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Coexistence of Familial Mediterranean Fever and Guillain Barre Syndrome

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Abstract

Familial Mediterranean Fever (FMF) is the most common autoinflammatory disease characterized by recurrent episodes of abdominal pain, fever and serositis. FMF is an autosomal recessively inherited and self- limiting disease. It is more common in countries around the Mediterranean. Guillain Barre Syndrome (GBS) is an acute, immune-mediated polyneuropathy affecting peripheral nerves and nerve roots. GBS is usually characterized by progressive flaccid paralysis and decreased deep tendon reflexes. Central nervous system involvement is not common in the course of FMF. Guillain Barre Syndrome developed in a patient who was followed with colchicine treatment for 1 year due to Familial Mediterranean Fever. In the literature review, no association of these two diseases was found. This case is presented to draw attention to the coexistence of immune-mediated Familial Mediterranean Fever and Guillain Barre Syndrome. In this case, it was thought that two inflammatory diseases may have affected each other or autoinflammatory diseases can be seen together.

Key words: Familial mediterranean fever; guillain-barre syndrome; immune system diseases.

Introduction

Familial Mediterranean Fever (FMF) is a common autosomal recessive autoinflammatory disease characterized by recurrent, self-limiting, fever and painful inflammation attacks(1). It is more common in countries around the Mediterranean. Neurologic involvement is very rare in patients with Familial Mediterranean Fever(2). Guillain-Barre Syndrome (GBS) is an acute, inflammatory immune disease of peripheral nerves and nerve roots. GBS is usually characterized by progressive flaccid paralysis and decreased deep tendon reflexes. It is an acquired acute polyradiculoneuropathy with diffuse sensory, motor and autonomic symptoms. GBS is usually diagnosed based on clinical criteria, but nerve conduction changes in electromyography (EMG) and albuminocytologic dissociation in cerebrospinal fluid (CSF) examinations help to confirm the diagnosis of GBS(3).In our case report, we present a patient who was diagnosed with FMF 1 year ago. The patient who was followed up with colchicine developed 2 FMF attacks in the last 1 year. Guillain barre syndrome developed in this patient following upper respiratory tract disease. In the literature, the coexistence of these two diseases was not found and this case study aims to present two immune-mediated diseases in one case.

Case

A 17-year-old male patient presented to the emergency department with the complaint of sudden onset of weakness in the hands and feet after upper respiratory tract infection 5 days ago. As a result of the initial evaluation of the patient, he was diagnosed as Guillain-Barre Syndrome by pediatric neurology at an external center. The patient's MRI showed thickening and increased contrast enhancement at the level of the conus medullaris and anterior neural roots and the patient's EMG was compatible with acute motor axonal neuropathy (AMAN). The patient did not ask for lumbar puncture. Clinical findings, the fact that the EMG was compatible with guillain barre and the presence of anterior root involvement on contrast-enhanced MRI were considered as guillain barre. 1 g/kg intravenous immunoglobulin (IVIG) 2 days treatment was organized for the patient. The patient who was consulted to us for rehabilitation was mobilized with a single support, sensory examination, range of motion was normal, right upper extremity muscle strength was 4/5,

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right lower extremity 3/5, left lower 4/5, bilateral foot dorsiflexion 1/5, deep tendon reflexes were hypoactive. In the patient's history, it was found that the patient received 2*0,5 mg colchicine treatment 1 year ago with the diagnosis of FMF (V726A heterozygote) according to tel-hashomer criteria and stated that he used colchicine regularly throughout the treatment and had 2 attacks in the last 1 year. He stated that he had no known comorbidities and 2 aunts and 1 uncle had FMF disease in his family history. When the patient's attacks before the diagnosis were interrogated, it was determined that fever was accompanied, but fever was not accompanied in the 2 attacks after colchicine. Three days after hospitalization, the patient had an attack of severe lower extremity myalgia, abdominal pain and chest pain. During the attack, the patient's vitals were normal, fever was 37.3, bowel sounds were normal with no defense rebound on physical examination, standing plain abdominal radiography and ECG were normal, cardiac enzymes were within normal limits, and C-reactive protein(CRP) among acute phase reactants was found to be elevated in laboratory tests (table 1). Physical examination revealed a 2 cm^2 erysipelas-like erythema area on the forearm and posterior lateral malleolus of the ankle.

Table 1: Patient's laboratory values during the attack

Hgb:	16.22;	11-16 g/dL	ALT:	112;	0-40 u/L	Albumin:4.7;	3.4-5.4 g/dL
WBC:	6.42;	4-10 10^3/uL	AST:	70;	2-35 u/L	Fibrinogen: 182;	200-400 mg/dL
Neutrophil:	3.21;	2-7 10^3/uL	Creatine:	0.61;	0.5-0.9 mg/ dL	Brucella : negatif	
Lymphocytes:	2.58;	0.8-4	CRP:	73;	0-5 mg/ dL	Full urinalysis: normal	
Platelets:	285;	100-400	ESR:	7;	0-30 mm/h	Creatin kinase:	216; 30-226 U/L
Troponin:	0.001;	0-0.004	CK-MB:	14.5	0-500 U/L		

