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Case Report

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First Case Report of McArdle Disease and Alive Kidney Transplantation

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ABSTRACT

McArdle disease (glycogen storage disease type V, MIM #232600) is an inherited disorder of glycogen metabolism affecting only skeletal muscles. A 56-year-old male patient had fatigue and muscle weakness beginning from the age of 8. He was diagnosed with glycogen storage disease type V at the age of 30. Despite the treatment, the patient had been followed up with chronic kidney failure for the last 11 years most probably due to recurrent episodes of rhabdomyolysis. The patient underwent preemptive kidney transplantation from his wife due to the progression to end-stage kidney disease. We report the first case of McArdle disease who developed chronic kidney failure and underwent kidney transplantation. We aim to present this process before and after the transplantation in order to contribute to the literature.

Keywords: Clinical nephrology, McArdle disease, kidney transplantation, rhabdomyolysis

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INTRODUCTION

Glycogen storage disease (GSD) is an autosomal recessive inherited carbohydrate metabolism disorder that develops as a result of the absence or insufficiency of one of the enzymes involved in glycogen synthesis or release.[1] McArdle disease or GSD type V, the most common muscle glycogenosis, is caused by the defective activity of myophosphorylase in muscle.[2] The disease was first reported by Brian McArdle.[3] The exact prevalence of McArdle disease is unknown but ranges from 1 in 50 000 to 1 in 200 000 in the United States.[4] There is no detectable glycogen phosphorylase activity in most of the patients.[1] It is inherited by the PYGM gene (11p13), which encodes 20 exons.[1] It is characterized by the onset of exercise intolerance and muscle cramps in childhood or adolescence.[2] Patients may develop rhabdomyolysis due to excessive exercise, and creatine kinase (CK) may rise above 100 000-1 000 000 UI/L during episodes, leading to the risk of developing acute kidney failure. Although the symptoms are present in the first decade, the patients typically present in adolescence or early adulthood with exercise intolerance, fatigue, muscle pain, cramps, muscle swelling, and weakness.[2,3] The aim of this study is to present a case of chronic kidney failure most probably due to recurrent episodes of rhabdomyolysis in McArdle disease, to examine the results of a living donor kidney transplantation before and after transplantation, and to share our observations and experiences.

CASE PRESENTATION

Informed consent was obtained from the patient included in this study. A 56-year-old male patient who was born to first-degree cousin marriage had fatigue, weakness, and muscle cramp since he was 8 years old. When he was 18 years old, he was misdiagnosed with glomerulonephritis due to the darkening of the urine after upper respiratory tract infection. No biopsy was performed on the patient at that time. In the follow-up,

