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Case Report

Distal Renal Tubular Acidosis can be the Cause of Hypokalemia in Graves' Disease: A Rare Association

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Abstract

Distal renal tubular acidosis (dRTA) may rarely occur in the course of autoimmune diseases. We present a patient who was followed up with Graves' disease and vitiligo and who was diagnosed with dRTA upon detection of hypopotasemia. A 9.2-year-old girl presented with complaints of sweating, palpitations, and hand tremors. The patient had vitiligo on examination and was diagnosed with Graves' disease per clinical and laboratory findings. The patient, who received methimazole and was followed up as a euthyroid, was found to have hypokalemia in biochemical examinations performed at the age of 13 years. While investigating the etiology of hypokalemia, the patient was diagnosed with dRTA. Since she had two autoimmune pathologies, it was thought that the dRTA might be of autoimmune origin. Checking serum potassium levels in the follow-up of patients with Graves' disease may allow early diagnosis and treatment of accompanying dRTA.

Keywords: Distal renal tubular acidosis, Graves' disease, vitiligo, autoimmune disorder

INTRODUCTION

Distal renal tubular acidosis (dRTA) is a rare disease caused by the impaired acid-secretory function of the distal kidney tubules. Since the hydrogen (H+) ion cannot be secreted, metabolic acidosis develops, and urinary pH gets inappropriately alkaline (pH>5.5) (1). In most pediatric cases, dRTA is primarily caused by genetic defects (ATP6V1B1, ATP6V0A4, SLC4A1, KCC4) in the channels or enzymes involved in H+ secretion in the distal renal tubules (2). The autosomal recessive form is often diagnosed in infancy and has a more severe clinical course. On the other hand, the diagnosis of the autosomal dominant disease is usually made at a later stage (1,3). Hypopotassemia, hyperchloremia, metabolic acidosis, normal plasma anion deficit, positive urinary anion deficit, hypercalciuria, and nephrocalcinosis are important and diagnostic findings suggesting distal RTA (1-3). Secondary dRTA often occurs after damage to the distal or collecting ducts due to drugs, renal diseases, calcium disorders, hypergammaglobulinemia, or autoimmune diseases (systemic lupus erythematosus, primary biliary cirrhosis, Sjogren's syndrome, autoimmune thyroiditis, rheumatoid arthritis, etc.) (2-4). DRTA in autoimmune thyroiditis (Graves' disease, Hashimoto's thyroiditis) has been reported in a small number of cases to date (5,6).

This article presents a case detected to have Graves' disease and vitiligo in the prepubertal period and diagnosed during puberty with dRTA as due to incidental hypopotassemia at follow-up.

CASE REPORT

A 9-years and 2-months-old girl presented with sweating, palpitations, and hand tremors. She reported an inability to gain weight and a state of nervousness despite the increase in appetite. On physical examination, her body weight was 22 kg (-1.83 SDS) and her height was 122 cm (-1.94 SDS). She was prepubertal and had stage 1 diffuse goiter, moderate exophthalmos, hyperthermia

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(body temperature 38.0 °C), hypertension (135/85 mmHg), and tachycardia (pulse 118/min). Vitiligo was present on the trunk, arms, legs, dorsal hand, and genital area. Her complete blood count, biochemistry profile, and complete urine tests were normal and the laboratory findings were as follows: free serum thyroxine (fT4): 3.2 ng/mL (N: 0.93-1.7), free triiodothyronine (fT3): 12.04 pg/mL (N: 1.86-4.6), and thyroid-stimulating hormone (TSH): 0.005 mIU/L (N: 0.35-4.94 mIU/L). In thyroid ultrasonography, the right thyroid lobe was 10x10x29 mm, the left lobe was 10x10x28 mm, and AP isthmus thickness was 1.7 mm. The contours of both lobes and isthmus were smooth, and the parenchyma echoes were heterogeneous. Thyroid peroxidase antibody (anti-TPO) requested to study autoimmune thyroid diseases was positive, and Thyroglobulin antibody (Anti-TG) was negative. Her thyroid-stimulating hormone receptor antibodies (TRAB) were measured as 2.14 IU/L (0-1.75). She was diagnosed with Graves' disease, and oral treatment with Methimazole 0.3 mg/kg/day was started. Propranolol 1mg/kg/day in 2 doses was initiated for her tachycardia. The tachycardia improved, and propranolol was discontinued at follow-up. The patient stopped Methimazole treatment after 6 months and applied to us 6 months after discontinuing methimazole. At this admission, she was euthyroid, but TRAB was positive.

The patient was followed up for 21 months without medication as euthyroid. When she was 11.5 years old, subclinical hyperthyroidism emerged, and the TRAB positivity continued. Hence, 5mg/day methimazole was started again. During the follow-up, 25 mcg/day L-thyroxine was added to the treatment because the patient developed hypothyroidism with low-dose antithyroid therapy. Upon progression of exophthalmos to moderate-severe levels (eyelid retraction and prominent exophthalmos) with the onset of puberty in the follow-up, the patient received 250 mg/dose methylprednisolone (MPZ) IV for 6 weeks, then 125 mg/dose weekly IV MPZ for another 6 weeks. After this treatment, a slight regression was observed in her exophthalmos.

