

Ankylosing Spondylitis Together with Familial Mediterranean Fever: A Concomitant Disease or a Feature of FMF?

Ailevi Akdeniz Ateşi ve Ankilozan Spondilit: Eşzamanlı Hastalık mıdır?

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Abstract

Familial Mediterranean Fever (FMF) is an autosomal recessive disease characterized with self-limited recurrent episodes of fever and serositis. The association of FMF with ankylosing spondylitis (AS) was reported in previous studies as a rare condition and the mechanism of this association still remains unknown. The possible forms of joint involvement in FMF are acute or chronic mono-oligoarthritis and seronegative spondyloarthropathy. We described a case of FMF with AS in the case of a patient who had been diagnosed as having acute rheumatic fever (ARF) 20 years ago. We suggest that FMF with AS must be kept in mind in the presence of articular symptoms in patients with FMF. (*Rheumatism 2007; 22: 110-13*)

Key words: Familial mediterranean fever, spondyloarthropathy, ankylosing spodylitis

Özet

Ailevi Akdeniz Ateşi (AAA), aralıklı gelen ateş ve serozit atakları ile karakterize, otozomal resesif geçiş gösteren bir hastalıktır. AAA ile ankilozan spondilit ilişkisini, bildiren çalışmalar vardır ancak bu nadir görülen klinik tablonun, hangi mekanizma ile ortaya çıktığı henüz bilinmemektedir. AAA seyrinde görülen eklem tutulumu, genellikle akut ya da kronik mono-oligoartrit ve seronegatif spondiloartropati şeklindedir. Biz bu yazıda 20 yıl önce akut romatizmal ateş tanısı almış olan ve AAA ve ankilozan spondilitin tanı kriterlerine uyan bir hastayı tanımladık. Eklem tutulumu olan AAA hastalarında ankilozan spondilitin de ortaya çıkabileceği unutulmamalıdır. (*Romatizma 2007; 22: 110-13*)

Anahtar kelimeler: Ailevi akdeniz ateşi, spondiloartropati, ankilozan spondilit

Introduction

Familial Mediterranean fever is a multisystemic genetic disease, characterized by recurrent episodes of febrile peritonitis, pleuritis, and synovitis (1). It is the most prevalent periodic fever syndrome, affecting more than 100.000 patients worldwide (2). Articular attack is a common feature of FMF which usually presents monoarthritis affecting most frequently the large joints of the lower extremities. Less common manifestations include erysipelas-like erythema, acute scrotal attacks, febrile myalgia, and chronic arthritis (3).

Herein we report a case of FMF with Ankylosing Spondylitis (AS) who had been diagnosed as having acute rheumatic fever (ARF) 20 years previously.

Case Report

Our patient, a 40 years old male, had been followed for FMF since 1999. His cousin and uncle have also been diagnosed with FMF.

He described joint pain and swelling, particularly at elbows, knees, and ankles. He had a history of lower back pain, which worsened at rest and improved with activity. The medical history was unremarkable for oral-genital ulceration, eye involvement, and inflammatory bowel disease. At the age of 10, he was diagnosed with acute rheumatic fever (ARF) for pain and swelling of bilateral knee and ankle joints. He had used salicylates, non-steroidal anti-inflammatory drugs (NSAIDs) and antibiotics for 5 years. Meanwhile he described arthralgia, stiffness and mild abdominal pain, but he had not attended his physician for regular routine controls. Although there were insignificant abdominal pain and chest pain, the first significant abdominal pain attack occurred at the age of 20. The patient has a history of appendectomy because of severe abdominal pain and fever when he was 20. Although the abdominal pain and arthralgia were

present after appendectomy, he was not given a regular treatment.

The patient described acute febrile abdominal attacks, chest pain and arthralgia recurring periodically at about one month intervals for 7 years. Attacks took about 6-10 hours and subsided spontaneously. He had inflammatory back pain worsened at rest and improved with activity, and morning stiffness lasting about 2 hours. He experienced the last episode about 3 weeks ago before he was referred to our clinic. He was diagnosed as FMF after attacks of abdominal pain, fever and arthritis. He was recommended colchicine therapy (1mg/day) but he did not use regularly before his first visit to our clinic.

