



Epilepsy and McArdle Disease in a Child

Bir Çocukta Epilepsi ve McArdle Hastalığı

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ABSTRACT

McArdle's disease, defined by the lack of functional glycogen phosphorylase in striated muscle, is inherited as an autosomal recessive trait. Patients typically suffer from reduced exercise tolerance, with muscle cramps and pain provoked by exercise, along with easy fatigability and weakness after exercise. Following prolonged exertion, contractures, rhabdomyolysis, and myoglobinuria may occur. Central nervous system symptoms have rarely been reported in McArdle disease. In this case report, a 13-year-old boy with epilepsy and McArdle's disease is presented.

Key words: McArdle's disease, epilepsy, coexistence.

ÖZET

McArdle hastalığı, çizgili kasta glikojen fosforilaz enziminin eksikliği sonucu gelişen, otozomal resesif kalitim gösteren bir hastalık olarak tanımlanmaktadır. Hastalar genellikle çabuk yorulma ve egzersiz sonrası güçsüzlük ile birlikte, kas krampları, ağrı ve azalmış egzersiz toleransından yakınırlar. Uzun süreli efor sonrası kontraktür, rabdomiyoliz ve miyoglobinüri oluşabilir. Merkezi sinir sistemi belirtileri McArdle hastalığında nadiren bildirilmiştir. Burada, epilepsi ve McArdle hastalığı olan 13 yaşındaki bir çocuk sunulmuştur.

Anahtar kelimeler: McArdle hastalığı, epilepsi, birliktelik.

INTRODUCTION

McArdle's disease is an autosomal recessive metabolic myopathy due to a genetic defect of the muscle-specific isozyme of glycogen phosphorylase (myophosphorylase)¹. The disease usually presents in childhood or adolescence, and is characterized by exercise intolerance, myalgia, cramps, increased resting serum creatine kinase (CK), and episodic myoglobinuria². Traditionally, diagnosis is based on the inability of the patient to produce lactate during a forearm exercise test, lack of muscle glycogen phosphorylase activity on muscle biopsy and, more recently, DNA studies in *PYGM*³.

Myophosphorylase expression is not muscle restricted. This enzyme is also expressed in astrocytes, where it has been reported to have a key role in neural energy metabolism. To date, there are only a few reliable report manifestations of central nervous system (CNS) in McArdle disease⁴⁻⁶. Here we report the case of an Turkish 13-year-old boy with McArdle disease and epilepsy.

CASE

A 9-year-old boy presented to the hospital with complex partial and secondarily generalized

seizures, since 1 month. His mother and father were first-degree cousins. The developmental milestones were normal. There are no members in his family with epilepsy.

On his examination, vital signs and anthropometric measurements were in normal limits. The physical and neurological examinations were unremarkable.

Laboratory studies including, serum electrolytes, glucose, liver and kidney test values were normal. Electroencephalography (EEG) showed normal background activity and epileptic focus on the left centro-parietal region. Cranial magnetic resonance imaging (MRI) was normal. He was started oxcarbazepine and controlled his seizures.

On 1 year of therapy, his seizures started again. His treatment was reviewed and increased dose of oxcarbazepine and controlled his seizures again. On laboratory results, all of the biochemical tests were found normal.

On the 2nd year, he complained of mild myalgia, and early fatigue since the past few days. His physical and neurological examination were normal. Laboratory tests showed the following results: serum electrolytes, glucose, bilirubin, gamaglutamyl transferase, and kidney functions were normal. The alanine transaminase (ALT) was 96 U/L, aspartate transaminase (AST) was 256 U/L, and serum creatinine kinase (CK) was 946 U/L (normal 0-171 U/L). Laboratory tests revealed no evidence of hemolysis. Oxcarbazepine was stopped due to abnormal laboratory tests results. Levetiracetam therapy was started for epilepsy. After seven days, all laboratory test results were found normal.

After six and nine months, he admitted to similar complaint of myalgia and fatigue. At presentation, results of laboratory tests showed increased levels of CK, ALT and AST. There was no myoglobinuria. Electromyography study was normal. We considered an extensive differential diagnosis, and excluded multiple events and conditions that may precipitate rhabdomyolysis by

history, including: exposure drugs except levetiracetam, crush or electrical injury, infections, and ischemic events. We have not found any things. We thought metabolic disorders such as McArdle disease or CPTII deficiency. The muscle biopsy, ischemic forearm test and muscle phosphorylase A activity could not performed. To confirm the diagnosis McArdle disease, we analyzed the *PYGM* gene sequencing in the patient, and revealed homozygous p.710delF (c.2128_2130delTTC) mutation.

DISCUSSION

Glycogen-storage diseases are the result of some enzyme defects. These enzymes normally catalyze reactions that ultimately convert glycogen compounds to glucose. Glycogen storage disease type V is called McArdle disease or myophosphorylase deficiency¹. Myophosphorylase, the deficient enzyme in McArdle disease, is found in the muscle tissue. The *PYGM* gene involved on it is located in the 11. chromosome³. The typical features of McArdle disease include exercise intolerance with myalgia, early fatigue, stiffness of exercising muscles, rhabdomyolysis, and myoglobinuria².

Central nervous system symptoms have been frequently reported in other glycogen storage diseases⁷, whereas, has rarely been reported in McArdle disease in literature. Among the first 112 described patients, seizures were reported in five cases⁵. Siciliano et al.⁶ reported, a 43-year-old male patient with McArdle disease who had a right hemiparesis 2 years before and a transient left hemiparesis the following year was reported in 1995. He had been suffering from generalized tonic-clonic seizures since the age of 24, attributed to a head trauma occurred at age 19. MRI of the brain showed multiple hemispheric lesions consistent with an ischemic process, as also suggested by single photon emission tomography of the brain; in an attempt to correlate brain with muscle pathology, a biopsy from an extracranial artery was taken off, but no evidence for glycogen

accumulation in smooth muscle cells of the temporal artery was obtained. Walker et al.⁸ describe a 33-year-old woman who had occult seizures. Mancuso et al.⁴ reported the case of a patient with McArdle disease and cognitive impairment. Here, we report an 13-year-old boy presenting with epilepsy and rhabdomyolysis due to McArdle disease.

To date, systematic studies about extramuscular involvement in McArdle disease are not available, probably because myophosphorylase has always been considered a muscle-restricted enzyme and, therefore, McArdle disease a "pure myopathy"¹. The lack of CNS involvement is attributed to the expression pattern of the three phosphorylase isoforms, each coded by genes on different chromosomes. Both the muscle and brain isoforms are expressed in brain, but the brain isoform is predominant and the lack of CNS symptoms is attributed to its abundant activity. A recent report of glycogen accumulation (as determined by 1H-magnetic resonance spectroscopy) in the brain of a patient with probable McArdle's disease awaits confirmation, but suggests that abnormal glycogen storage may occur in brain in some patients⁹.

In conclusion, to date the coexistence of epilepsy and McArdle disease has not been reported in children, and our patient is the first case in the literature. We are aware that the association of McArdle disease and CNS involvement. Finally, further studies in large groups of patients are needed in order to assess the prevalence of CNS involvement in this disease and to better characterize the clinical heterogeneity of the disease.

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