Case Report

A case of Becker muscular dystrophy and massive myoglobinuria with minimal renal manifestations

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Introduction

Myoglobinuria is the leading cause of acute renal failure (ARF) among outpatients. Even in the absence of muscle weakness and morphological abnormalities, Becker muscular dystrophy can be associated with exertional myoglobinuria. Renal damage caused by exertional myoglobinuria in patients with Becker muscular dystrophy has not been well documented.

We report the case of a 12-year-old boy who was found to have severe exertional myoglobinuria and marked elevation of creatine kinase (CK). Presumably the marked elevations of serum myoglobin and cytosolic CK were caused by increased permeability of the muscle cell membrane, a cellular abnormality common in patients with Becker muscular dystrophy. There was no muscle necrosis, and no evidence of fluid accumulation in muscle tissue. The patient was not hypovolaemic and not dehydrated. Despite severe myoglobinuria, the patient was found to have only minimal renal manifestations. The findings of this case document that haem proteins have minimal nephrotoxic effects in the absence of hypovolaemia, dehydration, and aciduria.

Case report

The patient, a 12-year-old boy, was referred to us for evaluation of pigmenturia. On the previous day, the patient participated in a school excursion when he complained of myalgia in his leg and dark coloured urine. Until referral, the patient had been healthy. The patient had no documented weaknesses. At 9 years old he had reported occasional exertional cramps in his legs. These cramps were never associated with dark coloured urine. The patient’s mother indicated that pregnancy and delivery were both normal. The family history was negative for neuromuscular diseases.

On examination, the patient had no swelling of muscle tissues and no muscular weaknesses. Hypertrophy of the calves was not noted. The patient appeared to be normally developed. Further investigation revealed the following: serum CK level 360,000 IU/l (normal < 160 IU/l); serum myoglobin 7100 ng/ml (normal < 70 ng/ml); urine myoglobin 370,000 ng/ml (normal < 20 ng/ml); serum aspartate aminotransferase 4100 IU/l; lactate dehydrogenase 14 665 IU/l; creatinine 70.7 mmol/l; blood urea nitrogen 2.0 mmol/l; and creatinine clearance 115.3 ml/min. Following plasma protein electrophoresis, muscle cytoplasmic CK-MM isoenzyme bands were prominent, while mitochondrial CK isoenzymes were not observed. The patient’s complete blood count was normal. Urinalysis revealed a pH of 6.5, 3+ protein, 3+ blood, and 6–9 red blood cells per high-power field. Urinary protein excretion was 413 mg/day. Urinary β2-microglobulin was 8,000 μg/l (normal 5–253 μg/l) and urinary N-acetyl β-D-glucosaminidase was 9.1 IU/l (normal < 11.0 IU/l).

Following admission, the patient was treated with alkaline solute diuresis for 4 days to prevent renal deterioration. The patient did not exhibit oliguria at any time. The patient indicated that his muscle cramps disappeared on the day he was admitted. On the 3rd day following admission, the patient’s urinalysis was normal. Over the course of the patient’s hospital stay, serum creatinine values were repeatedly measured and found to be between 70.7 and 114.9 mmol/l. On the 10th day after admission, renal biopsy specimens were collected. Renal biopsies revealed nearly normal histology. Casts in distal tubules did not stain positive for myoglobin antibody. DNA analysis of the dystrophin gene showed a deletion of exon 48 and exon 51. Following the identification of the dystrophin gene abnormality, the patient was diagnosed with Becker muscular dystrophy.

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Discussion

There is growing interest in the mechanism of haem protein-induced ARF. This case was characterized by markedly elevated serum CK and severe myoglobinuria without hypovolaemia, dehydration, and aciduria. Although muscle cytoplasmic CK-MM isoenzymes were demonstrated, mitochondrial CK isoenzymes were not present in the patient’s serum, indicating that there was no muscle tissue necrosis [1]. Furthermore the patient did not develop hypocalcaemia or hyperkalaemia, conditions associated with rhabdomyolysis. In addition, fluid accumulation, or third spacing, commonly seen with muscle-tissue necrosis, was not observed. Presumably serum myoglobin and cytosolic CK were elevated because of increased permeability of the muscle cell membrane secondary to the patient’s dystrophinopathy [2]. This case is unique because despite severe myoglobinuria and marked elevation of serum CK, the only renal manifestations observed were transient increases in urinary protein and β2-microglobulin excretion. Although the level of serum creatinine increased from 70.7 to 114.9 mmol/l on the third day of the patient’s hospital stay, the creatinine level returned to baseline by day 4. Urinary N-acetyl β-D-glucosaminidase was not elevated. Renal biopsy revealed nearly normal histology. The minor renal manifestations observed in this case may have been caused by transient tubular dysfunction.

This case suggests that the observation of haem-protein-induced ARF in experimental animal models may be relevant to human clinical disease. The most widely used experimental models of haem protein-induced ARF are haem protein infusions into dehydrated and/or volume-depleted animals or intramuscular injections of hypertonic glycerol [3]. These experimental animal models have demonstrated that haem proteins have minimal nephrotoxic effects without concomitant hypovolaemia, dehydration, and aciduria. Although the patient received forced alkaline solute diuresis treatment, the circumstances surrounding the case delayed this therapeutic intervention for more than 24 h following patient exertion. Better and Stein [4] suggested that 6 h was the upper time limit for effective forced alkaline solute diuresis to effect a favourable outcome in patients who experienced exertional myoglobinuria. It was reported that the incidence of myoglobinuria in Becker muscular dystrophy was nearly 3% [5]. However, ARF secondary to exertional myoglobinuria in patients with Becker muscular dystrophy has not been reported, suggesting that this combination of conditions has a low risk of ARF unless dehydration and hypovolaemia are also present. As this case indicates, even when there are no muscle weaknesses and no positive family history of myopathy, Becker muscular dystrophy should be considered among the possible causes of exertional myoglobinuria. Although non-traumatic myoglobinuria is much more typical of metabolic myopathies, since the introduction of dystrophin testing there has been an increase in the awareness that dystrophinopathies can be associated with myoglobinuria induced by exercise, even in the absence of appreciable muscle weakness [6,7]. In the present case, neither muscle weakness nor hypertrophy of the calf muscles were demonstrated. Nevertheless, DNA analysis revealed deletions in the dystrophin gene resulting in the diagnosis of Becker muscular dystrophy.

In summary, this case was characterized by severe myoglobinuria and marked elevation of cytosolic CK isoenzymes with only minor renal manifestations. This case suggested that haem proteins may have minimal nephrotoxic effects in the absence of hypovolaemia, dehydration, and aciduria. In this case, we concluded that the myoglobinuria was secondary to Becker muscular dystrophy. The diagnosis of Becker muscular dystrophy was made following discovery of deletions in the dystrophin gene in this patient.

References

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