IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 19, Issue 2 Ser.3 (February. 2020), PP 13-15
www.iosrjournals.org

Distal Renal Tubular Acidosis with Coexisting Primary Hypothyroidism

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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 withprimary hypothyroidism is a rare instance.On account of its rarity, wereport an interesting case of an adult man with primary hypothyroidism withhypokalemic paralysis, in whom the presence of hyperchloremic (non-anion gap) metabolicacidosis with alkaline urine led us to the diagnosis of dRTA.*
Keywords: *Distalrenal tubular acidosis, primary hypothyroidism, hyperchloremic metabolic acidosis*

Date of Submission: 17-01-2020 Date of Acceptance: 05-02-2020

I. Introduction:

Renal acid–base homeostasis is a complex process, effectuated by bicarbonate reabsorption and acidsecretion. 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 notknown. Primary dRTA can be inherited, but most cases are sporadic. Of the various clinicalsettings dRTA has been found to be associated with, an association of dRTA withprimary 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, wereport 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 emergencydepartment of our hospital on a ventilatory support and intravenous (IV) infusions ofnor-adrenaline and dopamine. The patient was a known case of hypertension for the pastthree 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 asquantity; few of the hypotensive episodes were severe enough to be associated withsyncope. He experienced generalized body pain and progressive weakness for the past sixmonths. The condition aggravated in the last 7–8 days, with loss of appetite andfever. Furthermore, the patient suffered an episode of cardiac arrest, the night before hewas brought to our hospital, which he survived with prompt cardiopulmonary resuscitationand IV infusions delivered by the distant hospital; however, he had been unconscious sincethen. 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 ofnephrolithiasis. Moreover, he did not have any relevant family history.

On examination, the patient was febrile, unconscious, intubated from the distant hospital, inview 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; serumchloride = 122 mEq/L; and random blood glucose = 102 mg/dL. Arterial blood gas analysisshowed arterial pH = 7.30; pCO_2 = 12 mmHg; pO_2 = 112 mmHg; and HCO_3 = 9.3 mmol/L,suggestive of metabolic acidosis. An anion gap of 14 mmol/L was noted. Urine examinationrevealed the following results: Urinary pH = 7.1, suggestive of alkaline urine; urinaryosmolality = 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 ofpotassium. His urine was negative for protein and glucose. Thyroid function tests weresuggestive of primary hypothyroidism: T3 = 70 ng/dL (normal 80–180 ng/dL); T4 = 2.1mcg/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 antithyroglobulinantibodies were elevated to 49.86 IU/mL (normal 0–18 IU/ mL) and

216.21 IU/mL (normal0–70 IU/mL), respectively, suggestive of an autoimmune basis. Other tests such as hepatitisB surface antigen, humanimmunodeficiency virus, anti-hepatitis C virus, anti-nuclearantibody titer, creatine kinase, serum bilirubin, liver enzymes, serum albumin, serumcalcium, serum magnesium and serum phosphorous were within normal limits. Theelectrocardiogram showed prominent u-waves and the chest radiograph was normal. Nerveconduction 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 withhypokalemic paralysis, in whom the presence of hyperchloremic (non-anion gap) metabolicacidosis with alkaline urine led us to the diagnosis of dRTA. He was treated with intravenouspotassium chloride infusion followed by oral supplementation, potassium sparing diuretics,and coconut water. For primary hypothyroidism, he was treated with levothyroxine, andendocrinology inputs were taken. He exhibited complete recovery from the weakness andwas discharged at the end of 1 week.

III. Discussion:

Hypokalemic paralysis classically presents in its familial form, but occasionally presents because ofexcessive gastrointestinal and/or urinary loss of potassium. Since the hypokalemic status of ourpatient did not resolve despite potassium supplements and there was no incidence of vomiting ordiarrhea 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 lessthan 3.8 mEq/L (3.8 mmol/L), the kidneys respond by conserving potassium, and urinary potassiumexcretion falls below 40 mEq/d. However, in patients with dRTA, the degree of potassium-wastingcontinues irrespective of the severity of hypokalemia.[6] This remarkable potassium wasting isbelieved to be a reflection dRTA.

The dRTA can present as a primary disorder or can be associated with a variety of systemicdisorderssuch as Wilson's disease, nephrocalcinosis, sickle cell disease, drugs, toxins, and autoimmunedisorders.[9] Of the endocrinal causes, it has rarely been reported in patients with thyroid dysfunctionincluding hyperthyroidism, Hashimoto's thyroiditis, and hypothyroidism. A defect in the renalacidification was observed in hypothyroid rats when compared tocontrols.[7] Moreover, it has beensuggested in the literature that the defect in acidification may be attributable to thyroxinedeficiency.[8] Furthermore, the combination of thyroid dysfunction and dRTA described in theliterature has suggested several changes in structure and function in experimental and clinicalhypo-thyroid state. Kidney weight has been found to be decreased, mainly because of a decrease inthe 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.[10] A regulatory role of thyroidhormone on membrane proliferation and cell growth has been postulated to be the mechanism forother 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.[11] The functional implications of these changes are transformed intodecrease in Na–K–ATPase activity, implicating a stimulatory effect of thyroid hormones on theNa– K–ATPase activity in the TAL of the outer medulla.[12]

Functionally, hypothyroidism is associated with impaired renal bicarbonate reabsorption afterbicarbonate loading, reduced hydrogen secretion in the distal nephron, a decreased urinary–bloodpCO2 gradient, typical of dRTA, and an impaired ability to acidify urine and excrete ammonium afteran acute ammonium chloride load.[13-15] Coexistence of non-autoimmune hypothyroidism anddRTA was described for the first time in 1996 by Fang et al. in a 68-year-old man with severepost-radioiodine ablation hypothyroidism. The patient presented with hyperkalemic dRTA, and avoltage-dependent defect was presumed to be the possible attributable mechanism. The patientwas put on L-thyroxine, and follow-up metabolic studies documented complete reversal ofmetabolic acidosis and normalization of serumpotassium.[16]

The case reported here is significant to be incorporated in the literature due to the rarity ofoccurrence of dRTA in association with autoimmune hypothyroidism. Whether the coexistencewas an incidental finding cannot be rule out; however, as the patient had abruptly stopped thethyroxine supplements and exhibited no other hidden pathology, it can be postulated that the dRTAwith 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.

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