Familial mediterranean fever with sacroiliac joint involvement: Report of two cases

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Özet

Ailesel akdeniz ateşi hastaliği'nda sakroiliak eklem tutuluşu: iki olgu sunumu

Az oranda görülmesi ve spondilartritler ile karıştırılabilmesi nedeniyle ailesel Akdeniz ateşi seyrinde sakroiliit gelişen iki olguyu sunmayı amaçladık. Her iki olguda da HLA-B27 testi negatif ve MEFV mutasyon analizi M694V için homozigot idi. Eklem yakınmaları düzenli kolşisin tedavisine rağmen mevcuttu. Tedavide klinik ve laboratuvar düzelmeyi sağlayabilmek için nonsteroid antiinflamatuar ilaçlarla birlikte sulfasalazin ve/veya kortikosteroid kullanılması gerekti.

Anahtar Kelimeler: Ailesel Akdeniz ateşi, Seronegatif spondilartrit, Sakroiliit, MEFV geni

Abstract

We report two cases of familial Mediterranean fever (FMF) with sacroiliac joint involvement. They had bilateral sacroiliitis and both were homozygous for M694V mutation of the MEFV gene. Both were HLA-B27 negative. There were articular symptoms despite the ongoing colchicine treatment. Sulphasalazine and/or corticosteroids are required in addition to non-steroidal anti-inflammatory drugs to achieve clinical and laboratory improvement.

Keywords: Familial Mediterranean fever, Seronegative spondyloarthropathy, Sacroiliitis, MEFV gene

Introduction

Familial Mediterranean Fever (FMF) is an autosomal recessive disease characterized by recurrent febrile peritonitis, pleuritis and synovitis. It mainly affects Turks, non-Askhenazi Jews, Arabs and Armenians. Acute, mono/oligo, transient, non-erosive, non-deforming arthritis of the large joints is a typical manifestation. Many joints may be involved subacutely or chronically. Erosive and deforming arthritis may also seen especially at hip joints and the duration of the arthritis may change from days to years (1,2) However, sacroiliac joints are rarely affected during the course of FMF (1-3). Clinical picture of sacroiliitis with FMF may change from asymptomatic cases with radiographic findings only, to lower back pain of different duration, and/or stiffness. The diversity and the nonspecificity of the various clinical manifestations of FMF can often obscure the diagnosis. To date, the identification of FMF gene and its various mutations enable the application of a noninvasive, sensitive molecular genetic testing for an accurate diagnosis. In this report, we present two cases of FMF with sacroiliac joint involvement.

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Case 1

A 29-year-old man was admitted with pain and swelling of his left knee. He was suffering from recurrent abdominal pain, fever, asymmetric arthritis and lower back pain attacks for 15 years. He gave the history of abdominal pain and fever attacks lasting for 3 or 4 days. However, arthritic attacks particularly of the knee were lasting more than one month. He also reported that arthritic symptoms were resolving with nonsteroidal anti-inflammatory drugs (NSAIDs). He has been diagnosed as FMF fourteen years ago. He has been on colchicine treatment regularly since the time of diagnosis until 1995. The frequency of the attacks was four or six times in a year prior to the initiation of colchicine treatment. Under colchicine treatment, the frequency of attacks was decreased to one or two in a year. Two years after the discontinuation of colchicine, abdominal pain attacks have begun. Also, there were complaints of intermittent low back pain which are unrelated to abdominal pain attacks. He gave no history of uveitis, upper respiratory tract or urinary tract infection and diarrhea on admission.

Physical examination revealed no restriction in lumber movements. Schober test was 5.5 cm. Sacral compression, Mennel and Patrick-Fabere tests were all positive. Other joint examinations were normal. His

chest expansion was 2.5 cm at the nipple line.
Complete blood count, urine examination, peripheral blood smear, routine biochemistry and chest roentgenogram were all normal. He was negative for rheumatoid factor and antinuclear antibodies. HLA-B27 was either negative. Pelvic x-ray revealed grade 3 sacroiliitis with evident subchondral sclerosis in both iliac and sacral margins, and narrowing in 1/3

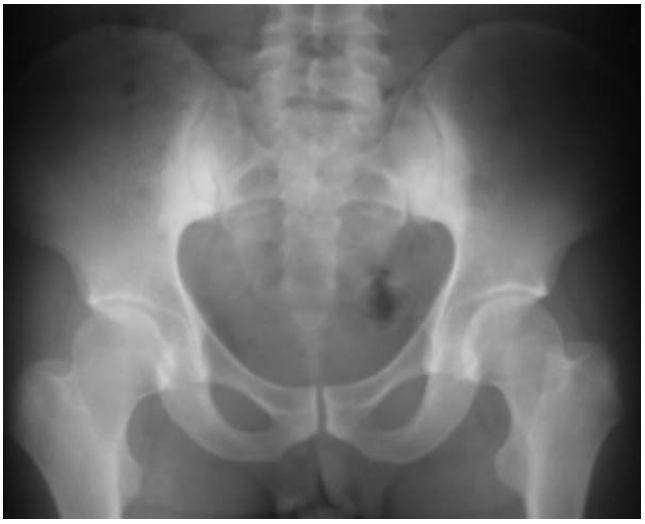

Figure 1. Direct radiography of sacroiliac joints demonstrating grade III sacroiliitis.

distal part of sacroiliac joints (figure 1). There was no abnormality of vertebra on x-ray examinations. ESR was 30 mm/h and CRP was 47.9 mg/l. He was homozygous for M694V mutation of the MEFV gene. He was diagnosed as having FMF with knee arthritis and bilateral sacroiliitis. He was given 0.5 mg/kg prednisolone daily and his knee arthritis symptoms resolved within three days. Corticosteroid treatment was decreased gradually and stopped in three weeks. He was also treated with 2g sulfasalazine, 1.5 mg colchicine and 75 mg indomethacin, daily. CRP decreased to 22.2 mg/l a week after the admission. His complaints completely resolved in 3 months. Then, sulfasalazine treatment was stopped. He continued to take only colchicine (1.5 mg/day). Six months later he presented again with arthritis on his left knee for two days. Indomethacin treatment of 75 mg daily was given in addition to colchicine treatment. One week later, arthritis symptoms regressed and treatment continued with colchicine only. He had no attack of abdominal pain, fever or back pain for twelve months up to latest control examination.

Case 2

A 24-year-old woman admitted with low back pain and morning stiffness for 18 months. She was suffering from fever and abdominal pain attacks, intermittent monoarticular joint swelling and pain of the ankles or the knees since she was 4 years old. She had been diagnosed as FMF since that time. The duration of fever and abdominal pain attacks was 3 days but the articular pain and swelling was protracting to one month. The arthritic attacks were asymmetric and generally monoarticular at the knees or ankles. Before colchicine treatment, her attacks were remitting once a month but she did not have abdominal pain and fever attacks for 6 months and arthritis for 2 years. She was prescribed 1.5 mg/day colchicine treatment which she was receiving irregularly since two years in the doses between 0.5 mg and 1.5 mg daily. Low back pain was characteristically inflammatory in nature. On physical examination, flexion with finger to floor distance was 10 cm. Schober test was 5 cm. Sacral compression, Mennel and Patrick-Fabere tests were positive. There was tenderness on her right sacroiliac joint. Straight leg rising and femoral stretch tests were negative. Laboratory investigations revealed a hemoglobin concentration of 11 g/dl, hematocrit of 30.5% and platelet count of 632 000 /mm^3. Erythrocyte sedimentation rate (ESR) was 70 mm/h and C-reactive protein (CRP) was 20 mg/l. Rheumatoid factor was negative. She was also negative for HLA-B27. On pelvic x-ray, bilateral irregularity and periarticular sclerosing of the sacroiliac joints were observed. This finding was more evident at the right side. Ophtalmological examination was negative for uveitis. Genetic analysis showed that she was homozygous for M694V mutation of the MEFV gene. She was treated with 2 g sulfasalazine, 1,5 mg colchicine and 75 mg indomethacin daily. 3 months after the first admission, she had no articular complaint and the physical examination was normal. ESR was 25 mm/h and CRP was 7 mg/l. Sulfasalazine was stopped gradually and she was followed up only with colchicine treatment (1.5 mg/day). She had no attacks of abdominal pain, arthralgia or arthritis for 12 months.

