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CASE REPORT

# McArdle disease in a patient with anorexia nervosa: a case report

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## Abstract

**Background** McArdle disease is an autosomal recessive genetic disorder caused by a deficiency of the glycogen phosphorylase (myophosphorylase) enzyme, which muscles need to break down glycogen into glucose for energy. Symptoms include exercise intolerance, with fatigue, muscle pain, and cramps being manifested during the first few minutes of exercise, which may be accompanied by rhabdomyolysis.

**Case presentation** This case report describes for the first time the clinical features, diagnosis and management of a 20 year-old patient with anorexia nervosa and McArdle disease, documented by means of muscle biopsy.

**Conclusion** Anorexia nervosa and McArdle disease interact in a detrimental bidirectional way. In addition, some laboratory parameter alterations (e.g., elevated values of creatine kinase) commonly attributed to the specific features of eating disorders (e.g., excessive exercising) may delay the diagnosis of metabolic muscle diseases. On the other hand, the coexistence of a chronic disease, such as McArdle disease, whose management requires the adoption of a healthy lifestyle, can help to engage patients in actively addressing their eating disorder.

**Keywords** Anorexia nervosa · Glycogen storage disease type V · McArdle disease · Cognitive behavior therapy · Treatment · Excessive exercise

## Introduction

McArdle disease, or glycogen storage disease type V (GSDV) [1], is an autosomal recessive genetic disorder caused by a deficiency of muscle glycogen phosphorylase (myophosphorylase) activity, determined by mutations in the myophosphorylase gene (PYGM) [2]. Without this enzyme, muscles cannot break down glycogen into simple sugars to meet the energy requirements of exercise. This makes individuals with McArdle disease suffer from exercise intolerance, characterized by fatigue, muscle pain, and cramps during the first few minutes of exercise. Typically, people with this disease experience a sudden drop in heart rate and improvement of exercise tolerance after about 7–10 min of walking or cycling, a phenomenon known as "second wind" [3]. This pathognomonic feature of the disease has been attributed to increased sympathoadrenal response and the release of extra-muscular energy substrates, free fatty acids, and glucose to compensate for the damaged glycogen breakdown [4]. Laboratory tests usually show increased serum creatine kinase (CK) levels at rest, with mean values frequently exceeding 1,000 IU/L (normal reference values: < 200 IU/L), and episodic myoglobinuria, which can eventually result in acute renal failure [4].

Diagnosis is based on clinical symptoms and histochemical/biochemical evidence of myophosphorylase deficiency in muscle biopsy. Although symptom onset is frequently in the first decade of life, diagnosis is often delayed, as myalgia and fatigability are dismissed/overlooked. This may increase the risk of significant fixed muscle weakness, life-threatening episodes of myoglobinuria, and premature death in swimming or climbing accidents [5]. Available data indicates that the prevalence of McArdle disease is 1 in 100,000 in the US [5] and 1 in 170,000 in Spain [6].

McArdle disease has never before been reported in anorexia nervosa. This case report describes a female with anorexia nervosa and concomitant McArdle disease, detailing the potential interaction between the symptoms of this

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disease and eating-disorder psychopathology, and how the case was diagnosed and managed.

## Case presentation

The patient reported the onset of the eating disorder at 18 years of age, a few months after her parents separated. At a body weight of 55 kg and a body mass index (BMI) of 18.4 kg/m$^2$, during the first Italian COVID-19 lockdown she started dieting and doing daily bodyweight exercises. Progressive intensification of dietary restriction and physical exercise, associated with her extreme concerns about shape and weight, produced a progressive weight loss and secondary amenorrhea.

When her body weight reached 46.2 kg, her parents obliged her to start a multidisciplinary specialist outpatient treatment for eating disorders. Despite the treatment, she continued to maintain extreme and rigid dietary rules and lost further weight. At a body weight of 43 kg, she was admitted to a medical unit to stabilize her medical condition. There she was treated with enteral nutrition, and was discharged after 3 months at a body weight of 44 kg. After discharge, despite attending a specialist outpatient treatment for eating disorders, she lost 1 kg in 1 month, and was referred to our inpatient eating disorder unit, where she was admitted on 5 October 2021.

Before admission, the patient participated in four preparatory sessions in which she agreed to be hospitalized, and to play an active role in addressing her eating-disorder psychopathology and its maintenance mechanisms via inpatient enhanced cognitive behavior therapy (CBT-E), which would necessarily entail weight regain [7].

