Reminder of important clinical lesson

Hypophosphataemia as a cause of acute confusional state

Sean Ninan,¹ David Lloyd,¹ Manoj Saraswat²¹Hull Royal Infirmary, Hull, UK²Medicine for the Elderly, Castle Hill Hospital, Hull, UK

Correspondence to Dr Sean Ninan, sean9n@hotmail.com

Summary

A 74-year-old gentleman presented with an acute onset of confusion and agitation. His symptoms were so severe that he had to be sedated and intubated for CT scan. All investigations were unremarkable, except a low serum phosphate. He was treated with intravenous phosphate and his symptoms improved in line with the rise in his serum phosphate. By discharge, he had returned to his previous state of health. The cause of the hypophosphataemia was not apparent; we have asked his general practitioner to monitor his serum phosphate.

BACKGROUND

This patient presented with acute severe agitation, requiring sedation and intubation for CT scan. The cause of this agitation was hypophosphataemia, and his symptoms improved in line with phosphate replacement.

Acute confusional state is a common clinical presentation and readers should be aware of hypophosphataemia as a cause. Readers should also be aware of methods and ideal rates of phosphate administration.

CASE PRESENTATION

A 74-year-old gentleman was admitted to hospital following a sudden onset of acute confusion and agitation. He was sitting in his living room, writing, when he suddenly started throwing things around and shouting in an aggressive manner. His wife called other members of the family, and then the general practitioner who arranged for admission to the emergency department via an ambulance.

This behaviour was out of character and unusual for him. There was no history of acute illness or symptoms of infection. The only other symptoms he had been complaining of recently were a mild intermittent headache over the past 2 weeks and aching of his calves.

His previous illnesses included Parkinson's disease, nocturnal visual hallucinations, anxiety and depression.

His regular medications consisted of citalopram, clonazepam, cocareldopa, entacapone, domperidone, quetiapine, terazosin and lactulose. There was no history of overdose or non-compliance.

He lived in warden-controlled accommodation with his wife and was independent with activities of daily living. He did not drink alcohol or smoke.

On examination, he was agitated and pulling out his lines and catheters. He was tachycardic. Cardiovascular and respiratory examinations were unremarkable. His abdomen was soft; there was mild left iliac fossa tenderness. There were no focal neurological findings.

INVESTIGATIONS

Blood tests including full blood count, urea and electrolytes, serum calcium, liver function tests and C reactive

protein were all unremarkable barring a serum phosphate of 0.39 mmol/l (lower limit of normal 0.70 mmol/l).

- ▶ Chest x-ray: clear lung fields
- ▶ Electrocardiogram: sinus tachycardia
- ▶ Arterial blood gas (15 litres oxygen, non-rebreath mask): pH 7.38, pCO₂ 4.5, PO₂ 51.9, bicarbonate 21.7 and lactate 2.0
- ▶ Capillary blood glucose 7.8
- ▶ CT of head: unremarkable appearances

DIFFERENTIAL DIAGNOSIS

Older people admitted with acute confusion should receive a full work-up. The differential diagnosis is wide and includes hypoxia, hypoglycaemia, sepsis, stroke, infection, constipation, urinary retention, intracranial haemorrhage, substance misuse or withdrawal, changes in medications, renal failure, liver dysfunction, psychiatric disorders and electrolyte or metabolic abnormalities.

Often, there may be a combination of causes, for example, constipation, dehydration and urinary retention, and all contributing factors should be addressed to help relieve symptoms.

TREATMENT

The patient received 10 mg diazepam, 5 mg midazolam and 5 mg haloperidol in the emergency department but was still difficult to manage so had to be sedated and intubated for CT scan. He was extubated shortly afterwards and transferred to the acute assessment unit, where he remained agitated but his behaviour was becoming more manageable. An intravenous phosphate infusion of 500 ml phosphate polyfusor (containing 50 mmol phosphate) was started later that day. There was some debate as to how quickly to administer the solution and it was eventually administered slowly at 7.5 ml/h on the advice of the ward pharmacist and in line with hospital policy.

OUTCOME AND FOLLOW-UP

His serum phosphate rose slowly, returning to within the normal range 4 days later. Over this time, his symptoms slowly improved and he was eventually discharged a week

after his initial admission, having returned to his prior state of health.

His parathyroid hormone level was normal, and the cause for his hypophosphataemia was not clear. We have asked his general practitioner to monitor his serum phosphate and to refer back to hospital if there is recurrent hypophosphataemia for further investigations.

