OLGU SUNUMU / CASE REPORT

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Piyelitten Miyozite: Uzamış Febril Miyalji Sendromlu Olgu

From Pyelitis to Myositis: Protracted Febrile Myalgia Syndrome – A Case Report

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ÖZ

Giriş: Uzamış febril miyalji sendromu (UFMS) şiddetli kas ağrısı ve ateş ile karakterize olup, ailevi Akdeniz ateşi (AAA) hastalarında nadir görülen bir durumdur. Daha önceden AAA tanısı olmayan ve piyelit nedeniyle takip edilirken uzamış febril miyalji atağı geçiren bir olguyu sunmayı amaçladık.

Olgu Sunumu: Yedi yaşında kız hasta karın ağrısı, yüksek ateş ve dizüri ile başvurdu. Akut faz reaktanlarının yüksek olduğu tespit edildi. Hastanın ultrason görüntülemesinde piyelit bulgusu saptandı ve antibiyotik tedavisine rağmen ateşi devam etmekteydi. Takibinde yaygın kas ağrısı ve aktivite kısıtlılığı gelişti. Hastaya, UFMS tablosu olması ve ardından da M694V homozigot mutasyonu saptanması ile AAA tanısı konuldu.

Sonuç: Şiddetli miyalji, ateş ve akut faz reaktan yüksekliği olan olgularda UFMS akılda tutulmalıdır.

Anahtar Kelimeler: çocuk, ailevi akdeniz ateşi, miyalji

ABSTRACT

Objective: Protracted febrile myalgia syndrome (PFMS) is a rare condition in patients with familial Mediterranean fever (FMF), characterised by severe muscle pain and fever. We present a case of protracted febrile myalgia in the setting of pyelitis in a patient with undiagnosed FMF.

Case Report: A seven-year-old patient was admitted with abdominal pain, high fever, dysuria and high acute phase reactants. The patient had an ultrasound imaging finding of pyelitis, persistent fever despite antibiotic therapy. The patient developed generalised myalgia, edema of the muscles and activity limitation. She was diagnosed with FMF followed by PFMS and detection of M694V homozygous mutation.

Conclusion: Protracted febrile myalgia syndrome should be considered in cases of severe myalgia, fever and elevated acute phase reactants.

Keywords: child, familial mediterranean fever, myalgia

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INTRODUCTION

Familial Mediterranean fever (FMF) is an autosomal recessive autoinflammatory disease characterised by self-limited recurrent fever, peritonitis, pleuritis, arthritis or erysipelas-like cutaneous manifestations [1]. Protracted febrile myalgia syndrome (PFMS) is characterised by severe muscle pain, limitation of movement and fever. It is a rare condition in FMF patients. PFMS was first defined by Langevitz et al in 1994 as episodes of severe activity-limiting myalgia, fever, high acute phase reactant levels and hyperglobulinemia lasting 4-6 weeks in patients with FMF [2]. Muscle enzymes are always within the normal range in patients. Frequently, at least one M694V mutation is detected [3,4]. Here we report a case of PFMS in which FMF was not previously diagnosed and which presented with pyelitis. Our case is important. Because the patient had not previously been diagnosed with FMF and was diagnosed with PFMS during follow-up with another diagnosis.

CASE REPORT

A seven years old female patient was admitted to our clinic with abdominal pain of 10 days duration. On physical examination, she had tenderness in the epigastric and left costovertebral region. Other systemic examinations were normal. Urinary ultrasonography (USG) showed an enlarged left renal pelvis with an AP diameter of 8.5 mm and mucosal enlargement of the proximal urethral mucosa with a mucosal thickness of 1.5 mm. These findings were consistent with pyelitis. Urinalysis was normal. Blood and urine cultures did not detect any microorganisms. Her fever persisted despite treatment with ceftriaxone. On day 3 of her clinical follow-up, the patient had generalized muscle pain and her activities were limited. Laboratory analysis showed hemoglobin (Hgb) 12.5 g/dL, white blood cell (WBC) 16.07x103/µL, platelet (PLT) 714x103/µL, C-reactive protein (CRP) 220 mg/L, erythrocyte sedimentation rate (ESR) 78 mm/h, ferritin 600 ng/mL, serum amyloid A >30 mg/dL, lactate dehydrogenase (LDH) 708 U/L, fibrinogen 595 mg/dL. Muscle enzymes were within normal limits. Her treatment was changed to vancomycin and cefepime due to persistent fever and elevated acute phase reactants. We investigated the patient for infectious factors, malignancy and rheumatological conditions. Brucella Wright test, Plasmodium polymerase chain reaction (PCR), Leishmania PCR, Influenza PCR, COVID-19 PCR, Ebstein Barr Virus and Cytomegalovirus serologies were negative. Echocardiography was normal. Bone marrow aspiration was performed because of hyperferritinemia and resistant fever. No haemophagocytic or blastic cells were seen in the bone marrow smear. Anti-nuclear antibodies were negative. Immunoglobulin and complement levels were in the normal range, C3 was 208 mg/dL and C4 was 37.9 mg/dL. Whole-body MRI showed diffuse T2A signal enhancement in both shoulder muscles, both arms and forearm muscles, hands, gluteal muscles, paravertebral muscles, bilateral thigh and crural muscles, and abdominal wall muscles, consistent with myositis. Increased signal was seen in the subcutaneous adipose tissue of both arms, forearms and hands (Figure 1). Muscle biopsy was performed. The patient was treated with 2 mg/kg/d prednisolone and 10 mg/week methotrexate (MTX) with a presumptive diagnosis of polymyositis based on the MRI findings. Muscle biopsy results were normal. Despite resolution of myalgia and fever on clinical follow-up, acute phase reactant elevation persisted. Treatment with colchicine was started for subclinical inflammation. Genetic analysis for autoinflammatory diseases was also performed. In the Mediterranean fever gene (MEFV) analysis, a homozygous M694V missense mutation was detected. Although there were no classic findings associated with familial Mediterranean fever, it was noted that she had recurrent short-term leg pain and inability to walk for the past year. Protracted febrile myalgia syndrome (PFMS) was diagnosed because the patient had fever, severe myalgia, elevated acute phase reactants and a homozygous M694V mutation. During follow-up, the patient achieved remission, steroids and MTX were discontinued and colchicine was continued.

