A case report of recurrent hypokalaemic periodic paralysis in a young male patient

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A 21-year-old normotensive male patient presented with acute-onset flaccid paralysis with the history of a similar episode a few months back. Clinical and laboratory evaluation revealed lower motor neuron type of flaccid quadriparesis with hypokalaemia, normal anion gap metabolic acidosis, bicarbonaturia and transtubular potassium concentration gradient more than 7. Subsequently, urine acidification test (by ammonium chloride challenge test) was performed and diagnosis of renal tubular acidosis was established. The patient ultrasound did not show nephrocalcinosis, and history of recurrent diarrhoea preceding the attack revealed that the patient also had coeliac disease. The patient responded to conservative management (Sohl's solution) and gluten-free diet.

Keywords:
ammonium chloride challenge test, distal renal tubular acidosis, hypokalaemic periodic paralysis, Sohl's solution

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Introduction

Distal renal tubular acidosis (dRTA) is a nonuremic syndrome of defective urinary acidification. It is characterized by presence of hypokalaemia, normal blood pressure, normal anion gap metabolic acidosis, alkaline urine, inability to acidify urine pH less than 5.5, nephrocalcinosis and features of rickets [1]. Primary dRTA can be inherited, but most cases are sporadic. An inherited case may be an autosomal dominant or autosomal recessive form. Secondary causes are Sjögrens syndrome, amphotericin B toxicity, chronic active hepatitis and systemic lupus erythrematous [2]. The treatment required is alkali administration in the form of Sohl's solution at doses 0.5–2 ml/kg in 4–6 divided doses per day. We report a case of a 21-year-old male patient presenting with periodic acute-onset flaccid quadriparesis with a diagnosis of dRTA after series of investigations.

Case report

A 21-year-old student boy was admitted with acute-onset quadriparesis evolving over a period of 24 h reaching up to the extent that he could only sit or stand with adequate support following 2-day history of diarrhoea. He had a similar episode 2 months back, which was preceded by diarrhoea and dehydration with hypokalaemia persisting even long after resolution of diarrhoea. On assessment of the previous records, it was revealed to be an episode of hypokalaemia leading to quadriparesis, recovered with oral KCl supplementation and discharged as hypokalaemic periodic paralysis with the advice to take oral KCl. However, this time there was no history of diarrhoea. General physical examination was completely normal. No features suggestive of thyrotoxicosis were present. Nervous system examination revealed normal higher functions, cranial nerves, sensory system, bladder and bowel and cerebellar functions. Motor examination revealed normal muscle bulk with hypotonia. Muscle power of the upper limb was 4/5 and lower limb was 3/5; deep tendon reflexes were present but diminished, and plantars were bilaterally flexor. Investigation showed haemoglobin –11.2 g%, total lymphocyte count –8 700/mm^3 (neutrophils –72%, lymphocytes –22%, eosinophils –4%), mean corpuscular hemoglobin –28.6 pg/cell, mean corpuscular hemoglobin concentration –31.4 g/dl and mean corpuscular volume — 91 fl. Random blood sugar was 108 mg/dl, creatine phosphokinase –303 U/l, Na^+ –135 mmol/l, K^+ –2.3 mmol/l, Ca^{2+} –9.8 mg/dl and Mg^{2+} –2.8 mg/dl (normal –1.5–2.6). Kidney function test was normal: blood urea = 20 mg/dl, s.creatinine = 0.8 mg/dl and uric acid = 3.5 mg/dl. ECG showed prolonged PR interval, T-wave flattening and U wave. Arterial blood gas (ABG) was performed: pH –7.38, pO_2 – 102 mmHg, pCO_2 –20 mmHg, HCO_3 –11.4 mEq/l, Na^+ –142 mEq/l, K^+ –2.6 mEq/l, Cl – 118 mEq/l, Ca^{2+} –4.2 mEq/l, anion gap –10.4 and plasma osmolality –302.5 mOsm/kg. The ABG report showed a combination of metabolic acidosis with hypokalaemia. This condition is usually found in two possible conditions, either gastrointestinal loss or RTA. Other investigations included ANA –negative, fT_3 –3.58 pg/ml, fT_4 –7.2 mcg/dl, thyroid-stimulating hormone –1.59 IU/ml, 24 h urine total volume –3180 ml, K^+ excretion –113.3 mEq/24 h, Osmolality was 436.7 mOsm/kg

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and pH 7. Transtubular potassium gradient was 6.2. Ultrasound did not reveal any nephrocalcinosis. As there was history of recurrent diarrhoea, we strongly suspected inflammatory bowel disease. Endoscopy revealed patchy areas of villous atrophy and tissue transglutaminase –34 U/ml (<10 U/ml). In the meantime, the patient was treated with oral potassium supplementation and patient markedly improved. To confirm our diagnosis after stabilization of the patient, we opted for an oral ammonium chloride challenge test. urinary tract infection was ruled out beforehand by urine microscopy and culture. Ammonium chloride was given orally at doses of 0.1 g/kg with fruit juice.

