CLINICAL VIGNETTE

Familial Mediterranean Fever in a 29-Year-Old Male with Chronic Cyclical Abdominal Symptoms and Fever

Shih-Fan Sun, MD and Hiroshi Suzuki, MD

Introduction

Familial Mediterranean Fever (FMF) is an autoinflammatory, usually autosomal recessive, disorder associated with mutations in the MEFV (Mediterranean Fever) gene. It is most prevalent in individuals of Turkish, Middle Eastern, Arab, Armenian, and Non-Ashkenazi Jewish descent around the Mediterranean basin. Patients with FMF often exhibit recurrent attacks of fever and serositis such as pericarditis, synovitis, pleuritis and peritonitis. Ninety percent of initial attacks occur before age 20.[1]

During attacks, symptoms are usually abrupt onset and self-resolve after few days. Frequency of the attacks is highly variable. The clinical manifestations of FMF can vary in different ethnicities. Recurrent episodes of fever and serositis are common in the Middle East, whereas headache is common in Japanese and European patients. Japanese and European patients also have different types of skin rash, rather than the erysipelas like erythema characteristic of FMF.[2] Given variable symptomatology, the diagnosis of FMF can easily be missed without a high level of suspicion. We present a patient with Familial Mediterranean Fever where the diagnosis was delayed for almost 20 years.

Case Report

A 29-year-old male presented with intermittent abdominal pain since age 10. He had multiple hospitalizations as a child for similar symptoms without clear diagnosis. Prior evaluation included two colonoscopies, most recently around age 12, which were reportedly unremarkable. During symptom flare ups, he reported intense abdominal pain, constipation and bloating. Laxatives and dicyclomine would help alleviate the pain. Some symptoms were associated with fever, night sweats, nausea or vomiting. Each flare would last 3-7 days. He denied bleeding and reports stress can trigger symptoms. His family is from Mexico in an area heavily colonized by Spaniards.

On exam, blood pressure was 115/77, pulse 89, temperature 36.1 Celsius. Abdomen exam was benign. Lipase was 16 U/L. Labs include: normal comprehensive metabolic panel with creatinine 0.90 mg/dL, urea nitrogen 11 mg/dL, total bilirubin 0.4 mg/dL, alkaline phosphatase 87 U/L, AST 38 U/L, ALT 62 U/L. Lipase was normal. CBC was normal. WBC 8.22 x10E3/uL, hemoglobin 16.7 g/dL, hematocrit 49.7%, platelet count 365 x10E3/uL. C-reactive protein < 0.3 mg/dL. Transglutaminase IgA <20.0 CU. TSH 0.46 mcIU/mL, fecal calprotectin 32 ug/g, Helicobacter pylori antigen stool antigen negative, vitamin B12 626 pg/mL, ferritin 241 ng/mL, anti-nuclear antibody < 1:40 titer, hepatitis B antigen nonreactive, hepatitis C viral antibody nonreactive. CT abdomen pelvis with contrast showed mild colonic diverticulosis without diverticulitis, otherwise unremarkable. Irritable bowel syndrome was considered likely and he was referred to gastroenterology.

Gastroenterology suspected Familial Mediterranean Fever given the cyclical pattern of fever and peritoneal symptoms. Familial Mediterranean Fever testing revealed heterozygosity for familial Mediterranean fever mutation M694I. The patient was started on daily colchicine 1.2 mg with improvement in symptoms.

Discussion

Familial Mediterranean Fever is an autoinflammatory disorder with variable symptomatology. Almost all cases have fever during flare ups.[2] Our patient was atypical with fever only sometimes present. Abdominal pain is present in up to 95 percent of Middle Eastern patients.[1] Chest pain is present in 33 to 84 percent.[2] Erysipelas-like rash is reported in 12 to 40 percent of patients.[3] Other symptoms can include joint pain, exertional myalgia, pericarditis and headache.

Common laboratory findings in Familial Mediterranean Fever include elevation of serum markers of systemic inflammation, such as leukocytosis, elevated erythrocyte sedimentation rate, fibrinogen, and C-reactive protein. Long term complications can include progressive secondary amyloidosis.[4] Therefore screening with urine protein/creatinine is important. The diagnosis of FMF is established with genetic testing, although diagnostic criteria are useful.

The goals of treatment of Familial Mediterranean Fever are to prevent acute attacks, minimize inflammation, and to prevent complications such as amyloidosis. Colchicine is considered first line treatment and should be started as soon as diagnosis is suspected and continued indefinitely. Following colchicine initiation, patients should be regularly followed to monitor for colchicine toxicity and therapeutic efficacy measured by attack frequency and severity. Complete blood count is used to monitor for colchicine induced leukopenia. Inflammatory markers

including erythrocyte sedimentation rate and C-reactive protein monitor disease response. Urine protein is used to screen for renal amyloidosis. Liver and kidney functions are monitored for colchicine dose adjustment. Colchicine's effectiveness and relative ease of treatment, make it essential to keep FMF on the differential for cases of cyclical abdominal symptoms especially with fever.

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