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CASE REPORT

SYSTEMIC LUPUS ERYTHEMATOSUS PRESENTING INITIALLY AS HYDROGEN ATPase PUMP DEFECTS OF DISTAL RENAL TUBULAR ACIDOSIS

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ABSTRACT

Tubulointerstitial involvement is well recognized in systemic lupus erythematosus. The tubular dysfunction is usually latent and usually presents after diagnosis of systemic lupus erythematosus. We report a case presenting that she is well previously and initially diagnosed as periodic paralysis of hypokalemia at emergency room and final diagnosis is systemic lupus erythematosus with H^+-ATPase pump defect of distal type renal tubular acidosis. Kidney biopsy showed lupus nephritis classified as mesangial proliferative glomerulonephritis WHO class II B. Her renal tubular acidosis was subsided after steroid therapy was administered.

Key Words: Systemic Lupus Erythematosus; Distal Renal Tubular Acidosis; Hypokalemia.

INTRODUCTION

Distal renal tubular acidosis is characterized by a decrease in net hydrogen secretion in renal collecting tubules such that the urine pH remains

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above 5.3 in a condition of acidemia. The most common identifiable causes in adults are autoimmune disorders, such as Sjogren syndrome, systemic lupus erythematosus (SLE), rheumatoid arthritis and drug related renal tubular acidosis, such as amphotericin B, lithium carbonate etc. (1,2). Tubulointerstitial involvement is well recognized in SLE. The tubular dysfunction is usually latent and usually presents after diagnosis of SLE (3–5). We report a case presenting that she is well previously and initially diagnosed as periodic paralysis of hypokalemia at emergency room and final diagnosis is SLE with H^+-ATPase pump defect of distal type renal tubular acidosis. Her renal tubular acidosis was subsided after steroid therapy was administered.

CASE REPORT

A 21-year-old female was admitted to the hospital because of progressive weakness of lower legs for 2 days via emergency room. Initially, hyperthyroidism associated with periodic paralysis was impressed because she had severe hypokalemia (potassium 1.7 mmole/L) after exercise and body weight loss with hand tremor was noted in recent one month.

On examination the patient was clear consciousness and well nutrition. The body temperature was 37.8°C, pulse rate 80/min and respiratory rate 20/min. The blood pressure was 120/74 mmHg. There is no malar rash and oral ulcer. The thyroid gland was firm and no bruit without enlargement. The jugular venous pressure was not elevated. The both lung fields were clear. The heart sounds were normal and abdominal examination showed mild obese abdomen without tenderness. There was no pitting edema, no cyanosis, no digital clubbing. There was no history of nephrolithiasis. Laboratory studies at emergency room revealed hemoglobin 8.7 gm/dL, hematocrit 26.3%, white blood cells 11300/mm^3 with segment 88%, band 4%, monocyte 6%, lymphocyte 1%, atypical lymphocyte 1%, serum creatinine 1.0 mg/dL, blood urea nitrogen 6.0 mg/dL, sodium 137 mmole/L, potassium 1.7 mmole/L, chloride 120 mmole/L. The arterial blood gas was: pH 7.233, PCo2 20.4 mmHg, PO2 114.4 mmHg, and bicarbonate 8.4 mmole/L. Urine pH was 8.0 with a specific gravity of 1.005 and hematuria (15–18/HPF) without proteinuria. Anion gap of serum was 8.6 mmole/L. The thyroxin (T4) concentration was 6.24 μg/dL and thyroid-stimulating hormone (TSH) was 0.62 IU/mL which were all in normal range. Hyperthyroidism associated periodic paralysis of hypokalemic renal tubular acidosis was considered unlikely after she was admitted to nephrologic ward and she was arranged the following studies of tubular function under impression of renal tubular acidosis.

Renal sonography showed renal parenchymal disease without evidence of nephrolithiasis & nephrocalcinosis. Sodium bicarbonate loading test was performed and the following arterial blood gas findings were observed: pH

7.403, PCO_2 14.3 mmHg, PO2 90 mmHg, bicarbonate 17.8 mmoles/L. Urine gas analysis showed pH 7.263, PCO_2 26.2 mmHg bicarbonate 11.8 mmoles/L. The fractional excretion of bicarbonate was 3.7%. Urine anion gap was positive 10.6 mmoles/L (urine sodium 84 mmoles/L, potassium 11.6 mmoles/L, chloride 85 mmoles/L). Serum sodium concentration was 138 mmole/L, potassium 3.0 mmole/L, chloride 120 mmole/L. The results of the studies were approved with the diagnosis of hypokalemic distal type(type I) renal tubular acidosis with low net distal H^+ secretion (severe distal H^+ secretory defect). H^+-ATPase pump defects of collecting tubules was diagnosed by low urine PCO_2 (<50 mmHg) and high urine pH (>6.0) (1,6). Antinuclear antibody (ANA) was 1:640 in speckle type, anti-double stranded DNA antibody titer was 1112 IU/ml, and anti-RNP antibody and anti-Sm antibody were strongly positive (>100 U/ml). C3 25.5 mg/dL (normal range 73–134 mg/dL), C4 < 5.73 mg/dL (normal range 18.2–45.5 mg/dL) were depressed. Immunoglobulin was IgG 2920 mg/dL, IgA 249 mg/dL, IgM 104 mg/dL, IgE 241 mg/dL. Anti-HCV antibody and hepatitis B surface antigen were negative. Erythrocyte sedimentation rate (ESR) was 63 mm/hr and C-reactive protein (CRP) was less than 3 mg/L. Systemic lupus erythematosus with distal renal tubular acidosis was highly suspected.

