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Two Cases of Hypothyroidism Complicated by Renal Dysfunction

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ABSTRACT

We report two patients in whom hypothyroidism was considered to cause renal dysfunction. Case 1 was a 65-year-old woman who stopped taking levothyroxine sodium for hypothyroidism. After 6 months, she developed proteinuria, edema, weight gain, and renal dysfunction. Renal biopsy revealed focal segmental proliferative glomerulonephritis. After re-administration of levothyroxine sodium, thyroid function and renal function both recovered. Case 2 was a 51-year-old man who presented with edema, difficulty in swallowing, muscular weakness, and fatigue. We diagnosed hypothyroidism, and focal segmental proliferative glomerulonephritis was revealed by renal biopsy. After administration of levothyroxine sodium, his symptoms resolved and his thyroid function and renal function both improved. Our experience suggests that hypothyroidism should be taken into consideration as one of the causes of renal dysfunction.

Key words: *Hypothyroidism, Renal dysfunction, Levothyroxine sodium*

Hypothyroidism is known to cause many complications, with hyperlipidemia, arteriosclerosis, and heart failure being especially important for the prognosis. It also causes renal dysfunction, with a decrease of the glomerular filtration rate (GFR) and renal plasma flow (RPF), alterations of the renal concentration and sodium re-absorption capacity, and sometimes proteinuria[6,10]. However, there have been few reports about renal dysfunction due to hypothyroidism. This is probably because other symptoms of hypothyroidism occur before nephropathy and lead to treatment of the patient.

Here we report two rare cases of hypothyroidism that were left untreated until renal dysfunction appeared.

CASE REPORT

Case 1: The patient was a 65-year-old woman who was diagnosed as having hypothyroidism in 1994 and was treated with levothyroxine sodium, which she stopped taking of her own accord in November 1997. From December 1997, proteinuria, palpebral and cervical edema, weight gain, and renal dysfunction were noted. She was admitted to our hospital for further investigation in June 1998. She had taken analgesic drugs for 10 years because of headache, but had no history of hypertension, diabetes, macroscopic hematuria, or purpura.

On admission, her height was 155.2 cm, her weight was 52.6 kg, and her temperature was 35.7°C. The blood pressure was 134/74 mmHg and the heart rate was 62/min (regular). Her conjunctivae were slightly pale and not icteric. The thyroid gland was slightly enlarged. There was no heart murmur, the lungs were clear, and the abdomen was normal. There was mild ankle edema. Peripheral sensation was mildly reduced. The chest X-ray film showed a cardiothoracic ratio of 46% and the ECG was normal. Intravenous pyelography showed a complete double pelvis on the left side, but no atrophy or vesicoureteral reflux. Her urine was negative for protein, but occult blood was positive. The urine volume was 1100~1450 ml/day. Hematology tests showed that the red blood cell (RBC) count (2.85×10^6/mm^3), hemoglobin (Hb) (10.5 g/dl) and hematocrit (Ht) (31.9%) were decreased. Biochemistry tests showed increases of glutamic oxalacetic transaminase (GOT) (46 U/liter), lactate dehydrogenase (LDH) (717 U/liter), creatine kinase (CK) (1469 U/liter), and myoglobin (173 ng/ml;<61). Total cholesterol (TC) (305 mg/dl), triglycerides (TG) (180 mg/dl), blood urea nitrogen (BUN)(33 mg/dl), creatinine (Cr) (1.32 mg/dl), and β_2-microglobulin (β_2m) (1.94 μg/ml) were also slightly increased. Her creatinine clearance (Ccr) was 54.4 ml/min, the GFR was 40 ml/min, RPF was 212 ml/min, renal blood flow (RBF) was 305 ml/min, and fractional excretion of sodium (FE_{Na}) was 1.41%. Free triiodothyronine (FT_3) was 1.1 pg/ml, free thyroxine (FT_4) was 0.2ng/dl, and thyroid-stimulating hormone (TSH) was 186.2 μU/ml. The antinuclear antibody (ANA) titer was ×320, the anti-microsomal antibody titer was >×409600, the anti-thyroglobulin antibody titer was >×409600, C-reactive protein (CRP) was

<0.3 mg/dl, and the erythrocyte sedimentation rate (ESR) was 41 mm/hr.

