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Familial Mediterranean fever in two brothers aged seven and five years old

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ABSTRACT

Familial Mediterranean fever (FMF) is an inherited disease characterized by fever and intermittent abdominal pain. Due to amyloid deposits in the kidneys and gastrointestinal tract, untreated FMF can lead to severe complications such as end-stage renal disease and malabsorption. The present study reports two brothers aged seven and five years, who presented with fever, abdominal pain, and anorexia. Based on their clinical history and ruling out other possible diagnoses, FMF was definitively diagnosed, and both patients underwent colchicine treatment.

Implication for health policy/practice/research/medical education:
The present study reports two brothers, aged seven and five years old, who presented with intermittent fever, abdominal pain, and anorexia during the last two years. Based on their clinical history and ruling out other possible diagnoses, familial Mediterranean fever was definitively diagnosed, and both patients were successfully controlled with colchicine.

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Introduction

Familial Mediterranean fever (FMF) is an autosomal recessive disease characterized by recurrent attacks and inflammation of the serous membranes. Due to amyloid deposits in the kidneys and gastrointestinal tract, untreated FMF can lead to serious complications such as end-stage renal disease and malabsorption. In 1958, Heller described the clinical board and diagnostic criteria for the disease and the genetic properties, racial limitations, and subsequent joint syndrome and called it FMF (1). The main symptoms of this disease include painful and feverish attacks accompanied by a significant increase in body temperature and acute peritonitis, pleuritis, and synovitis. These attacks are short-duration, and the patient does not feel uncomfortable between these periods. Abdominal attacks occur in 90% of patients; the body temperature reaches 39-40 °C, and the pain spreads throughout the abdomen during the attack (2). These attacks lead to arthritis, the second most common symptom, affecting 75% of patients.

This disease should be diagnosed and treated as soon as possible due to its specific complications, the most important of which is amyloid. If left untreated, due to amyloid deposits in the kidneys and gastrointestinal tract, the disease can lead to serious complications such as end-stage renal disease and malabsorption (3). Other complications of the disease are mainly secondary to the misdiagnosis of the illness and iatrogenic complications such as unnecessary surgeries, unnecessary and costly diagnostic and therapeutic procedures (4).

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Cases Presentation

The family that is introduced is from the Kurdish people of Ilam province. Patients' parents are related. The patients were two brothers, 5 and 7 years old, referred to Imam Khomeini medical center in Ilam for high fever, stomachache, and anorexia. Patients had no similar family history. The patients had a more severe fever and cough during sleep, and they had taken acetaminophen for fever, but it was ineffective. Intermittent fever and stomachache in both patients had started two years earlier, and treatment had given temporary relief, but similar attacks occurred again a week to a month later. Patients' fever recurred 1-2 times a month. The fever did not respond to antibiotics and lasted for 2-3 days. Patients had generalized and continuous pain and had a history of previous admissions due to fever and stomachache. Both patients had minor thalassemia anemia, and the younger brother complained of nausea, vomiting, and diarrhea. Clinical examinations revealed the patients had normal heart, lung, kidney, and skin. During palpation, the abdomen was soft and had no organomegaly, mass, or tenderness. To rule out other diseases and perform differential diagnoses, an upper gastrointestinal series, abdominal and pelvic ultrasound, urinalysis for proteinuria, genetic tests transmission for diagnosis of possible FMF and anti–cyclic citrullinated peptide (anti-CCP) antibodies, and routine laboratory tests were performed. The laboratory test results are shown in Table 1. Abdominal and pelvic ultrasonography and upper gastrointestinal series showed no positive results, and anti-CCP antibody was negative.

Considering the above results and that other differential diagnoses were ruled out, the results of examinations of peripheral blood samples for pathogenic FMF-induced mutations and MEFV gene mutation analysis in both patients showed compound heterozygous R202Q mutation; both patients received a definitive FMF diagnosis. Colchicine treatment was started on the first day of admission, and the patient's symptoms were controlled. On day three of treatment, patients were discharged with colchicine treatment (0.5 mg every 12 hours).

As the colchicine treatment began, both patients exhibited a dramatic response and experienced no abdominal pain or fever for 6 months of treatment and follow-up. Liver, kidney, and urine tests were checked every 3 months.

