An uncommon cause for severe hypophosphataemia after transsphenoidal pituitary surgery

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Electrolyte abnormalities are common during the peri-operative period; this can lead to life-threatening cardiac arrhythmias, alteration in mental status, muscle weakness, muscle rigidity and respiratory failure. Failure to recognise these abnormalities may lead to misdiagnosis, which increases the morbidity or mortality.[1] Alteration in serum sodium is the common electrolyte abnormality seen in neurosurgical patients.[2-4] Potassium and calcium abnormalities are also seen but hypophosphataemia is rare, in a healthy patient undergoing surgery. We report a case of acute on chronic hypophosphataemia caused by chronic hypokalaemia, presenting with severe skeletal muscle weakness and paraesthesia, following a transsphenoidal excision of prolactinoma. An informed written consent was obtained from the patient for publication of this case report.

A 41-year-old female (height 166 cm, weight 60 kg) was scheduled for an endoscopic transsphenoidal excision of pituitary adenoma. She had presented with galactorrhoea, on investigation, was found to have 1.8 × 1.3 × 1.1 cm prolactinoma. She was treated with oral bromocriptine 1.25 mg once daily, for more than one year duration, which failed to control her symptoms. Her past medical history included hypothyroidism, which was controlled with 50 mcg of levothyroxine per day. She also gave history of heavy vaginal bleeding due to uterine fibroid for which she was on subcutaneous leuprolide acetate injection, an gonadotropin releasing hormone (GnRH) analog, once a month for a year. Her previous anaesthetic history for appendectomy and caesarean section was uneventful. She was a non-smoker and non-alcoholic. Her physical and airway examinations were normal. Pre-operative blood investigations including the thyroid function test were normal except for the serum potassium (K^+) of 3.3 mmol/L.

Her anaesthetic management consisted of intravenous induction with midazolam (1 mg), fentanyl (150 µg), propofol (150 mg) and rocuronium (50 mg), followed by endotracheal intubation. Anaesthesia was maintained with air, oxygen, sevoflurane (1 MAC) and a low dose of remifentanil infusion (0.05-0.1 µg/kg/min). Monitoring consisted of 5-lead ECG, non-invasive and invasive blood pressure, pulse oximetry, capnography, oesophageal temperature and urine output. Before surgery, nasal cavity was prepared by packing with epinephrine soaked pledgets (1 in 10,000) followed by sub mucosal infiltration of epinephrine (1 in 200,000). Intra-operatively her vitals were stable and end tidal carbon dioxide was maintained within normal limit (32-35 mm Hg). The blood loss (<250 ml) was very minimal. She received 2 L of crystalloids during surgery. Her urine output was 300 ml over 3 h. Intra-operative blood work revealed hypokalaemia (K^+ 2.5 mmol/l) and was treated with 40 mmols of potassium chloride (KCl) as an intravenous infusion over 2 h. Her repeat serum K^+ level was 3.0 mmol/L. At the end of surgery, neuromuscular blockade was reversed and she was extubated awake in the operating room. In the post-anaesthesia care unit (PACU), she was haemodynamically and neurologically stable and received further supplementation of 20 mmols of KCl. Repeat K^+ revealed persistent hypokalaemia (2.4 mmol/L) and received another 20 mmol of KCl and was started with the maintenance fluid of 0.9% normal saline (NS) with 40 mmol of KCl at the rate of 100 ml/h. After 4 h of stay in PACU, she was transferred to neuro critical care step-down unit (NCCU) for monitoring.

Two hours later, she complained of severe weakness of both upper, lower extremities, over the cheeks and could not open her mouth. She also complained that she could not feel her upper, lower extremities and the cheeks. On examination, she was anxious, tachypnoeic, tachycardic (120 bpm), hypertensive (190/110 mmHg) and her oxygen saturation was 100% with the 5 L of oxygen by a face mask. Her temperature was 37.4°C and the arterial blood gas analysis revealed respiratory alkalosis with the P_H of 7.5, $PaCO_2$ of 24 mmHg, PaO_2 of 109 mmHg with the HCO_3 of 19 mmol/L. Neurological examination revealed severe weakness (grade 2/5) of both extremities.

In view of difficulty in mouth opening with associated tachycardia and hypertension, a clinical possibility of malignant hyperthermia (MH) was considered as one of the differential diagnosis. However, presence of severe muscle weakness instead of muscle rigidity, normothermia

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with low $PaCO_2$ (24 mmHg) excluded the possibility of MH. Further investigations revealing a low potassium (3.3 mmol/L) and normal creatine kinase of 41 IU/L with no myoglobin in urine ruled out MH. Rest of her blood investigations including calcium and magnesium were normal except for severe hypophosphataemia with phosphate levels of 0.28 mmol/L (normal 0.8-1.45) and mild hypokalaemia (3.3 mmol/L). Hypophosphataemia was treated with two doses of intravenous potassium phosphate (15 mmol in 250 ml of 0.9% NS each over 2 hours). Her symptoms improved after correction and she was started with oral supplements of sodium acid phosphate (500 mg three times daily) and potassium (60-80 mmols/day) for 72 hours. She remained asymptomatic and got discharged from the hospital on the 7th post-operative day in a good clinical state. We did not find any other reports in the literature describing this presentation.

Chronic hypokalaemia has been shown to decrease the renal tubular re-absorption of phosphate thereby increasing the phosphate clearance in urine and can cause hypophosphataemia.[5-7] Studies have shown that a decrease in phosphate clearance and a return of the plasma phosphate concentration to normal levels occurred after correction of the potassium deficit.[7] There was a recent report by food and drug administration (FDA), which showed 78 cases of hypokalaemia among 4487 users of leuprolide acetate for various causes.[8] There are case reports of hypokalaemia after the use of leuprolide acetate for advanced prostatic cancer.[9,10] In our patient, the use of leuprolide acetate may be the possible reason for the chronic hypokalaemia. Chronic hypokalaemia could have been the cause for chronic hypophosphataemia. Intra-operative use of epinephrine, steroid and post-operative anxiety-induced hyperventilation could have caused further decrease in serum phosphate and potassium by intra-cellular shift.

Hypophosphataemia is commonly missed or misdiagnosed due to non-specific signs and symptoms at presentation.[11,12] It can cause considerable morbidity and mortality due to cardio respiratory dysfunction.[13] The common causes for acute hypophosphataemia during the peri-operative period include, fluid shift, drug-induced renal excretion[14] (diuretics) and intra-cellular shift of phosphate (hyperglycaemia, use of insulin, epinephrine and corticosteroid or hyperventilation).[15,16] The common cause for chronic hypophosphataemia is nutritional depletion. However, we did not check phosphate and albumin level during the pre-operative visit as the patient was healthy. Post-operative albumin of 3.3 g/dL excluded a nutritional depletion. Hence, chronic hypokalaemia-induced phosphate loss in the urine could be the possible cause for hypophosphataemia in our case. Retrospectively, it was felt that a complete bundle of electrolyte workup should have been done during the immediate post-operative period, which could have prevented the symptoms and the delay in treatment of hypophosphataemia and the intensive care unit (ICU) admission.

Our report presents a case of acute on chronic hypophosphataemia caused by chronic hypokalaemia, manifesting as severe paresthesia and skeletal muscle weakness. Complete electrolyte bundle work up is warranted routinely in surgical patients who present with chronic hypokalaemia.

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