Case report

Coexistence of myasthenia gravis with hypokalemic periodic paralysis: a rare presentation

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SUMMARY

Bilateral symmetrical weakness of acute onset is not very uncommon and the differential varies widely from life-threatening neurological illnesses to metabolic and electrolyte derangements. We report the case of a young female with severe muscle weakness, respiratory distress and hypokalemia who required immediate intubation on arrival to emergency department. During hospital course, even after normalisation of serum potassium and some improvement in limb weakness, patient failed multiple attempts of extubation because of type II respiratory failure. Subsequently, acetyl cholinesterase antibodies were checked which came out positive, and diagnosis of myasthenia gravis and hypokalemic periodic paralysis was made. She was successfully extubated after intravenous pulse steroids, pyridostigmine and plasmapheresis. Patient was finally discharged home on oral steroids, pyridostigmine and azathioprine. In a patient presenting with hypokalemic weakness, the suspicion of a second disorder should be very high if weakness fails to resolve following correction of hypokalemia.

BACKGROUND

Bilateral symmetrical weakness of acute onset is not very uncommon and the differential varies widely from life-threatening neurological illnesses to metabolic and electrolyte derangements. There are a number of neurological disorders ranging from myasthenia gravis (MG), Lambert-Eaton syndrome, spinal cord haemorrhages and Guillain-Barre syndrome, which cause weakness of acute onset. A thorough history and detailed neurological examination supported by relevant laboratory investigations are of utmost importance in reaching the diagnosis. The common extraneurological disorder causing recurrent weakness is hypokalemia, and the frequent causes are hypokalemic periodic paralysis and renal tubular acidosis (RTA). However, at times it becomes very difficult to find out the exact cause of hypokalemia if the patient has already received potassium supplements or if the presentation is acute and there is no time to send the detailed work up and correction of hypokalemia is urgent.

We report the case of a young female with severe muscle weakness, respiratory distress, hypokalemia and normal anion gap metabolic acidosis who required immediate intubation on arrival to emergency department. An initial diagnosis of hypokalemic periodic paralysis secondary to underlying RTA was made. Despite correction of serum

potassium, she was not getting off mechanical ventilator and going into type II respiratory failure. Subsequently, her serum acetylcholine receptor antibodies (AChR-Ab) were checked that came out positive and she was successfully extubated after plasmapheresis and pulse intravenous (IV) steroids. This case presented to us with the major diagnostic challenge as there is no clear association of hypokalemic periodic paralysis (HPP) with MG in the literature.

CASE PRESENTATION

A 40-year-old Asian woman presented to emergency department with 1-week history of generalised weakness, decreased oral intake and sudden onset of shortness of breath. The weakness was bilateral and symmetrical involving both proximal and distal muscles. For these complaints, she was initially taken to a nearby hospital where she was found to have bilateral flaccid paralysis and serum potassium level of 1.8 mmol/L. She was started on IV potassium chloride, but she started having shortness of breath so transferred to our centre. In the past, she had experienced similar attacks of weakness of much less intensity, which were completely reversed by potassium replacement. Work up at that time revealed normal renal functions and remaining electrolytes. Her renin, aldosterone and cortisol were done, which were within normal range. She was advised to take oral potassium supplements, which she was taking intermittently.

On presentation, her blood pressure was 118/65 mm Hg with a regular heart rate of 104 beats per minute. Oxygen saturation was 94%, but breathing was rapid and shallow at a rate of 40/min. On examination, she was very pale and 1⁺ pedal oedema was present. She was not moving her limbs, tone was decreased and power was 2/5 in all four limbs. Reflexes were absent and planter reflex was equivocal. There was no sensory deficit. Her chest, abdomen and cardiac examinations were within normal limits. Because of severe respiratory distress, the patient was electively intubated in emergency department and shifted to intensive care unit.

INVESTIGATIONS

Haemoglobin of 8.1 g/dL; sodium 165 mmol/L; potassium 2.2 mmol/L; bicarbonate 16 mmol/L; chloride 132 mmol/L; anion gap 14; creatinine 1.1 mg/dL; calcium 7.5 mg/dL; magnesium 1.8 mg/dL; liver function tests including alanine aminotransferase and aspartate aminotransferase were

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normal; spot urinary potassium 42 mmol/L; spot urinary sodium 84 mmol/L; spot urinary chloride 111 mmol/L; urine anion gap 15; urine DR showed pH of 7; proteins +2; leucocytes 05; total serum proteins 6.0 g/dL; albumin 2.6 g/dL; antineutrophil antibody negative; anti-double-stranded DNA antibody negative; thyroid-stimulating hormone 1.03 μ IU/mL; creatine phosphokinase 185 IU/L; aldolase 5 U/L; AChR-Ab 15.85 nmol/L; repetitive nerve stimulation (RNS) test negative.

