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Systemic lupus erythematosus and renal tubular acidosis associated with hyperthyroidism

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Abstract

A case of a 42-year-old female with hyperthyroidism was subsequently diagnosed to have systemic lupus erythematosus with distal RTA. The clinical examination on admission showed swelling of the knee joints and the urinalysis showed pH 6.5, pro 3+. Her blood routine results were as follows: white blood cells 1.85×10^9/L, platelets 100×10^9/L, erythrocyte 3.06×10^{12}/L. The serum potassium was 3.11 mmol/L, 24 hour urinary electrolyte: K 68.87 mmol/24 H, antinuclear antibodies (ANA) 1:1 000, speckled pattern. The anti-double stranded DNA antibody (anti-dsDNA), anti SS-A(52) antibody and anti SS-A(60) antibody were positive. The light microscopy and immunofluorescence showed diffuse proliferative lupus nephritis. These data were compatible with the diagnosis of systemic lupus erythematosus. The diagnosis of hyperthyroidism and distal RTA is clear. This report showed that other autoimmune disease in the diagnosis of hyperthyroidism should not be ignored.

CASE REPORT

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic and multi-system autoimmune disorder characterized by dysregulated immune responses and production of pathogenic autoantibodies by immune cells such as B-cells, T-cells and dendritic cells(Yuen & Cunningham 2014). The clinical presentations of SLE include rash, oral ulcers, fatigue and arthralgias, and the course of the disease is unpredictable with periods of flares alternating with remission (Yuen & Cunningham 2014). Renal tubular acidosis (RTA) is a metabolic acidosis caused by impaired excretion of hydrogen ions reabsorption of bicarbonate. The most common causes of distal renal tubular acidosis in adults are autoimmune disorders including Sjögren's syndrome, systemic lupus erythematosus, rheumatoid arthritis and autoimmune thyroiditis of the thyroiditis states. Graves, disease-associated RTA is a rare disease (Sim *et al.* 2013). Autoimmune thyroid disease (AITD) results from a dysregulation of the immune system leading to an immune attack on the thyroid. AITD is T cell-mediated organ-

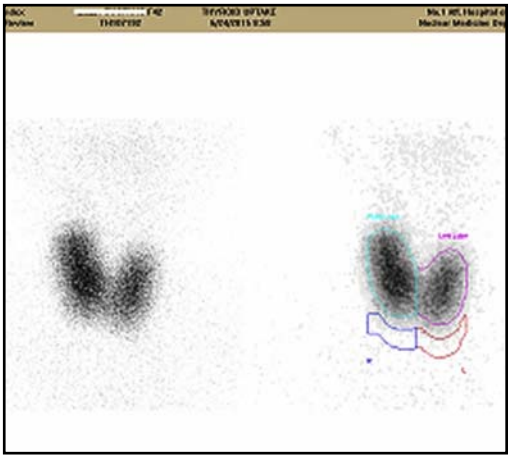

Fig. 1. Radionuclide imaging of thyroid gland.

specific autoimmune disorders. Associations exist between AITD and other organ specific, or systemic autoimmune disorders (Sjögren's syndrome, rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis, cryoglobulinemia, sarcoidosis, and psoriatic arthritis) (Alessandro *et al.* 2015).

Here, we present a woman case with systemic lupus erythematosus, renal tubular acidosis, and hyperthyroidism.

CASE REPORT

A 42-year-old women was referred to us for management of hyperthyroidism. Two years ago, she presented to her physician with fatigue, inappetence and weight loss. A diagnosis of hyperthyroidism was made. She started on propyl-thiouracil and propranolol tablets, and was initially treated with 150 mg/day. Her propyl-thiouracil requirements did not change greatly over these years. She admitted to having noticed inappetence with occasional pukes for nearly a month. She had been referred to our hospital due to progressive deterioration of her liver functions. There was a history of nocturia. She did not have a history of vomiting, loose motions, fever or high carbohydrate diet intake. The vital signs at presentation were shown as follows: blood pressure 115/72 mmHg, pulse rate 120/min, and body temperature 37.0 °C. Physical exam showed her hands had a slight tremor and her skin was moist. There was exophthalmos and stare. A small diffuse goiter was noted while there was no pretibial dermopathy. Swelling of the knee joints was noted. No obvious skin erythema, hair loss or lymph node swelling were observed. The