The patient's consents were obtained and approved by the hospital. Patients have provided informed written consent for the release of their case details.

Discussion

Familial Mediterranean is characterized by recurrent fever and serous inflammation (e.g., peritonitis, pleuritis, synovitis). Most people (80%) are infected before the age of 10 years and 90% before the age of 20. The disease may occur in older ages, but only rarely after 40 years (3). Most patients with FMF (95%) experience abdominal pain, either localized or widely spread, which may be the first symptom in half of the patients. Patients may present with a slight dilation as well as severe peritonitis. As these patients showed acute abdominal symptoms, they were diagnosed with FMF. Appendectomy and laparotomy may be performed incorrectly (5). The radiological findings of the patients in our study did not confirm the acute abdomen. Molecular genetic diagnostic testing was used to confirm the FMF diagnosis, but the diagnosis was still largely based on clinical criteria (3).

The first point to be discussed is the clinical diagnosis of FMF based on Tel-Hashomer clinical criteria (6). According to the criteria shown in Table 2, the presence of two major symptoms, i.e., recurrent attacks of fever and abdominal pain or serous inflammation such as arthritis or pleuritis, and appropriate response to colchicine treatment, are sufficient for clinical confirmation of FMF. The presence of two major criteria and one minor criterion makes a definite diagnosis, and the presence of one major criterion and one minor criterion suggests a possible diagnosis (6).

After ruling out other possibilities and diagnostic criteria, the disease was diagnosed with complete certainty for the patients in the present study. Reports have shown

Table 1. Patients' laboratory test results

	Patients 1 (7-year-old)	Patients 2 (5-year-old)	Normal values
WBC, 10^9/L	5.4	3.5	0.5-14.5
RBC, 10^9/L	5.7	5.8	3.8-4.8
Hb, g/dL	11.1	12	10.3-14.1
MCV, fL	60	60.17	68-85
MCH, pg	19.47	20.69	24-30
Lymphocyte, %	60	52	32-52
ESR, mm	3	2	
Urinalysis (UA)	Negative for proteinuria	Negative for proteinuria	
CRP, mg/L	Negative	Negative	

WBC, White blood cells; RBC, Red blood cells, HB, Hemoglobin; ESR, Erythrocyte sedimentation rate; CRP, C-reactive protein; MCV, Mean corpuscular volume; MCH, Mean corpuscular hemoglobin.

Table 2. Tel-Hashomer clinical criteria, for the clinical diagnosis of FMF (6)

Major criteria	Minor criteria
Recurrent febrile episodes with serositis (peritonitis, synovitis or pleuritis)	Recurrent febrile episodes
Amyloidosis of AA type without a predisposing disease	Erysipelas-like erythema
Favorable response to regular colchicine treatment	FMF in a first-degree relative
Diagnosis: 2 major criteria or 1 major and 2 minor criteria	

that 90% of patients with FMF develop recurrent attacks of fever and acute abdominal pain, of whom about 50% undergo surgery (7). FMF treatment focuses on preventing painful attacks and amyloidosis. Nonsteroidal anti-inflammatory drugs (NSAIDs) may be used to treat people in acute periods, although they are not always effective. Colchicine has been the mainstay of FMF treatment since 1972. Optimal response to colchicine treatment may be one of the most valuable criteria for the FMF diagnosis (5), as the disease becomes controllable and a significant improvement is observed in patients when colchicine treatment is started upon admission. Genetic analysis plays a major role in the diagnosis. The gene responsible for FMF (MEFV) is located on chromosome 6p13.3 and contains ten exons. FMF exhibits an apparent autosomal dominant inheritance pattern, and patients experience compound homozygous or heterozygous mutations (3). When peripheral blood samples were examined for pathogenic mutations causing FMF in the present study, the results showed that both patients had two different compound heterozygous mutations in two different exons of the MEFV gene.

Conclusion

Two cases of FMF in children undergoing colchicine treatment have been described. It is suggested that FMF should be considered in the differential diagnosis of patients with recurrent fever syndrome.

Authors' contribution

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Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

This case report was conducted in accordance with the World Medical Association Declaration of Helsinki. The patient has given us written informed consent for publication as a case report. Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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