A percutaneous renal biopsy was performed and pathology showed glomeruli with mild mesangial hyperplasia and interstitium had moderate chronic inflammation. Immunofluorescence revealed glomeruli with 3+IgG, 3+IgA, 2+IgA, 3+IgA, 3+C3, 2+Clq deposition in mesangium. All studies were consistent with lupus nephritis classified as mesangial proliferative glomerulonephritis WHO class II B. She was treated initially with methylprednisolone pulse therapy (methylprednisolone 500 mg intravenous infusion for 3 days) and followed by prednisolone 1.0 mg/kg daily for 8 weeks which dosing was gradually tapered thereafter.

After 8 weeks of steroid therapy, she did not receive alkali therapy and potassium supplements any more. Laboratory studies showed serum sodium concentration was 139 mmole/L, potassium 3.4 mmole/L, chloride 111 mmole/L, CO_2 24.6 meq/L. Urine pH was 5.3 with a specific gravity of 1.020 and without proteinuria & hematuria. C3 (99 mg/dL) and C4 (22 mg/dL) level were all in normal range. Anti-double stranded DNA antibody titer was 14 IU/mL. She did not experience episode of hypokalemia any more after steroid therapy was administered for SLE.

DISCUSSION

The presence of distal type renal tubular acidosis should be suspected in any patient with a normal anion gap metabolic acidosis and a urine pH greater than 5.3 in adults. Many different conditions have been associated with distal type renal tubular acidosis. The major causes of this disorder

includes primary idiopathic disease, hereditary disease such as Wilson's disease, disorders of calcium metabolism and nephrolcalcinosis, autoimmune diseases, drugs, toxins, urinary tract obstruction and sickle cell anemia (1). Impaired tubular function in SLE is most often present in patients with acute nephritis or nephrotic syndrome. In our patient, she had symptomatic hypokalemia of distal renal tubular acidosis without any other physical sign of SLE. Only mild hematuria and autoantibodies were detected. It is difficult to make a diagnosis from such a patient presenting hypokalemia only without any manifestation of SLE. From this experience, to check antinuclear antibody, anti-double stranded DNA antibody titer, anti-RNP antibody, anti-Sm antibody and complement level is recommended for unexplained hypokalemia with renal tubular acidosis.

Distal tubular acidosis has been well documented in the presence of a variety of autoimmune disorders including thyroid disease, Sjogrens syndrome, systemic lupus erythematosus et al. What is the possible mechanism responsible for this patient with lupus nephritis related renal tubular acidosis? Three mechanisms were conceivable: (1) defect in H^+-ATPase pump of the cortical and/or medullary collecting tubules; (2) reduction in cortical sodium reabsorption, thereby diminishing the degree of luminal negativity and producing a voltage-dependent defect which will lead to a concurrent impairment in potassium secretion and result in hyperkalemia, A reduction in sodium-potassium-ATPase activity may be responsible for the reduction in sodium resorption; (3) an increase in membrane permeability, which allows back-diffusion of hydrogen ions or possibly bicarbonate (1). In our patient, her sodium bicarbonate loading test revealed the fractional excretion of bicarbonate was 3.7%. Urine anion gap was positive. The diagnosis of hypokalemic distal type (type I) renal tubular acidosis with low net distal H^+ secretion (severe distal hydrogen secretory defect) was made. H^+-ATPase pump defects of collecting tubules was confirmed by low urine PCo_2 (<50 mmHg) and high urine pH (>6.0). Taken together, these data suggest a defect in H^+-ATPase pump of the cortical and/or medullary collecting tubules as the underlying mechanism of lupus nephritis (1,6).

Tubulointerstitial involvement is well recognized in systemic lupus erythematosus. The tubular dysfunction is usually latent and usually presents after diagnosis of SLE(3–5). Complete distal renal tubular acidosis preceeding of SLE is rare and only one case report in a 10-year-old girl with distal renal tubular acidosis for 4 years preceded other manifestations of SLE (7). Tubular atrophy, interstitial infiltration and fibrosis are seen in 50–70% of patients in SLE with tubular dysfunction and occasional reports have indicated the possibility of interstitial nephritis in the absence of glomerular changes in SLE (2,4,5,8,9). In our patient, her renal histologic examination was glomeruli with mild mesangial hyperplasia and moderate chronic inflammation of interstitium. Tubular had mild atrophy. All of the findings were compatible with the previous reports which SLE was recognized for several

months, but our patient did not initially present the other manifestations of SLE at diagnosis. The laboratory findings showed renal tubular acidosis subsided after 8 weeks of steroid therapy and suggested reversible tubular function could be expected if early intervention of steroid was prescribed.

In summary, we report a previously unrecognized lupus case presenting as SLE associated with hypokalemic distal type renal tubular acidosis which is possibly due to lupus nephritis with inflammation of interstitium. The underlying mechanism of these tubular defects may be related to H^+-ATPase pump defects of collecting tubules resulting in severe defects of hydrogen secretion. Distal renal tubular acidosis resolved after steroid therapy was implemented and activity of SLE was under well controlled.

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