CASE REPORT

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Severe Hypokalaemia with Metabolic Alkalosis in an Adult: Bartter Syndrome or Gitelman Syndrome?

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Abstract

Renal tubular disorders can present with various electrolyte abnormalities. Sometimes the combination of electrolyte abnormalities can be confusing and may not match one particular disease. We here present the case of a 35-year-old female from Eastern India, who presented with severe hyponatraemia, hypokalaemia, hypochloraemia, hypocalcaemia and metabolic alkalosis. Also, there was presence of mild hypomagnesaemia and hypercalciuria (high urinary Ca:Cr molar ratio). The patient responded to fluid and electrolyte replacement and on follow-up, is maintaining stable serum electrolyte values. Literature regarding such tubular disorders has also been discussed at length.

Key words: Bartter syndrome, Gitelman syndrome, metabolic alkalosis, hypokalaemia.

Introduction

The renal tubular system is vital for acid-base homeostasis, and fluid and electrolyte balance in the body. Hence, any structural or functional disorder of these tubules can cause imbalance in one or more of these components[1]. Renal tubular disorders can present with a variety of electrolyte abnormalities. The tubular disorders can be congenital or acquired. Even in congenital disorders with specific mutations, the manifestations are protean. Although most of the cases present at a young age, patients can present at any age with varying clinical manifestations. Since electrolyte abnormalities can occur in a wide range of disorders, a high degree of suspicion is needed to diagnose renal tubular disorders in patients presenting with dyselectrolytemia. The specific tubular disorders usually have certain typical electrolyte changes, which can help in their identification. But, sometimes, the presenting electrolyte abnormalities may be confusing and may not conform to one particular disease. We here present such a case from Eastern India.

Case report

A 35-year-old female was admitted with generalised weakness and gradually progressive altered consciousness for three days. She had a few successive episodes of vomiting three days ago, after which these symptoms were noticed. Both of the symptoms were progressive and at the time of admission, the patient was delirious, with marked hypotonia in all four limbs. There was no similar previous history. The patient did not have history of any recent travel or exposure to animals. Neck rigidity was absent and pupils were reactive. Plantar response was bilaterally flexor. Fever was absent and there was no suggestion of poisoning. There was no significant past medical or surgical history and she was not on any medicines (like diuretics) at the time of admission. The next of kin of the patient could not answer questions about her birth history.

Examination of vital signs on admission revealed a pulse rate of 48/minute and blood pressure of 80/50 mm of Hg. Capillary blood glucose was 152 mg/dl. SpO2 was 96% on room air. The patient was immediately shifted to the critical care unit where an ECG revealed (Fig. 1) sinus bradycardia with prolonged QT interval (corrected QT by Bazett formula: 766 ms), T wave flattening and reduced PR interval. Arterial blood gas (ABG) at the point of admission showed pH of 7.57, HCO3 52.6 mmol/l, Na 103 mmol/l, K 1.0 mmol/l, chloride 78 mmol/l, Ca^{2+} 0.78 mmol/l (3.12 mg/dl). Thus, the patient was found to have metabolic alkalosis with severe hyponatraemia, hypokalaemia and hypocalcaemia. The hypocalcaemia was responsible for the ECG changes. Urine output of the patient was 2.5 l/24 hours. Urinary pH was 6, with specific gravity of 1.01.

The patient was resuscitated with appropriate fluid and electrolytes. Her serum sodium level normalised and she fully regained consciousness. But serum potassium remained persistently low. The blood pressure increased to 110/80 mm of Hg. On the 3rd day of admission, her serum potassium fell to 0.63 mmol/l. She was immediately given, i.v., potassium salt through a central line. However, a repeat

