Hyperosmolar non-ketotic diabetic coma and rhabdomyolysis

Dorothy Trump, Shaun O'Hanlon, Michael Rinsler and Patrick Sharp

Northwick Park Hospital and Clinical Research Centre, Watford Road, Harrow HA1 3UJ, UK

Summary: Rhabdomyolysis is a rare but potentially fatal complication of hyperosmolar states. We report a case of severe hyperosmolar non-ketotic diabetic coma causing rhabdomyolysis in a young man. Despite very high levels of creatine kinase there was no detectable myoglobinuria. Creatine kinase estimation should be a standard investigation in all patients presenting with a hyperosmolar state.

Introduction

Rhabdomyolysis associated with diabetic hyperosmolar non-ketotic coma was first reported 18 years ago.¹ It has recently been recognized that subclinical rhabdomyolysis occurs commonly in this condition but is usually not suspected.^{2,3} We describe a classic example of hyperosmolar non-ketotic diabetic coma, complicated by rhabdomyolysis in a patient not previously known to be diabetic. The timing of the rise in creatine kinase and the severity of his muscular symptoms led to a diagnostic dilemma and a muscle biopsy was performed. This revealed changes consistent with rhabdomyolysis.

Case history

A 40 year old Afro-Caribbean male student presented to the Accident and Emergency department with a reduced conscious level. History elicited from a friend was of polyuria, polydipsia and loss of appetite over the preceding week. He had previously been well with no significant past medical history and was taking no regular medication. For 2 days prior to admission he had become increasingly weak and on the day of admission was breathless and sweating. He lost consciousness 1 hour before arrival in the Accident and Emergency department. There was no history of trauma, prolonged coma, ingestion of drugs or excessive exercise.

On admission he was pyrexial with a temperature of 39.6°C, dyspnoeic with a tachycardia but normotensive. He was unconscious and

unresponsive to pain, and had no gag reflex. He was areflexic but no other focal neurological signs could be elicited.

Initial investigations revealed a blood glucose of 65.9 mmol/l with a sodium of 181 mmol/l, potassium of 4.3 mmol/l, creatinine of 206 µmol/l, a serum osmolality of 428 mosm/kg and mild hypocalcaemia. He had a respiratory acidosis (pH 7.24, PO_2 6.6 kPa, PCO_2 8.13 kPa, bicarbonate 25 mmol/l), and an electrocardiogram (ECG) showed sinus tachycardia with ST depression and widespread T wave inversion. A full blood count and chest X-ray were normal, urinalysis revealed glycosuria but no ketones. The creatine kinase was 7,600 IU/l (normal 20–175), with a normal MB fraction.

A diagnosis of hyperosmolar non-ketotic diabetic coma was made, and he was managed in the standard way with intravenous fluids and an infusion of intravenous insulin. The electrolytes measured 6 hours later showed profound hypokalaemia of 1.7 mmol/l and a glucose of 34 mmol/l.

He received 8 l of fluid with potassium replacement intravenously over the first 24 hours. Intravenous heparin therapy was initiated to prevent thromboembolic complications and intravenous broad-spectrum antibiotics were administered. His ECG returned to normal.

His clinical state improved and he regained consciousness within 5 hours of admission. The next day he was found to have microscopic haematuria and his platelet count had dropped to $73 \times 10^9/l$ with normal clotting and fibrinogen degradation products. This was attributed to the heparin which was stopped. No myoglobin was found in two urine samples.

He continued to improve both clinically and biochemically, and his platelet count rose following the withdrawal of heparin. He maintained a good

Correspondence: D. Trump, M.R.C.P., MRC Molecular Medicine Unit, Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Road, London W12 0NN, UK.

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diuresis. Four days later he was converted to subcutaneous insulin.

However, his serum creatine kinase level had risen to 66,000 IU/l by day 6 of the admission with no change in renal function (Figure 1). He developed painful swollen muscles proximally and was unable to weight bear. The creatine kinase rose further to 95,000 IU/l the following day.