Renal biopsy was performed on June 24, 1998. One of the 14 glomeruli obtained showed global sclerosis, while the other 13 glomeruli had focal and segmental mild mesangial cell proliferation and matrix expansion. Adhesions were present in 3 of the 13 glomeruli, but no crescents were found. Capillary tufts were normal. Tubular atrophy, tubular necrosis, and interstitial fibrosis, edema, and inflammatory cell infiltration were all mild. Immunofluorescence studies failed to detect immunoglobulin (Ig) G, IgA, IgM, C3, C4, or fibrinogen. Electron microscopy revealed no electron dense deposits in the glomerulus. Therefore, a diagnosis of focal segmental proliferative glomerulonephritis was made.

After admission, she was given 25μg/day of levothyroxine sodium and the dose was increased gradually. Her thyroid function and renal function both improved (FT_3 to 2.1 pg/ml, FT_4 to 1.5 ng/dl, TSH to 4.16μU/ml, BUN to 19 mg/dl, Cr to 0.84 mg/dl, and Ccr to 67.2 ml/min) (Fig. 1).

Case 2: The patient was a 51-year-old man who had been in good health. He became aware of palpebral edema and edema of the upper limbs in April 1998. He consulted a local doctor and was diagnosed as having renal dysfunction, but there were no abnormalities on urinalysis. At the end of April, he noted difficulty in swallowing, muscle weakness and fatigue, and he was referred to our hospital on May 22, 1998. We treated him with 50μg/day of levothyroxine sodium and he was admitted to hospital for further investigation on June 25, 1998. His father had diabetes, but there was nothing else in the family history.

On admission, his height was 174.7 cm, his weight was 67.6 kg, and his temperature was 36.5°C. The blood pressure was 120/68 mmHg, and the heart rate was 66/min (regular). His conjunctivae were not pale or icteric. The thyroid gland was slightly enlarged. There was no heart murmur, the lungs were clear, and the abdomen was normal. There was no peripheral edema and sensory function was normal. The chest X-ray film showed a cardiothoracic ratio of 51.2% and the ECG was normal. Intravenous pyelography showed small areas of calcification in the right kidney, but no renal atrophy. Ultrasonography of the thyroid gland showed a low internal echo. Urinary protein was equivocal and occult blood was negative. The urine volume was 1400~1900 ml/day. His WBC count (9800/mm^3) was slightly increased. Biochemistry tests showed an increase of GOT (75 U/liter), glutamic pyruvic transaminase (50 U/liter), LDH (603 U/liter) and CK (1163 U/liter). Myoglobin (37 ng/ml) was normal, but TC (273 mg/dl), BUN (22 mg/dl), Cr (1.32 mg/dl) and uric acid (7.6 mg/dl) were slightly increased. In addition, Ccr was 48.7 ml/min, GFR was 68 ml/min, RPF was 222 ml/min, RBF was 366 ml/min, FENa was 0.68%. His FT_3 level was 1.1 pg/ml, FT_4 was 0.1 ng/dl, and TSH was 125.1μU/ml. ANA was <×80, the anti-microsomal antibody titer was

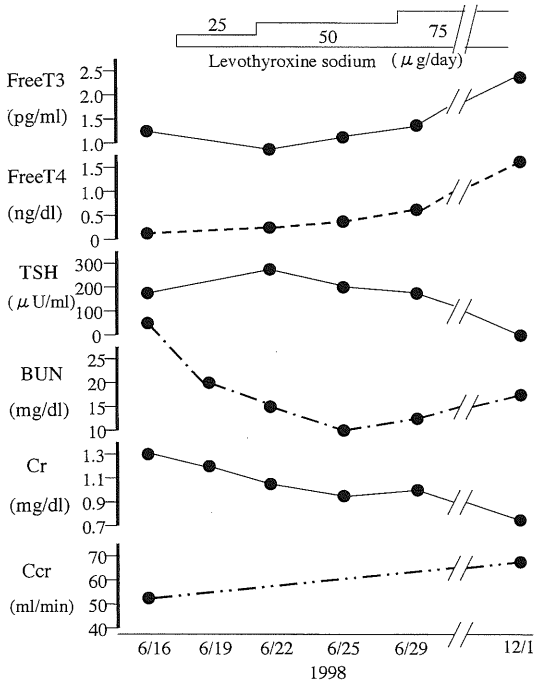

Fig.1. Clinical course of case 1.
After re-administration of levothyroxine sodium, thyroid function and renal function both improved.