The patient was euthyroid when she came to control at the age of 13, under Methimazole and Levothyroxine treatments. Incidentally, hypopotassemia (K: 2.9 mEq/L) was detected in the biochemical analysis without active complaints. As the control biochemistry analysis revealed hypopotassemia three days later (K: 2.5 mEq/L), the etiology was investigated. Her serum biochemistry analyses returned the following results: glucose 82 mg/dl, urea 13.6 mg/dl, creatinine 0.67 mg/dl, calcium 9.5 mg/dl, phosphorus 4.2 mg/dl, sodium 139 mEq/L (136-145), potassium 2.5 mEq/L (3.4 -4.7), chlorine 116 mEq/L (98-107). While urine pH was 7 and density was 1001, potassium excretion in spot urine was 34 mEq/L. Blood gas analysis revealed the following: pH: 7.23, PCO2: 38.8, HCO3: 15.7, and BE: - 9.6. The 24-hour urinary calcium level was 5.36 mg/kg/day (>4mg/kg/day), which was high. The plasma anion gap was normal at 10.3 mmol/l. The urine anion gap was 30 mmol/l. Bilateral grade 2 medullary nephrocalcinosis was observed in the abdominal ultrasonography. Plasma renin activity and plasma aldosterone levels were normal. As a result, the patient was diagnosed with hypokalemic hyperchloremic metabolic acidosis and nephrocalcinosis with dRTA. The hearing test was normal, and celiac antibodies tested for additional autoimmune pathologies were negative. There were no clinical signs of systemic lupus erythematosus in the patient. However, she had positive antinuclear antibody and anti-dsDNA results. The patient started oral potassium citrate 1 mEq/kg/day and sodium bicarbonate 1 mEq/kg/day orally. In the follow-up, the patient's serum electrolyte and blood gas values returned to the normal range within 2 weeks. The patient is still being followed up with Methimazole, Levothyroxine, potassium citrate, and sodium bicarbonate treatments.

DISCUSSION

The etiology of hypopotassemia detected during the follow-up in an adolescent patient who was followed up with Graves' disease and vitiligo was investigated, resulting in the diagnosis of dRTA. One of the causes of hypokalemia in hyperthyroid patients is thyrotoxic hypokalemic periodic paralysis (THPP), a rare complication of hyperthyroidism. THPP is characterized by reversible muscle weakness and paralysis attacks due to the intracellular blockade of K+ by excessive thyroid hormones. The situation often disappears with the recovery of hyperthyroidism (7). In our case, unlike THPP, when hypokalemia was detected, there were no clinical and laboratory findings of hyperthyroidism, and there was no acute muscle weakness or paralysis. Therefore, THPP was not considered in this patient. In addition to hypokalemia, a diagnosis of dRTA was made with the findings of hyperchloremia, metabolic acidosis, normal plasma anion deficit, positive urinary anion deficit, alkaline urine, hypercalciuria, and nephrocalcinosis.

The association of hyperthyroidism and RTA was first described in 1959. After the diagnosis of hyperthyroidism in a 40-year-old female patient, hypercalcemia, nephrocalcinosis, and RTA were detected in the follow-up. Since the x-ray evidence shows that nephrocalcinosis develops in the hyperthyroid process, it has been suggested that the distal RTA in the patient arose due to the hypercalciuria and tubular damage secondary to nephrolithiasis caused by hyperthyroidism (8). It should be kept in mind that nephrocalcinosis due to hypercalciuria can also be seen in the course of primary dRTA. Wu et al. detected hyperthyroidism due to hypokalemia, RTA, and autoimmune lymphocytic thyroiditis in a 34-year-old patient who presented with proximal muscle weakness. Since hypercalcemia and nephrocalcinosis were not found in the patient, hyperthyroidism was improved with antithyroid and radioactive iodine treatment but dRTA continued, they proposed that RTA was not caused by metabolic mechanisms but by immunological mechanisms (9). A 20-year-old female patient was reported from

Korea, followed up with Graves' disease for three months. She was diagnosed with hypokalemic periodic paralysis and dRTA in the period of recurrent hyperthyroidism after discontinuing the treatment (5).

Furthermore, Guerra-Hernandez et al. reported dRTA in two children with acquired autoimmune hypothyroidism and suggested that dRTA may have developed due to hypothyroidism or autoantibodies (6). In our adolescent girl who was followed up with a diagnosis of Graves' disease and vitiligo, dRTA was detected while she was euthyroid. It was thought that the dRTA in our patient could be of autoimmune origin since she did not currently have hyperthyroidism but had autoimmune diseases. However, a histopathological evaluation was not performed.

The pathophysiological explanation of dRTA associated with autoimmunity is not fully resolved. The mechanism in dRTA seen with Graves' disease has not been fully explained, and the exact target of autoimmunity in the kidney has not been determined. It has been suggested that antibodies against TSH receptors may cross-react against the epithelial Na+ channel, carbonic anhydrase II enzyme, acid-base transporters, intercalated cells, or specific antibodies against these structures may exist in an autoimmune background (4,5,9,10). No antibody against renal tubules could be shown in Graves' disease.

In conclusion, it should be kept in mind that although distal RTA is generally a hereditary condition in children, it may also develop in the course of autoimmune diseases. Screening for dRTA at regular intervals (serum potassium levels, blood gas analysis, renal USG) will be appropriate in the follow-up of patients with Graves' disease.

What is new?

-Distal renal tubular acidosis (dRTA) can be seen in children during the course of autoimmune thyroid disease.

-In the course of Graves' disease in children, dRTA is the first case to develop.

- Screening for dRTA at regular intervals (serum potassium levels, blood gas analysis, renal USG) will be appropriate in the follow-up of patients with Graves' disease.

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