Urine pH was subsequently recorded as follows:

- First hour –6.69
- Second hour –6.19
- Third hour –6.63
- Fourth hour –6.1
- Fifth hour –6.17

ABG –Second hour

- pH –7.29
- HCO_3 –9.9 mEq/l
- Base excess –14.5
- Na^+ –133 mEq/l, K^+ –2.4 mEq/l

ABG –Fourth hour

- pH –7.31
- HCO_3 –10.8 mEq/l
- Base excess –13.7 mmol/l
- Na^+ –139 mEq/l, K^+ –2.4 mEq/l, Cl –118 mmol/l

Therefore, the urine pH did not decrease below 5.5, despite plasma HCO_3 being persistently below 20 mEq/l. Hence, our diagnosis of dRTA (type 1) was confirmed. Treatment with Sohl's solution (Na-citrate 500 mg, K-citrate 550 mg and citric acid 334 mg/5 ml) was initiated. A volume of 1 ml of this solution is equivalent to 1 mEq of Na^+, 1 mEq of K^+ and 2 mEq of HCO_3. It was initiated at a dose of 1 mmol/kg per day in divided doses. After 1 week of starting the therapy, serum K^+ was 4 mEq/l, Cl^-–102 mEq/l, pH–7.4 and HCO_3-23.8 mEq/l. ECG at discharge was normal. At follow-up, the patient is performing well.

Discussion

RTA is a medical condition that involves an accumulation of acid in the body due to a failure of the kidneys to appropriately acidify the urine either by failure to recover sufficient (alkaline) bicarbonate ions from the filtrate in the early portion of the nephron (proximal tubule) or by insufficient secretion of (acid) hydrogen ions into the latter portions of the nephron (distal tubule) [1]. dRTA is the classical form of RTA, characterized by a failure of acid secretion by the α intercalated cells of the cortical collecting duct. This leads to an inability to acidify the urine to a pH of less than 5.5. The clinical features of dRTA include normal anion gap metabolic acidosis/acidaemia, hypokalaemia, urinary stone formation (related to alkaline urine, hypercalciuria and low urinary citrate) [2], nephrocalcinosis (deposition of calcium in the substance of the kidney) and bone demineralization (causing rickets in children and osteomalacia in adults) [3]. Our patient had low pCO_2, which can be explained by chronic metabolic acidosis due to bicarbonaturia leading to hyperventilation for removal of excess acid. The diagnosis of dRTA can be made by the observation of a urinary pH of greater than 5.5 in the face of a systemic acidaemia (usually taken to be serum bicarbonate of 20 mmol/l or less). The test usually performed is the short ammonium chloride test [4], in which ammonium chloride capsules are used as the acid load. Secondary causes include autoimmune disease (e.g. Sjögrens syndrome) [5], mutations of Band 3, subunits of the apical proton pump vH^+-ATPase, renal transplantation, sickle cell anaemia, toxins including ifosfamide [6], toluene [7], lithium carbonate [8] and amphotericin B [9] and chronic active hepatitis [10]. In contrast, periodic paralysis due to hypokalaemia is often due to hypokalaemic periodic paralysis, an inherited channelopathy [11]. As the clinical features of both RTA type I and RTA type II can be similar, distinguishing between them can be a diagnostic challenge. These two causes of nonanion gap acidosis with hypokalaemia can be distinguished relatively easily, with some laboratory testing. The easiest and most readily tested laboratory examination is the urine pH. In RTA I, the distal tubule is unable to acidify the urine and results in a urine pH that is above 5.5. RTA type II, however, has intact distal acidification, which, together with an ability of the proximal tubule to reabsorb filtered bicarbonate once its concentration has fallen below its abnormally low tubular reabsorptive capacity, results in a urine pH less than 5.5. Medullary nephrocalcinosis was not present. In all cases, secondary causes such as coeliac and inflammatory bowel disease should be searched. With these mechanisms, RTA II usually does not cause profound serum acidosis as RTA I. However, because the clinical manifestations of hypokalaemia are mainly muscle weakness, it may be difficult, in some cases, to discriminate between a paralytic attack of hypokalaemic periodic paralysis and an episode of weakness associated with hypokalaemia of another cause (e.g. reduced potassium intake, enhanced renal excretion or digestive loss) requiring varied investigations.

In our case, all possible causes were excluded by appropriate investigations and diagnosis of dRTA was established by ABG, 24 h urinary potassium excretion,

transtubular potassium concentration gradient and ammonium chloride challenge test. Treatment with Sohl's solution and gluten-free diet was followed by rapid recovery.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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