

# McArdle Disease and Pregnancy

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## ABSTRACT:

McArdle disease (Glycogen Storage Disease type V) is a rare hereditary disease, frequently diagnosed in adulthood. It is associated with exercise intolerance and severe rhabdomyolysis. There are only a few reported cases of pregnancy in these patients, and in most of them there was no worsening of the disease.

The authors report the case of a young woman presenting with severe rhabdomyolysis by the age of 28, being diagnosed with McArdle. She complained about exercise intolerance since childhood, but never had valued these symptoms. The authors also describe two pregnancies in the same patient. During the first pregnancy, there was improvement of the patient's complaints, but it was not observed during the second one.

The basis of the therapy of this disease consists of aerobic exercise and ensuring euglycaemia and enough protein intake. With these measures, it is possible to control the symptoms and complications of the disease.

**Keywords:** Rhabdomyolysis, Glycogen Storage Disease Type V, Pregnancy

**Palabras clave:** Rabdomiolisis. Enfermedad de Almacenamiento de Glucógeno de Tipo V. Embarazo

## Introduction

McArdle disease, despite being the most common of the glycogen storage diseases<sup>1</sup>, is a rare disease, which is sometimes diagnosed late in life<sup>2,3</sup>. The diagnosis is rarely made during childhood or adolescence<sup>4</sup>. The reported case illustrates these situations, where the patients frequently ignore the symptoms.

Also, there are only a few described cases of pregnancy and labour in patients with McArdle disease<sup>5-12</sup>. Therefore, the fact that this patient had two pregnancies can be helpful to understand the behaviour of this disease during pregnancy.

## Case presentation

The authors describe the case of a 28-year old female patient, who presented to the Emergency Department after a fall, without altered mental status. The fall occurred in context of a sudden generalized muscle weakness. She also complained of reddish urine, suprapubic discomfort and nausea without vomiting.

When asked about it, she also referred recurrent muscle cramps, of high intensity, since the age of 9, with associated exercise intolerance. Besides these complaints, she had always been healthy before. She had two siblings, both with the same muscular symptoms.

At physical examination there were no relevant changes, especially at neurological examination, where there were no deficits or asymmetries. She was afebrile and with no evidence of acute infection. From the preliminary laboratory results, the highlight goes to a severe rhabdomyolysis, with Creatine phosphokinase (CPK) of 272430 U/L (ref: 30 – 170U/L), Myoglobin of 24892 ng/mL (ref: 10 – 92 ng/mL) and Lactate dehydrogenase (LDH) of 21389 U/L (ref: 313 – 618 U/L). There was also an elevation in liver enzymes, in a cytolytic pattern, with Aspartate aminotransferase (AST)

of 1157 U/L (ref: 15 – 46 U/L) and Alanine aminotransferase (ALT) of 240 U/L (ref: 13 – 69 U/L), while Alkaline phosphatase and gamma-Glutamyltransferase remained within the reference range. Urinalysis was normal, as was the superior abdominal ultrasonography. The patient was then admitted to the ward in order to treat and investigate the rhabdomyolysis.

Autoantibody (Antinuclear antibodies, Anti-Jo1 and Extractable Nuclear Antigens) assays were all negative. The same happened with serologies for infectious agents, which were all negative, either bacterial (*Chlamydia*, *Leptospira*, *Mycoplasma*, *Rickettsia*, *Brucella* and *Legionella*) or viral (Coxsackie, Echovirus, Adenovirus, Hepatitis B virus, Hepatitis C virus and Human Immunodeficiency Virus).

An electromyography, an echocardiography and respiratory function tests were performed, being all these results normal.

A muscular tissue biopsy was also performed, and the histopathology showed the enzymatic deficit of myophosphorylase, with subsarcolemmal vacuoles. Even though phosphorylase staining can lead to false positive diagnosis, the presence of those subsarcolemmal vacuoles confirmed the diagnostic of Glycogen Storage Disease type V (McArdle disease).

Rhabdomyolysis can occur in various situations, mainly infectious or inflammatory status, but also in metabolic diseases. In this case, the differential diagnosis, taking into account the age of the patient, was between an infectious disease, an autoimmune disease and other genetic metabolic diseases. These metabolic diseases include other glycogen storage diseases, mainly type II (Pompe disease), or other diseases that affect mainly the muscle metabolism.

In hospital, the patient was treated with intravenous fluids in order to improve the rhabdomyolysis and prevent kidney injury secondary to myoglobinuria.

