Learning from errors

Secondary hypokalaemic paralysis

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Summary

A 28-year-old man presented with acute onset, ascending-type and bilateral symmetrical areflexic motor paralysis. There was a history of fever 3 days prior to paralysis, multiple episodes of vomiting, chloroquine use and intravenous dextrose administration. Investigations revealed metabolic alkalosis with normal serum potassium level but ECG showed characteristic changes of hypokalaemia based on which patient was managed successfully. This case highlights the importance of ECG findings of hypokalaemia in the presence of non-confirmatory laboratory values while evaluating a case of acute flaccid quadriplegia.

BACKGROUND

Acute hypokalaemic paralysis, a clinical syndrome characterised by acute systemic weakness and low-serum potassium, is an uncommon, but treatable cause of acute weakness. Early and correct diagnosis is necessary to prevent morbidity and mortality from respiratory failure and cardiac arrhythmias.

CASE PRESENTATION

A 28-year-old man presented to the emergency department on 10 March 2011 at around 16:00 with the complaints of inability to move all limbs since morning. As per the patient he was in his usual state of health till 4 days back (6 March), when he started having fever which was of moderate grade, continuous, without chills and rigors. On 7 March he consulted a doctor who prescribed him chloroquine and antipyretics. Next day the patient developed 15–20 episodes of non-projectile vomiting, though his fever was relieved. For this he got admitted at a peripheral hospital where he was treated symptomatically with antiemetics and intravenous fluids. He was discharged from the hospital on 9 March with relief in vomiting. Same day by evening patient started feeling generalised weakness and lethargy though he was able to do his routine activities. Next day, patient woke up at around 5:00 with the urge to pass urine, as soon as he tried to get up from the bed he fell down and found that he is not able to bear weight on his legs. Two of his family members supported him to the toilet for passing urine and stool. He also noticed difficulty in lifting his arms above his head. By afternoon when he presented to the emergency department, he was not able to move all his limbs. There was no history of trauma, headache, neck pain, loss of consciousness, bowel bladder involvement, loose stools, pain abdomen, band-like sensation over the trunk, similar episode in the past, recent vaccination, difficulty in breathing, difficulty in swallowing, drooling of saliva or visual disturbance. There was nothing contributory in history. None of his family members had ever had this kind of illness.

At presentation his vitals were within normal limits and there was no orthostatic hypotension. His respiratory rate, single breath count and breath holding time was normal. The patient was conscious, oriented with normal speech and intelligence. All cranial nerves were intact. All limbs were flaccid with power grade 0/5 in all muscle groups. Bilateral biceps, triceps, supinator, knee and ankle jerks were absent. Plantar reflexes were equivocal. All sensory tracts were intact. There was no spinal deformity. Abdominal examination revealed sluggish bowel sounds. Rest of the systemic examination was normal.

INVESTIGATIONS

On investigation, haemoglobin, 13 g/dl; total leucocyte count, 6100/mm³; differential leucocyte count: polymorph 68%, lymphocyte 26%, eosinophil 4%, monocyte 2%, serum creatinine 1.0 mg/dl (0.6–1.2), blood urea 28 mg/dl (20–40), serum sodium (Na⁺) 139 mmol/l (135–145), potassium (K⁺) 4.2 mmol/l (3.5–5), magnesium 1.8 mmol/l (1.6–2.4), liver function test, urine analysis, blood sugar random and x-ray chest were within normal limits, urinary potassium 14 mmol/l/day (25–100). Arterial blood gas analysis—pH-7.5, PaCO₂-52, PaO₂-78, HCO₃-38 mmol/l suggestive of metabolic alkalosis. Thyroid function test—T3-146 ng/dl (75–195), T4-9.6 µg/dl (4.6–11.2) and TSH-3.8 mU/l (0.5–5). ELISA for HIV was negative. Cerebrospinal fluid study was within normal limit. Electromyography showed reduced number of motor units. ECG done at the time of presentation revealed prominent U-waves and ST-segment depression suggestive of hypokalaemia (figure 1A).

