

Severe hypophosphataemia in anorexia nervosa

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Summary: In addition to well-described acid–base and electrolyte disturbances, anorexia nervosa may be complicated by severe hypophosphataemia. We report a case of anorexia nervosa complicated by life-threatening hypophosphataemia manifesting as generalized muscle weakness and bulbar muscle dysfunction, resulting in an aspiration pneumonia and cardiorespiratory arrest.

Introduction

Anorexia nervosa is a complex psychosocial disorder which, when severe, is associated with well-described metabolic and endocrine disturbances. Reviews on acid–base and electrolyte disturbances that may accompany this disorder have concentrated on hypochloraemic alkalosis and depletion of sodium and potassium.¹ We wish to draw attention to severe life-threatening hypophosphataemia which may also occur.

Case report

A 21 year old woman with a 3-year history of anorexia nervosa, characterized by severe dietary restriction only, was admitted to the psychiatric ward 10 days earlier because of progressive loss of weight, feeling generally weak, and marked fatigue. Her premorbid weight was 56 kg whereas on admission it was 35 kg (body mass index of 12.5 kg/m²). She had severe anorexia, and was able to manage only 500–700 ml of a liquid polymeric preparation (Ensure@ Ross-Abbott Laboratories) and little else.

In view of her inability to maintain nutrition and her progressive weakness, which now confined her to bed, she was referred to the gastrointestinal unit for further management. On examination she was fully conscious, markedly emaciated and dehydrated with a blood pressure of 100/70 mmHg with a 40 mmHg systolic postural drop. Heart sounds were normal and the chest clear. Abdominal examination was normal. She was mentally alert and her speech normal. She had generalized weakness (grade 3), which was more marked proximally. Bulbar muscle function was normal. Reflexes were

all present but depressed. A mild peripheral sensory neuropathy was present. Chvostek's and Trousseau's signs were negative. The only investigations available at the time revealed a haemoglobin of 11.1 g/dl (reference range (RR) 11.6–15.6), white cell count $3.5 \times 10^9/l$ (RR 3.7–5.3), platelets $68 \times 10^9/l$ (RR 164–432), sodium 131 mmol/l (RR 135–145), potassium 3.8 mmol/l (RR 3.5–5.5), urea 8.9 mmol/l (RR 1.7–6.7), creatinine 70 $\mu\text{mol/l}$ (RR 75–115). Red blood cell morphology was grossly abnormal with numerous anisocytes, acanthocytes, microcytes with hypochromasia, spherocytes, and poikilocytes. Her chest X-ray revealed a small heart size and clear lung fields. The electrocardiogram was normal.

In view of her clinical evidence of dehydration, the patient was given 2 litres of a 0.9% sodium chloride/5% dextrose solution over 12 hours. Over the next 12 hours her generalized weakness worsened, with the development of dysphagia and nasal speech. Her gag reflex was weak. Arterial blood gases on room air revealed a pH 7.40 (RR 7.38–7.42), PaCO₂ 4.2 kPa (RR 4.5–6.1), PaO₂ 14.4 kPa (RR 10.0–13.3), bicarbonate 24.9 mmol/l (RR 21–24). Serum biochemistry revealed the following: sodium 126 mmol/l, potassium 3.4 mmol/l, urea 1.4 mmol/l, creatinine 29 $\mu\text{mol/l}$, corrected calcium 2.05 mmol/l (RR 2.10–2.60), magnesium 0.67 mmol/l (RR 0.70–1.00), creatine kinase 34 IU/l (RR 0–110). Liver function tests were unremarkable. The most dramatic abnormality was an extremely low serum inorganic phosphate of 0.08 mmol/l (RR 0.70–1.00).

The severe hypophosphataemia was corrected with 30 mmol of phosphate administered as potassium phosphate diluted in 500 ml normal saline infused intravenously over 12 hours. Although blood tests shortly after completion of the infusion showed improvement in her biochemistry with serum inorganic phosphate of 0.61 mmol/l, cor-

rected calcium 1.90 mmol/l, magnesium 0.59 mmol/l and potassium 3.5 mmol/l, her condition further deteriorated with the development of respiratory distress and signs of a right lower lobe pneumonia. She had a sudden cardiorespiratory arrest and required ventilatory support for the next 10 days. Nerve conduction studies during this period were normal and electromyography showed features of a myopathic process. A normal serum inorganic phosphate level was maintained on continued oral supplementation. She was fully ambulant, although still weak, 4 days after being weaned off the ventilator.

Discussion

This patient, with a background of near starvation due to anorexia nervosa, developed progressive weakness and became bedridden over a 10-day period during refeeding. After receiving an intravenous dextrose-containing solution, there was further deterioration of her muscle weakness, with the development of a bulbar palsy, complicated by an aspiration pneumonia. The serum creatine kinase was normal and normal nerve conduction studies excluded the presence of a motor neuropathy. The first available serum inorganic phosphate level was obtained at the time of maximum weakness and was found to be extremely low (0.08 mmol/l). The bulbar palsy resolved within 4 days of correcting the serum inorganic phosphate with gradual improvement in her general weakness. In the absence of earlier serum inorganic phosphate values, we cannot be certain that acute hypophosphataemia was the cause of her sudden deterioration. However, the clinical picture was similar to that previously ascribed to severe hypophosphataemia.²

The cause of this patient's severe hypophosphataemia is probably multifactorial. A diet deficient in phosphorus is rare as it is widely distributed in all natural foodstuffs. However, a prolonged period of near starvation, as in our patient, can lead to total body phosphorus depletion. Phosphorus is predominantly an intracellular anion, and the serum inorganic phosphate level is thus a poor reflection of the intracellular and total body phosphorus status.

