Recurrent Acute Kidney Failure Due to McArdle Disease

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We present an adolescent with McArdle disease and recurrent acute kidney failure due to rhabdomyolysis. The patient was admitted with acute kidney failure for 3 times and due to a history of proximal weakness, fatigue, and muscular cramps after physical activities a glycogen-storage disease was suspected. Serum creatine phosphokinase and urine myoglobin were found to be elevated. McArdle disease was diagnosed based on pathologic examination of muscle tissue specimen. Patients presenting with rhabdomyolysis following strenuous exercise should be evaluated for McArdle disease.

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Case Report

INTRODUCTION

Treatment of underlying factors in acute kidney failure (ARF) may improve kidney function. One of them is rhabdomyolysis. This problem is usually due to crush injury.[1] Clinical findings may be absent on physical examination, and delayed diagnosis may make the problem irreversible. In other conditions such as glycogen-storage disease (GSD), especially its type V—namely *McArdle disease*—hidden rhabdomyolysis may occur.[2] Patients with McArdle disease may have a persistently low level of myoglobin in the blood due to ongoing muscle damage and repair.[3] The clinical course of ARF due to rhabdomyolysis is not different from other causes of ARF and mortality has been reported to be up to 29.3% in these patients.[3] An extreme or prolonged bout of myoglobinuria could cause kidney failure and even require a person to undergo transient or even permanent dialysis.[4] We present herein an adolescent with McArdle disease and recurrent ARF due to rhabdomyolysis.

CASE REPORT

A 12-year-old boy was admitted to Sina Hospital in Tabriz, Iran, with peripheral edema, elevated blood pressure, and reduced urine volume. He did not have any familial history of kidney disease. Laboratory studies revealed elevated levels of blood urea nitrogen (BUN; 45 mg/dL), serum creatinine (2.5 mg/dL), and serum potassium (5.6 mEq/L). Urinalysis showed microscopic hematuria, and ultrasonographic finding of both kidneys was a 4-mm left kidney calculus without any hydronephrosis. With conservative therapy (diuretics, antihypertensive drugs, and correction of electrolytes level), his BUN and serum creatinine returned to the reference level, and then, edema and hypertension disappeared after 13 days. At this time, he was discharged with a good general condition and unremarkable laboratory examination.

At the age of 15, he was again admitted with another episode of ARF (BUN, 52 mg/dL and serum creatinine, 3.2 mg/dL). Urinalysis showed microscopic hematuria, but ultrasonography did not show any abnormality. Other serologic indicators including antistreptolysin O test, complement 3, complement 4, erythrocyte sedimentation rate, and C-reactive protein were with reference ranges. On physical examination, no problem was found and the patient did not have any compliant. Despite conservative therapy, BUN and serum creatinine rapidly rose to 148 mg/dL and 7.2 mg/dL, respectively, and hemodialysis was initiated. After 3 sessions of hemodialysis, urine output was alleviated and kidney function tests showed improved levels. Hence, hemodialysis was discontinued.

The 3rd episode occurred when the patient was 17 years old, admitted with periorbital edema to Sina hospital. His serum creatinine and BUN were 3.2 mg/dL and 140 mg/dL, respectively. Serum potassium level was 6.2 mEq/L. He noted proximal weakness, fatigue, and muscular cramps after physical activities and exercise at school. Accordingly, a muscular disease led to rhabdomyolysis was suspected. Serum creatine phosphokinase (CPK) and urine myoglobin were found to be elevated. Hydration and administration of alkaline diuretics were considered, immediately, and thereafter, urine output increased and serum creatinine level decreased to 1.1 mg/dL.

For documentation of diagnosis, electromyography and nerve conduction velocity test were done. Electromyography revealed a decrement with contracture formation in repetitive stimulation at high frequency (15 Hz), but nerve conduction velocity was normal. We obtained biopsy of the quadriceps muscle. Initially, pathologic examination was indicative of GSD. Ischemic forearm test was positive and staining for myophosphorylase was negative. Based on the above evidence, a diagnosis of McArdle disease was made. The patient was recommended restricting vigorous physical and muscular activities, drinking of enough water, and going on a protein-rich diet. At 1-year follow-up visit, he did not have any muscular cramps, weakness, fatigue, or symptoms ARF.