The differential diagnosis included rhabdomyolysis and myositis and a muscle biopsy was performed. Subsequently oral steroid therapy was commenced. Other investigations were unhelpful (ESR, C-reactive protein, anti-nuclear antibody). An ultrasound examination of the pancreas was normal.

The muscle biopsy (Figure 2) showed focal chronic inflammation and occasional regeneration of muscle fibres, indicating muscle damage and excluding myositis. A diagnosis of rhabdomyolysis was made and the corticosteroid therapy was stopped.

The patient improved and was able to walk 3 days later and the creatine kinase had dropped to 7,100 IU/l. He was discharged home 7 days later on twice daily subcutaneous insulin, by which time the creatine kinase was 452 IU/l and the creatinine had dropped to 121 $\mu\text{mol/l}$.

On review 1 week later his treatment was changed to oral hypoglycaemic agents which were subsequently stopped 6 weeks later. His diabetes is now controlled with diet alone.

Figure 2 Muscle biopsy results showing chronic inflammatory cells. A dead cell can be seen in the centre on the field of view.

Figure 1 Results of biochemical investigations during admission. The normal range for sodium and creatinine is indicated by the hatched area. In normal circumstances creatine kinase is less than 175 UI/l in males.

Discussion

Our patient is a classic example of hyperosmolar non-ketotic coma and exhibits all of the expected biochemical abnormalities. He was found to have a high creatine kinase on admission which had been measured because his electrocardiography was abnormal. The ECG abnormalities resolved and in retrospect were attributed to his abnormal blood chemistry. The creatine kinase originated from skeletal muscle and on day 6 rose to a very high peak when the patient developed muscular symptoms. This was unexpected as the patient was otherwise much improved, and his glucose and electrolytes had returned to normal by day 4 of the admission. The results of the muscle biopsy were consistent with generalized muscle damage. Very similar muscle histology has been reported in a case of rhabdomyolysis associated with diabetic ketoacidosis.⁴

Rhabdomyolysis is known to occur in the hyperosmolar state and was first reported 20 years ago⁵ in a military recruit who became confused and was found to be pyrexial, hypotensive and had a

high serum sodium. Ten years before this, myoglobinuria was reported in a 36 year old man with diabetic ketoacidosis,⁴ and in 1974 rhabdomyolysis was reported in a case of hyperosmolar non-ketotic diabetic coma.¹ More recently rhabdomyolysis has been reported to be associated with those cases of hyperosmolar non-ketotic coma which have severe biochemical disturbance, in particular a low initial potassium level (particularly less than 2.0 mmol/l),² and a linear relationship has been found between serum creatine kinase and both serum sodium and osmolarity.³

In previous reports of rhabdomyolysis associated with hyperosmolar non-ketotic diabetic coma, the peak level of creatine kinase is described as occurring within the first 48 hours. The creatine kinase level in our patient reached a maximum on day 6 of his admission. Only one other reported case has such a late peak.⁶ In our patient this timing may be due to the continuing biochemical disturbance and resulting muscle insult which persisted for 4 days after his admission.

Despite such high levels of creatine kinase, indicating continuing muscle breakdown, we did not demonstrate any myoglobinuria. This has been reported previously in the hyperosmolar state.^{1,6}

The use of myoglobinuria alone as a diagnostic test for rhabdomyolysis in this condition is therefore not advisable. The serum level of creatine kinase is a more reliable indicator of muscle breakdown.

On admission, our patient had renal impairment. No deterioration in his renal function was observed throughout his illness. He maintained a diuresis initially due to his hyperglycaemia and subsequently due to his treatment. This prevented further impairment in his renal function but improvement was only seen when the creatine kinase levels fell.

Rhabdomyolysis is known to occur in severe metabolic derangement. This case, which is a good example of both hyperosmolar non-ketotic diabetic coma and of rhabdomyolysis, serves as a reminder of this type of muscle damage. The diagnosis should be considered in any patient with a hyperosmolar state and creatine kinase levels estimated.

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