Type 4 Renal Tubular Acidosis in a Patient With Lupus Nephritis

Davut Akin, Sehmus Ozmen

Department of Nephrology, Dicle University School of Medicine, Denizli, Turkey

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Although renal tubular acidosis (RTA) is a rare complication of systemic lupus erythematosus (SLE), type 4 RTA associated with lupus nephritis is extremely rare. A 20-year-old woman presented with malaise and edema in the lower extremities and face. She had multiple lymphadenopathies. There were 20% eosinophil in blood smear and 32% in bone marrow aspiration. Serology revealed positive antinuclear antibody at 1:1000 titer, positive double-stranded DNA antibodies, and low complements C3 and C4 levels. Urinary sediment was active and urinary protein excretion was 4.8 g/d. The SLE Disease Activity Index score was 23. A high SLE Disease Activity Index scores was proposed as a potential risk factor for type 4 RTA. Type 4 RTA may complicate SLE, and specifically, patients with high SLEDAI scores and lymphadenopathy may pose a high risk. Our patient responded successfully to immunomodulatory therapy.

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INTRODUCTION

Type 4 renal tubular acidosis (RTA) is associated with hyperkalemia and mild renal impairment. Causes of RTA include idiopathic, tubulointerstitial disease, secondary to autoimmune diseases and toxins. Some drugs cause type 4 RTA, such as nonsteroid anti-inflammatory drugs, potassium-sparing diuretics (amiloride, triamterene, and spironolactone), and angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and cyclosporine. Generally, RTA is a rare complication of systemic lupus erythematosus (SLE) and may pose diagnostic challenges, and type 4 RTA associated with lupus nephritis is extremely rare.[1-3] We describe a case of a woman with a rare acute presentation of SLE, with hypereosinophilia, lymphadenopathy, high SLE Disease Activity Index (SLEDAI) score, and type 4 RTA, responding successfully to immunomodulatory therapy.

CASE REPORT

A 20-year-old woman presented with malaise and bilateral pedal edema for 1 year. She also complained of fatigue and polyarthralgia of the wrists, hands, and feet. There was no past medical history of note, in particular no respiratory tract illnesses and no history of allergy. She took no prescribed or over-the-counter medications. Raynaud phenomenon was not present.

On examination, her body temperature was 36.5°C, the blood pressure was 140/80 mm Hg, the pulse rate was 80 beats per minute, and the respiratory rate was 20 breaths per minute. She had no skin lesions. There was a mobile right axillary lymph node, 2 cm in diameter, anterior cervical lymphadenopathy (0.5 cm to 1 cm in diameter), and post-auricular lymphadenopathy. Her chest sounds were clear with no friction rubs or wheezing, and she had no murmurs. There was periorbital and pretibial edema.

Blood chemistry investigations revealed the following: serum sodium, 136 mmol/L; serum potassium, 5.8 mmol/L; serum chloride, 115 mg/dL; blood urea, 55 mg/dL; and serum creatinine, 1.05

Case Report

mg/dL. Acute phase reactants levels were normal. A complete blood count showed a leukocyte count of 22.8×10^9/L and a platelet count of 452×10^9/L. Hemoglobin level was 10.6 g/dL. Blood smear revealed 20% eosinophil. Bone marrow aspiration revealed hypereosinophilia (32%). In urinalysis, urine was cloudy; protein level was 3+ (300 mg/dL); and there were up to 12 to 20 leukocytes, 15 to 20 erythrocytes (30% dysmorphic), 1 to 2 granular casts, and many epithelial cells per high-power field. Urinary pH was 5.0. Nitrite and leukocyte esterase were negative. Urinary protein excretion was 4.8 g/d. Transtubular potassium gradient was 3.7. Serum cortisol level was 11.8 mg/L. Plasma renin activity and serum aldosterone concentrations were 0.19 ng/mL/h (reference range, 0.2 ng/mL/h to 3.4 ng/mL/h) and 25 pg/mL (reference range, 30 pg/mL to 160 pg/mL), respectively.

Tests for hepatitis A, B, and C, human immunodeficiency virus 1 and 2, and tuberculosis; repeated examination for bacterial infection (blood, urine, sputum, and stool,); and tests for parasitic infection were all negative. Serology investigations, however, revealed positive anti-nuclear antibody at 1:1000 titer, positive double-stranded DNA antibodies (Farr assay), positive anti-nucleosome antibody (3+), and low complement C3 (26 mg/dL; reference range, 79 mg/dL to 152 mg/dL) and C4 levels (3.9 mg/dL; reference range, 16 mg/dL to 38 mg/dL). Antibodies to neutrophil cytoplasmic antigens, myeloperoxidase, and proteinase 3 were negative. Arterial blood gas tests showed to have adequate oxygenation on air with evidence of acidosis (pH, 7.34; pO_2, 91 kPa; pCO_2, 34 kPa; standard bicarbonate, 18.3 mmol/L; and base excess, 4 mmol/L) and serum anion gap was normal. Serum immunoglobulin E level and spirometry were within normal ranges and rheumatoid factor was negative. Echocardiography showed that there was minimal pericardial effusion. Her serum potassium increased to 6.8 mmol/L during hospitalization.