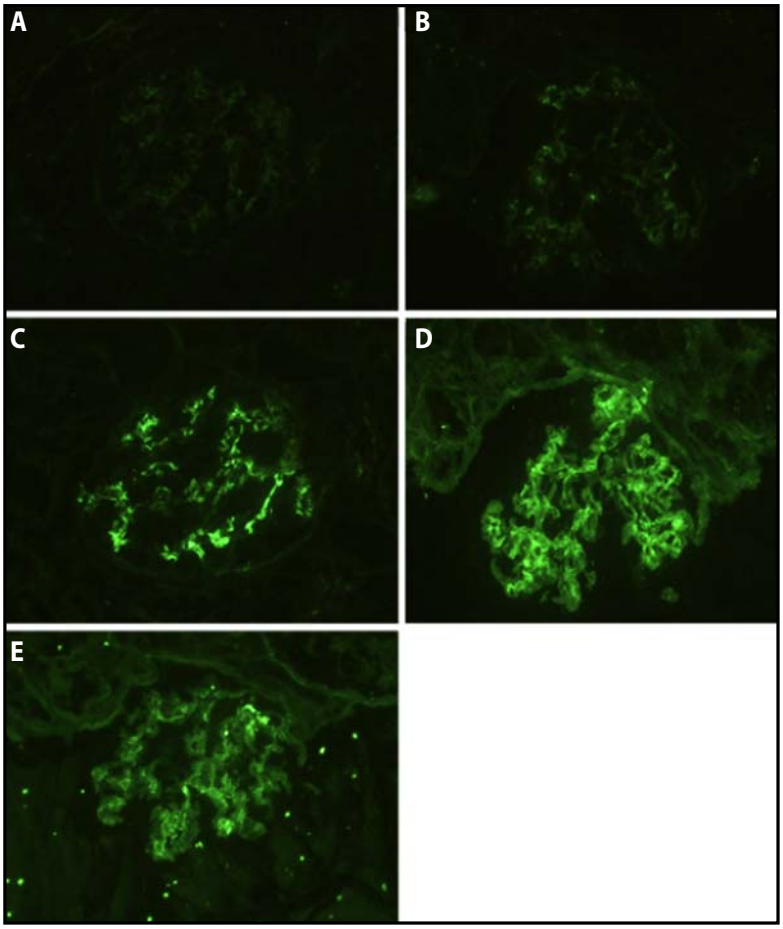

Fig. 2. Immunofluorescence staining of kidney tissue (A: IgA +, B: C1q ++, C: C_3 +++, D: IgG ++, E: IgM ++)

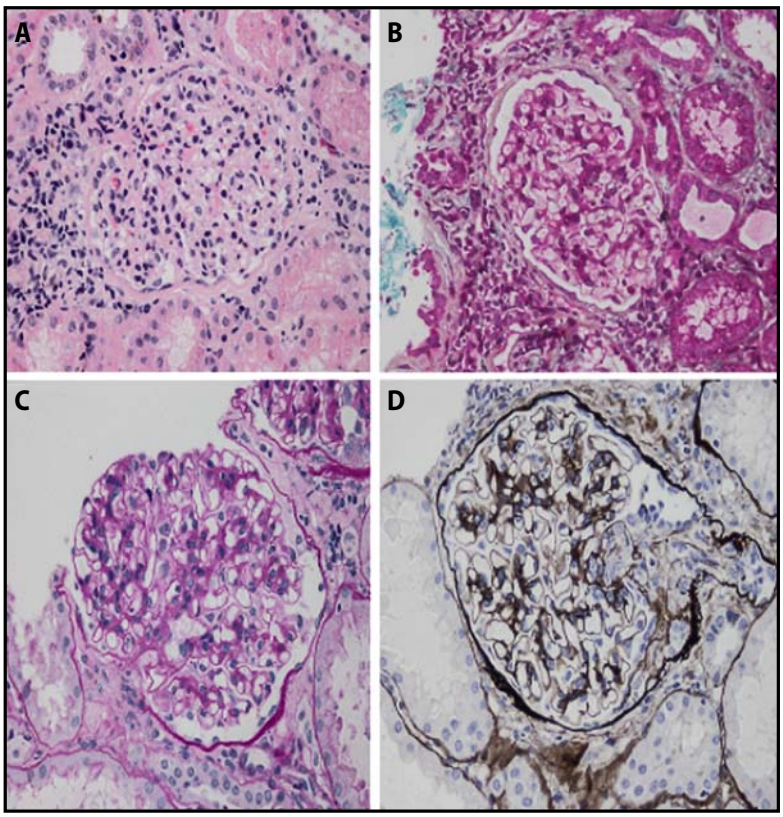

Fig. 3. Pathological examination revealed lupus nephritis (A: HE staining, B: Masson staining, C: PAS staining, D: PASM staining)

Tab. 1. Relevant laboratory data on the patient.