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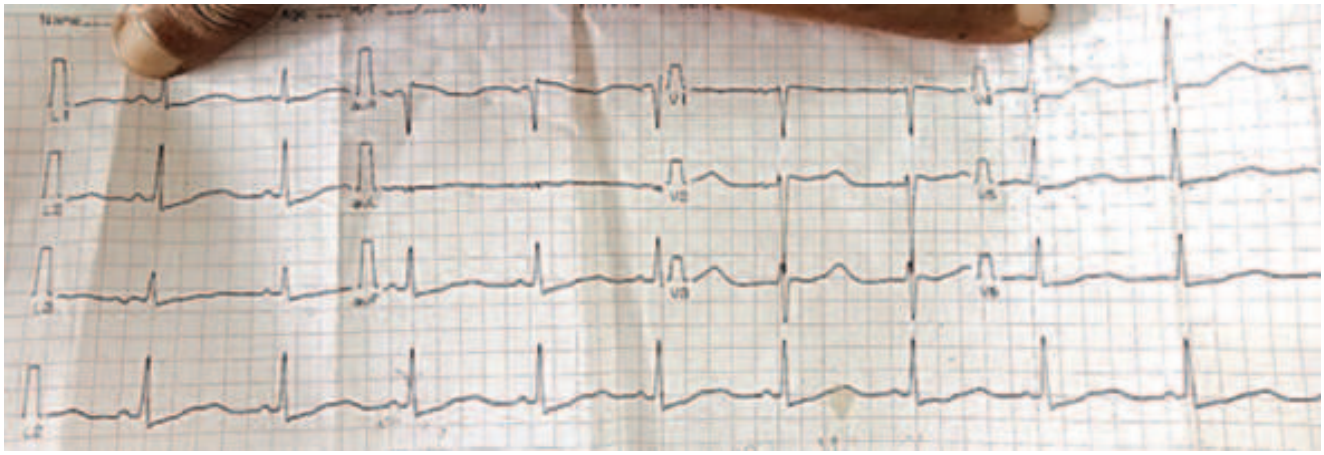

Fig. 1: *ECG of the patient showing QT prolongation, loss of T waves and short PR intervals.*

ABG showed a pH of 7.64 with K: 1.2 mmol/l. Other test results included serum magnesium of 1.24 mg/dl. In view of the persistent hypokalaemia with alkalosis, serum cortisol (8 AM) was done which came as 12.28 µg/dl (N: 6 - 18) and serum aldosterone came as 4.6 ng/dl (supine; after correction of serum sodium) (N: ≤ 21). Anti-nuclear factor was negative.TSH was 4.6 µIU/ml.To investigate the cause of hypokalaemia, urinary chloride was done, which came as 178 mmol/l (N: 110 - 250); urinary calcium was 8.3 mg/dl and creatinine was 38.2 mg/dl.The Ca:Cr ratio was 0.21 mg/mg, the urinary molar Ca:Cr ratio was 0.61. Urinary potassium excretion was 2.54 mmol/l of creatinine. On ultrasonography of the abdomen, there was no renal calcinosis.The patient refused renal biopsy.

The patient was discharged on oral potassium chloride salt, oral magnesium replacement and spironolactone 100 mg daily.Indomethacin was started but had to be stopped due to severe gastric intolerance. On follow-up, the patient had borderline hypokalaemia 2.7 mmol/l and blood pH remained between 7.5 and 7.55. She has had no further episodes of generalised weakness.

Discussion

The major renal tubular disorders which cause dyselectrolytaemia include Bartter syndrome, Gitelman syndrome,renal tubular acidosis (RTA),Fanconi syndrome, nephrogenic diabetes insipidus and idiopathic hypercalciuria, just to name a few[2]. Usually, these are diagnosed at a very young age with clinical features like failure to thrive, bony deformity and/or polyuria[2]. But these disorders can present at any age and even Bartter syndrome has been rarely reported to present in the 4th decade of life[3].Thus, any severe dyselectrolytaemia in adult patients, especially with the typical constellation of electrolyte abnormalities, should be evaluated for renal tubular disorders. Blood pH can be a good starting point for such evaluation. Presence of marked metabolic alkalosis, as in our case, rules-out RTA, Fanconi syndrome and idiopathic hypercalciuria.

Both Bartter syndrome and Gitelman syndrome present with metabolic alkalosis with hypokalaemia. But there are other electrolyte changes, both in the serum and urine, which help in differentiating the two disorders. But in some cases, the changes may be so overlapping that a clear diagnosis is impossible.Then,only genetic testing can help in separating the two conditions. But in a country like India, where the health system runs on very limited resources, genetic testing is often difficult to procure.

