1-1-2011

Protracted Febrile Myalgia in a Child as the Presenting Sign of Familial Mediterranean Fever: Case Report and Review of the Literature

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Balkan Med J 2011; 28: 222-223 • DOI: 10.5174/tutfd.2009.02972.3

Protracted Febrile Myalgia in a Child as the Presenting Sign of Familial Mediterranean Fever: Case Report and Review of the Literature

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ABSTRACT

Protracted febrile myalgia (PFM) is a rare form of vasculitic disease which is an uncommon dramatic manifestation of familial Mediterranean fever (FMF), characterized by severe crippling myalgia and high fever. We describe a 14-year-old boy who presented with fever, abdominal pain and severe myalgia in all his muscles for 5 days. The diagnosis of PFM was considered based on the presence of fever, paralyzing myalgia with normal CPK, elevated CRP and ESR. Thus, we started prednisolone treatment and his symptoms disappeared and acute-phase reactants declined rapidly. Mutational analysis of the MEFV gene demonstrated homozygote M694V mutation. Thus, he was diagnosed as PFM and FMF. In this report, we present a child with PFM as the sole feature preceding the diagnosis of FMF, and draw attention to the PFM for the diagnosis of FMF even the patient does not fulfill the criteria for the clinical diagnosis.

Key Words: Familial Mediterranean fever, myalgia, protracted febrile myalgia, children

Received: *08.07.2009* ***Accepted:*** *18.08.2009*

Introduction

Familial Mediterranean fever (FMF) is an autosomal recessive disease characterized by recurrent self-limited attacks of fever accompanied by peritonitis, pleuritis, and arthritis. The disease is predominantly seen in Mediterranean populations (Jews, Armenians, Arabs, Turks). Several types of vasculitis are associated with FMF: Polyarteritis Nodosa (PAN) and Henoch-Schonlein Purpura (HSP) are the best delineated ones. Protracted febrile myalgia (PFM) is another rare form of vasculitic disease which is an uncomman dramatic manifestation of FMF. PFM may occur despite colchicine therapy and requires treatment with corticosteroids. PFM, first described by Langevitz et al. (1) in 14 FMF patients in 1994, is characterized by severe paralyzing myalgia and high fever, sometimes accompanied by abdominal pain, diarrhea, and arthritis/arthralgia, and in a few patients by transient vasculitic purpura mimicking HSP. The episode lasts for 4-6 weeks, except in those patients treated with corticosteroids. High ESR, hyperglobulinemia, normal CPK, and subtle nonspecific inflammatory myopathic changes on EMG are the other characteristics (1, 2). In this report, we present a child with PFM as the sole feature preceding the diagnosis of FMF and draw attention to the PFM for the diagnosis of FMF even the patient does not fulfill the criteria for the clinical diagnosis.

Case

A 14-year-old boy presented with fever (38.5°C) and severe myalgia in all his muscles for 5 days. Due to the myalgia, he was unable to walk without help. He was the second child of a consangineous marriage, and he had two healthy siblings. Family history was negative for FMF.

Physical examination revealed normal anthropometric development. His blood pressure was normal. He had muscular tenderness over the extremities, neck, and shoulders. The remaining physical examination was normal. Laboratory evaluation showed normal urinalysis; hemoglobin 11.6 g/dL, leukocyte count 10.900/mm^3, and thrombocyte 349.000/mm^3. In a peripheral smear of leukocytes, 76% were PMNL. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), ASO titer, and fibrinogen were 52 mm/h, 76.4 mg/dl, 350 IU/mL, and 583 mg/dL, respectively, and all were elevated. Serum glucose, urea, creatinine, creatine phosphokinase (CPK), transaminases, alkaline phosphatase, calcium, sodium, potassium, magnesium, phosphate, uric acid, total protein and albumin were all within normal limits. Serum C3 and C4 levels were normal. ANA, antidsDNA, p-ANCA, and c-ANCA were negative. Blood, urine, and throat cultures were sterile. Occult blood in the stool was negative. Serology for brucellosis and salmonellosis was negative. Chest x-ray and abdominal ultrasonography, including Doppler examination of the liver and kidney were normal.