Urinalysis		Reference range	Serological and Immunological data		Reference range
pH	6.5	4.8~8.0	Anti TPO antibodies (U/ml)	59.20	0.00–60.00
Pro	(+++)		Antithyoglobulin antibody (U/ml)	29.00	0.00–60.00
Hemogram			TSH receptor antibodies (U/L)	18.00	<12
RBC ($\times10^{12}$/L)	3.06	4.30~5.80	ACL-IgA (RU/ml)	5	0~20
Hb (g/L)	77	130~175	ACL-IgG (RU/ml)	17	0~20
HCT (%)	23.00	35.00~45.00	ACL-IgM (RU/ml)	4	0~20
WBC ($\times10^{9}$/L)	1.85	3.50~9.50	β2-GP1-IgA (RU/ml)	3	0~20
NEUT (%)	56.30	40.00~75.00	β2-GP1-IgG (RU/ml)	12	0~20
Plt ($\times10^{9}$/L))	100	125~350	β2-GP1-IgM (RU/ml)	6	0~20
24 hour urinary electrolyte			c-ANCA	(–)	
K (mmol/24H)	68.87	25.00-100.00	Anti-PR3	(–)	
Ca mmol/24H)	4.73	2.50-7.50	p-ANCA	(+)1:80	
CL (mmol/24H)	213	170-250	Anti-MPO	(+)	
Mg (mmol/24H)	3.17	2.10-8.20	Antinuclear antibodies(ANA)	(+)1:1000	
Na (mmol/24H)	236	130-260	speckled pattern;anti-double stranded DNA antibody (anti-dsDNA)	(+)	
P (mmol/24H)	16.77	22.00-48.00	SS-A(52) antibody	(+)	
Urine acidification function			SS-A(60) antibody	(+)	
pH	6.8	5.32-6.16	Anti-histone antibody	(–)	
HCO3- (mmol/L)	2.90	0.84-3.54	anti-JO-1antibody	(–)	
titratable acid (TA) (mmol/L)	12.0	13.59-27.93	anti-SCL-70 antibody	(–)	
NH_4- (mmol/L)	15.0	17.66-42.54	anti-ribonucleo protein antibody	(–)	
Blood chemistry			anticentromere B anti-body (ACA)	(–)	
K (mmol/L)	3.11	3.50~5.10	anti- SS-B/La antibody	(–)	
Na (mmol/L)	140.3	137.0~145.0	anti-SmD1 antibody	(–)	
Cl (mmol/L)	108.8	98.0-107.0	anti-ribosomal P protein antibody	(–)	
Ca (mmol/L)	2.20	2.10-2.55	anti-nucleosome antibody	(–)	
P (mmol/L)	1.69	0.81-1.45	human immunoglobulin (Ig)G (g/L)	25.46	7.60–16.60
Mg (mmol/L)	0.67	0.70-1.00	human immunoglobulin (Ig)A (g/L)	3.01	0.71–3.35
HCO3- (mmol/L)	19.00	20.0-30.0	human immunoglobulin (Ig)M (g/L)	0.99	0.48–2.12
Fasting blood glucose (mmol/L)	5.39	3.89-6.11	Total serum immunoglobulin E (mIU/ml)	13	0–100
CPK (μ/L)	19	26~140	Complement C3 (g/L)	0.51	0.87–1.41
CKMB (μ/L)	18	0~24	Complement C4 (g/L)	0.06	0.10–0.40
ALT (μ/L)	39	7~40	ASO (IU/ml)	30	0–200
AST (μ/L)	37	13~358	rheumatoid factor(RF) (IU/ml)	13.0	0.0–14.0
LDH (μ/L)	156	109~245	u-hs CRP (mg/L)	16.62	0.00–3.00
BUN (mmol/L)	6.56	3.20~7.10	ESR (mm/h)	90	0–20
CRE (μmol/L)	84.0	44.0~99.0			
T_3 (nmol/L)	11.8	0.92-2.79			
T_4 (nmol/L)	363.20	58.10-161.30			
FT_3 (pmol/L)	21.70	3.50-6.50			
FT_4 (pmol/L)	75.60	11.50-22.70			
TSH (μIU/ml)	0.007	0.550-4.780			
Thyroglobulin (ng/ml)	7.10	1.70-55.60			

nervous system examination was normal, and the systemic examination was otherwise unremarkable. The laboratory results were shown in Table 1. The stool routine was normal. The flow of tears and saliva measurement were normal. The laboratory tests revealed RTA.