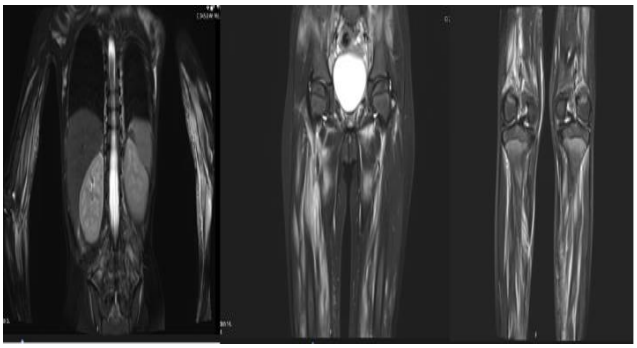

Figure 1. Whole body MR images. Widely T2A signal increases in both shoulders, both arms and forearm muscles, abdominal muscles, paravertebral muscles, bilateral thigh and crural muscles.

DISCUSSION

Patients with FMF are easily diagnosed when they present with classic symptoms such as recurrent fever, abdominal pain and serositis. However, diagnosis can be difficult when patients present with an atypical symptom such as myalgia, arthralgia or subclinical inflammation. Our patient did not describe a typical clinical attack and there was no family history of FMF. In our case, the initial diagnosis was pyelitis based on urinary USG findings. As the fever persisted and did not resolve with broad-spectrum antibiotics, we investigated the unknown aetiology of the fever. She was diagnosed with PFMS based on myositis findings, persistent acute phase reactant elevation and homozygous MEFV mutation. She was subsequently also diagnosed with FMF. There are three types of febrile urinary tract infection (fUTI). These are pyelitis, acute pyelonephritis and lower urinary tract infections. Pyelitis is an inflammation of the kidney pelvis. Acute phase reactant levels may be lower in pyelitis than in acute pyelonephritis. Dimercaptosuccinicacid (DMSA) is normal because pyelitis does not involve the renal parenchyma [5]. Although urinalysis has the highest sensitivity in the diagnosis of fUTI, it has a high false-positive rate and a low positive predictive value. A negative urine culture was found in 10-35% of cases of acute pyelonephritis diagnosed with DMSA [6]. Therefore, radiological imaging is also important in the diagnosis of fUTI. In our patient, urinalysis was also normal and pyelitis was diagnosed by ultrasound imaging. Myalgia in FMF occurs in three clinical forms: spontaneous, exercise-induced and protracted febrile myalgia. PFMS accounts for 11% of myalgia in FMF [3]. In the literature, the M694V mutation has been associated with a more severe clinical course of FMF and PFMS [2,4]. The detection of the M694 homozygous mutation in our case supported the diagnosis of PFMS. In a multicentre cohort study conducted in 2007, severe myalgia lasting at least 5 days, normal muscle

enzyme levels and a family history of FMF were mandatory criteria for PFMS. High fever, at least one M694V mutation and elevated acute phase reactants were also reported as supportive findings [7]. Our case had two of the mandatory criteria and all the supportive findings. Similar to our case, FMF cases in which PFMS is the first finding have been reported in the literature [4,7,8,9]. Prolonged febrile myalgia attacks can last up to 4-6 weeks if not treated appropriately. Colchicine is the main treatment option for FMF but does not prevent the development of PFMS attacks. Treatment for PFMS includes non-steroidal anti-inflammatory drugs and glucocorticoids. In addition, some studies have shown that an IL-1 antagonist is also beneficial [3,10]. In our patient, no recurrence of the prolonged febrile myalgia attack was observed after glucocorticoid treatment.

CONCLUSION

Protracted febrile myalgia syndrome is a rare clinical entity in FMF. Complaints of severe myalgia, fever and acute phase reactant elevation may be the first presentation of PFMS and FMF, even patients may apply to infectious diseases clinics. MEFV gene analysis should be requested in these cases.

Informed Consent: The patient's informed consent was obtained.

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