CASE REPORT

Panic-related hyperventilation resulting in hypophosphataemia and a high lactate

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SUMMARY

A 22-year-old lady presented to the emergency department with dyspnoea and pleuritic chest pain. Life-threatening asthma, pulmonary embolus and pneumothorax were all excluded. However, investigations did show an unexplained hypophosphataemia and raised lactate, both of which were subsequently attributed to hyperventilation with a component of panic. Here we explore the mechanism of these findings and the management of hypophosphataemia.

BACKGROUND

Hypophosphataemia is a common biochemical finding in hospital inpatients.^{1 2} Identifying the cause is important as management varies depending on the cause. Rapid treatment is crucial as the consequences of hypophosphataemia can be severe.^{1 3 4}

CASE PRESENTATION

A 22-year-old lady was admitted to the emergency department complaining of dyspnoea, pleuritic chest pain and feeling wheezy. She had a background of mild asthma and rarely required her salbutamol inhaler. She also took the oral contraceptive pill. She had no medical history or family history of anxiety disorder or mood disorder.

During transfer to the acute care unit she suffered a sudden deterioration. Her examination findings were a high respiratory rate of 38 breaths/min; BP 118/95 mm Hg; pulse of 125 bpm; oxygen saturation was 100% on 15 l of oxygen. She appeared tremulous, sweaty and frightened and complained of a worsening of her original symptoms. Her cardiovascular, respiratory and abdominal examinations were unremarkable.

INVESTIGATIONS

An arterial blood gas on room air showed a respiratory alkalosis with a raised lactate. Biochemical and haematological investigations were normal with the exception of a low phosphate of 0.33 mmol/l. Peak expiratory flow (PEF) readings were low with a best of three readings being 220 l/min (50% of predicted).⁵ However, the technique was poor.

DIFFERENTIAL DIAGNOSIS

Severe shortness of breath in a known asthmatic with a sudden deterioration coinciding with the presence of pleuritic chest pain raised the possibility of acute severe asthma or a pneumothorax. Given the use of the oral contraceptive pill we also needed to exclude a pulmonary embolus (PE).

A normal chest x-ray excluded pneumothorax while a CT pulmonary angiogram (CTPA) excluded a PE. Acute severe asthma explains the low peak expiratory (PEF) readings but does not explain the remaining abnormal investigations of low phosphate and a raised arterial lactate. However, these can all be explained by panic-related hyperventilation resulting in hypophosphataemia as discussed below. We believe that the trigger for this panic attack was the patient's perception that transfer from the emergency department to the acute care unit suggested a deterioration in condition, of which she was fearful.

TREATMENT

A 3-day course of oral phosphate was prescribed and completed.

OUTCOME AND FOLLOW-UP

Phosphate levels were subsequently checked a week later and were within the normal range. She was seen 4 weeks later in the acute medical outpatient clinic and her physical symptoms had resolved. She had suffered from no further panic attacks and intervention for this was deemed unnecessary.

DISCUSSION

Phosphate is absorbed in the gut and filtered and excreted in the kidney. Under normal conditions approximately 80% of filtered phosphate is reabsorbed.² It is stored in bones and teeth, the intracellular fluid of soft tissues and in the extracellular fluid.² Phosphate homeostasis is regulated by parathyroid hormone and calcitriol. Parathyroid hormone is released in response to hypocalcaemia, which it corrects, and inhibits renal phosphate reabsorption resulting in phosphaturia. The response to hypophosphataemia is co-ordinated by calcitriol, a vitamin D derivative, whose active moiety is formed by hydroxylation in the kidney. Calcitriol stimulates gut absorption of phosphate and in high concentrations stimulates osteoclastic bone reabsorption. Both of these raise plasma phosphate levels (figure 1).

Low phosphate, <0.8 mmol/l, can result from three processes: insufficient dietary intake or intestinal absorption, raised renal losses or redistribution of body phosphate stores. These include insufficient absorption (malabsorption, vomiting); renal losses (hyperparathyroidism, fanconi syndrome) and redistribution (hyperventilation, refeeding syndrome).⁶⁻⁸ There was no clinical evidence of insufficient absorption or renal losses, and no evidence of these on investigation.