A second contributory factor is 'nutritional recovery syndrome', one of a small number of clinical situations described to cause severe hypophosphataemia, that is, less than 0.32 mmol/l.³ During the anabolic state induced by refeeding, there is an influx of inorganic phosphate from the extracellular to the intracellular compartment. This patient had 10 days of a balanced liquid polymeric preparation with a phosphate content of 14.5 mmol/l prior to her first serum inorganic

phosphate determination. However, more importantly, immediately prior to this blood sample being taken, she had received 2 litres of a dextrose-containing solution intravenously. The administration of glucose results in the release of insulin, which promotes uptake of both glucose and phosphorus into cells, thus causing a slight decline in serum phosphorus levels. This phenomenon has been shown to be much more pronounced when glucose is administered to a starving individual.⁴ These three factors seem to be the most likely explanation for the life-threatening hypophosphataemia that occurred in our patient. This illustrates well the brittle metabolic state of severely malnourished patients, which can easily be upset by unbalanced nutrient solutions such as glucose.

The cause of her cardiorespiratory arrest is unclear but may have been due to aspiration secondary to a weak gag reflex, respiratory muscle weakness, and/or cardiomyopathy secondary to starvation and hypophosphataemia. The clinical manifestations of severe hypophosphataemia mainly involve the neuromuscular and cardiovascular systems.² Paraesthesia and numbness, muscle weakness, acute rhabdomyolysis, acute respiratory failure, acute bulbar symptoms, as well as central nervous system abnormalities such as tremors, confusion, seizures and coma, have all been described. It has been implicated as a cause of reversible cardiomyopathy.⁵ In a report of three cases of anorexia nervosa complicated by sudden death, one case had severe hypophosphataemia (0.06 mmol/l) on the day of the event, which was characterized by the development of a wide-complex idioventricular rhythm.⁶ Our patient had a normal serum inorganic phosphate level for at least 36 hours prior to her cardiorespiratory arrest. There is no documentation of ventilatory failure prior to this event. She maintained her small heart size and normal electrocardiogram during her hospitalization, and at no stage was there evidence of heart failure.

Haematological abnormalities associated with severe hypophosphataemia include haemolytic anaemia, impaired leucocyte phagocytic function and possibly disordered platelet function. Anorexia nervosa itself commonly leads to haematological abnormalities, which are reversible on improved nutrition and is the likely explanation for the abnormalities seen in this patient.⁵ The mechanisms postulated to play a role in most of the clinical manifestations of hypophosphataemia include depletion of cellular adenosine triphosphate, tissue hypoxaemia due to reduced erythrocyte 2,3 diphosphoglycerate resulting in impaired oxygen release and partial blockade of glycolysis due to lack of phosphorus as an important cofactor.

Although the hypophosphataemia was corrected within 24 hours, the bulbar muscle weakness was

fully recovered after 4 days. Her generalized weakness recovered even more gradually but this recovery period was complicated by an admission to the intensive care unit with a period on a ventilator. To what extent this delayed return of normal muscle power is uncertain. A similar hypophosphataemia-related bulbar palsy has been previously described, with full resolution of neurological signs 3 days after commencing treatment.² There appears to be a delay in reversal of the neurological signs despite normalization of the serum inorganic phosphate. However, normal serum levels do not indicate intracellular repletion. All the intracellular effects of phosphorus depletion are not known, whether some are irreversible, and what the lag phase is for cellular recovery after phosphorus repletion.

The treatment of severe hypophosphataemia has been reviewed by Lentz *et al.*⁸ Intravenous therapy is recommended when the serum inorganic phosphate levels are below the life-threatening level of 0.32 mmol/l, at an initial dose of between 0.08 and 0.16 mmol/kg body weight infused over 6 hours,

with subsequent therapy determined by serum inorganic phosphate levels. The much safer oral route of supplementation should be used as soon as the serum levels are above 0.32 mmol/l. It has already been mentioned that serum levels are a poor reflection of total body phosphorus. The urinary phosphorus excretion is a much better guide to adequate phosphorous repletion as the urine may be free of phosphorus in the depleted state due to avid retention by the kidneys, and reappear only after body stores are replete.

Sudden death is a well-described complication in anorexia nervosa and in other starvation situations. There has been no consistent electrolyte abnormality relating to this complication, although some patients may have a prolonged Q-T interval on the electrocardiogram as a prodrome.⁶ This case highlights the need for careful metabolic monitoring of malnourished patients with anorexia nervosa and the need to maintain a cautious, balanced infusion of nutrients during early recovery.

References

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