Hypernatremia and Hypophosphatemia in Distal Renal Tubular Acidosis: A Case Report of Acid-base and Electrolyte Misadventure

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Research Article

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Abstract

Introduction: Distal renal tubular acidosis (RTA) is easily recognized in patients with hypokalemia and normal anion gap acidosis. Other concurrent electrolyte abnormalities could change the diagnosis. We describe a newly diagnosed distal RTA complicated with severe hypernatremia and hypophosphatemia while admitted to the intensive care unit.

Case report: A 12-year-old girl presented with worsening paralysis. Initial investigations revealed low serum potassium of 1.8mmol/L, pH 7.2mmol/L, bicarbonate 12mmol/L and high urine pH (8.0) suggesting distal RTA. She required mechanical ventilation due to severe metabolic acidosis and hypokalemia. Resuscitation strategies initially focussed on intravenous hydration with 0.9% normal saline and potassium repletion. Delayed correction of acidosis with sodium bicarbonate led to severe hypernatremia (180mmol/L) and slow recovery of serum potassium level. Hypernatremia was also contributed by concurrent nephrogenic diabetes insipidus. Interestingly, her serum phosphate was persistently low (0.4mmol/L) leading to more workup to investigate proximal tubulopathy. It persisted till resolution of hypernatremia and acidosis. Meanwhile she developed sepsis with multiple thromboses attributed to disseminated tuberculosis. Screening for connective tissue diseases were negative. She recovered well and was discharged with anti-tuberculosis drugs, anticoagulation and potassium supplements.

Conclusion: In conclusion, correction of acidosis in distal RTA should be prioritised to avoid prolonged hypokalemia and significant increase in serum sodium. Hypophosphatemia in a critically ill patient should be interpreted with caution, correlating with serum sodium and arterial blood gas to avoid incorrect diagnoses.

Introduction:

Distal renal tubular acidosis (RTA) is a common referral to nephrology units worldwide. Reported prevalence varies between 2.8–25% depending on the population [1, 2]. The α-intercalated cells of the distal tubules and cortical collecting ducts are unable to excrete excess hydrogen ions which results in potassium wasting to maintain electrical neutrality. While adult onset is usually caused by autoimmune diseases, children are more commonly associated to primary distal RTA [3]. It is important to recognize distal RTA early as treatment involves prompt correction of acidosis, without which results in futile replacement of potassium. Distal RTA, if left untreated, could lead to nephrolithiasis, osteomalacia and chronic kidney disease. It is distinguished from proximal RTA by the presence of raised urine pH and positive urine anion gap. Hypophosphatemia is often associated to proximal RTA in Fanconi syndrome [4]. Its presence in distal RTA without other evidence of proximal tubular dysfunction, to the best of our knowledge, has not been reported. It is rarely discussed but commonly seen in the critically ill [5]. Low phosphate levels amongst intensive care unit patients are multifactorial owing to redistribution, renal losses, malabsorption and acute dialysis [6]. Careful interpretation with clinical correlation is vital to avoid incorrect diagnoses. We present a case of newly diagnosed distal renal tubular acidosis with

disseminated tuberculosis complicated with hypernatremia and hypophosphatemia. The dynamic electrolyte changes are explained according to the clinical manifestations which unfolded throughout her hospital stay.

Case Report:

A 12-year-old girl was brought in to the Emergency Department by her parents for progressive weakness of all 4 limbs over 3 days. She had nausea and vomiting over the preceding 4 days but there was no fever, diarrhoea, or other positive history. She had a past history of smear positive pulmonary tuberculosis after coming into close contact with a school mate. Treatment was completed 7 months prior to presentation.

On examination she was tachypnoeic and exhibited paralysis over all 4 limbs with lower motor neuron findings. She was otherwise alert. Blood investigations revealed severe hypokalemia with normal anion gap metabolic acidosis. Serum potassium was 1.8mmol/L, sodium 145mmol/L, chloride 120mmol/L, pH 7.2mmol/L bicarbonate 12mmol/L and partial pressure carbon dioxide (pCO_2) 16mmHg. Urea and creatinine was 5.1mmol/L and 71µmol/L respectively. Transtubular potassium gradient was raised at 14.

She was initially treated as acute gastroenteritis with hypokalemic periodic paralysis. However, after aggressive intravenous hydration with 0.9% normal saline and multiple doses of potassium correction amounting to a total of 6gm in 12 hours, serum potassium continued to remain low and metabolic acidosis worsened requiring intubation and mechanical ventilation in the intensive care unit (ICU). Further laboratory tests indicated a high urine pH at 8.0 and positive urine anion gap. A trace of past history via the hospital electronic medical records revealed a baseline low potassium of 2.3mmol/L more than 1 year prior to admission which had gone unnoticed with the patient being asymptomatic. A nephrology consult and a diagnosis of distal renal tubular acidosis was made.

She was then initiated on intravenous infusion of sodium bicarbonate. With the correction of acidosis, serum potassium gradually picked up at the expense of serum sodium which increased steadily, peaking at 180mmol/L even after discontinuation of sodium bicarbonate and sodium containing intravenous fluids. While the obvious cause was iatrogenic, she started to have polyuria, more than 3L per day. 2 doses of subcutaneous desmopressin 0.1mcg was given at 12 hours apart resulting in a slight increase of urine osmolality (221 to 350mOsm/kg) suggesting a partial nephrogenic diabetes insipidus. The sodium was slowly corrected by calculated replacements of water deficit with dextrose 5% solution.