At admission, the patient had a body weight of 44 kg and a BMI of 14.6 kg/m$^2$, an oral temperature of 36.1℃, a heart rate of 67 bpm, and a blood pressure of 100/80 mmHg. Her eating-disorder psychopathology, assessed via the Eating Disorder Examination (EDE.170D) [8], was characterized by the overvaluation of shape and weight, severe dietary restriction, and more than 1 h a day of bodyweight exercises. Her EDE global score was 3.62, > 1 standard deviation (SD) above the community mean (i.e., above 1.74) [9]. The following laboratory test results were outside the normal range: alanine aminotransferase (ALT) 96 IU/L (normal values < 33 IU/L), aspartate aminotransferase (AST) 72 IU/L (normal values < 32 IU/L), ferritin 159 ng/ml (normal values 13–150 ng/ml), lactate dehydrogenase (LDH) 285 IU/L (normal values 135–214 IU/L), and CK 1868 UI (normal values 135–214 IU/L). We initially ascribed the increased CK to the episodes of excessive exercising reported by the patient before admission, and the other laboratory alterations to her undereating and being underweight, as abdominal ultrasound was negative.

The patient began treatment well, and took a very active role in applying the strategies and procedures for addressing weight regain (including assisted eating), and her preoccupation with shape and weight. Laboratory tests repeated during the first month of the treatment showed normalization of her ALT, AST, and ferritin levels as she began to regain weight, but CK values continued to increase, ranging from 1,782 IU/L to 14,626 IU/L.

As the patient had apparently stopped excessive exercising, which she was never seen to do by the nurses in the unit, and as the CK values were so persistently high (unprecedented in our unit even in patients known to practice extreme excessive exercising) we prescribed leg electromyography. This was negative, so we discussed the case with a neurologist expert in muscle diseases, who recommended muscle biopsy of the left vastus lateralis. Analyzed at the University of Verona Neuropathology Laboratory, the sample revealed the histological-histochemical features of myopathy, namely atrophic and numerically reduced type 1 fibers, glycogen accumulation in the periodic acid–Schiff (PAS) preparation, and lack of histochemical reactivity for myophosphorylase. As this picture was compatible with McArdle disease, an enzyme assay was performed on the muscle biopsy tissue. This showed low phosphorylase (0.19 μmol/min/g tissue; normal values: 27.19 + / − 5.12 μmol/min/g tissue), histochemically confirming the phosphorylase defect.

When informed that muscle biopsy demonstrated the presence of McArdle disease and educated about the exercise intolerance determined by this disease, the patient was relieved; she now realized that her problems exercising were not related to psychological weakness, as she had thought, but to a rare genetic disorder. She disclosed having experienced fatigability and myalgia upon exercising since childhood—information that had not revealed at the intake interview. She recounted that at elementary school she had often been mocked by her classmates due to her poor performance during physical education (PE) lessons, which became very stressful and scary times for her. In fact, she became very anxious about exercising in general, and made excuses to avoid PE and any other situation involving exercise (e.g., walking or biking with friends, going walking in the mountains, etc.). She also reported some "traumatic" experiences related to her difficulties in exercising. One day, for example, the PE teacher scolded her because she stopped during a run, and her classmates laughed and teased her. On another occasion, during a class trip, she felt humiliated because her classmates started running so as not to miss the bus, but she was unable to keep up with them, being derided by the bus driver for being lazy.

These difficulties with exercising, and comparing her physical performance with that of her peers, led her to believe that she was, in fact, weak and lazy. This negative self-belief was reinforced by recurrent comments from her

father, who attributed her difficulties to a lack of motivation and a problem with her "mind".

During the COVID-19 lockdown she started, for the first time in her life, to do light bodyweight exercises alone. She realized that, after an initial sensation of fatigue and a short break of 1 or 2 min, she was able to continue exercising without difficulties for a long period of time (the "second wind"). Exercise and dietary control made her feel happy and strong because she was able to control her "mind" and body shape.

Following her diagnosis, the patient was educated on how some features of her eating disorder (i.e., excessive exercising and strict carbohydrate cutting) could aggravate the symptoms of fatigue and myalgia, and in the long term increase the risk of fixed muscle weakness and life-threatening episodes of myoglobinuria, potentially resulting in premature death [5]. She was also informed that, while individuals with McArdle disease had in the past been advised to abstain from any type of exercise to reduce the risk of rhabdomyolysis, recent evidence suggests that regular, progressive, moderate-intensity aerobic exercise accompanied by a tailored diet can help to improve muscle metabolism [4]. We also informed her that muscle crises could be prevented by avoiding acute bouts of intense exercising (e.g., running or lifting weights) [4].