Upon admission, her temperature was 36.5, pulse 88/min-regular and blood pressure 110/60 mmHg. Cervical motions were limited flexion: 20° (0-45°), extension: 15° (0-45°), lateral flexion: 10° (0-45°), right and left rotation: 30° (0-90°). Chest expansion: 1.5cm, occiput to wall distance: 2 cm, tragus-to-wall distance: 15cm, finger-to-floor distance: 21cm. The sacroiliac joints were painful

with compression. Modified Schober test was 3 cm, Patrick-Fabere, Gaenslen and Mennel tests were bilaterally positive, Bilaterally hip flexion: 90° (0-120°), extension: 5°, internal rotation:10° (0-35°), external rotation: 10° (0-45°). Prominences of the calcaneus were bilaterally tender to palpation. The patient was consulted with the departments of chest disease and cardiology. His pulmonary function tests, and computed tomography of chest was normal. Pathergy test was negative. The echocardiography findings showed mild mitral valve stenosis (valve 2.8 cm²).

Laboratory evaluations were as follows: Hemoglobin was 11.2 g/dL (12-18 g/dl), ESR: 54 mm/1 h (0-15 mm/h), CRP: 15.3 mg/dL (0.0-0.8), rheumatoid factor were negative, antistreptolysin O (ASO): 430 IU/L, HLA B27 were negative. Assays for ANA, anti-dsDNA, HIV, brucella, and hepatitis antigen were negative. Serum routine chemistry tests were normal. Blood, urine and throat cultures were negative. We could not have the opportunity for the analyses of MEFV gene in our hospital.



Figure 1. Sacroiliac joint graphy shows bilateral sacroiliitis

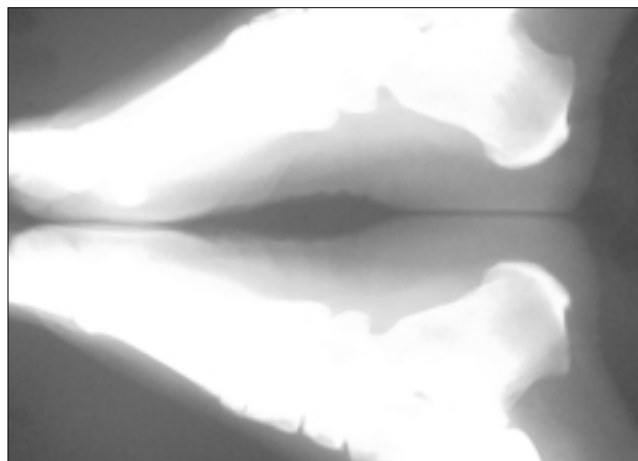


Figure 3. Lateral feet radiograph shows bilateral erosions of the postero-superior aspect of the calcaneus

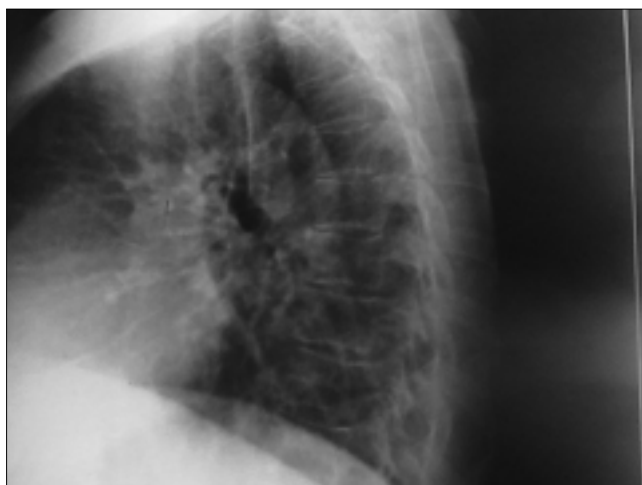


Figure 2. Lateral lumbosacral graphy shows squaring of vertebral bodies with osteopenia

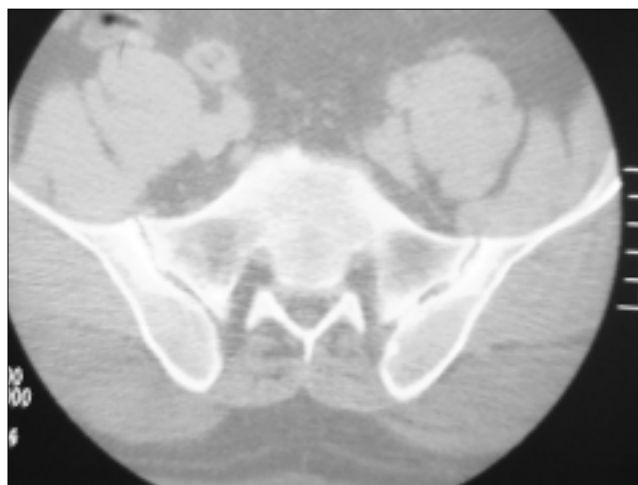


Figure 4. Computed tomography of sacroiliac joints shows bilateral grade 3 sacroiliitis

Radiological examinations demonstrated bilateral sacroiliitis (Fig.1), and lateral lumbosacral vertebrae showed the squaring of vertebral bodies with osteopenia (Fig.2). Lateral feet radiographs revealed bilateral erosions of the posterosuperior aspect of the calcaneus (Fig.3). Computed tomography of sacroiliac joints disclosed bilateral grade 3 sacroileitis (Fig.4).

The clinical features and results of various diagnostic tests met the modified New York Criteria for AS (4) The diagnosis of AS which occurs in the course of FMF was established in our case. The medical history and cardiologic evaluations proved that the patient had also been suffered from ARF when he was a child.

The patient was prescribed 1.5 mg/day colchicine 2 g/day sulfasalazine and 25 mg/day NSAID. After the fourth week of the treatment, he started to feel better, and he did not have chest, abdominal and lower back pains. Morning stiffness improved considerably. Laboratory results revealed ESR: 22 mm/1h (0-15), CRP: 1.3mg/dL (0.0-0.8). He had been attending regularly to our clinic for 5 months he had not experienced periodically occurring symptoms. We observed a dramatic improvement in his complaints.

Discussion

The articular involvement of FMF presents as an abrupt onset of acute arthritis, accompanied by high fever, redness, warmth, tenderness, and swelling (5). It is often monoarticular and generally affects the large joints of the legs (6). Another possible form of joint involvement in FMF is sacroiliitis, which is the characteristic feature of seronegative spondyloarthropathy (SNSA) (7). The true prevalence of SNSA among FMF patients is not known. It has been reported that the prevalence of SNSA in FMF is 0.4% (8). Some of SNSA cases, which present with FMF, can display an AS clinical course like our case. The exact relationship between FMF and AS is a challenge. Occurrence of FMF and AS in the same patients has been described by several authors (9, 10, 11, 12). In a series of 3,000 FMF patients, which included 160 patients with chronic arthritis, 11 patients had SNSA meeting criteria (12). Majeed and Rawashdeh reported only one case developed AS in a study group including 95 patients with chronic arthritis of FMF (13).

Medical history, cardiologic examination, electrocardiography, and echocardiography of our patient indicated that he had suffered from ARF in his childhood. The presence of high levels of ASO antibodies and streptococcus-associated diseases such as acute poststreptococcal glomerulonephritis (AGN) and acute rheumatic fever (ARF) have been reported in patients with FMF. Authors suggested that patients with FMF have an exaggerated response to streptococcal antigens and might be susceptible to poststreptococcal non-suppurative complications,

such as ARF (14, 15, 16). Tekin et al. (17) reported that nine patients with FMF (5.5%) were considered to have ARF and three of them (1.85%) also had rheumatic heart disease in 162 FMF patients. In normal population, the incidence of ARF is 0.37% (18). We thought that, developing ARF in our patient was the result of the increased acute-phase responsiveness, which is considered to important mechanism in pathogenesis of the FMF.

Sacroiliitis and spondyloarthritis can be seen in patients with FMF (19). The FMF-AS combination predominantly affects males and the FMF usually precedes the AS (20). However, the nature of this association and whether it is just a coincidence or an unexplained common etiology remains to be explored. Dilsen and coworkers have been reported that the association of FMF and AS was frequently seen in Turkey (21).

HLA B27 was negative in our patient. The absence of HLA-B27 by no means rules out the diagnosis of SNSA (22). HLAB27 is not counted among the criteria for diagnosis of spondyloarthropathy (11). The association of familial Mediterranean fever and AS is frequently seen with negative HLA-B27 antigen. Langevitz and co-workers proposed that the association of FMF and AS were seen in 11 patients in a series of 3000 patients with FMF. Further, there were nine patients who had a negative HLA-B27 antigen in 11 patients with FMF and AS (12).

In conclusion, we reported a case of FMF and AS who also had been suffered ARF. Although, the possible pathogenetic mechanisms that probably link these conditions are still unknown, we thought that coexistence of FMF and AS was not coincidental, and FMF patients might be prone to ARF. FMF with AS must be kept in mind in the presence of sacroiliitis in patients with FMF. Further studies are required to clarify whether coexistence of FMF and AS is only a coincidence or AS is one of the clinical presentations of FMF.

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