranean fever (FMF) · Intraosseous amyloidosis · Protracted arthritis

Introduction

Familial Mediterranean fever (FMF) is an autosomal recessively inherited disorder affecting mainly those of Jewish, Armenian, Arab, and Turkish descent. It is now being recognized that FMF also occurs in other Mediterranean populations, including Italians and Greeks.[1]

The clinical manifestations of FMF are characterized by recurrent periods of fever, peritonitis, pleuritis, arthritis, and eryspelas-like erythema (ELE).[2] The articular disease is the second most common manifestation after abdominal pain. The articular disease occurs in 70%–75% of patients and in one-third of these as the first presenting sign.[3] The most common articular attack is an acute, exquisitely painful, large joint monoarthritis usually affecting the knee or hip lasting for a few days, but protracted attacks persisting for months or even years have been reported.[4–6] The most severe complication of FMF is the development of systemic amyloidosis, ultimately leading to renal failure.[3]

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In this report we present a patient with bilateral degenerative joint damage of the hips secondary to FMF with protracted arthritis, who was finally able to be treated by bilateral total hip arthroplasty, while intraosseous amyloidosis of the femoral head was determined by biopsy.

Case report

A 23-year-old man suffering from prolonged hip pain was admitted to our department. The initial attack of the patient was abdominal pain which occurred when he was 12 years old. His first arthritis attack, lasting 3 days, occurred on the left knee in the following year. The attacks of arthritis were accompanied or unaccompanied by abdominal attacks and fever at intervals. He was already under treatment of colchicine over a period of 11 years.

The patient had been suffering prolonged hip pain for the last 2 years. In addition, during the last 6 months his daily activities were restricted due to limited movement of the hip joints.

Diagnosis of FMF was based on the criteria of Livneh et al.[7] and preoperative clinical examination based on the Harris Hip Score.[8] Total Harris Hip scores were 38 for the right hip and 42 for the left hip. Laboratory values were as follows: hemoglobin 13.7 g/dl, white blood cell count 9500/mm^3, platelet count 250000/mm^3, erythrocyte sedimentation rate (ESR) 41 mm/h, C-reactive protein (CRP) 9.02 mg/dl, rheumatoid factor (RF) and HLA-B27 were negative. Radiological examination revealed joint space narrowing, local and regional demineralization, and sclerosis (Fig. 1).

A bilateral cementless total hip prosthesis was inserted through the lateral approach 3 months later. The patient received antibiotics and low-dose heparin therapy for 5 days. At 6-month follow-up total Harris Hip Scores were assessed as 96 for the right hip and 94 for the left hip. Colchicine treatment was continued throughout the whole period. The removed femoral heads were examined histopathologically. Bilateral cementless total hip arthroplasty

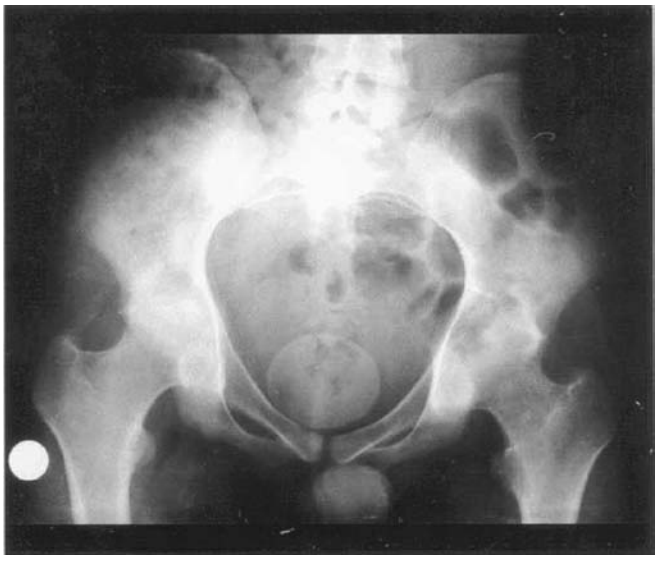

Fig. 1. Anteroposterior pelvic radiograph made before arthroplasty revealed joint space narrowing, local and regional demineralization, and sclerosis

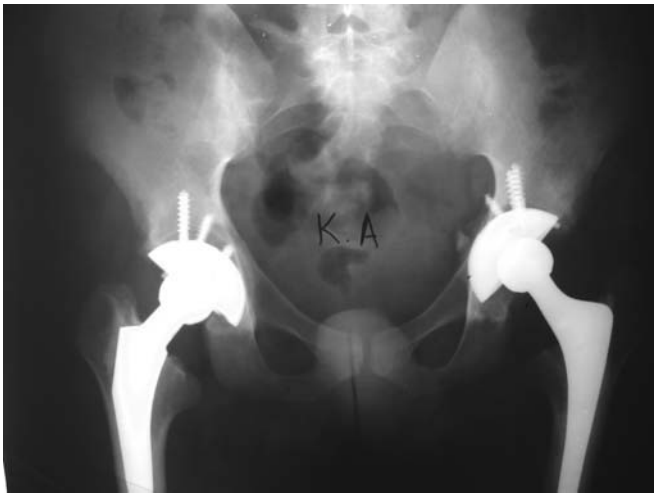

Fig. 2. Anteroposterior pelvic radiograph taken 1 year postoperatively

resulted in painless hip joints with almost a full range of motion (Fig. 2). Postoperative Harris Hip Scores were recorded. Histopathological studies that were carried out by means of crystal violet revealed chronic degenerative changes, and focal amyloidosis in vessels and in chondroid matrix (Fig. 3).