DISCUSSION

The incidence of hypophosphataemia is around 0.2–3.1% in hospital inpatients although this may be higher in selected groups, for example, patients with sepsis, alcoholism, critical illness and malnutrition.¹

Hypophosphataemia can be classified as moderate (serum phosphate 0.32–0.65 mmol/l) or severe (serum phosphate <0.32 mmol/l). Symptoms tend to occur when serum levels are in the severe range and clinical manifestations can be widely ranging. Neurological manifestations such as seizures,² coma,³ visual hallucinations,⁴ central pontine myelinolysis⁵ and Wernicke's encephalopathy⁶ have been reported. Cases reported in the literature often occurred in the setting of alcohol abuse,^{3 5 6} critical illness³ or refeeding after a period of malnutrition.² The mechanism of encephalopathy is poorly understood but it is possible that tissue ischaemia is a causative factor due to reduced 2,3-diphosphoglycerate which leads to reduce oxygen release by increasing the affinity of haemoglobin for oxygen.⁷

Our case was unusual in that the patient neither had another acute illness, nor did he have a chronic condition that would predispose him to hypophosphataemia. His symptoms were severe despite not falling into the (arbitrary) severe range of hypophosphataemia. It was not possible to identify the cause for this presentation. The patient was well nourished. He did not have any symptoms to suggest gastrointestinal losses, nor was he on any medication that could have caused phosphate losses. His parathyroid hormone level and acid–base status were normal. Given that this was a one-off event, we have elected to monitor his serum phosphate. If hypophosphataemia recurs, then further tests to evaluate, for example, renal losses may be appropriate. This can be done by measuring the fractional phosphate excretion using the following formula:

Percentage reabsorption = $100 \times (1 - (\text{urine phosphate level} \times \text{serum creatinine level}) \div (\text{serum phosphate level} \times \text{urine creatinine level}))$.

If the cause of a low phosphate was extrarenal, percentage reabsorption should be close to 100% in the setting of a low serum phosphate.

The treatment of hypophosphataemia is dependent on the cause, severity and duration. Moderate hypophosphataemia should be managed with oral replacement therapy unless symptoms necessitate more rapid repletion. Oral replacement can be complicated by gastrointestinal side effects, for example, diarrhoea and doses should be divided throughout the day to limit this.

Intravenous therapy is advised if hypophosphataemia is severe or the patient is suffering from sequelae of hypophosphataemia. Correction can sometimes be unpredictable and rapid infusions have sometimes been associated with complications such as hyperphosphataemia, hypotension, hypocalcaemia, tetany, renal failure and ECG abnormalities.^{8 9} Infusion rates between 5 and 20 mmol/h have been evaluated and considered to be safe although rates of 15–20 mmol/h were associated with mild hyperphosphataemia, mild hyperkalaemia and mild hypocalcaemia.⁸

This patient was given a 50 mmol/500 ml bag of polysfusor infusing at 7.5 mls/h over nearly 3 days, working out at a replacement rate of 0.75 mmol/h, on advice of our ward pharmacist. Our hospital policy allows for replacement rates of up to 1.5 mmol/h on the ward; higher rates of replacement are probably safe but require close monitoring of vital signs, cardiac rhythm and serum biochemistry.

Learning points

- ▶ Hypophosphataemia is a cause for an acute confusional state.
- ▶ Treatment of hypophosphataemia may result in cessation of symptoms.
- ▶ Intravenous phosphate should be administered in cases of severe or symptomatic hypophosphataemia.
- ▶ Rapid phosphate repletion requires careful monitoring of vital signs, cardiac rhythm and serum biochemistry.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **Gaasbeek A**, Meinders AE. Hypophosphatemia: an update on its etiology and treatment. *Am J Med* 2005;**118**:1094–101.
2. **Silvis SE**, Paragas PD Jr. Paresthesias, weakness, seizures, and hypophosphatemia in patients receiving hyperalimentation. *Gastroenterology* 1972;**62**:513–20.
3. **Lee JL**, Sibbald WJ, Holliday RL, *et al.* Hypophosphatemia associated with coma. *CMAJ* 1978;**119**:143–5.
4. **Barbe B**, Lejoyeux M, Bouleau JH, *et al.* Visual hallucination related to severe hypophosphataemia. *Lancet* 1991;**338**:1083.
5. **Michell AW**, Burn DJ, Reading PJ. Central pontine myelinolysis temporally related to hypophosphataemia. *J Neurol Neurosurg Psychiatry* 2003;**74**:820.
6. **Vanneste J**, Hage J. Acute severe hypophosphataemia mimicking Wernicke's encephalopathy. *Lancet* 1986;**1**:44.
7. **Weisinger JR**, Bellorin-Font E. Magnesium and phosphorus. *Lancet* 1998;**352**:391–6.
8. **Geerse DA**, Bindels AJ, Kuiper MA, *et al.* Treatment of hypophosphatemia in the intensive care unit: a review. *Crit Care* 2010;**14**:R147.
9. **Shackney S**, Hasson J. Precipitous fall in serum calcium, hypotension, and acute renal failure after intravenous phosphate therapy for hypercalcemia. Report of two cases. *Ann Intern Med* 1967;**66**:906–16.

This pdf has been created automatically from the final edited text and images.

Copyright 2012 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.

BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Ninan S, Lloyd D, Saraswat M. Hypophosphataemia as a cause of acute confusional state. *BMJ Case Reports* 2012;10.1136/bcr-2012-006960, Published XXX

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow