Familial Mediterranean Fever Accompanied by Ankylosing Spondylitis: Case Report

Ailevi Akdeniz Ateşine Eşlik Eden Ankilozan Spondilit

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ABSTRACT Arthritis is the second most common form of familial Mediterranean fever (FMF) attacks; lower extremity joints, such as knees and ankles, are frequent involvement sites for FMF. Sacroiliitis and spinal involvement is the hallmark of ankylosing spondylitis (AS) and a possible but infrequent feature of FMF. About 10% of the patients experience protracted attacks, usually knees or hips are involved, but sacroiliitis occurs only in 2%. We present and discuss a rare case of FMF accompanying to AS. The diagnosis of FMF must be made on clinical grounds. The combination of irregularly recurrent attacks comprising short, febrile episodes of abdominal pain, pleuritic chest pain or arthritis in children or young adults are the main features of diagnosis. FMF should be considered in the differential diagnosis in patients with inflammatory involvement of the lumbar spine and arthritis in the knees or ankles.

Key Words: HLA-B27 antigen; Familial Mediterranean Fever; spondylitis, ankylosing

ÖZET Diz ve ayak bileği gibi büyük eklem artriti, Ailevi Akdeniz Ateşi (AAA) ataklarının 2. en sık görülen bulgusudur. Ankilozan spondilitin (AS) belirgin özelliği olan lomber spinal tutulum, AAA'da görülse de oldukça nadirdir. AAA olgularının yaklaşık %10'unda uzamış diz ve kalça art riti görülür. Buna karşın uzamış sakroiliit sadece %2 oranında bildirilmiştir. Burada AAA'ya eşlik eden AS olgusunu takdim ederek tartıştık. AAA tanısı; çocuk veya genç erişkinlerde tekrarlayan karın ağrısı, artrit, plevral semptomlara eşlik eden ateş ataklarının varlığı ile konulmaktadır. Bununla birlikte diz, ayak bileği ve lomber vertebral eklem tutulumunun olduğu olgularda da ayırıcı tanıda dikkate alınmalıdır.

Anahtar Kelimeler HLA-B27 antiyojeni; Ailevi Akdeniz Ateşi; ankilozan spondilit

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Familial Mediterranean Fever (FMF) is a genetic disease with an autosomal recessive inheritance and most commonly occurs in Jews, Turks, Armenians, and Arabs. FMF is characterized by recurrent and self-limited attacks of fever accompanied by peritonitis, pleuritis, synovitis, or erysipelas-like erythema.[1] The recent identification of the FMF gene, named MEFV located on the 16th chromosome is apparently expressed in neutrophils and encodes a protein called pyrin or marenostrin. Arthritis is among the most common manifestations of FMF. Most typical joint involvement is monoarticular arthritis of the knee or other large joints. Polyarticular arthritis accounts for less than 20% of all joint involvements in FMF.[2] Sacroiliitis may occur in the course of the disease. However, it is infrequent compared to arthritis of the knees or ankles.[3]

AS is the most common inflammatory disorder of the axial skeleton with a male dominance of 2-5:1.[4] Symptoms usually become apparent in adolescence and present with back pain persisting for more than 3 months. Pain is localized to the sacroiliac joint and is accompanied by morning stiffness. Thirty percent of the patients with AS have arthritic involvement other than the sacroiliac joint.[5] Extraarticular manifestations are anterior uveitis, pulmonary fibrosis and cardiac involvement including aortic insufficiency and conduction defects.

Herein, we present a case of FMF accompanied by AS and review the literature for sacroiliac joint involvement in FMF patients.

CASE REPORT

A 27-year-old male patient, with a history of pain and limitation of motion of the lower back and hip, presented to our center with abdominal pain, nausea, vomiting and fever. He was diagnosed as AS and had a history of irregular treatment with methylprednisolone and sulfasalazine 6 years ago. Skin and mucous membrane and eye lesions were negative. Physical examination revealed limitation of motion of the lower back. Finger to floor distance was 21 cm and back pain emerged during examination. Sacroiliac compression and Mennel tests were bilaterally positive, Schober's test was 4 cm, chest expansion was measured at 3 cm with full inspiration (5 cm considered normal), and occiput to wall distance was 2 cm. He was neurologically intact and no nerve root tension signs were elicited. Rebound tenderness was evident by abdominal palpation. Bilateral involvement was evident in sacroiliac and coxafemoral joints in radiological examination. Bilateral sacroiliitis was detected in computerized tomographic examination (Figure 1). In the laboratory examination, leukocyte count was 22.900/μL, hemoglobin was 13.7 g/dL, platelet count was 289.000/μL and erythrocyte sedimentation rate was 64 mm/h. No abnormality was detected in abdominal ultrasonography. Patient was admitted to various hospitals with abdominal symptoms several times since he was 15 years old and had a history of appendectomy. Laparotomy