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Figure 1 The calcitriol axis.

Hyperventilation results in increased loss of carbon dioxide from the lungs, resulting in a fall in the partial pressure of carbon dioxide in arterial blood (PaCO_2). As carbon dioxide is a weak acid, a fall in its partial pressure generates an alkalosis. This is demonstrated by the equation $\text{CO}_2 + \text{H}_2\text{O} \rightleftharpoons \text{HCO}_3^- + \text{H}^+$ which becomes left-shifted as a result of a fall in carbon dioxide.⁷

As carbon dioxide diffuses freely across cell membranes the alkalosis becomes both intracellular and extracellular. One consequence of intracellular alkalosis is the stimulation of phosphofructokinase, the rate-limiting enzyme in glycolysis (figure 2). This reaction causes the consumption of intracellular phosphate. As a result, phosphate is redistributed into the intracellular space thus reducing extracellular phosphate concentration and causing hypophosphataemia.^{6,7}

As well as consuming phosphate, glycolysis produces lactate. The increased production of lactate in response to intracellular alkalosis is not mitigated by an increase in Krebs cycle activity because Krebs cycle activity is determined by the demand for ATP, not the availability of substrates such as pyruvate. This explains how hyperventilation can cause both hypophosphataemia and a raised lactate.^{6,7}

Phosphorous plays a key role in many processes including the maintenance of cell structure, cellular metabolism, regulation of intracellular enzymes and acid-base homeostasis.² Hypophosphataemia therefore affects a wide range of body systems. The clinical manifestations usually result from the effect of low phosphate on the musculature, resulting in weakness; blood cells whose function is impaired and the nervous system.

Figure 2 The glycolysis reaction.

These manifestations usually only arise in the context of severe hypophosphataemia of $<0.4 \text{ mmol/l}$.³ The clinical consequences of hypophosphataemia can include skeletal muscle weakness, rhabdomyolysis, haemolysis, altered mental state and panic.

The management of hypophosphataemia should focus on treating the cause with replacement being reserved for cases of sustained or severe hypophosphataemia. Replacement can be either with oral phosphate or, if severe, with intravenous potassium phosphate. Other than in exceptional circumstances phosphate administration should be cautious as sudden phosphate administration can cause clinically significant hypocalcaemia and widespread calcium deposition as a result of calcitriol inhibition.^{2,3}

The diagnosis of panic attack was made in line with the Diagnostic and Statistical Manual of mental disorders IV (DSM-IV) criteria: 'a brief period of intense fear or discomfort' during which four of 13 criteria are 'developed abruptly' and reach 'a peak within 10 min' (box 1).⁹ Our patient was fearful and experienced a tachycardia, sweating, tremor and a worsening of her shortness of breath. While panic attacks are correlated with other psychiatric diagnosis they can occur in their absence, as in this case.⁹

Box 1 The diagnostic criteria for panic attack

DSM-IV criteria for panic attack

A discrete period of intense fear or discomfort in which four or more of the below develop abruptly and reach a peak within 10 min

- Palpitations, pounding heart or accelerated heart rate
- Sweating
- Trembling or shaking
- Sensation of shortness of breath or smothering
- Feeling of choking
- Chest pain or discomfort
- Nausea or abdominal distress
- Feeling dizzy, unsteady, lightheaded or faint
- Derealisation or depersonalisation
- Fear of losing control or going crazy
- Fear of dying
- Paraesthesiae
- Chills or hot flushes

DSM-IV, Diagnostic and Statistical Manual of mental disorders-IV

Learning points

- ▶ Resuscitate the acutely unwell patient and exclude life-threatening pathology first.
- ▶ Reassure and comfort the patient and treat symptoms. Panic can cause true clinical deterioration.
- ▶ The causes of hypophosphataemia can be divided into decreased intake, increased loss or redistribution. Management depends upon the cause.
- ▶ If you correct hypophosphataemia, do so cautiously.

Competing interests None.

Patient consent Obtained.

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