For long-term therapy, the established plan consists essentially in aerobic training and correct carbohydrate and protein intake in order to maintain euglycaemia and muscular mass.

The patient was hospitalized for 11 days, with a great improvement of the symptoms and of the rhabdomyolysis. By the time of discharge, she was referred to the internal medicine clinic, to keep her monitoring in an outpatient basis. There were no other episodes like the one who lead to hospitalization.

In the first 5 years of monitoring, CPK levels kept elevated but stable between 998 and 4691 U/L. During this period she was globally asymptomatic while resting or with mild physical activity, but moderate exercise (even in work) was usually associated with relapse of muscle symptoms. There were two CPK isolated values of 11032 and 15985 U/L, associated with even higher physical activity, but promptly treated with rest and increased fluid intake.

At the fifth year of follow-up, the patient got pregnant, being observed an improvement of the rhabdomyolysis, associated with an increase exercise tolerance. The patient's CPK levels were between 156 and 694 U/L, occurring for the first time within the normal range. During this pregnancy, the patient mentioned that she could endure higher physical activity without pain. The delivery occurred by caesarean, without any complications or worsening of rhab-

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domyolysis. This decision was based on a suspected fetopelvic incompatibility, and was made early in the process in order to avoid excessive muscular effort during parturition. After this pregnancy, there was a slight worsening of the laboratory profile, with CPK levels between 1259 and 5790 U/L, and a return to the previous clinical state had occurred, with the patient having symptoms again with moderate physical activity.

Two years after the first pregnancy, the patient got pregnant again. However, during the second pregnancy there was no improvement on exercise tolerance and rhabdomyolysis, with CPK levels between 1484 and 3651 U/L. Nevertheless, she kept asymptomatic in resting state during this pregnancy, but had symptoms associated with mild to moderate exercise. The delivery was also by caesarean, based again on a suspected fetopelvic incompatibility, and, as occurred in the first one, had no complications.

## Discussion

McArdle disease (Glycogen Storage Disease type V) is a hereditary metabolic disease, characterized by a deficit of the enzyme myophosphorylase<sup>1</sup>. This enzyme is essential to the carbohydrates metabolism. It converts muscular glycogen into glucose-1-phosphate<sup>13</sup>. Despite being the most common of the glycogen storage diseases, it is an uncommon disease, being transmitted as a recessive autosomal trait<sup>4</sup>. There are incidence reports from 1:100000 inhabitants in Texas to 1:650000 inhabitants in Norway<sup>7,14</sup>. Its features are essentially exercise intolerance, with premature fatigue, myalgia and muscle cramps. The “second-wind” phenomenon, which is specific of McArdle disease, is described as sudden improvement in tolerance to aerobic exercise after a short period of exertion<sup>15</sup>. Even though this phenomenon is very specific of this disease, a large proportion of patients do not identify it. Most of the patients present symptoms since childhood, but are only diagnosed in adult age<sup>4</sup>. This happens due to the fact that the patients and their families often ignore these symptoms<sup>2,3,16</sup>. That is exactly what happened with the described patient, who had symptoms since the age of nine and was only diagnosed when she was 28 years old, due to a more severe episode. The laboratory tests show, especially in a physical activity context, an elevation of rhabdomyolysis enzymes (CPK and myoglobin), as well as cytolysis enzymes (AST, ALT and LDH) without hepatic injury. There may also occur myoglobinuria. The main complication is the acute kidney injury, secondary to myoglobinuria, and which can lead to hemodialysis in more severe cases<sup>13</sup>.

The treatment of this disease is based in exercise and dietetic measures. Even though there are not randomised controlled trials on these subjects, two Cochrane reviews suggest aerobic exercise and dietary measures such as high protein

intake<sup>4,17,18</sup>.

In pregnancy, even though there are only a few cases described, the worsening of the disease is rare, occurring frequently an improvement of rhabdomyolysis, with the patients being asymptomatic or referring improvement of exercise tolerance. In a series of 20 pregnancies in 14 women, published in 2010, an improvement was seen in 13 of the patients<sup>7</sup>. Two other individually described cases also improved during pregnancy<sup>5,6</sup>. There are more pregnancies described, but there is not enough data to know if there was an improvement of the symptoms<sup>8-12</sup>.

Pregnancy is not defined as a risk factor in McArdle disease and normal delivery is not contraindicated<sup>5-8</sup>.

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