The diagnosis of PFM was considered based on the presence of fever, paralyzing myalgia with normal CPK, elevated CRP and ESR. Thus, we began treatment with 2 mg/kg prednisolone per day, his symptoms disappeared and acute-phase reactants declined rapidly, supporting the diagnosis of PFM. Mutational analysis of the MEFV gene demonstrated homozygote M694V mutation and 2x0.5 mg colchicine was added to the treatment. Thus, he was diagnosed as PFM and FMF.

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Discussion

FMF, also known as paroxysmal polyserositis, is an autosomal recessive inflammatory disease characterized by a lifelong course and recurrent attacks of inflammation of serosal membranes and fever resulting in acute abdominal, chest, and/or joint pain (3, 4). Among rare symptoms of the disease, muscular manifestations may be seen as one of the main clinical manifestations or as its sole feature and should be recognized. PFM was first described in a group of FMF patients who had profound myalgia, fever, arthritis, and purpura lasting more than 1 month (1).

In our patient, the possibility of underlying FMF was suggested after the appearance of PFM, and the patient was later found to be a homozygote for the FMF mutation. PAN which is reported to be coincidental with FMF, shares common findings of PFM such as fever, abdominal pain, arthralgia, and myalgia. These are shared symptoms with PFM which were also present in our patient; however, there was no sign of renal involvement, ANCA was negative, and no visceral vascular aneurysm was detected; thus, no histopathologic or radiologic sign of vascular inflammation required for the diagnosis of PAN was present (5). Fever, severe musculoskeletal pain, and elevated ESR could be associated with malignancy, especially hematologic malignancies. Our patient's hematologic evaluation showed normal hemoglobin and platelet count, and leukocytosis with PMNL predominance. He had no hepatosplenomegaly, or lymphadenopathy. Also, there was no atypical cell in the peripheral smear, excluding the possiblity of malignancy.

Although PFM is an uncommon finding in FMF, it causes severe paralyzing myalgia. Similarly, in our patient, myalgia was so severe that he was unable to walk without help. PFM characterized by severe crippling myalgia and tenderness, is usually bilateral and in the lower extremities. In some patients, all muscles ache (6). Similarly, our patient had severe myalgia in all muscles. Treatment consists of prednisolone, beginning with 1-2 mg/kg per day with slow tapering, which will result in immediate relief, as we observed in our patient. In addition to response to steroids, all the clinical and laboratory findings of our patient were compatible with PFM.

Majeed et al. examined the expanded clinical profile of FMF prospectively in a large group of Arab children seen in pediatric FMF clinics from January 1991 through December 1998, and found the incidence severe myalgia to be 11% (52/476) (7). Majeed et al. also studied the frequency and clinical patterns of myalgia prospectively in a group of 264 children with FMF seen from September 1995 through September 1999, and found the incidence of myalgia to be 25% (65/264) (2). They defined myalgia as pain or tenderness, or both, in the extremities distant from the joints in the absence of joint swelling and signs of underlying osteomyelitis. Three clinical patterns of myalgia were identified: An exercise-induced pattern of myalgia (81% of all cases of myalgia) was more common than the others and defined as the onset of myalgia within 8 hours of exercise. In these children the episode lasted for 1-3 days, similar to the duration of the other serosal attacks of FMF. Furthermore, the response to colchicine was also similar, with a success rate of 97%. The spontaneous pattern of myalgia (8% of cases) was mild to moderate myalgia, not related to exercise or any other precipitating factor, that lasted for about 8 hours. PFM comprised 11% of all cases of myalgia (2, 7). Majeed et al. presented 407 children with FMF, of whom 12 (3%) developed PFM (8). Similarly, Odabaş et al. reported that 3 of 96 (3%) patients with FMF had PFM in their series (9).

Kaplan et al. presented an analysis of patients with PFM and proposed clinical criteria for diagnosis in a multicenter cohort study in 2007 (10). They proposed criteria for a working diagnosis including: severe disabling myalgia of at least 5 days in a young patient with FMF, associated with fever, elevated levels of inflammatory markers and the presence of at least one M694V mutation (10). However, it was also reported that PFM may occur as a first attack before being diagnosed as having FMF (2, 6, 10, 11). Similarly, in our patient, the first FMF attack was characterised by PFM. In conclusion, we emphasise that PFM is an uncomman dramatic manifestation of FMF and may occur as the presenting sign preceding the diagnosis of FMF even the patient does not fulfill the criteria for the clinical diagnosis.

Conflict of Interest
No conflict of interest was declared by the authors.

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