CASE REPORT

Severe hypophosphataemia: a rare cause of postoperative muscle weakness

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SUMMARY

We report a case of severe generalised muscle weakness in a 66-year-old man who underwent revision of left knee arthroplasty. On postoperative day 1, he developed non-focal muscle weakness and shortness of breath which progressed over a 6-hour period. Serum phosphorus level was severely low at 0.5 mg/dL, along with mild degree of hypokalaemia, hypocalcaemia and hypomagnesaemia. His symptoms completely resolved after emergent phosphorus replacement. The authors believe this case is of educational interest to physicians as generalised muscle weakness is an uncommon presentation of severe hypophosphataemia. In a postoperative setting, hypophosphataemia is often multifactorial, thought to result from combination of perioperative catecholamine surge, administration of saline, diuretics, glucose and antacids, poor oral intake and respiratory alkalosis secondary to pain. We report this case to raise awareness among physicians on severe phosphate imbalance as the primary aetiology for acute generalised muscle weakness and respiratory failure, especially after a surgery.

BACKGROUND

Hypophosphataemia is commonly reported in hospitalised patients, especially in the intensive care setting. Severe hypophosphataemia (<1 mg/dL or 0.32 mmol/L) is uncommon, but associated with significant morbidity and mortality. The most common symptoms reported with severe hypophosphataemia are rhabdomyolysis, proximal muscle weakness, respiratory failure from diaphragmatic weakness, congestive heart failure and arrhythmias. We report a case of severe hypophosphataemia in a postsurgical patient presenting as severe generalised acute myopathy.

CASE PRESENTATION

A 66-year-old man was admitted for elective revision of loosened femoral component of left knee arthroplasty. His history was significant for hypertension, hyperlipidaemia, chronic pain syndrome and left total knee arthroplasty performed in the distant past for post-traumatic arthritis. His medications included atenolol, hydrochlorothiazide, lisinopril, atorvastatin and oxycodone on as needed basis. He denied perioperative use of antacids. He was a carpenter by occupation, non-smoker and never used alcohol. He also admitted to having a normal appetite prior to surgery. He underwent an uncomplicated revision of left total knee

arthroplasty with an estimated blood loss of 50 mL. He received 1500 mL of crystalloids during the procedure and required no blood product transfusions. On postoperative day 1, he noted weakness of all four extremities. Over the next 6 hours, he developed shortness of breath at rest and chest discomfort. On examination, he appeared to be in mild respiratory distress. He was awake, verbal and oriented. Vitals signs showed blood pressure of 116/67 mm Hg, respiratory rate of 16 per minute and oxygen saturations at 98% on room air. Cardio-pulmonary examination was within normal limits. Examination of cranial nerves revealed weakness of facial muscles and inability to raise both eyebrows or protrude tongue. He had intact sensations and generalised profound weakness in both proximal and distal components of all four extremities with grade 2 strength. Muscle tone was diminished. Deep tendon reflexes were hypoactive and Babinski's sign was absent.

INVESTIGATIONS

A 12-lead ECG and serial troponins were performed and acute coronary syndrome was ruled out. The serum phosphorus level was severely low at 0.5 mg/dL, potassium was 3.1 mmol/L, ionised calcium at 4.29 mg/dL and magnesium level was 1.6 mg/dL; renal and liver function tests were within normal limits. Thyroid stimulating hormone level, parathyroid hormone and parathyroid hormone-related peptide levels were also normal. Urine analysis was unremarkable without proteinuria or glycosuria. Urine electrolytes showed phosphate of 32 mg/dL and a calculated fractional excretion (FePhos) of 27.17% (reference range: 10%–20%); however, these were tested after instituting phosphate replacement. Total vitamin D level was mildly low at 21 ng/dL. Arterial blood gas showed mixed respiratory and metabolic alkalosis with pH 7.50, bicarbonate 30 mmol/L and pCO₂ 38 mm Hg. An alcohol level prior to the day of surgery was <11 mg/dL.

Additional workup showed mildly elevated creatine kinase level at 363 units/L (normal range: 52–336 units/L). The serum calcitonin and vasoactive intestinal peptide levels were normal. Serum protein electrophoresis and free light chain assay performed to rule out multiple myeloma were also within normal limits.

DIFFERENTIAL DIAGNOSIS

The differential diagnoses considered in this case prior to the laboratory data included ischaemic

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stroke, intracranial haemorrhage, spinal cord inflammation or compression, Guillane-Barre syndrome, alcoholic myopathy, electrolyte imbalance and hypothyroidism.

TREATMENT

After initial laboratory results revealed severe hypophosphataemia and mild hypomagnesaemia, hypokalaemia and hypocalcaemia, electrolyte replacement was initiated intravenously. He received 30 mmol of potassium phosphate, 30 mmol of sodium phosphate intravenously and 16 mmol of oral phosphorous for a total of 48 mmol phosphorous administered over the subsequent 12 hours. This resulted in normal inorganic phosphorus level of 4.0 mg/dL on subsequent recheck 12 hours later.