DIFFERENTIAL DIAGNOSIS

At that time, our differentials included HPP secondary to underlying RTA as she had hypokalemia with normal anion gap metabolic acidosis, positive urine gap and urine pH of >5.5. She had prior history of weakness although not very severe, which used to subside with potassium supplements.

Another differential of muscle weakness included Guillain-Barre syndrome but as potassium was very low, it was ruled out.

TREATMENT

The patient was started on IV potassium replacement and later oral potassium citrate was added. The power in lower limbs improved, and she started moving her limbs against gravity but not against resistance. On day 3 of admission, she failed a trial of extubation and had to be reintubated again because of type II respiratory failure. Serum potassium was at the upper limit of normal at that moment. Later, weaning was attempted multiple times but patient could not tolerate it. At that time, AChR-Ab were sent which came out positive; however, RNS test did not reveal any decremental response suggestive of MG. Neurology was taken on board and patient was started on pulse IV steroids, pyridostigmine and plasmapheresis. After three sessions of plasmapheresis, she was successfully extubated but required non-invasive mechanical ventilation for few days postextubation. She underwent total five sessions of plasmapheresis.

OUTCOME AND FOLLOW-UP

After remaining in hospital for 16 days, the patient was finally discharged on oral steroids 30 mg two times per day, pyridostigmine 60 mg three times per day and azathioprine 50 mg two times per day. Throughout these days, her serum bicarbonate remained within range without any bicarbonate supplement, but she continuously required 5 mEq of potassium chloride daily. The final diagnosis of HPP and MG was made.

After discharge, her condition gradually improved. She started tolerating orally, nasogastric tube was removed and she was able to walk without support. Her serum potassium and bicarbonate were maintained at 4–4.5 mmol/L and 24 mmol/L, respectively; however, she continuously required 5 mEq of potassium chloride per day without any bicarbonate supplement. On her first outpatient follow-up visit, she revealed that she used to get fatigue after minor exertion such as bathing, combing hair and also while eating, but it was always attributed to low potassium levels. Although she was underweight, anaemic with low albumin levels, she denied any history of diarrhoea and weight loss. After 6 weeks of discharge, the patient was readmitted with drug-induced pancytopenia and cavitary pneumonia. Unfortunately, she died of septic shock and severe respiratory failure.

DISCUSSION

MG is associated with a number of autoimmune disorders such as autoimmune thymic hyperplasia, grave's disease, rheumatoid arthritis and diabetes mellitus.¹ HPP, on the contrary, is a rare

heritable neuromuscular disorder that may be familial or associated with thyrotoxicosis, hyperaldosteronism, RTA and certain drugs. Both MG and HPP have been associated with thyrotoxicosis, but the simultaneous occurrence of MG and HPP has rarely been reported.^{2,3}

The repeated episodes of weakness associated with low serum potassium levels with almost normal serum potassium levels in-between the attacks differentiate HPP from other disorders. Our patient had history of intermittent weakness, which used to get better with potassium supplements. Moreover, she also described fatigue after minor exertion, which was not worked up and was also ascribed to hypokalemia. MG can present with both localised and generalised muscle weakness along with fatigue, but the latter is also a common occurrence in electrolyte disorders especially chronic hypokalemia.

The exact association between MG and HPP is not well understood, but it is assumed that this may be secondary to the presence of certain autoantibodies, which affect the nicotinic AChR in MG as well as dihydropyridine and calcium channel receptors in HPP.⁴

Even though the existence of MG and HPP together may be coincidental, there are case reports in literature that support an association between the two disorders.^{2,3} Our patient had also presented with weakness and hypokalemia and found to have MG; however, she presented with myasthenia crises, and the diagnosis was made on the basis of positive AChR-Ab as RNS came out normal. Although AChR-Ab is positive in more than 90% of patients with MG,^{5,6} the frequency of positive RNS is slightly less at around 75% to 80% but it increases to more than 90% in patients with myasthenic crises.^{7,8} In a study of RNS test in myasthenic crises, 92% patients showed abnormal response,⁷ which is in contrast to another study that showed abnormal response in only one out of nine patients with myasthenic crises.⁹

The factors that predict a higher risk of death in MG are disease severity at diagnosis, presence of AChR-Ab, duration of disease and thymic pathology,¹⁰ whereas in HPP, deaths have been reported due to aspiration pneumonia. Our patient had severe disease with dual pathology and despite showing initial improvement, she died of severe infection and respiratory failure.

Learning points

- In a patient presenting with hypokalemic weakness, the suspicion of a second disorder should be very high if there is associated fatigue and weakness fails to resolve following correction of hypokalemia.
- Patients presenting acutely may have normal gap metabolic acidosis on presentation. However, associated hypokalemia does not always mean underlying renal tubular acidosis and therefore, before labelling a patient, a thorough work up and serial electrolytes should be done.
- In myasthenia gravis, there is high sensitivity and specificity of acetylcholine receptor antibodies and repetitive nerve stimulation can be normal even in myasthenic crises. Hence, a normal repetitive nerve cannot rule out myasthenia gravis.

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