DIFFERENTIAL DIAGNOSIS

In view of acute onset, ascending-type and bilateral symmetrical areflexic motor paralysis, diagnosis of Guillain-Barre syndrome was considered but characteristic ECG findings pointed towards hypokalaemia as the cause of paralysis.

Figure 1 (A) ECG at presentation showing ST depression (blue arrow) and prominent U (red arrow) suggestive of hypokalaemia C1–C6 corresponds to chest leads V1–V6. (B) ECG on second day after giving 100 mmol of potassium overnight showing disappearance to ST depression and U-wave in the same chest leads. (C) Normal ECG on third day after 200 mmol of potassium showing reappearance of normal T-wave (encircled in lead C3) and absence of ST depression and U-wave, along with full recovery of patient.

TREATMENT

Syndromic diagnosis of acute onset flaccid quadriplegia without sensory and bowel bladder involvement was

made. The patient was admitted in intensive care unit and low-molecular-weight heparin was started for deep vein thrombosis prophylaxis. Though the laboratory

report revealed normal potassium level, considering characteristic ECG findings, patient was given 100 mmol of potassium intravenously overnight the first day. Next day morning, the patient's neurological examination did not show any improvement but patient was subjectively feeling some strength in both his hands. Repeat ECG (figure 1B) showed reversal of ST segment depression and disappearance of U-wave. These changes in the ECG finding and patient's feeling of improvement were an indirect evidence of underlying hypokalaemia that was being corrected, moreover repeat serum potassium was 2.2 mmol/l which made us believe that there was some laboratory error in previous potassium measurement. The patient was given 200 mmol of potassium intravenously over next 24 h. Same day by evening, the power in all limbs increased to 2/5. Areflexia was still present. Next day (third day) morning, the patient regained power in all limbs and was able to walk without any support. Neurological examination revealed 4/5 power in all the muscles groups. All reflexes were present. ECG (figure 1C) was normal with appearance of normal T-waves and serum potassium was 3.3 mmol/l. Patient was started on oral potassium chloride. Final diagnosis in this case was acute secondary hypokalaemic paralysis.

OUTCOME AND FOLLOW-UP

The patient was discharged after 15 days with serum potassium 4.2 mmol/l and was not advised to continue potassium supplementation. Since then, he is receiving regular follow-up, and has not experienced a similar episode of weakness.

DISCUSSION

Hypokalaemia, one of the common electrolyte disturbances, is diagnosed if plasma potassium (K^+) concentration is less than 3.5 mmol/l. Mild hypokalaemia (3–3.5 mmol/l) is usually asymptomatic, but greater degree of hypokalaemia can result in signs and symptoms that reflect the fundamental role of potassium in neuromuscular transmission. Severe hypokalaemia (< 2.5 mmol/l) can result in life-threatening arrhythmia or respiratory failure.

Hypokalaemia can occur either due to K^+ depletion or due to transcellular shift of K^+ . The most common cause of K^+ depletion is the use of diuretics.^{1 2} High-dose glucocorticoid administration promotes K^+ excretion indirectly.³ Potassium depletion and hypokalaemia are almost invariable consequences of metabolic alkalosis.^{3–5} This acid-base disorder is most commonly the result of selective chloride losses induced by vomiting or by diuretic administration. Metabolic alkalosis can also exist independent of chloride depletion, most commonly caused by primary hyperaldosteronism, or more rarely by other states of mineralocorticoid excess. Two rare genetic abnormalities, Liddle's syndrome and 11 β -hydroxysteroid dehydrogenase deficiency, can produce hypokalaemia by stimulating K^+ secretion independent of aldosterone secretion.^{4 6} Potassium depletion and hypokalaemia occur in type 1 and in some forms of type 2 renal tubular acidosis (RTA).⁴ Magnesium depletion, regardless of its cause, can lead to renal K^+ wasting.⁴ A wide variety of β_2 -adrenergic agonist drugs shift K^+ into cells and cause transient hypokalaemia. These drugs include decongestants, bronchodilators and tocolytic agents.⁴ Chloroquine also causes