She was started, as recommended [4], on a diet containing 65% carbohydrate, especially at breakfast and lunch, and 20% fat, associated with a program of indoor light cycling (i.e., 40 watts, 3 days a week, duration 20 min, increasing gradually to 50 watts, duration 30 min) under the supervision of our physiotherapist. The patient was discouraged from weightlifting and isometric exercises, as these would require pre-exercise carbohydrate ingestion that might interfere with the CBT-E regular eating procedure.

The patient was compliant with the proposed protocol. During her stay, she had no episodes of excessive exercising, and showed improvements in her eating-disorder psychopathology. Her body weight gradually normalized, reaching 59 kg, BMI 19.6 kg/m$^2$, at discharge, when her global EDE score was 1.8. She was referred to individual outpatient CBT-E, and continued indoor cycling 3 times a week supervised online by our physiotherapist.

## Discussion

Although comorbid anorexia nervosa with McArdle disease will never be encountered by most clinicians, the coexistence is of clinical interest as an example of how an eating disorder and a general medical disease may interact in a detrimental way. In this case, for example, excessive exercising and poor dieting, two typical features of the patient's eating disorder, seem to have exacerbated the muscle damage caused by McArdle disease, and in the long term could have accentuated the risk of developing fixed muscle weakness and life-threatening kidney failure. Contemporaneously, the feeling of physical weakness during exercise was interpreted by the patient as a sign of mental weakness, leading her to strive especially hard to control her shape, weight and eating to overcome her sense of worthlessness.

It is also important to note that an eating disorder may delay the diagnosis of a coexisting general medical disorder. Indeed, in this case, the elevated CK values were attributed by both the clinicians in the internal medicine unit who administered enteral nutrition and also, initially, by our team, to the consequences of excessive exercising. This underlines the importance of always doing an accurate differential diagnosis to assess whether the coexisting medical alteration is a spurious comorbidity, i.e., secondary to the eating disorder, or in fact a true comorbidity.

Despite the promising improvements achieved via the treatment in this patient, no definitive conclusions can be drawn about the long-term prognosis of either the eating disorder or the McArdle disease. Indeed, a subgroup of patients with anorexia nervosa relapse upon discharge from inpatient CBT-E [7], and McArdle disease patients are at risk of persistent rhabdomyolysis, even following a 20 year period of inactivity [10].

That being said, the case illustrates how the presence of a severe chronic disease that requires the adoption of a healthy lifestyle, such as McArdle disease, may help to engage the patients in actively addressing their eating disorder, if the treatment can be appropriately adapted to accommodate the general medical disorder.

## Conclusion

Anorexia nervosa and McArdle disease interact in a detrimental bidirectional way. In addition, some laboratory parameter alterations (e.g., elevated values of creatine kinase) commonly attributed to the specific features of eating disorders (e.g., excessive exercising) may delay the diagnosis of metabolic muscle diseases. On the other hand, the coexistence of a chronic disease, such as McArdle disease, whose management requires the adoption of a healthy lifestyle, can help to engage patients in actively addressing their eating disorder via a specially adapted form of an evidence-based treatment.

### What is already known on this subject?

- McArdle disease, caused by a deficiency of the myophosphorylase enzyme, encoded by the PYGM gene, hampers glycogen breakdown in muscle cells and interferes with the function of muscle cells, causing exercise intolerance.

- No case reports have previously described the coexistence of McArdle disease and anorexia nervosa.

### What this study adds

- This case report describes the detrimental bidirectional interaction between anorexia nervosa and McArdle disease.
- It shows that the diagnosis of a severe muscle disease may delayed in people with anorexia nervosa by interpreting elevated creatine kinase as the result of excessive exercising.
- It also illustrates that the presence of a medical disease, in this case McArdle disease, may be harnessed to engage the patients in actively addressing their eating disorder.

## Financial interests

The authors declare that they have no financial interests to disclose.

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## Declarations

**Conflict of interest** On behalf of all authors, the corresponding author states that there is no conflict of interest.

**Ethics approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee, and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Informed consent** The patient provided informed written consent for this anonymous Case Report.

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