Distal Renal Tubular Acidosis with Coexisting Primary Hypothyroidism

Ashutosh Tiwari¹, Sudha Kansal²

¹(Senior Registrar, Medical Intensive Care Unit, Indraprastha Apollo Hospitals, Delhi, India)
²(Senior Consultant, Critical Care and Pulmonary Medicine, Indraprastha Apollo Hospitals, Delhi, India)

Abstract: Renal acid–base homeostasis is a complex process and an impairment of urinary acidification is called renal tubular acidosis (RTA). Distal RTA(dRTA) characterized by the presence of hypokalemia, normal blood pressure, normal anion-gap metabolic acidosis, and an alkalineurine (inability to acidify urine with pH <5.5) is the commonest to be encountered. dRTA has been found to be associated with several clinical settings, and an association of dRTA with primary hypothyroidism is a rare instance. On account of its rarity, we report an interesting case of an adult man with primary hypothyroidism with hypokalemic paralysis, in whom the presence of hyperchloremic (non-anion gap) metabolic acidosis with alkaline urine led us to the diagnosis of dRTA.

Keywords: Distal renal tubular acidosis, primary hypothyroidism, hyperchloremic metabolic acidosis

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I. Introduction:

Renal acid–base homeostasis is a complex process, effectuated by bicarbonate reabsorption and acid secretion. Impairment of urinary acidification is called renal tubular acidosis (RTA), with distal RTA(dRTA) being the commonest of the RTA syndromes.[1] It is characterized by the presence of hypokalemia, normal blood pressure, normal anion-gap metabolic acidosis, and an alkalineurine (inability to acidify urine with pH <5.5). The prevalence and incidence of dRTA is not known. Primary dRTA can be inherited, but most cases are sporadic. Of the various clinical settings dRTA has been found to be associated with, an association of dRTA with primary hypothyroidism is a rare instance, and to the best of our knowledge, very few suchcases have been reported till date in the literature.[2,5,16] Thus, on account of its rarity, we report a case of an adult man with primary hypothyroidism and dRTA.

II. Case Report:

A 47-year-old male patient was transferred from a distant hospital to the emergency department of our hospital on a ventilatory support and intravenous (IV) infusions of nor-adrenaline and dopamine. The patient was a known case of hypothyroidism for the past three years and was reported to have multiple hypotensive episodes for the last two years, with history of poor drug compliance for hypertension, both in terms of quality as well as quantity; few of the hypotensive episodes were severe enough to be associated with syncope. He experienced generalized body pain and progressive weakness for the past six months. The condition aggravated in the last 7–8 days, with loss of appetite and fever. Furthermore, the patient suffered an episode of cardiac arrest, the night before he was brought to our hospital, which he survived with prompt cardiopulmonary resuscitation and IV infusions delivered by the distant hospital; however, he had been unconscious since then. The patient also had a history of hypothyroidism for the past one and a half years; however, he had abruptly stopped the medication for it. There was no history suggestive of nephrolithiasis. Moreover, he did not have any relevant family history.

On examination, the patient was febrile, unconscious, intubated from the distant hospital, in view of poor sensorium and metabolic acidosis. Preliminary blood investigations revealed the following results: Hemoglobin = 14 gm/dL; blood urea = 26 mg/dL; serum creatinine = 1.3 mg/dL; serum potassium = 1.8 mEq/L; serum chloride = 122 mEq/L; and random blood glucose = 102 mg/dL. Arterial blood gas analysis showed arterial pH = 7.30; pCO₂ = 12 mmHg; pO₂ = 112 mmHg; and HCO₃⁻ = 9.3 mmol/L, suggestive of metabolic acidosis. An anion gap of 14 mmol/L was noted. Urine examination revealed the following results: Urinary pH = 7.1, suggestive of alkaline urine; urinary osmolality = 500 mOsm/L; urine potassium = 119 mEq/L; and 24-h urinary calcium = 240 mg. The calculated trans-tubular potassium gradient (TTKG) was 38, suggestive of renal loss of potassium. His urine was negative for protein and glucose. Thyroid function tests were suggestive of primary hypothyroidism: T₃ = 70 ng/dL (normal 80–180 ng/dL); T₄ = 2.1 mcg/dL (normal 4.6–12 mcg/dL); and thyroid stimulating hormone (TSH) = 41.6 mcIU/mL (normal 0.5–5.5 mcIU/mL). The titers of antithyroperoxidase and antithyroglobulin antibodies were elevated to 49.86 IU/mL (normal 0–18 IU/mL) and...
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216.21 IU/mL (normal 0–70 IU/mL), respectively, suggestive of an autoimmune basis. Other tests such as hepatitis B surface antigen, human immunodeficiency virus, anti-hepatitis C virus, anti-nuclear antibody titer, creatine kinase, serum bilirubin, liver enzymes, serum albumin, serum calcium, serum magnesium and serum phosphorus were within normal limits. The electrocardiogram showed prominent u-waves and the chest radiograph was normal. Nerve conduction study and electromyography were normal. Ultrasonogram of the abdomen was normal without any evidence of nephrocalcinosis.