Hgb: hemoglobine, **WBC:** White blood cell, **ALT:** alanine aminotransferase, **AST:** aspartate aminotransferase, **CRP:** C-reactive proteine, **ESR:** erythrocyte sedimentation rate, **CK-MB:** creatine phosphokinase-MB

The patient who was consulted to neurology in terms of GBS relapse was not found to be significant in terms of relapse. Colchicine treatment was continued and 1 mg/kg methyl prednisolone treatment was organized. In terms of amyloidosis, proteinuria was found to be 78 mg/day and creatine 720 mg/day in 24-hour urine test. After the attacks, the patient's colchicine was regulated as 3*0,5 mg and due to the severe neuropathic pain of the patient, gabapentin was gradually increased and 3*600 mg treatment was organized with the recommendation of neurology. For physical therapy, range of motion exercises, stretching and strengthening exercises, parallel bar walking exercises, transcutaneous electrical stimulation (TENS) modalities were performed in all 4 extremities. Physiotherapy rehabilitation for muscle weakness was completed. The patient was able to walk a short distance without support, deep tendon reflexes were normal and patient's discharge was planned.

Discussion

In the literature studies, no coexistence of these two diseases was found. In this case, it was thought that two inflammatory diseases may have affected each other. Considering that autoinflammatory diseases can be seen together and in recent studies, diseases such as infection, vaccination, birth, surgical operation etc. may cause GBS development. considering these situations, it was thought that FMF may trigger GBS formation. FMF is an autosomal recessively inherited disease characterised by fever and inflammation which may be localised with peritoneal, pleural, joint and cutaneous findings(3). FMF is a disease generally seen in Turkish, Jewish, Armenian and Arab communities, and although it varies in ethnic groups, its incidence is generally between 1/200 and 1/1000(4). The prevalence of FMF in Turkey is estimated to be approximately 1/1000 (5,6,7). In the pathophysiology of FMF, it occurs as a result of mutation in the MEFV gene located on chromosome 16. The MEFV gene located on chromosome 16 encodes the pyrin protein(8, 9). Pyrin, which is mostly found in neutrophils and macrophages, has an important role in apoptosis and inflammatory pathways (8,10). Mutated pyrin causes an exaggerated inflammatory response with uncontrolled interleukin-1 (IL-1) secretion (10). Guillain-Barre Syndrome is an acute, inflammatory immune disease of peripheral nerves and nerve roots. GBS is an acquired acute polyradiculoneuropathy characterised by diffuse sensory, motor and autonomic symptoms, usually with progressive flaccid paralysis and deep tendon reflex decline. In GBS, the diagnosis is usually

made on the basis of clinical criteria. In addition, nerve conduction changes in electromyography (EMG) and detection of albuminocytological dissociation in cerebrospinal fluid (CSF) examinations help to confirm the diagnosis of GBS(11). Colchicine-induced neuromyopathy and acute intermittent porphyria are diseases that should be considered in the prediagnosis of a fmf patient with muscle weakness and neuromyopathy. Colchicine-induced neuromyopathy involves the proximal muscles; acute intermittent porphyria involves the proximal muscles, autonomic symptoms such as tachycardia and hypertension and is accompanied by hypnatremia. However, in our case, the diagnosis of guillain barre was primarily considered because of the presence of clinical findings of ascending muscle weakness and absence of autonomic symptoms. Contrast uptake in MRI and EMG supported the diagnosis of guillain barre. Lumbar puncture is another diagnostic support but the patient did not want a lumbar puncture. Guillain Barre Syndrome develops 2 to 4 weeks after gastroenteritis, respiratory infection or vaccination in 50-70% of cases. Camplylobacter jejuni is the infectious agent most commonly associated with the axonal form of Guillain Barre Syndrome, while cytomegalovirus infection is associated with the GBS form characterised by sensory symptoms and cranial nerve involvement. Rare cases occur following surgery or in the course of other diseases (12). Guillain Barre Syndrome is thought to be an autoimmune disease resulting in the production of antibodies against antigenic proteins of peripheral nerves as a result of T cell activation. Infectious agents such as Ebstein-Barr virus, Cytomegalovirus, Mycoplasma pneumoniae and Campylobacter jejuni, vaccination, surgery or childbirth trigger the production of antibodies. Although antibodies target myelin proteins, axonal structures are the primary target of immune-mediated damage in some cases (13).

Conclusions

Inflammation is involved in the pathogenesis of both FMF and GBS. In addition to this association, the fact that GBS involves the nervous system and FMF is a disease that causes systemic inflammation and is characterised by multiorgan involvement is what distinguishes the two diseases. The role of genetics in the etiology of FMF disease can be predicted to be responsible for the genetic substructure in GBS. Different genetic-based studies have been performed in GBS, but no MEFV gene mutation study responsible for FMF has been found in GBS patients in the literature. Although more studies are needed to understand whether FMF is a risk factor or a prognostic factor for GBS or whether this is a coincidental association, this case is worth presenting in order to emphasise that GBS development should be considered in patients with FMF in the light of studies and case examples that the MEFV mutation, which is the gene responsible for FMF, may have an effect on the pathogenesis or prognosis of GBS.

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