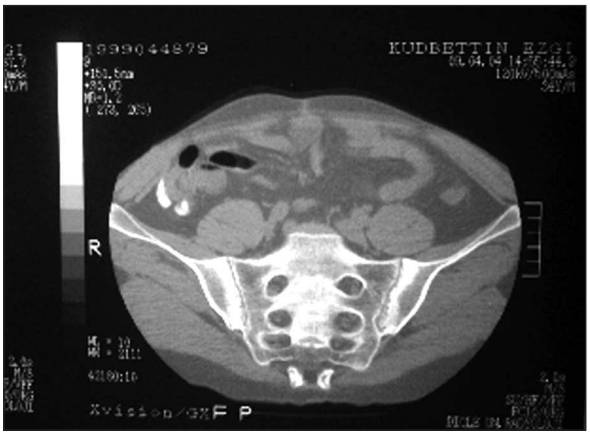

FIGURE 1: Bilateral sacroiliitis was detected in tomographic examination.

was performed 6 months ago and widespread peritoneal inflammation suggesting primary peritonitis was present. Attacks of abdominal pain were recurring at approximately 2-month intervals and each attack persisted for 2 to 3 days. Fibrinogen level was 507 mg/dL (normal range 212-488 mg/dL) and CRP was 208 mg/L (normal range 0-5 mg/L). IL-6 and TNF-α levels were 19.4 (normal range 0-12) and 15.8 (normal range 4-10) pg/mL respectively. In the clinical follow up, abdominal pain diminished progressively and disappeared completely. In the following week, erythrocyte sedimentation rate was 9 mm/h, CRP was 3.85 mg/L, fibrinogen was 297 mg/dL and the levels of cytokines were within normal range. For differential diagnosis, dermatologic and colonoscopic examinations were performed and were normal. Urine and throat cultures were negative. Mild polyclonal gammopathy was detected in protein electrophoresis and autoantibodies such as antinuclear antibody, anti-smooth muscle antibody and rheumatoid factor were negative. HLA-B27 was positive. One of his brothers had a history of FMF for 6 months and was treated with colchicine.

Both medical and family history and clinical manifestations of the patient resembled FMF and the definitive diagnosis of FMF was made by using Tel-Hashomer criteria for the diagnosis of FMF. The diagnosis of FMF was confirmed in our clinic with genetic analysis, which revealed homozygote M694V mutation. Colchicine and sulphasalazine therapy was initiated. Attacks of abdominal pain

improved and the patient did not describe abdominal pain or fever in regular outpatient service visits in the following 7 months.

DISCUSSION

FMF is characterized by recurrent episodes of unprovoked inflammation involving the joints, pleural and peritoneal cavities and less frequently the skin. Physical and emotional stress, menstruation and high fat diet may trigger attacks.[6] Some patients report a prodromal period preceding an attack. The frequency of the attacks is variable and often unpredictable. The severity of the attacks and their frequency usually decrease throughout the person's life-span.[7]

Arthritis is a cardinal and the second most common feature of FMF.[8] The articular disease is a common manifestation that occurs in 70-75% of the patients and it is the initial manifestation in approximately 10-15%.[2,9] Joint involvement may be acute monoarthritis or chronic oligoarthritis of lower extremities. Arthritis rarely causes deformities and recovery of joint function between attacks usually occurs. Patients with homozygote M694V mutation have higher tendency to arthritic involvement than the FMF patients with other MEFV gene mutations.[10] Although patients with FMF have variable articular presentations, articular attacks usually resolve within 10-14 days. Generally, less than 10% of patients develop protracted arthritis lasting for months.[11]