DISCUSSION

Glycogen-storage diseases are the result of enzyme defects. These enzymes normally catalyze reactions that ultimately convert glycogen compounds to glucose.[5] Most patients experience muscular symptoms such as weakness and cramps, and certain GSDs manifest with specific syndromes such as hypoglycemic seizures or cardiomegaly. Glycogen-storage disease type V is called *McArdle disease* or *myophosphorylase deficiency*.[2] Myophosphorylase, the deficient enzyme in McArdle disease, is found in the muscle tissue.[5] Diagnosis is made based on the findings from the patient's history and physical examination, creatine kinase testing, muscle biopsy, electromyelography, and ischemic forearm testing. Biochemical assay for enzyme activity can lead to definitive diagnosis.[6]

During intense exercise, glucose from glycogen stored in the muscles becomes the predominant resource. Fatigue develops when the glycogen supply is exhausted. Exertional rhabdomyolysis may cause ARF. Burgundy-colored urine has been reported. It is thought to be a result of rhabdomyolysis after intense exercise. Diagnosis of myoglobinuria is made by a positive orthotoluidine test in a urine sample free of erythrocytes and elevated CPK and myoglobin in serum. The orthotoluidine test is not very sensitive, and hence, other tests like spectrophotometry should be done for a definite diagnosis.[7] A urine sediment with tubular epithelial cells, pigmented granular casts, and occasional erythrocytes is the usual finding in cases of myoglobinuric kidney failure.[8] The microscopic hematuria observed in our patient was probably due to urethral catheterization. Microscopic hematuria in myoglobinuric ARF can occur due to traumatic rhabdomyolysis. Since the urinary dipstick test and orthotoluidine test do not distinguish between hemoglobin and myoglobin in the presence of erythrocytes in urine, diagnosis of rhabdomyolysis with myoglobinuria is made by demonstrating a positive test on the supernatant urine sample, normal color of serum (ie, absence of hemolysis), and elevated CPK and aldolase.[9]

Patients presenting with rhabdomyolysis following strenuous exercise should be evaluated for McArdle disease. Uberoi and colleagues[10] reported 7 cases of rhabdomyolysis over a period of 6 years with ARF due to exercise-induced myoglobinuria in the absence of heat stress. Another series of 8 cases was reported from a naval officers training institute.[11] Ramamoorthy and colleagues[12] described myoglobinuria with ARF in a 19-year-old boy, who had performed a three hours continuous dance program in a hot humid summer afternoon. The major life-threatening complication of myoglobinuria is acute tubular necrosis, as occurred in our patient. The exact mechanism by which ARF results from myoglobinuria is not well understood. Postulated mechanisms are direct tubulotoxic effect of ferriheme or myoglobin, obstruction of tubular lumen by myoglobin casts, back diffusion of glomerular filtrate through a break in the epithelium, and decreased glomerular filtration rate.[7] Dehydration, heat stress, hypovolemia, and acidification of urine are crucial precipitating factors. Renal involvement is characterized by oliguria, exceptionally high creatinine levels, hyperkalemia, hyperphosphatemia, and hyperuricemia.[2] Alkaline

solute diuresis and infusion of mannitol or sodium bicarbonate improve kidney function, if initiated early. The clinical course of ARF due to rhabdomyolysis is not different from other causes of ARF.[10]

Our patient recovered completely, possibly because he was otherwise healthy and had the benefit of early diagnosis and energetic management. There is only one report of McArdle disease presenting with ARF in the absence of a past history of exercise-induced muscle pain and stiffness.[11] In general, no specific treatment exists for GSDs. In some cases, diet therapy is helpful. Meticulous adherence to a dietary regimen may reduce liver size, prevent hypoglycemia, allow for reduction in symptoms, and allow for growth and development. A high-protein diet may increase exercise tolerance in some cases, although this practice is controversial.[4]

CONFLICT OF INTEREST

None declared.

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