Besides a deranged potassium, sodium and acid base status, she also had hypophosphatemia needing regular replacements with intravenous potassium dehydrogenase phosphate. Serum phosphate was 0.4mmol/l while fractional excretion was 25%. While ventilated, her pCO_2 was maintained at a low level, ranging 22-32mmHg. Serum magnesium and uric acid was normal while urine glucose was negative. Ultrasound of the kidneys was normal with no evidence of nephrolithiasis. Once the acidosis and sodium levels were corrected, the phosphate level also normalized without needing supplements.

During the ICU admission her condition was complicated with multiple thromboses and sepsis. Imaging confirmed cavernous sinus thrombosis and right lower limb arterial and venous thromboses. Screening tests for autoimmune diseases such as systemic lupus erythematosus (SLE) and Sjögren's syndrome were negative. The contrasted CT Brain suggested tuberculoma. Tracheal aspirate sample sent for mycobacterium tuberculosis polymerase chain reaction was positive. Lumbar puncture for confirmation of neurological involvement was not done as her parents did not consent. She was treated with heparin infusion which was converted to warfarin and initiated on anti-tuberculosis treatment with the addition of oral prednisolone for tuberculous meningitis.

A final diagnosis of disseminated tuberculosis with distal renal tubular acidosis was made. She was extubated and transferred out to ward for physiotherapy and rehabilitation before being discharged home well. She is doing well on follow-up reviews and continues to be on potassium and sodium bicarbonate supplements with normal serum potassium, sodium, bicarbonate and phosphate.

Discussion:

This patient had distal renal tubular acidosis in which secondary screening turned out negative. In order to correct the potassium deficit, one must first address the acidosis. Correcting the acidosis will prevent further potassium wasting. She was incorrectly diagnosed with hypokalemic periodic paralysis (HPP) on admission, which should be a diagnosis of exclusion. In HPP the defect is in the muscle ion channels causing intermittent transcellular shift of potassium triggered by stressors such as fasting, sugar load and illness. Patients usually do not have acid base disturbances. Delayed recognition of the severe metabolic acidosis not amenable to hydration hampered the efforts of potassium correction leading to clinical deterioration and mechanical ventilation.

During the course of her admission her dynamic electrolyte abnormalities include hypokalemia, hypernatremia and hypophosphatemia. Although the severe hypernatremia was clearly due to the sodium load from correction of acidosis, she also exhibited partial nephrogenic diabetes insipidus transiently. Nephrogenic diabetes insipidus have been reported to occur in both proximal and distal RTA due to defective aquaporin 2 channels, hypercalciuria, cystinosis and Sjögren syndrome as a result of tubulointerstitial nephritis [7, 8]. As it lasted very briefly, it is unlikely due to a chronic tubular disease, rather more likely due to acute tubular injury sustained from haemodynamic instability, sepsis and iodinated contrast agents while she was in the intensive care unit.

Hypophosphatemia in this case, raised confusion and led treating doctors to consider concurrent proximal tubulopathy. However, it was also transient and existed till mechanical ventilation was weaned off and hypernatremia resolved. There was also no other evidence of Fanconi's syndrome. Postulated causes for the hypophosphatemia are severe hypernatremia and respiratory alkalosis. Due to the severe metabolic acidosis our patient had respiratory compensation and post intubation was maintained in a hyperventilated state. This increases intracellular pH leading to increased cellular uptake of phosphate [6]. Besides that, the hypernatremia would cause a negative feedback mechanism resulting in reduced

sodium reabsorption in the proximal tubule and therefore phosphate its reabsorption is mediated by a sodium phosphate cotransporter. These hypotheses were reinforced when she no longer required phosphate supplements once the sodium and acid-base disturbances were normalized.

There is no documented evidence of tuberculosis manifesting as tubulopathy. Renal tuberculosis usually leads to obstructive uropathy due to ureteric strictures. Treatment with rifampicin has been shown to cause distal RTA via tubulointerstitial nephritis but our patient's potassium was low even before initiating anti-tuberculous drugs. Common secondary causes of distal RTA are autoimmune disorders such as Sjögren's syndrome, SLE, drugs, hypercalciuria and medullary sponge kidneys. As screening for these conditions were negative we concluded that she had undiagnosed primary distal RTA which was exacerbated by her septic condition.

Conclusion:

Understanding the pathophysiology of distal RTA is important for clinicians in order to institute treatment efficaciously. Correction of acidosis should be prioritised to avoid prolonged hypokalemia and avoidable increase in serum sodium. Hypophosphatemia in a critically ill patient is not uncommon and usually multifactorial. Dynamic electrolyte changes should be interpreted carefully with clinical correlation. Further studies are needed to determine if renal tuberculosis can manifest as tubulopathy.

Declarations

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On behalf of all authors, the corresponding author states that there is no conflict of interest.

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Not applicable

Code availability :

Not applicable

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All authors contributed to the case write up. The first draft of the manuscript was written by Hashvina Sukesh and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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