A diagnosis of type 4 renal tubular acidosis was made, with probability of being linked to lupus nephritis. The SLEDAI score was 23 (based on scores obtained by global assessment, urinary microscopic finding, urinary protein excretion, pleurisy, complements, and presence of anti-double stranded DNA antibodies). The right supraclavicular lymph node excisional biopsy specimen examination revealed that there were only reactive changes (reactive follicular lymphoid hyperplasia). No caseating or noncaseating granuloma, giant cell, or inflammatory exudate was observed.

The patient was promptly treated with 3 consecutive pulses of methylprednisolone (1 g/24 h). Then, methylprednisolone, 1 mg/kg, and mycophenolate mofetil, 2 g/d, were started. The patient's clinical and laboratory findings improved and she was discharged with normal kidney function, serum potassium, serum bicarbonate, and blood eosinophil count. She was well and had normal electrolyte level on the examinations performed 4 months later.

DISCUSSION

Our patient had rare manifestations of SLE, eosinophilia with a type 4 RTA, which are two distinct disease entities. Systemic hypereosinophilic syndromes have also only rarely been described in relation to SLE. Case reports are confined to a young man with SLE and hypereosinophilia, whose Loeffler endocarditis and acute pulmonary capillaritis was only diagnosed postmortem[4]; a patient with quiescent SLE, who developed hypereosinophilia[5]; and a patient who developed late onset asthma and hypereosinophilia after 26 years of SLE, which progressed to meet the American College of Rheumatology criteria for diagnosis of Churg-Strauss syndrome.[6] The lack of premorbid respiratory tract disease or allergy and spirometric findings made a Churg-Strauss like syndrome unlikely in our case. Other causes of hypereosinophilia were excluded and hypereosinophilia was attributed to SLE in our patient.

Sjogren syndrome is highly associated with SLE. We ruled out Sjogren syndrome in our patient because she did not have dry eye or dry mouth, and was not positive for anti-rheumatoid factor or anti-lupus arthritis. The potential of direct cytotoxicity of eosinophils for proximal tubule epithelial cells was demonstrated previously in kidney allograft rejection. Therefore, we supposed that hypereosinophillia caused by SLE might have a role in tubular injury and type 4 RTA in our patient.[7] Overall, frequency of enlarged lymph nodes in patients with active SLE is 26% to 69%.[8,9] Although the presence lymphadenopathy in our patient might be attributed to the disease, we excluded a possible malignancy by excisional biopsy because

of wide distribution of lymphadenopathies. Patients with lymphadenopathy have significantly more constitutional symptoms of fatigue, fever, and weight loss; more cutaneous symptoms and signs; a higher rate of hepatomegaly and splenomegaly; increased anti-double-stranded DNA antibodies; and decreased complement levels. Disease activity index is higher among patients with lymphadenopathy,[9] as was the case for our patient.

Systemic lupus erythematosus can be associated with a variety of tubular defects. Impaired tubular function in SLE is often present in patients with acute nephritis or nephritic syndrome. In addition, type 4 RTA is an extremely rare event in SLE. Systemic lupus erythematosus accounts for 12% of distal RTA.[10] We found only a few cases of type 4 RTA associated with SLE in literature.[1-3] Li and coworkers[3] reported 6 cases with SLE and RTA. Two of them had type 4 RTA and higher SLEDAI scores (23 and 32) than patients with type 1 RTA (8 to 17). There was no medullary nephrocalcinosis or renal urolithiasis in our patient with type 4 RTA. High SLEDAI score in our case with type 4 RTA supports their idea supposing an association between high SLEDAI score and presence of type 4 RTA. Although knowledge about the presence of eosinophilia and lymphadenopathy, reported in only a few cases of SLE with type 4 RTA, is lacking, the presence of eosinophilia and lymphadenopathy may be associated with the occurrence of type 4 RTA by an unknown mechanism in patients with SLE.

CONFLICT OF INTEREST

None declared.

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Correspondence to:
Davut Akin, MD
Denizli State Hospital, Denizli, Turkey
E-mail: drdavutakin@gmail.com

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