In our patient, there was a combination of severe hyponatraemia, hypokalaemia and hypocalcaemia. Also, there was hypomagnesaemia and hypochloraemia.Usually, hypomagnesaemia is a feature of Gitelman syndrome (GS)[4]. The exact cause of hypomagnesaemia in GS is not known[5]. The main molecular pathology in GS is dysfunction of the thiazide sensitive Na-Cl cotransporter[5].This can explain the other electrolyte abnormalities but not hypomagnesaemia. But magnesium deficiency is universal in GS and patients require lifelong magnesium therapy. The magnesium deficiency can manifest as tetany resistant to calcium supplementation[4].In our patient,there was no tetany.

Another notable feature of GS is hypocalciuria. There is increased distal convoluted tubule reabsorption of calcium in these kidneys. But in our patient, urinary Ca:Cr molar ratio was 0.61. Ca:Cr ratio > 0.2 is an indication of hypecalciuria and is usually found in Bartter syndrome[6]. In Bartter syndrome, as sodium reabsorption in ascending limb of loop of Henle is impaired, the reabsorption of calcium ions (which is coupled to Na) is also impaired and there is excess urinary loss of both Na and Ca ions[4]. But in spite of the hypercalciuria, our patient did not have renal calcinosis. Thus, this patient had serum and urinary electrolyte changes overlapping both these disorders.

The main presenting feature of our patient was altered consciousness due to severe hyponatraemia. Since both Bartter syndrome (BS) and GS are salt-losing tubulopathies, some degree of hyponatraemia is quite common. But the severe form, as seen in our case, is quite rare in both. However, hyponatraemia is considered to be commoner in BS than in GS[7]. The exact mechanism for this is not known but it is thought that there is more severe salt and volume loss in BS, in general[7]. In our patient, in addition to the tubular disorder, the recent vomiting may have contributed to the hyponatraemia.

A case similar to ours was reported from Karnataka in 2015, where a 40-year-old male presented with severe hyponatraemia, mild hypomagnesaemia, hypercalciuria and metabolic alkalosis[8]. In that case, in the absence of genetic study, the authors concluded it to be an acquired Bartter-like phenotype[8]. Thus, despite one or two aberrant results favouring Gitelman syndrome, the majority of the results in our case were also in favour of a Bartter-like phenotype. BS has various types. Many of them (like types I and II) manifest themselves at birth[9]. But some varieties, especially type III with chloride channel disorder, may manifest in adulthood and this variety also has mild hypomagnesaemia as a feature[9]. Thus, mild hypomagnesaemia can occur in some varieties of Bartter syndrome too. Also, our patient had hypochloreamia as a prominent feature (serum chloride 78 mmol/l). Hypochloraemia is known to occur in BS type III[10]. But hypochloraemia is not specific for either BS or GS. It can occur in a variety of conditions, in addition to BS/GS, like vomiting, dehydration, metabolic alkalosis or diuretic use.

Pseudo-Bartter syndrome is a condition where the electrolyte changes of BS or GS can occur without any renal tubular pathology[4]. The main causes are prolonged vomiting, laxative abuse or bulimia[4]. In these cases, the main investigation is urinary chloride. In all of these cases, urinary chloride level will be low. In a case like ours, where a patient has an initial episode of vomiting followed by severe electrolyte abnormalities, urinary chloride can help in deciding whether vomiting is the cause of the dyselectrolytaemia.

In our case, urinary chloride was normal (178 mmol/l) in the face of marked hypochloraemia, thereby pointing to a tubular salt wasting disorder. Urinary chloride levels is a good screening test to differentiate between renal and extra-renal cause of metabolic alkalosis[11]. If high urinary chloride is found, it indicates a significant renal loss. In such cases, the replacement for sodium and potassium deficiency should preferably by with a chloride salt, so as to replace both cations and anions adequately.

Conclusion

Renal salt wasting disorders may present in adults with a variety of electrolyte abnormalities. Careful consideration of serum and urinary electrolyte values can often help in elucidating the cause, even in the absence of genetic studies. Concomitant diuretic use/abuse must be enquired in these cases.

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