hypokalaemia by transcellular shift of potassium.⁷ Theophylline and caffeine stimulate cell membrane Na^+/K^+ ATPase and promote K^+ entry into cells. Severe hypokalaemia is a characteristic feature of theophylline toxicity.^{8 9} Accidental ingestion of barium salts blocks K^+ exit from cells and causes hypokalaemia. In addition to drugs and toxins, hypokalaemia rarely occurs as a complication of hyperthyroidism, presumably from stimulation of activity of Na^+/K^+ ATPase by thyroid hormone.⁴ Familial hypokalaemic periodic paralysis is caused by a mutation in a cell membrane Ca^{++} channel that causes paroxysmal severe episodes of hypokalaemia brought on by a high-carbohydrate or high-sodium intake or by exercise.¹⁰

Hypokalaemic paralysis may be primary (familial) or secondary. The primary type is more common and has an autosomal-dominant inheritance. The primary type is associated with normal serum potassium during the asymptomatic period and usually reduced the potassium level during the period of muscle weakness. Secondary hypokalaemic paralysis is less common. In patients who have their first attack of weakness in adulthood a secondary cause must be searched for.¹¹ The secondary hypokalaemic paralysis lacks a family history. Differential diagnosis of secondary hypokalaemic paralysis includes transcellular shift of K^+ (causes are—thyrotoxic periodic paralysis and barium poisoning), actual potassium depletion which may be via renal loss (Type 1 RTA, Type 2 RTA and Conn's syndrome) or via extrarenal loss (gastroenteritis, villous adenomas, vasoactive intestinal peptide tumors, vomiting and excessive sweating).

Hypokalaemia is a relatively common biochemical abnormality found on routine screening in the accident and emergency department. In addition to the biochemical diagnosis, the emergency physician should be aware of the ECG manifestations that may result from hypokalaemia. The effect of hypokalaemia on the cell membrane is to increase the resting membrane potential, and increase the duration of the action potential and refractory period, which are potentially arrhythmogenic.¹² The classical ECG changes described are (1) a reduction in the T-wave amplitude, (2) depression of the ST-segment and (3) U-waves that are usually seen as a small positive deflection after the T-wave, best seen in mid-precordial leads. In severe hypokalaemia giant U-waves have been described that can be mistaken for peaked T-waves.¹³ In addition to these ECG manifestations, hypokalaemia has been shown to increase the risk of various malignant ventricular arrhythmias.

Treatment of hypokalaemic paralysis is to address the underlying cause and potassium replacement. Because of the risk of hyperkalaemia, oral route of potassium replacement is preferred. Intravenous replacement is reserved for life-threatening hypokalaemia that causes cardiac arrhythmias and severe paralysis.

Our patient suffered from life-threatening secondary hypokalaemic paralysis. The diagnosis was suspected upon the presence of characteristic ECG changes of hypokalaemia. Events that have led to severe hypokalaemia in our case are chloroquine use, multiple episodes of vomiting and possible intravenous dextrose administration to correct dehydration and generalised weakness following vomiting. Vomiting causes hypokalaemia by direct gastrointestinal

loss, transcellular shift and metabolic alkalosis and renin angiotensin aldosterone system activation. Intravenous dextrose causes hypokalaemia by insulin-mediated transcellular shift of K^+ . In our case ECG played pivotal role in establishing the correct diagnosis and prompt management of life-threatening emergency. Had ECG changes been missed in this case, it could have resulted in life-threatening cardiac arrhythmias and/or respiratory paralysis.

Learning points

- ▶ Hypokalaemic paralysis can present like Guillain-Barre syndrome.
- ▶ ECG should be an essential part of initial evaluation of acute flaccid quadriplegia.
- ▶ Physician recognising the ECG changes of hypokalaemia may be able to provide life-saving treatment before receiving biochemical confirmation.
- ▶ If intravenous fluids are given to patients with excessive vomiting, the fluids should contain potassium and patient's potassium levels should be monitored until the vomiting has resolved.
- ▶ It is imperative to recheck laboratory data that is crucial to confirm a diagnosis, if an initial value obtained is inconsistent with the clinical scenario.

Competing interests None.

Patient consent Obtained.

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