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Mitochondrial neurogastrointestinal encephalomyopathy

Mitokondrial nörogastrointestinal ensafalomyopati

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Mitochondrial neurogastrointestinal encephalomyopathy is an autosomal recessive disease characterized by progressive ophthalmoplegia, peripheral neuropathy, mitochondrial abnormalities and gastrointestinal involvement. We describe a 19-year-old male having chronic intestinal pseudoobstruction associated with ophthalmoplegia and proximal muscle weakness. The clinical and radiologic features suggested the diagnosis of mitochondrial neurogastrointestinal encephalomyopathy. Mitochondrial genetic defects should be considered in the differential diagnosis of unexplained chronic gastrointestinal symptoms accompanied by neurological findings, especially in families where there is more than one individual with the same kind of symptoms.

Key words: Mitochondrial neurogastrointestinal encephalomyopathy, intestinal pseudoobstruction

Mitokondrial nörogastrointestinal ensafolomyopati, progresif oftalmopati, periferik nöropati, mitokondrial anormallikler ve gastrointestinal tutulum ile karakterize otozomal resesif geçişli bir hastalıktır. Biz, oftalmopleji ve proksimal kas güçsüzlüğü ile birlikte kronik intestinal psodoobstruksiyonlu 19 yaşında bir erkek hastayı tanımladık. Klinik ve radyolojik özellilkleri mitokondrial nörogastrointestinal ensefalomyopatiyi destekliyordu. Nörolojik bulguların eşlik ettiği, açıklanamayan kronik gastrointestinal semptomların ayırıcı tanısında, özellikle ailede aynı semptomlardan yakınan birden fazla birey varlığında mitokondrial genetik eksiklikler düşünülmelidir.

Anahtar kelimeler: Mitokondrial nörogastrointestinal ensefalomyopati, intestinal psödoobstruksiyon

INTRODUCTION

Mitochondrial disorders have clinical manifestations reflecting the fact that nearly all organ systems utilize oxidative metabolism. Clinical features often involve tissues with high energy requirements such as central and peripheral nervous systems, and eye, muscle, kidney and endocrine organs (1). Mitochondrial neurogastrointestinal encephalomyopathy (MNGIE), an autosomal recessive disease, is one of the mitochondrial disorders, and is a multisystem disease clinically defined by progressive ophthalmoplegia, peripheral neuropathy, leukoencephalopathy, mitochondrial abnormalities and severe gastrointestinal involvement (2, 3). Generally, age of onset is in the second decade (4), but it might be observed from infancy to middle age; most of the patients die by age 58 (2).

CASE REPORT

Our patient was a 19-year-old man suffering from poor appetite, nausea, vomiting and diarrhea since January 2001. He had a normal prenatal history, but parents reported difficulties walking, running, and climbing the stairs after five years of age. His physical examination revealed cachexia, weight 39 kg, and height 160 cm. Blood pressure and pulse were normal. All system examinations were interpreted as normal except neurological system. Neurological examination showed external ophthalmoparesis. He had proximal muscle weakness at four extremities. Plantar responses were negative. All deep tendon reflexes were absent. The patient was mentally intact. In laboratory examination complete blood count, biochemistry, arterial blood gases, erythrocyte sedimentation rate, ferritin, iron, complete urine examination, urine culture, thyroid function tests, stool microscopy, stool culture, aPTT, PTZ, and INR were in normal ranges. Autoimmune markers such as ANA, anti-dsDNA, anti-Scl-70, anti-Jo-1, and anti-nRNP were negative. Stomach was dilated

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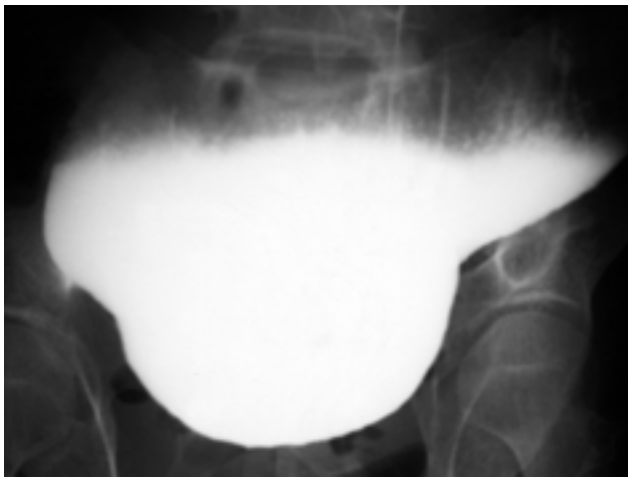

