Case Report

Adult-Onset Distal Renal Tubular Acidosis with Hypokalemic Quadriparesis in a Patient with Autoimmune Hypothyroidism

L. Naveen, Santoshi Malkarnekar

Department of Medicine, Sri Devaraj Urs Medical College, Tamaka Kolar, Karnataka, India

Abstract

A 40-year-old lady, a known case of hypothyroidism, presented with 1-day history of progressive weakness in all four limbs and reported a history of similar episodes since 3 years. Clinical examination revealed grade 2 hyporeflexic quadriparesis without any bulbar involvement. Workup revealed hypokalemia, non-anion gap hyperchloremic metabolic acidosis and alkaline urine suggestive of distal renal tubular acidosis (RTA). Antiperoxidase and antithyroglobulin antibodies were positive, suggestive of an autoimmune basis for hypothyroidism. She was managed with intravenous potassium chloride, thyroid replacement and bicarbonate therapy, following which remarkable recovery was noted. One week later, she was discharged on oral thyroxine and oral sodium bicarbonate and she remained weakness-free for a follow-up period of over 1 year. RTA presenting in a setting of autoimmune hypothyroidism is a rare occurrence and the possible role of immunological mechanisms and thyroxine deficiency in the pathogenesis of acidification defect seems most likely.

Key words: Autoimmune, distal renal tubular acidosis, hypothyroidism, hypokalemic quadriparesis

Key Messages: This case study emphasizes the fact that recurrent hypokalemic paralysis warrants the search for an underlying cause, which must be adequately addressed to prevent the persistence or recurrence of paralysis.

INTRODUCTION

Renal tubular acidosis (RTA) is one of the leading causes of secondary hypokalemic paralysis. RTA is defined as an inability of the renal tubule to acidify urine, which is out of proportion to any reduction in the glomerular filtration rate. The case study herein described depicts that of an adult woman with hypokalemic paralysis as a consequence of distal renal tubular acidosis in a setting of primary autoimmune hypothyroidism. RTA occurring in association with autoimmune hypothyroidism is a rare event. We have reviewed similar cases in the literature and discussed these in the context of our case. To the best of our knowledge, only three cases of RTA in association with autoimmune hypothyroidism presenting with hypokalemic paralysis have been reported earlier in the literature.[1-3] Hence, we report this case study on account of its rarity.

Address for correspondence: Dr. Santoshi Malkarnekar, Department of Medicine, Sri Devaraj Urs Medical College, Tamaka Kolar, Karnataka - 563 101, India.
E-mail: drsantoshi85@gmail.com

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CASE REPORT

A 40-year-old woman presented to the emergency room with acute progressive weakness in all four limbs for 1 day. There was no preceding history of fever, vomiting, loose motions and drug intake. She had a notable past medical history of having similar episodes on and off for the past 3 years. Old medical records revealed a diagnosis of hypokalemic paralysis; however, no further evaluation was performed for the same. She was also known to have primary hypothyroidism since 5 years and was non-compliant with treatment. There was no history suggestive of nephrolithiasis. She did not have any notable family history. On examination, the patient was moderately built, with a pulse rate of 86/min and blood pressure of 110/80 mmHg. There was no thyromegaly and no clinical features of hypothyroidism were noted. Neurological examination revealed grade 2 hyporeflexic quadriparesis without any bulbar, sensory and bowel/bladder involvement. Other systemic examination