OUTCOME AND FOLLOW-UP

Aggressive electrolyte replacement, especially phosphorus, resulted in complete resolution of muscle weakness. Further replacement was stopped and the inorganic phosphorus level stayed within normal limits during the rest of his hospital stay. He underwent physical rehabilitation during his stay in the hospital which he tolerated well. He continued to recover from the revision surgery and was discharged home 4 days later. At follow-up 1 week after discharge, inorganic phosphorus levels stayed normal and the patient was free of symptoms.

DISCUSSION

Hypophosphataemia is a common finding in hospitalised patients, especially in the intensive care unit. However, acute severe myopathy causing generalised muscle weakness as seen in our patient is rarely reported.¹ The clinical significance of mild to moderate hypophosphataemia is unknown except for patients on mechanical ventilation, where diaphragm weakness resulting from low phosphorus levels can delay liberation from the ventilator. Severe hypophosphataemia, defined as less than 1 mg/dL, is less common and is associated with increased morbidity and mortality mainly from cardiac dysfunction and acute respiratory failure.²

Severe hypophosphataemia may also present as symmetric muscle weakness with absent reflexes, mimicking Guillain-Barre syndrome. The mechanisms contributing to development of hypophosphatemia are outlined in the [box 1](#). The aetiology in postsurgical patients is often multifactorial.³ Interestingly, in a study of 121 patients with severe hypophosphataemia (defined as <2 mg/dL), 42.5% of patients were postsurgical and medications were considered as the cause in 81.5% of these patients.² Additionally, release of catecholamines, respiratory alkalosis secondary to pain, volume expansion, combined with reduced oral intake contributes to a low serum phosphate levels postoperatively.¹

The pattern of weakness in our patient with a completely intact sensory system and preserved reflexes indicated muscle weakness as the primary process. The history and physical examination suggested against malnutrition or antacid use. Hypovitaminosis D results in reduced intestinal absorption of phosphate. Vitamin D levels in our patient were not low enough to explain the severe degree of hypophosphataemia, also the parathyroid hormone levels were within normal limits. Thyroid stimulating hormone level, protein electrophoresis and serum free light chain assay was normal, thereby ruling out hypothyroidism and multiple myeloma. Volume expansion with administration of saline causes increased renal phosphate clearance. However, our patient received 1500 mL of Ringer

Box 1 Causes of hypophosphataemia.⁴

Causes

Pseudohypophosphataemia

- ▶ Mannitol.

Cellular redistribution

- ▶ Insulin, fructose, glucose, during refeeding syndrome.
- ▶ Acute respiratory alkalosis, catecholamine surge.
- ▶ Hungry bone syndrome.
- ▶ Rapid cellular proliferation with erythropoietin, granulocyte-monocyte colony stimulating factor.

Decrease in intestinal absorption

- ▶ Inadequate intake, malnutrition, chronic diarrhoea.
- ▶ Vitamin D deficiency.
- ▶ Antacids, phosphate binders.

Increased renal clearance

- ▶ Diuretics (mostly thiazides), acetazolamide.
- ▶ Fanconi's syndrome.
- ▶ Primary or secondary hypoparathyroidism.
- ▶ Vitamin D deficiency or resistance.
- ▶ Oncogenic osteomalacia.

Removal by renal replacement therapies

Learning points

- ▶ Severe hypophosphataemia commonly presents as rhabdomyolysis, acute respiratory failure secondary to diaphragmatic weakness, congestive heart failure, arrhythmias and haemolytic anaemia.
- ▶ Acute generalised muscular weakness may result from severe electrolyte disturbances such as low serum phosphate levels.
- ▶ Severe hypophosphataemia after a surgery could be multifactorial, resulting from a combination of prior diuretic use, perioperative catecholamine surge, administration of glucose and antacids, volume expansion, poor oral intake and respiratory alkalosis secondary to pain.

lactate intraoperatively. The high FePhos points towards renal wasting; however, the electrolytes were tested after initiating electrolyte replacement, thus making it unreliable. Also, the absence of glycosuria on urinalysis and renal tubular acidosis argued against Fanconi's syndrome. Notably, our patient was on a thiazide diuretic. Thiazides lead to increased phosphate clearance via a direct effect on the distal tubules, thereby partly explaining the high FePhos. The mild respiratory alkalosis which resulted from postoperative pain could have contributed to some extent. Additionally, perioperative catecholamine surge causes phosphate to shift intracellularly.

We therefore concluded that the aetiology of hypophosphataemia in our patient was multifactorial. The use of diuretics, mild respiratory alkalosis, vitamin D deficiency and perioperative catecholamine surge together contributed to the hypophosphataemia. We thereby recommend maintaining a high index of suspicion for severe hypophosphataemia as a potential cause for postoperative acute generalised myopathy in association with respiratory failure.

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