Figure 1. At radiologic evaluation stomach was dilated and enlarged to pelvis

and enlarged to pelvis at radiologic evaluation (Figure 1). Esophagogastroduodenoscopy revealed antral gastritis. Stomach was hypotonic and dilated with food products. Several biopsies were taken from bulbus, and the result was evaluated as chronic inflammation. In radiologic examination of the small intestine, mega duodenum was observed. Barium enema of colon was normal. No diverticulosis was detected. Mechanical obstruction was not present at any segment of the gastrointestinal system. His electrocardiography and echocardiography were normal. Because of abnormalities in neurological examination, cranial tomography was performed, and demyelinization of white matter was clear. The result of magnetic resonance imaging of the cranium exhibited the widespread and symmetric dysmyelinated regions of the periventricular and supraventricular white matter (Figures 2, 3). Electromyography demonstrated the sensorimotor demyelinization. We had planned muscle biopsy but the patient refused. Based on the findings of gastrointestinal system dysmotility, cachexia, ophthalmoparesis, proximal muscle weakness, and leukoencephalopathy, we considered this patient as MNGIE. The mother and father of our case were first-degree relatives. They had eight children, four of whom were healthy and the remaining four sick. Two of the four sick siblings died with unknown diagnosis, the first of whom was a 30-year-old male with the same complaints who died suddenly. His EMG result was sensorimotor demyelinated polyneuropathy, but the exact diagnosis was unkown. The second deceased sibling was a 28- year-old female who admitted to our hospital with the same complaints. On admission, her height was 170 cm and weight 29 kg. Gastric decompression was inefficient. Small intestinal radiography exhibited that the stomach was hypotonic and ptotic. The patient died with unknown etiology. We were unable to complete our research. Another sibling, a 27-year-old female, had the same symptoms 10 years ago.

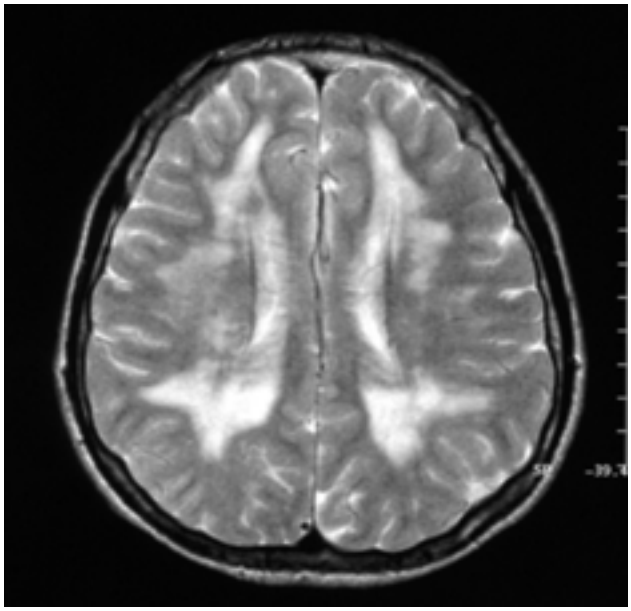

Figure 2. Magnetic resonance imaging of demyelinization of deep white matter at T2 axial level