Discussion

These cases are presented to remind physicians that sacroiliac joint involvement must be kept in mind in the presence of articular symptoms in patients with FMF. Sacroiliac joint involvement is one of the less frequent arthritis type seen in patients with FMF (1,3,5-9). The patients with radiographically sacroiliac joint involvement who suffer from inflammatory back or neck pains are named as seronegative spondyloarthropathy (SNSA). Most of the authors conclude that SNSA is one of the musculoskeletal manifestations of FMF (1,3). The relationship between FMF and SNSA was investigated by Langevitz et al. who

studied features of SNSA in 2000 Sephardic Jewish FMF patients (3). In this study, the frequency of SNSA was 0.4% among FMF patients and 11 patients were reported among 160 with chronic arthritis. Clinical presentation of sacroiliitis in patients with FMF may also differs from other joint involvement types. Brody et al reviewed 43 patients with FMF, six of whom presented radiographic changes in the sacroiliac joints consisting loss of normal cortical definition, sclerosis on both sides of the joint with or without erosion and fusion. These changes were noted despite the absence of clinically symptomatic joint disease (6). Sacroiliitis of an FMF case without any findings in pelvic x-ray was also reported in pediatric age group which was diagnosed by computerized tomography (CT) (4). On the other hand, another case was reported as longstanding sacroiliitis with FMF that later developed Behçet's disease. The comment was made as both were diseases with the common etiopathogenetic mechanism (8). Asymptomatic accidental radiographical findings of sacroiliitis, HLA-B27 positive arthritis of ankylosing spondylitis or with symptomatic back pain of SNSA with various durations of FMF are all reported in the literature (1,3,4,6,9).

Sacroiliitis due to FMF is generally HLA-B27 negative and it is distinguished by this way from other causes of sacroiliitis (4). Even though the sacroiliac joint involvement is seen in HLA-B27 negative patients with FMF, HLA-B27 positive ankylosing spondylitis (AS) patients with FMF are also reported in the literature (3). Patients with FMF may have abnormal sacroiliac joints without other features of AS. This may be a source of diagnostic confusion in the association of sacroiliitis with FMF. Both of our patients' manifestations are satisfied the modified New York criteria for AS as well as the spondyloarthropathy criteria of European Spondyloarthropathy Study Group. However, our patients lacked some characteristic manifestations of AS, including syndesmophytes, bamboo spine and uveitis. The chest expansion and schober tests were within normal limits. For our patients, although their features suggest AS diagnosis, it seemed reasonable to consider their sacroiliac involvements as SNSA of FMF. Both of them were negative for HLA-B27 test while they were homozygous for M694V mutation. The diagnosis depended on the clinical course of their disease and positive genetic mutations.

The sacroiliac joint arthritis generally occurs despite the ongoing colchicine treatment and the NSAID or second line nonsteroidal anti-inflammatory agents such as corticosteroids and sulfasalazine are required for the treatment (3). Sulfasalazine and/or corticosteroid treatment is also needed in our patients to resolve arthritic symptoms.

In conclusion, sacroiliac joint involvement is one of the rare presentations of the arthritis in patients with FMF. Mutation analysis is of value in such situations of diagnostic uncertainty. Despite sacroiliitis is a manifestation of FMF it provides a different treatment alternative other then the classical colchicine and NSAID treatment. Clinicians should be aware of different clinical presentations of this situation and consider taking a pelvic x-ray for the diagnosis of the sacroiliac joint involvement. When the x-ray finding is negative in a patient with symptomatic back pain, sacroiliac CT should be considered.

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