A Case of McArdle Disease: Efficacy of Vitamin B6 on Fatigability and Impaired Glycogenolysis

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Abstract

McArdle disease is a glycogenetic myopathy caused by a deficit of myophosphorylase inherited in an autosomal recessive pattern. Here, we report a case of McArdle disease in which fatigability was the only subjective complaint. Objective neurological findings were normal except for very mild muscle weakness in limbs and an elevated serum creatine kinase level. Ischemic forearm exercise test showed deficient glycogenolysis. In the muscle biopsy specimen, periodic acid Schiff (PAS) stained subsarcolemmal glycogen was increased and the muscle phosphorylase A activity was decreased. After administration of vitamin B6, fatigability was diminished and ischemic forearm exercise test showed improved glycogenolysis. Vitamin B6 may be beneficial for McArdle disease, especially for its easy fatigability.

Key words: fatigability, McArdle disease, vitamin B6


Introduction

McArdle disease is a glycogenetic myopathy caused by an inherited deficit of myophosphorylase, the skeletal muscle isoform of the enzyme glycogen phosphorylase (1). The patients typically show symptoms of myophosphorylase deficiency with exercise intolerance such as early fatigability, myalgia, contractures and sometimes myoglobinuria induced by exertion. Persistent and progressive muscle weakness and atrophy may occur in aged patients. However, in cases of mild McArdle disease, the patients do not notice such typical symptoms and they have had disadvantages in social activity and the diagnosis goes overlooked. We encountered a mild McArdle disease patient whose only complaint was general fatigue; her fatigability as well as lactic acid response in an ischemic forearm exercise test was improved by vitamin B6 supplementation.

Case Report

A 21-year-old woman had exercise intolerance since childhood. She experienced myalgia, cramps, and easy fatigability with mild exercise. Therefore, she learned to limit the amount of exercise to avoid such symptoms. None of her family members had such symptoms. At age twenty, she had difficulty in continuing her physically demanding job because of the fatigability. She was diagnosed as having psychological problems in other hospitals because of her minimal physical abnormalities. Finally, she was referred to our hospital since her serum creatine kinase (CK) level had been found to be higher than 1,000 IU/L.

Neurological examination showed only slight weakness in proximal muscles of the four extremities. The serum CK level was elevated to 2,499 IU/L, but other laboratory data were all within normal ranges. There was no auto-antibody detected. Though electromyography did not show typical myogenic nor neurogenic patterns, muscle cramps were easily observed at strong optional muscle contraction of the quadriceps femoris. The appearance of muscle cramps and unchanged lactic acid levels after the ischemic forearm exercise test suggested glycogen storage disease. An additional interview revealed an episode of a sudden, marked improvement in the tolerance to exercise (second wind). Therefore, we took a muscle biopsy from the biceps brachii. Periodic acid Schiff (PAS) staining of the muscle biopsy specimen
Figure 1. Hematoxylin and Eosin staining and PAS staining of the muscle biopsy sample from the biceps brachii. An increased subsarcolemmal space suggests accumulated glycogen.

Figure 2. Ischemic forearm exercise test before/after pyridoxine hydrochloride (Vitamin B6) supplement (90 mg/day). Ischemic forearm exercise test revealed an elevation of lactic acid suggesting the activity of myophosphorylase was improved by the pyridoxine hydrochloride (Vitamin B6) supplement.

revealed an increased amount of subsarcolemmal glycogen (Fig. 1). Muscle phosphorylase A activity was decreased to 0.24 μmol/min/gm/tissue (normal range >12.0), which is compatible with McArdle disease. She did not want to have genetic analysis.

After the diagnosis was made, we started to treat her with pyridoxine hydrochloride (vitamin B6) supplement (90 mg/day). About two months later, she was aware of an improvement of muscle fatigability. Ischemic forearm exercise test three months after the treatment became close to the normal response of lactic acid. These findings suggest improved myophosphorylase activity by vitamin B6 supplement (Fig. 2). Her serum CK level also decreased to 318 IU/L.

Discussion

The clinical symptoms of McArdle disease usually begin in young adulthood with exercise intolerance. Almost all McArdle disease patients (96%) show some kind of exercise intolerance like early fatigability, myalgia, contracture and sometimes myoglobinuria induced by exertion (2). In addition, they usually experience “second wind”, which probably results from a switch in the metabolic pathway from the glycolytic pathway to oxidative phosphorylation and is a characteristic feature of this disease (3, 4). Both exercise intolerance and second wind may be the most important manifestation suggesting McArdle disease in patients with easy fatigability. In patients with a glycolytic defect, the ischemic forearm exercise test shows no increase in pyruvate and lactic acid levels in venous blood flowing from contracting ischemic forearm muscles. The high sensitivity of this test (about 93%) may be beneficial to avoid overlooking McArdle disease (2).

On the other hand, Servidei et al collected atypical cases of McArdle disease and divided them four groups (5), as follows: 1. Mild fatigability or lack of stamina without my-
Table 1. Several Cases that Manifested Fatigability as the Only Subjective Complaint and were Finally diagnosed as McArdle Disease

<table>
<thead>
<tr>
<th>case</th>
<th>author</th>
<th>sex</th>
<th>age</th>
<th>family history</th>
<th>complain</th>
<th>clinical symptom</th>
<th>CK (IU/L)</th>
<th>exercise intolerance</th>
<th>second wind</th>
<th>ischemic forearm exercise test</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Present case</td>
<td>F</td>
<td>21</td>
<td>no</td>
<td>fatigue</td>
<td>normal</td>
<td>1000</td>
<td>yes</td>
<td>yes</td>
<td>positive</td>
</tr>
<tr>
<td>3</td>
<td>Nakasato et al [7]</td>
<td>M</td>
<td>15</td>
<td>no</td>
<td>fatigue</td>
<td>hypertrophy in deltoid, calf</td>
<td>234</td>
<td>yes</td>
<td>yes</td>
<td>positive</td>
</tr>
<tr>
<td>4</td>
<td>Watanabe et al [8]</td>
<td>F</td>
<td>25</td>
<td>yes</td>
<td>fatigue</td>
<td>normal</td>
<td>768</td>
<td>yes</td>
<td>yes</td>
<td>positive</td>
</tr>
<tr>
<td>5</td>
<td>Watanabe et al [8]</td>
<td>M</td>
<td>27</td>
<td>yes (case 4’s brother)</td>
<td>fatigue</td>
<td>normal</td>
<td>788</td>
<td>no</td>
<td>no</td>
<td>positive</td>
</tr>
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**References**