was unremarkable. Preliminary blood investigations revealed the following results: Hemoglobin = 10 gm/dL; blood urea = 25 mg/dL; serum creatinine = 1.1 mg/dL; serum potassium = 1.8 mEq/L; serum chloride = 122 mEq/L; and random blood glucose = 92 mg/dL. Arterial blood gas analysis showed arterial pH = 7.32; 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 examination revealed the following results: Urinary pH = 7 suggestive of alkaline urine; urinary osmolality = 500 mOsm/L; urine potassium = 119 mEq/L; and 24-h urinary calcium = 250 mg. The calculated Trans tubular potassium gradient (TTKG) was 38, suggestive of renal loss of potassium. Her urine was negative for protein and glucose. Thyroid function tests were suggestive of primary hypothyroidism: T3 = 72 ng/dL (normal 80-180 ng/dL); T4 = 2.2 mcg/dL (normal 4.6-12 mcg/dL); and thyroid stimulating hormone (TSH) = 31.6 mcIU/mL (normal 0.5-5.5 mcIU/mL). The titers of antithyroperoxidase and antithyroglobulin antibodies were elevated to 39.86 IU/mL (normal 0-18 IU/ mL) and 206.21 IU/mL (normal 0-70 IU/mL), respectively, suggestive of an autoimmune basis for the hypothyroidism. 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 phosphorous were within normal limits. The electrocardiogram showed prominent u waves and the chest radiograph was normal. While the ultrasonogram of the thyroid revealed a bulky gland, that of the abdomen was normal without any evidence of nephrocalcinosis. Nerve conduction study and electromyography were normal. Thus, here was an interesting case of a lady with autoimmune hypothyroidism with hypokalemic paralysis in whom the presence of non-anion gap hyperchloremic metabolic acidosis with alkaline urine ultimately led us to the diagnosis of distal RTA. She was treated with intravenous potassium chloride infusion followed by oral supplementation, oral thyroxine 100 mcg/day and oral sodium bicarbonate (325 mg)-two tablets thrice daily. She made complete recovery from the weakness and was ultimately discharged at the end of 1 week. At follow-up, she had attained an euthyroid state and all the laboratory investigations were normal. She claimed to be in good physical and mental health and was weakness-free for over 1 year of follow-up.

DISCUSSION

Hypokalemic paralysis is a form of metabolic myopathy that represents a heterogeneous group of disorder characterized by hypokalemia, acute flaccid paralysis and potentially fatal episodes of muscle weakness through the involvement of the respiratory muscles, and life-threatening cardiac arrhythmias. Hypokalemic periodic paralysis can be a primary disorder, which may be familial with an autosomal-dominant inheritance or sporadic, or it may be secondary with causes like RTA, thyrotoxic periodic paralysis, primary hyperaldosteronism, Gitelman syndrome, barium poisoning and diarrhea.[4] Distal RTA is one of the leading causes of secondary paralysis. RTA is a constellation of syndromes arising from different derangements of tubular acid transport. The clinical syndrome of distal RTA consists of hypokalemia, hyperchloremic metabolic acidosis, inability to lower urine pH below 5.5 in the presence of systemic acidosis, nephrocalcinosis and nephrolithiasis. RTA type I is either inherited or acquired. In the acquired form, the disorder can be caused by drugs, autoimmune diseases or by infection.[5] Of the endocrine disorders, RTA has rarely been reported in patients with thyroid dysfunction, including hyperthyroidism, Hashimoto's thyroiditis and hypothyroidism. The acidification defect has been presumably related to thyroxine deficiency.[6,7] In another recent study in rats with induced hypothyroidism, the investigators demonstrated a reduced expression of Na+/H+ exchanger NHE3, the Na+−phosphate co-transporter NaPi-IIa and the B2 sub-unit of the vacuolar H+−ATPase in the brush-border membrane of the proximal tubule, paralleled by a lower abundance of the Na+/HCO3-co-transporter NBCe1 and a higher expression of the acid-secretory type A intercalated cell-specific Cl−/HCO3− exchanger AE1.[8] The study concluded that thyroid hormones modulate the response to an acid challenge and alter the expression of several key acid-base transporters. Thyroid hormone increases membrane cell Na+ K+ ATPase pumps. In hypothyroidism, the content and function of these pumps are reduced, which causes a decreased elimination of H+ ions, exacerbating the acidosis state caused by RTA. Although the exact mechanisms remain unclear, the concurrence of RTA and autoimmune diseases is well documented, especially with Sjogrens syndrome and systemic lupus erythematosus. According to one study, the association of an autoimmune cause influences the renal acidification mechanisms through dysfunctions of various transporters and co-transporters involved in the acidification in the renal tubular system.[1]

The case herein described is noteworthy for various reasons. RTA occurring in association with autoimmune hypothyroidism, as seen in our case, is a very rare event, and, till date, very few cases have been reported. The concurrence of RTA and autoimmune thyroid disease is more than fortuitous, and it is believed that immunological mechanisms may be responsible for the pathogenesis. RTA in our patient developed 2 years after the diagnosis of

hypothyroidism. The systemic acidosis and hypokalemia disappeared following thyroid replacement therapy and the patient showed complete sustained recovery even after withdrawal of bicarbonate therapy at follow-up. Hence, the possibility of thyroxine deficiency also causing the acidification defect in our patient cannot be ruled out. This case study emphasizes on the fact that recurrent hypokalemic paralysis warrants the search for the underlying cause, which must be adequately addressed to prevent the persistence or recurrence of paralysis.

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