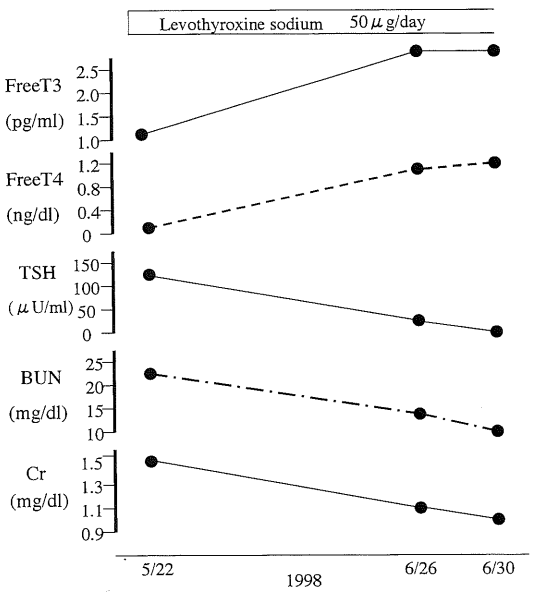

Fig.2. Clinical course of case 2.
After administration of levothyroxine sodium, thyroid function and renal function both improved.

>409600, anti-thyroglobulin antibody titer was ×400, CRP was <0.3 mg/dl, and ESR was 10 mm/hr.

Renal biopsy was performed on July 1, 1998. Three of the 18 glomeruli showed global sclerosis, two of the remaining 15 glomeruli showed segmental matrix expansion, and 3 showed segmental mesangial cell proliferation. Adhesions were present in 2 out of 15 glomeruli, but crescents were not found and capillary tufts were normal. The tubules and interstitium were also normal. Immunofluorescence studies were negative for IgG, IgA, IgM, C3, C4, and fibrinogen. Electron microscopy revealed no electron dense deposits in the glomerulus. A diagnosis of focal segmental proliferative glomerulonephritis was made from these findings.

After admission, he was continued on 50μg/day of levothyroxine sodium. Subsequently, his symptoms of difficulty in swallowing, muscle weakness, and fatigue had resolved, and thyroid function and renal function both showed an improvement (FT_3 2.7 pg/ml, FT_4 1.0 ng/dl, TSH 24.2μU/ml, BUN 12 mg/dl, and Cr 1.06 mg/dl)(Fig. 2).

DISCUSSION

With respect to renal dysfunction arising secondary to hypothyroidism, many points are still unclear. Some authors have suggested that hemodynamic changes are a cause of renal dysfunction, since cardiac output is decreased by hypothyroidism and this may reduce RPF and GFR[4]. In fact, both RPF and GFR were decreased in our two patients. Because of the generalized decrease in metabolism due to hypothyroidism, acidic mucopolysaccharides may accumulate in the glomeruli and the tubulo-interstitial region[1]. Thickening of the glomerular and tubular basement membranes and the presence of hyaline droplets in the epithelial cells, tubular cells, and intertubular connective tissue have been seen on light microscopy, as well as thickening of the basement membrane and an increase of mesangial matrix on electron microscopy[2,7]. There were no specific deposits detected by Sudan III, Alcian blue staining or electron microscopy in our two patients. It has also been suggested that abnormal muscle metabolism and mobilization of muscular enzymes and myoglobin may cause renal tubular obstruction, as occurs with rhabdomyolysis[9].

However, renal dysfunction associated with hypothyroidism is usually mild[8] and not all hypothyroid patients develop renal impairment. If we look at other possible causes in our two cases, some influence of chronic analgesic therapy can be considered in case 1. In case 2, it is conceivable that prerenal factors were involved because FENa was less than 1%. Multiple factors that impair renal function may eventually result in overt renal dysfunction. However, hypothyroidism was one of the causes, because improvement of thyroid function by administration of levothyroxine sodium relieved the symptoms of our patients and renal function was improved simultaneously.

It is unclear how far renal function would have deteriorated if hypothyroidism had not been treated in our patients, but it is impossible to investigate clinically whether end-stage renal failure would occur or some lesser degree of impairment. There is another view that the increase of serum creatinine is secondary to increased production of creatinine in patients with hypothyroidism[5].

There have also been reports[3] that renal failure is associated with thyroid function because of suppression of conversion from T_4 to T_3, a decline of affinity for thyroxine-binding globulin (TBG), and suppression of the production of TBG.

In both of our patients, hypothyroidism and renal function were improved by levothyroxine sodium therapy. Accordingly, hypothyroidism should be taken into consideration as one of the possible causes of renal dysfunction.

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