Discussion

The discovery of the gene responsible for FMF[9] has led to the development of molecular-based diagnosis, and some phenotype–genotype correlations have now been established. Among them, the most important seems to be the preferential association of amyloidosis with the M694V

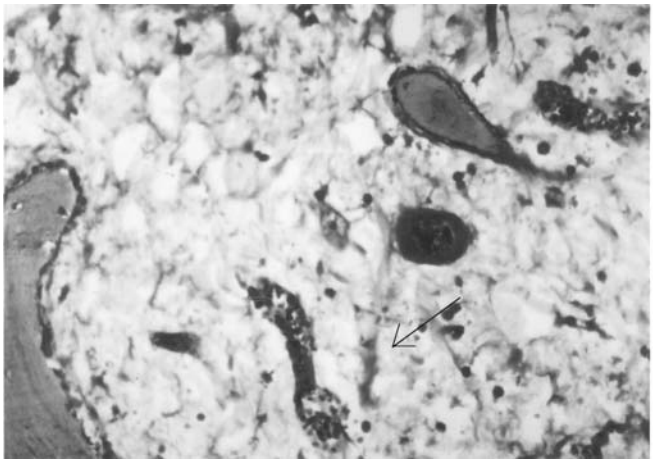

Fig. 3. Histologic findings made by means of crystal violet revealed intraosseous amyloid accumulation, which shows metachromatic staining

mutation at the Mediterranean fever gene (MEFV).[10] Nevertheless, the diagnosis of FMF still remains clinical. The disease is characterized by peritoneal (95% of cases), articular (75%), and pleural (40%) attacks.Three unique types of arthritis have been described: acute, chronic, and abortive. Acute attack represents 95% of the reported cases, and is characterized by short duration and self-limited episodes of arthritis. The second type is the abortive attack, with arthralgia as the only manifestation. Chronic arthritis which lasts more than a month accounts for 5% of cases. Effusion is often large and pain is severe. Radiologically, osteoporosis, and lytic and degenerative changes may be seen.[3] The striking feature of protracted FMF arthritis is full recovery without any sequelae, except for hip involvement.

Colchicine at a recommended dose of 1–2 mg daily can effectively prevent febrile attacks and development of amyloidosis.[11] During an acute articular attack, the drug of choice is a non-steroidal anti-inflammatory (NSAID). In a chronic disease like FMF there is no place for narcotic analgesics. The place of synovectomy in the treatment of chronic inflammatory disease is still questionable.

The most significant complication of FMF is amyloidosis, usually affecting the kidneys, which leads to nephrotic syndrome and renal failure.[11] Colchicine therapy prevents this complication and reduces the rate of mortality associated with renal failure.[11] However, in spite of the colchicine therapy our patient was observed to have protracted arthritis attacks and intraosseous amyloidosis of the femoral head. Many reports have described the deposition of amyloid in various tissues like the transverse carpal ligament, rectum and, less commonly, intraosseous locations, especially in those patients on long-term hemodialysis.[12,13] Reports of intraosseous amyloidosis in the literature are all associated with primary amyloidosis, plasma cell dyscrasias, or long-term hemodialysis patients, but our patient had none of these conditions.[14–16]

In patients who have restricted daily living activities due to degenerative arthritis with FMF, total hip arthroplasty

can be a treatment of choice. Salai et al.[17] preferred cementless prosthesis in FMF patients because loosening in time might be an indication for revision in these young patients and progression of the inflammatory process, perhaps in bone, might be a cause of loosening. In their histologic findings they pointed out progressive arterial occlusion in the synovial and capsular vessels. Even though colchicine is supposed to inhibit both of the phases of amyloidogenesis,[18] in our patient arterial occlusion is thought to stem from amyloid deposition. Recently Younes et al.[19] reported on ten patients with FMF who suffered from hip involvement, but only four of these patients had isolated FMF disease and two required hip arthroplasty. They strongly emphasized and documented the association of FMF and ankylosing spondylitis, although the pathogenic mechanisms that link these two conditions remain unknown.

In conclusion, we can expect that the age and number of FMF patients with chronic inflammatory hip joint disease who require total hip arthroplasty will increase, and research that studies the relationship between amyloidosis and chronic inflammatory joint disease should be carried out in the future.

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