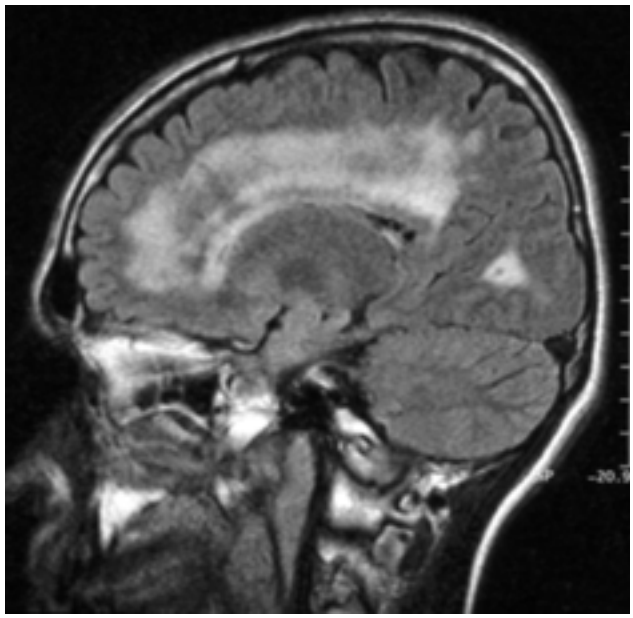

Figure 3. Magnetic resonance imaging of demyelinization of deep white matter at T2 sagittal level

Unknown gastric operations were performed at that time, at another center. She is still alive, but thin and weak. Her file documents could not be obtained.

DISCUSSION

Mitochondrial neurogastrointestinal encephalomyopathy is an autosomal recessive condition characterized by severe gastrointestinal dysmotility, cachexia, ptosis with progressive external ophthalmoparesis, peripheral neuropathy, leukoencephalopathy and laboratory evidence of mitochondrial dysfunction (2). It is associated with multiple deletions and depletion of mtDNA in skeletal muscle (5-6). In 1976, Okamura and associates (7) reported the first case as congenital oculoskeletal myopathy with abnormal muscle and liver mitochondria. Since then, more than 35 additional individuals with MNGIE have been described (5, 6, 8, 9). There were no metabolic, endocrine or nutritional causes for the disorder in our patient. The major clinical finding was chronic intestinal pseudoobstruction. Intestinal pseudoobstruction is a clinical syndrome characterized by ineffective intestinal propulsion (10). Based on clinical presentation, pseudoobstruction syndromes can be divided into acute and chronic forms. The most common type is the acute variety which is usually self-limited and related to surgical procedures (10) such as obstetric or gynecologic, orthopedic, or urologic surgeries and renal transplantation (11). Chronic intestinal pseudoobstruction is much less common and may be idiopathic or secondary to a known systemic disease (12-13). It has also been associated with several myopathies, such as myotonic dystrophy (14), familial visceral myopathy (15), dermatomyositis (16) and mitochondrial diseases. The association of mitochondrial disorders with gastrointestinal dysfunction has been reported in several cases (8-9), mostly as a part of the syndrome known as MNGIE (3). The most common neurological features of MNGIE are peripheral neuropathy, ptosis, ophthalmoparesis and hearing loss (2). As indicated in several cases, neuropathy was clinically mild, and this was the case in our patient as well. In neurological examination, pupils were normal with good response to light. Ocular movements were restricted to a few degrees in any direction. Ophthalmoplegia was evident. It is a striking but nonspecific clinical sign which occurs in different diseases. In some instances, it is a part of well-defined neuromuscular disorders, for example, myasthenia gravis, thyrotoxicosis, myotonic dystrophy, and mitochondrial myopathy (17). In our case, deep tendon reflexes were absent. No fasciculation was observed. No dementia or mental retardation was detected. Cranial magnetic resonance imaging was demonstrative for white matter demyelinization. The patient we described fits the characteristics of those reported by Nishino et al. (2). These authors found diffuse leukoencephalopathy in all 27 of their patients. In their report, dementia was not detected and mental retardation was seen in only one. In the report of Nishino and associates, serum lactic acidosis was present in 12 of 18 patients with the syndrome. However, in our case serum lactic acid level was in the normal range.

With the diagnosis of MNGIE, we started the patient on a treatment of broad spectrum antibiotics and domperidone, but no response was observed. There is no known efficient treatment modality for such patients.

In conclusion, mitochondrial genetic defects should be considered in the differential diagnoses of unexplained chronic gastrointestinal symptoms accompanied by neurological findings, especially in families in which more than one individual suffers from such symptoms.

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