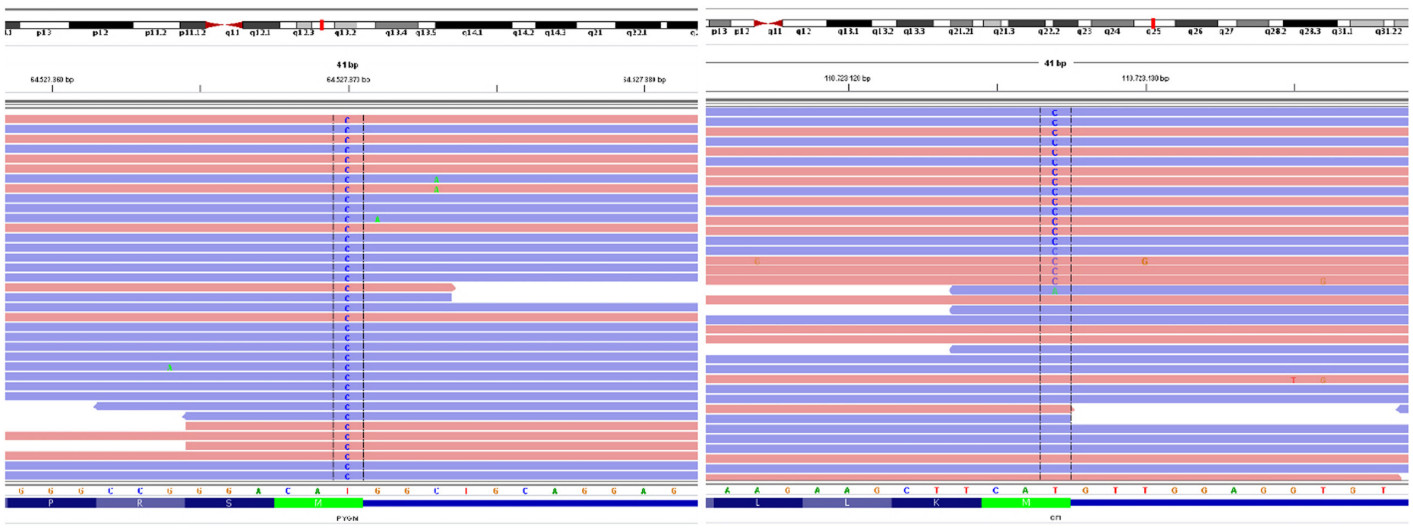

Figure 1. PYGM: c.1A>G (p.M1V) homozygous mutation on next-generation sequencing. CFI: c.1A>G (p.M1V) heterozygous mutation on next-generation sequencing. Both genes are located on the reverse strand.

myoglobinuria, muscle cramps, weakness, and elevated CK were detected in the patient. Muscle biopsy was performed when the patient was 35 years old with recurrent muscle cramps, elevated CK, and myoglobinuria attacks. Glycogen accumulation was detected in the muscle biopsy. As a result of PYGM gene analysis, the patient was diagnosed with McArdle disease. Afterward, myophosphorylase deficiency was detected in his 6 cousins with the family screening. Carbohydrate-rich diet was recommended to the patient. Despite medical nutrition therapy, the patient had repetitive episodes of rhabdomyolysis. The patient, who had a persistent increase in creatinine levels, was followed up in the nephrology clinic. Kidney biopsy was planned. However, it could not be performed due to lack of patients' approval. When the patient was diagnosed with chronic kidney failure, he did not have diabetes, hypertension, or glomerulonephritis. There was no pyuria, leukocyturia, proteinuria, or crystalluria in routine urine analysis. Urine sediment was normal. Except the reduced kidney volume, no pathological findings such as cystic lesion or glomerulosclerosis were observed in the urinary ultrasonography. The patient was followed for 11 years with chronic kidney failure. He had been using antihypertensive drugs for hypertension for the last 6 years. In the follow-up, no hemolysis or thrombocytopenia was observed. The mean frequency of rhabdomyolysis episodes was 18 (SD ± 5, min: 6 and max: 25 episodes) per year. Preparations for preemptive kidney transplantation were made as the creatinine level of the patient increased over time. Since McArdle disease and chronic kidney failure have not been reported in the literature before, whole exome sequencing (WES) was performed to explain other possible causes in the patient. As a result of molecular analysis, both pathogenic mutations, homozygous c.1A>G (p.M1V) in PYGM gene and heterozygous c.1A>G (p.M1V), in CFI gene were detected. Integrative Genomics Viewer (IGV) images of mutations are shown in Figure 1.

MAIN POINTS

- Recurrent episodes of rhabdomyolysis in McArdle disease may facilitate or accelerate the development of end-stage kidney disease (ESKD).
- To our knowledge, this is the first case report in the literature in which ESKD developed in McArdle disease.
- In addition, this is the first case of McArdle disease in which kidney transplantation has been performed in the literature.

In addition to the routine transplantation preparations for the donor and recipient, a carbohydrate-rich diet was prescribed to the patient. The appropriate intravenous (IV) anesthetics and neuromuscular blockers and IV hydration were administered to prevent the possible malignant hyperthermia and rhabdomyolysis. Dantrolene sodium was also kept available due to the possible risk of malignant hyperthermia. To reduce the risk of rhabdomyolysis, the rocuronium bromide was administered for the purpose of neuromuscular blockage. Intravenous anesthetics (propofol and remifentanil hydrochloride) were preferred instead of inhaler anesthetics. There were no intraoperative complications. A successful kidney transplantation was performed. The laboratory values of the patient before and after transplantation are shown in Figure 2. There was a significant decrease in CK and creatinine values in the following days after the transplantation. CK elevation or rhabdomyolysis attacks has never been observed in the following 6 months after the transplantation.