Thus, it was an interesting case of an adult man with primary hypothyroidism with hypokalemic paralysis, in whom the presence of hyperchloremic (non-anion gap) metabolic acidosis with alkaline urine led us to the diagnosis of dRTA. He was treated with intravenous potassium chloride infusion followed by oral supplementation, potassium sparing diuretics, and coconut water. For primary hypothyroidism, he was treated with levothyroxine, and endocrinology inputs were taken. He exhibited complete recovery from the weakness and was discharged at the end of 1 week.

III. Discussion:

Hypokalemic paralysis classically presents in its familial form, but occasionally presents because of excessive gastrointestinal and/or urinary loss of potassium. Since the hypokalemic status of our patient did not resolve despite potassium supplements and there was no incidence of vomiting or diarrhea after his admission to the hospital, the possibility of gastrointestinal loss was ruled out: TTKG = 38, suggestive of renal loss of potassium, hyperchloremic (non-anion gap) metabolic acidosis, and alkaline urine were suggestive of dRTA. When healthy individuals sustain hypokalemia of less than 3.8 mEq/L (3.8 mmol/L), the kidneys respond by conserving potassium, and urinary potassium excretion falls below 40 mEq/d. However, in patients with dRTA, the degree of potassium-wasting continues irrespective of the severity of hypokalemia. This remarkable potassium wasting is believed to be a reflection of dRTA.

The dRTA can present as a primary disorder or can be associated with a variety of systemic disorders such as Wilson’s disease, nephrocalcinosis, sickle cell disease, drugs, toxins, and autoimmunedisorders. Of the endocrinial causes, it has rarely been reported in patients with thyroid dysfunction including hyperthyroidism, Hashimoto’s thyroiditis, and hypothyroidism. A defect in the renal acidification was observed in hypothyroid rats when compared to controls. Moreover, it has been suggested in the literature that the defect in acidification may be attributable to thyroxine deficiency. Furthermore, the combination of thyroid dysfunction and dRTA described in the literature has suggested several changes in structure and function in experimental and clinical hypo-thyroid state. Kidney weight has been found to be decreased, mainly because of a decrease in the cortical volume. A reduction in the peritubular diameter of the proximal and thick ascending limb (TAL) and a decrease in cell height in the TAL have been documented. A regulatory role of thyroid hormone on membrane proliferation and cell growth has been postulated to be the mechanism for other kidney changes like decrease in cross-sectional area of the TAL of outer and inner strip of outermedulla. Moreover, there is a significant decrease in surface area of the apical and basolateralplasma membrane of the TAL. The functional implications of these changes are transformed into decrease in Na-K-ATPase activity, implicating a stimulatory effect of thyroid hormones on the Na-K-ATPase activity in the TAL of the outer medulla.

Functionally, hypothyroidism is associated with impaired renal bicarbonate reabsorption after bicarbonate loading, reduced hydrogen secretion in the distal nephron, a decreased urinary-blood CO2 gradient, typical of dRTA, and an impaired ability to acidify urine and excrete ammonium after an acute ammonium chloride load. Coexistence of non-autoimmune hypothyroidism and dRTA was described for the first time in 1996 by Fang et al. in a 68-year-old man with severe post-radioiodine ablation hypothyroidism. The patient presented with hyperkalemic dRTA, and a voltage-dependent defect was presumed to be the possible attributable mechanism. The patient was put on L-thyroxine, and follow-up metabolic studies documented complete reversal of metabolic acidosis and normalization of serum potassium.

The case reported here is significant to be incorporated in the literature due to the rarity of occurrence of dRTA in association with autoimmune hypothyroidism. Whether the coexistence was an incidental finding cannot be rule out; however, as the patient had abruptly stopped the thyroxine supplements and exhibited no other hidden pathology, it can be postulated that the dRTA with hypokalemic paralysis might be associated with the existing hypothyroidism. Thus, investigations in cases of dRTA must warrant enough to adequately address the rare coexisting, yet, etiological pathologies.

References:


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