Although sacroiliitis is infrequent and is among the likely joint involvements in FMF, there are many FMF cases accompanied with spondyloarthropathy (SpA) reported by many authors. Usually such cases have homozygote M694V mutation and negative HLA-B27. Langevitz et al carried out a study in 3000 FMF patients to determine the association of seronegative SpA and FMF. One hundred sixty patients had chronic arthritis and 11 of 160 patients met the criteria of seronegative SpA. Three patients fulfilled the criteria of the diagnosis of AS.[12] Keleş et al also reported a case of FMF accompanied with AS.[13] Our patient had homozygote mutation for M694V mutation and it was associated with severe disease, earlier age of onset, frequent attacks and higher risk of amyloidosis and arthritis.[14]

The diagnosis of FMF must be made on clinical grounds. The combination in healthy child, or young adult of irregularly recurrent, short, febrile episodes, abdominal, arthritic or pleuritic symptoms, a favorable response to colchicine therapy, and AA amyloidosis in the absence of another disease are the main features on which the diagnosis should be based. FMF must be considered for patients with arthritic involvement of the lumbar spine as well as knees and ankles, which are frequently involved in FMF. Determination of MEFV gene mutations would be appropriate for patients with specific ethnicity, family history or clinical presentation resembling FMF. Earlier initiation of colchicine therapy would minimize the severity of disease and risk of amyloidosis. It remains unclear whether the association of FMF and AS is coincidental or these two entities have a common pathogenetic mechanism.

REFERENCES

1. Sohar E, Gafni J, Pras M, Heller H. Familial Mediterranean fever. A survey of 470 cases and review of the literature. Am J Med 1967;43:227-53.
2. Uthman I, Hajj-Ali RA, Arayssi T, Masri AF, Nasr F. Arthritis in familial Mediterranean fever. Rheumatol Int. 2001;20:145-8.
3. Beşbaş N, Ozdemir S, Saatçi I, Bakkaloğlu A, Ozen S, Saatçi U. Sacroiliitis in familial Mediterranean fever: an unusual presentation in childhood. Turk J Pediatr 1999;41: 387-90.
4. Dougados M, van der Linden S, Juhlin R, Huitfeldt B, Amor B, Calin A, et al. The European Spondylarthropathy Study Group preliminary criteria for the classification of spondylarthropathy. Arthritis Rheum 1991;34: 1218-27.
5. Ball GV. Ankylosing spondylitis. In: McCarthy DJ, Koopman WJ, eds. Arthritis and Allied Conditions. 12th ed. Philadelphia: Lea & Febiger; 1993.p.1051-60.
6. Ben-Chetrit E, Levy M. Familial Mediterranean fever. Lancet. 1998;351:659-64.
7. Nir-Paz R, Ben-Chetrit E, Pikarsky E, Hassin D, Hasin Y, Chajek-Shaul T. Unusual presentation of familial Mediterranean fever: Role of genetic diagnosis. Ann Rheum Dis 2000;59:836-8.

8. Heller H, Gafni J, Michaeli D, Shahin N, Sohar E, Ehrlich G, et al. The arthritis of familial Mediterranean fever (FMF). Arthritis Rheum 1966;9:1-17.
9. Yalçinkaya F, Tekin M, Tümer N, Ozkaya N. Protracted arthritis of familial Mediterranean fever (an unusual complication). Br J Rheumatol 1997;36:1228-30.
10. Brik R, Shinawi M, Kasinetz L, Gershoni-Baruch R. The musculoskeletal manifestations of familial Mediterranean fever in children genetically diagnosed with the disease. Arthritis Rheum 2001;44:1416-9.
11. Ince E, Cakar N, Tekin M, Kendirli T, Ozkaya N, Akar N, et al. Arthritis in children with familial Mediterranean fever. Rheumatol Int 2002;21:213-7.
12. Langevitz P, Livneh A, Zemer D, Shemer J, Pras M. Seronegative spondyloarthropathy in familial Mediterranean fever. Semin Arthritis Rheum 1997;27:67-72.
13. Keleş I, Aydin G, Tosun A, Inal E, Keleş H, Orkun S. Familial Mediterranean fever and ankylosing spondylitis in a patient with juvenile idiopathic arthritis: A case report and review of the literature. Rheumatol Int 2006;26:846-51.
14. Dewalle M, Domingo C, Rozenbaum M, Ben-Chétrit E, Cattan D, Bernot A, et al. Phenotype-genotype correlation in Jewish patients suffering from familial Mediterranean fever (FMF). Eur J Hum Genet 1998;6:95-7.