Radionuclide imaging showed diffuse thyroid lesions (Figure 1). The thyroidal 99mTc uptake was 14 percent (normal 0.24–3.34%) at 30 minutes. The USG abdomen revealed kidneys were normal in size with no evidence of renal calcification. After receiving informed consent of the patient, we performed a renal biopsy. The light microscopy and immunofluorescence showed diffuse proliferative lupus nephritis (Figures 2 and 3). The bone marrow aspirate revealed hyperplasia of grain was obvious and hyperplasia of red tie reduced. The bone marrow biopsy showed there were erythrocytosis, guanulocytosis and thrombocytosis in bone marrow.

Patient started on oral potassium supplements concurrently with radioactive iodine to treat early hyperthyroidism. Metabolic acidosis was corrected with bicarbonate supplements. The corticosteroids was used in combination with immunosuppressive agents.

DISCUSSION

Systemic lupus erythematosus (SLE) is an autoimmune condition heterogeneous from a clinical and immunological point of view, and it is with variable and unpredictable course, intermingled with periods of flares and remission (Chan *et al.* 2013). This female patient was diagnosed with SLE in accordance with the criteria of the American College of Rheumatology (2009) (Petri 2009): i) Polyarthritis, ii) leucopenia, iii) renal involvement, iv) positive for antinuclear antibodies (ANA+), v) positive for anti-dsDNA. The thyroid function abnormalities and thyroid auto antibodies have been frequently described in patients with systemic rheumatologic autoimmune diseases such as SS, rheumatoid arthritis, SLE and SSc (Antonelli *et al.* 2010). A recent study showed that there was a greater prevalence of the association between AITD and rheumatic diseases which highlighted the possibility of common pathogenic mechanisms among them (Robazzi & Adan 2012).

Many studies underlined the importance of a common genetic susceptibility in AITD patients and systemic autoimmunity. Genetic influence was suggested in a study of 35 families with several cases of SLE concomitant with AITD, in which a gene of susceptibility was identified in 5q14.3-q15 (major locus of susceptibility for SLE and it was also found in AITD).This locus can be shared by patients with SLE and AITD, evidencing a potential genetic link between both diseases (Namjou *et al.* 2005).

Recent reports have shown that the serum and/or the tissue expressions of CXCL10 increased in organ specific autoimmune diseases such as AT, GD, T1D and/or systemic rheumatological disorders like RA, SLE, SSc MC, underlining the importance of a common immunopathogenesis of these disorders, characterized by a Th1 prevalent autoimmune response in the initial, and/or active phases of these diseases (Antonelli *et al.* 2014).

Distal renal tubular acidosis (dRTA) is caused by inability of the kidney collecting duct to acidify urine (Unwin *et al.* 2002). dRTA may be inherited or acquired by drugs, hypercalciuria, or an underlying autoimmune disorder. The condition has been reported in various autoimmune disorders including Sjögren's syndrome, primary biliary cirrhosis, autoimmune hepatitis, systemic lupus erythematosus, and rheumatoid arthritis (Rodriguez 2002). Although our patient had anti-Ro antibodies, she did not meet the criteria for Sjögren's syndrome for she had anti-Ro antibodies and the Sjögren's syndrome might manifest itself at a later stage. The reason of dRTA caused by these autoimmune disorders is not well known. Cases of RTA-associated hyperthyroidism were reported previously (Huth *et al.* 1959; Krane *et al.* 1956). The mechanism underlying this association is unclear.

Most cases of hypokalemic are caused by a single disease. However, in our patient, hypokalemic was not only caused by hyperthyroidism but also by distal RTA. Metabolic acidosis was coexistent with renal potassium loss. It has been suggested that hyperthyroidism causes RTA by disturbing calcium metabolism and thus causes nephrocalcinosis (Huth *et al.* 1959; Mason & Golding 1970). As our patient did not exhibit nephrocalcinosis, the possibility that hyperthyroidism contributed to the disturbance in calcium metabolism seems unlikely. The development of RTA after hyperthyroidism indicates it is more likely that an autoimmune mechanism is responsible for the association between RTA and hyperthyroidism. Further investigations of the causes of these effects are warranted. The long-term loss of potassium-can causes denaturalization and necrosis emerges in the epithelial cell of renal tubule. The hyposthenuria leads to nocturia.

We conclude that patients with hyperthyroidism, especially female ones with atypical metabolic features, should be investigated for possible precipitating factors.

Conflict of interest: *The authors declare that they have no conflict of interest.*

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