DISCUSSIONS

McArdle disease is the most common type of autosomal recessive inherited muscle energy metabolism disorders. The

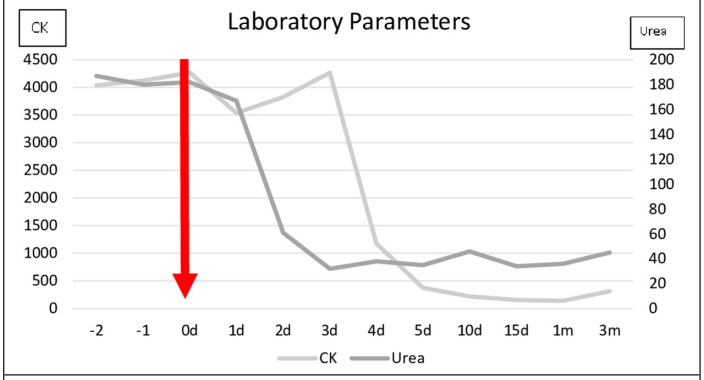

Figure 2. Creatine kinase and urea values of the patient before and after transplantation (black arrow marks the day of transplantation).

typical form is manifested by increased muscle weakness and cramps after exercise, often presenting in the second and third decades of life.[2] The most common laboratory results are myoglobinuria and elevated CK levels.[5] The recurrent myoglobinuria attacks are seen in more than 50% of patients. Rhabdomyolysis is a serious clinical picture that can lead to electrolyte balance disorders, compartment syndrome, disseminated intravascular coagulation, peripheral neuropathy, as well as acute kidney failure and hyperkalemia, as a result of the addition of intracellular materials to the systemic circulation as a result of the destruction of muscle cells. Myoglobin is excreted by the kidney and can cause kidney injury. Myoglobinuria has a toxic effect on kidney tubular cells and causes damage through tubular obstruction.[6,7] Acute kidney disease is extremely rare in McArdle disease. In the Spanish national registry, acute kidney injury has been reported at a rate of 4%.[8] In a study in the United Kingdom, myoglobinuria and acute kidney injury are reported at the rate of 62% and 11%, respectively.[9]

No relationship has been reported between recurrent episodes of rhabdomyolysis and chronic kidney failure. It is a known fact that tubular damage occurs during rhabdomyolysis. In McArdle disease, rhabdomyolysis attacks can be seen even with minimal exercise, without any electrolyte imbalance. The frequency of attacks varies depending on the enzyme activity level of the patient and the mutation he has. The mean rhabdomyolysis episodes was 18 per year in McArdle disease which was associated with severe disease. The damage caused by frequent rhabdomyolysis episodes on the kidney is inevitable. In our patient, there was a history of hypertension which started with elevated creatinine levels. He had no prior high blood pressure levels, glomerulonephritis, or diabetes which can cause end-stage kidney disease (ESKD). No cause other than recurrent rhabdomyolysis that could cause ESKD was found in the patient. Kidney biopsy would be a guide to determine the exact cause. However, biopsy could not be performed due to lack of patients' approval. In addition, there was no history of habits such as cigarette and alcohol or comorbid diseases, which could explain the ESKD. We performed WES analysis to explain the etiology of chronic kidney failure in our patient. As a result of molecular analysis, in addition to the PYGM gene, pathogenic heterozygous mutation in the CFI gene was detected. We found that the CFI gene mutation causing hemolytic uremic syndrome (HUS) type 3 had never caused HUS in our patient before. However, can the CFI gene be a facilitating factor in the development of chronic kidney failure with recurrent rhabdomyolysis episodes? In the future, further research may clarify this. In this case report, we presented the pre-transplantation and post-transplantation process of McArdle patient who had kidney transplantation from a living donor. Kidney transplantation in McArdle disease has not been reported in the literature yet, and chronic kidney failure has not been reported either. To the best of our knowledge, this is the first case in the literature. The rhabdomyolysis following the kidney transplantation, delayed graft rejection, and even graft loss were among the possible post-transplantation risks. Rhabdomyolysis has been reported in kidney transplantation cases due to the immunosuppression used (tacrolimus and CD25 monoclonal antibody).[10] We did not observe rhabdomyolysis in the postoperative period in our case in which tacrolimus and anti-thymocyte were used as induction or immunosuppressant agents. Kidney transplantation can be performed in McArdle disease with ESKD in the appropriate preoperative and postoperative conditions.

CONCLUSION

We reported a glycogen storage type V patient who underwent kidney transplantation due to ESKD. This is the first case in the literature.

Ethics Committee Approval: Ethical committee approval was granted by the local committee of Diyarbakir Gazi Yaşargil Research and Training Hospital (Date: June 1, 2022, Decision No: 1043).

Informed Consent: Written informed consent was obtained from the patient who participated in this study.

Peer-review: Externally peer-reviewed.

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Declaration of Interests: The authors have no conflicts of interest to declare.

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