The Case of a Mother Who Was Also Diagnosed with Familial Mediterranean Fever Following Her Children's Diagnoses

Çocuklarının Tanısından Sonra Kendisi de Ailevi Akdeniz Ateşi Tanısı Alan Anne Vakası

The Case of a Mother with Familial Mediterranean Fever

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Özet

Ailevi akdeniz ateşi (AAA) otozomal resesif bir hastalık olup, genelde periyodik ateş, karın, göğüs, eklem ağrısı, eritem benzeri deri lezyonları ile kendisini gösterir. Erişkinlerde görülebilse de, esas olarak genellikle 5-15 yaşları arasında semptom veren bir çocukluk çağı hastalığıdır. Bu çalışmada tekrarlayan ateş, karın ağrısı, bacak ağrısı atakları olan, AAA tanısı alan 3 çocuğundan sonra kendisi de AAA tanısı alan hastadan bahsedilecektir.

Anahtar Kelimeler

AAA; Anne; M680I

Abstract

Familial Mediterranean fever (FMF) is an autosomal recessive disease that manifests itself with periodic fever, stomach ache, chest pain, and skin lesions such as erythema. Although it can be seen in adults, it is most often a childhood disease with symptoms generally occurring between 5-15 years of age. This study discusses a patient who had repeating fever, stomach ache, and leg pain attacks and was also diagnosed with FMF after her three children had received the same diagnosis.

Keywords

FMF; Mother; M680I

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Introduction

Familial Mediterranean fever (FMF) is an autosomal recessive disease that manifests itself with periodic fever, stomach ache, chest pain, and skin lesions such as erythema. But the disease may manifest itself with very different clinical presentations. It is more common in males. The average onset age is reported as 9.6 years and average age at diagnosis as 16.4 years. The occurrence rate of FMF in Turkey is known to be 1/1000. Various studies have reported occurrence rates ranging from 15-34%. FMF is common in the Middle East. It is especially seen in Jews, Turks, Arabians, Armenians, and Kurds, and less commonly in Jews of European origin [1]. Many mutations have been detected in the MEFV gene held responsible for the disease. The diagnosis is rather difficult since there are no significant pathognomonic symptoms and the tests made with biochemical or other methods are not definitively diagnostic. This study discusses a patient who had been experiencing repeating fever, stomach ache, and leg pain attacks for years and who referred to the Family Healthcare Center. She was diagnosed with FMF; her three children had received the same diagnosis earlier.

Case Report

Our 35-year-old patient is married and has three children. She came to the Family Healthcare Center complaining of diffuse stomach ache, left leg pain, and fever in August 2015. In her anamnesis, it was learned that these complaints occurred three or four times per month as attacks; they did not respond to analgesic and antipyretic treatment satisfactorily and ended spontaneously. She did not experience other complaints such as headache and sore throat, cough with mucus, diarrhea, or burning sensation during urination. She said that she had had the complaints for years but had been unwilling to visit a doctor.

There were no significant findings from systemic examination. Among the vital findings, her fever was 38.2º C and blood pressure, pulse, and respiratory rate were normal. The patient did not have any chronic diagnosis or drug use. She did not smoke or consume alcohol. She did not have any surgeries or allergies. It was learned that all her children previously had been diagnosed with FMF and received colchicine treatment and also that the children of her brother and sister have this disease. Her husband is not an FMF patient.

Her first child is male, now 15 years old. When he was 7 years old, suspicion of FMF prompted a genotype analysis that revealed a heterozygote M680I(G/C) and heterozygote M694V mutation among MEFV gene mutations. Her second child is female, now 13 years old. When she was suspected of FMF at the age of 12, FMF fragment analysis was performed. Using the hybridization (primary + probe) based SNP analysis method, which is the only nucleotide change detector, the MEFV gene Exon 2,3,5 and Exon 10 were examined and M680I(G/C) heterozygote mutation was detected. The third child, a female now 9 years old, underwent the same testing at the age of 8, with the same finding.

In the examinations made on the patient, complete blood count, liver and kidney function tests, complete urine analysis, and posteroanterior lung graphy were normal. Erythrocyte sedimentation rate (ESR) was 21 mm/h (0-20), fibrinogen 3.08 g/dl (1.8-3.5), and C-reactive protein (CRP) 0.297 mg/dl (0-0.35). The patient was transferred for genetic examination with FMF pre-diagnosis. In FMF sequence analysis, the bilateral florescent DNA serial analysis method was used. The MEFV gene Exon 2,3,5 and Exon 10 were examined and M680I(G/C) homozygote mutation was detected. After the patient was given colchicine treatment (2mg/day), the number of attacks decreased to one per month and the severity also decreased. Following diagnosis, she did not delay the treatment of her children or herself.

Discussion

Although typically children's FMF diagnosis follows diagnosis of the parent, in this case the mother was diagnosed with FMF after the diagnosis of her children. FMF is a genetic and autoinflammatory disease [2]. Although it can be seen in adults, it is most often a childhood disease, with symptoms generally occurring between 5-15 years of age. There are no diagnostic physical examination findings or specific laboratory tests for FMF. Findings of leucocytosis, serum amyloid A level, ESR increase, fibrinogen, and CRP increase during attack aid in diagnosis but are not specific. Although definition of the disease gene is helpful for diagnosis, the anamnesis is primarily depended on for clinical progress. While there were no significant findings in the laboratory values of our patient, the detection of M680I(G/C) homozygote mutation in genetic analysis made the diagnosis of the disease easier. The MEFV gene was localized in the shorter arm of the chromosome (16p13.3) and codes a protein with 781 amino acids (pyrine). It is stated that pyrine protein plays a role in inflammation inhibition and neurophil activity in the inflammation location during FMF attacks [3]. MEFV gene related mutations were examined in 197 cases referred with FMF pre-diagnosis in the study by Yeşilada et al. The most common homozygote mutations were M694V (n=12) and M680I(G/C) (n=3) and the most common heterozygote mutations were M694V (n=22) and E148Q (n=12) [4]. Different criteria have been developed for diagnosis; the most common among these are the Tel-Hashomer criteria. According to Tel-Hashomer, a major criterion for FMF is recurrent fever attacks occurring with polyserositis with AA type amyloidosis for which no other explanations are found and that respond well to ongoing colchicine treatment. Recurrent fever attacks, rashes similar to erysipelas, and the presence of FMF in first-degree relatives are minor criteria. Definitive FMF diagnosis is made with the combination of two major or one major and two minor criteria [5].

Amyloidosis has been defined as the most serious complication of FMF. But no connection has been demonstrated between the occurrence of amyloidosis and FMF starting age, frequency of attacks, and duration [6]. Colchicine treatment plays a significant role in preventing amyloidosis development [7]. Anakinra, rilonacept, canakinumab, and tocilizumab are recommended in the 5-10% of patients resistant to colchicine [8].

FMF is a common disease in Turkey and its diagnosis is problematic. It can be seen both in children and adults. The people who are known FMF carriers and are planning to marry should be evaluated for FMF. It is important to support the diagnosis with genetic testing in situations where FMF is suspected.

Competing interests

The authors declare that they have no competing interests.

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