A rare cause of acute kidney injury: hypothyroidism

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Akut böbrek hasarının nadir bir nedeni: Hipotiroidizm

Abstract: Kidneys and thyroid are two basic organs that interact with each other, and when one of them becomes ill, functions of the other are affected. Although electrolyte disturbances are the most common symptoms reported due to hypothyroidism, some are case reports in the literature suggested that acute kidney injury developed due to hypothyroidism. Despite this, we doubt that this information comes into mind in routine clinical practice. To report a case of reversible hypothyroidism-induced acute kidney injury, and review those two clinical conditions, which are often overlooked in the nephrology practice, in the light of the literature. We reported a 75-year-old female patient who admitted for acute kidney injury associated with deep hypothyroidism, required hemodialysis, and underwent a renal biopsy since no etiological factors were detected for acute kidney injury. We emphasized that the patient’s creatinine concentrations gradually returned to normal following hormone replacement therapy. Renal dysfunction in presence of hypothyroidism is a known, but frequently overlooked entity. Hypothyroidism should not be overlooked as the cause of reversible kidney injury since it is easy to treat, and there is almost complete response to treatment in terms of renal failure.

Keywords: Acute kidney injury, Hypothyroidism, Thyroid hormone replacement

1 Introduction

Both hyper- and hypothyroidism affect functions of various organs including heart, brain and muscles. However, hypothyroidism is often overlooked in the etiology of renal dysfunction. It has been known that thyroid hormones affect renal functions. Thyroid dysfunction may lead to alterations in renal blood flow, glomerular filtration rate (GFR), and tubular renal functions, and it also causes structural changes in kidneys [1–3]. It has been known that the serum creatinine concentration increases in case of hypothyroidism, it reduces after L-thyroxin administration, and this is
more obvious in the elderly [4]. Acute kidney injury (AKI) associated with hypothyroidism is rare, and although there are several case reports in the literature concerning such an association, we doubt that this information comes into mind in routine clinical practice.

In this paper, we aimed to present this rare clinical condition in the light of the literature. We presented a case that was followed up with the diagnosis of AKI and diagnosed with deep hypothyroidism, and emphasized that her serum creatinine concentrations reduced significantly following thyroid hormone replacement.

2 Case Report

A 75-year-old female with the history of diabetes mellitus for 5 years, and hypertension for 10 years presented with weight gain, edema, and asthenia over the previous 4–5 months. Her serum creatinine concentration had been measured as 80 µmol/L two months ago on a routine check-up, but her creatinine concentration was 539 µmol/L on admission to hospital with aforementioned complaints. She was admitted to nephrology clinic with diagnosis of AKI. Her history revealed that she was on thyroid hormone replacement due to hypothyroidism, but she had not been taking her medications over previous three months. Her physical examination showed a blood pressure of 120/70 mmHg, a peak heart rate of 60/minute, and a body temperature of 37°C. On chest auscultation, she had reduced breath sounds at inferior pulmonary regions bilaterally, and her cardiac examination revealed muffled cardiac sounds. Non-pitting pretibial edema was evident in both lower extremities. Examination of fundus oculi indicated grade 1 hypertensive retinopathy. Blood test results were as follows: Urea 49 mmol/L, creatinine 672 µmol/L, sodium 133 mmol/L, potassium 3.96 mmol/L, total protein 56 g/L, albumin 31 g/L, creatinine kinase (CK) 75 U/L (26–140 U/L), TSH >100 mIU/L (0.34–5.6 mIU/L), free T4 <2.5 pmol/L (7.8–19 pmol/L), free T3 <0.1 pmol/L (0.03–0.06 pmol/L), erythrocyte sedimentation rate 61 mm/h, hemoglobin 12.4 g/dL, and white blood cell count 9.2x10⁹/L (Table 1). Other hematologic and biochemical parameters were normal. Twenty-four-hour protein excretion was 5.6 g, and her urine sediment was normal. Anti-nuclear antibody, peripheral and cytoplasmic anti-neutrophil cytoplasmic antibody, anti-double-stranded DNA antibodies, anti-glomerular basal membrane antibody, rheumatoid factor, and cryoglobulins were all negative. Serum and urinary immunofixation electrophoresis did not show any monoclonal gammopathies. Her renal ultrasonography (USG) demonstrated normal kidney size and echogenicity. Renal arterial and venous color Doppler USG did not demonstrate any stenoses in the renal arteries or veins. Concentrations of thyroid autoantibodies were high: anti TPO was 528 IU/mL (0–9 IU/mL), and anti TG was 263.8 IU/mL (0–4 IU/mL). The thyroid USG was compatible with chronic thyroiditis.

The patient was diagnosed with Hashimoto’s thyroiditis, administered 50 µg/day L-thyroxine due to hypothyroidism, and then the dose gradually increased to 150 µg/day. Because creatinine concentrations did not decrease during follow-up and there was no obvious cause for AKI, a renal biopsy was obtained to distinguish glomerular and tubular proteinuria. Renal biopsy revealed that three of 10 glomeruli had segmental sclerosis, and other glomeruli were normal (Fig. 1). There were no abnormalities other than mild regenerative changes of the tubules in the interstitium, and patch-like focal mononuclear cell infiltration (Fig. 2). The patient was hemodialyzed every other day for two weeks due to metabolic acidosis refractory to treatment. During follow-up, the patient’s urinary output increased, edema diminished, and metabolic acidosis improved, and she did not need hemodialysis anymore. After 8 weeks of thyroid hormone replacement, her TSH was 5.76 mIU/L, and her creatinine concentration reduced to 106 µmol/L. The patient was discharged from the hospital.

3 Discussion

Functional interaction of kidneys and thyroid gland has been known for years. Renal diseases cause thyroid dysfunction, and thyroid dysfunction affects renal physiol-
ogy. Patients with kidney injury may simultaneously have hypothyroidism, but it is rarely the underlying cause. However, questions for hypothyroidism is not included in the routine history in patients with renal dysfunction.

Hyperthyroidism causes predisposition to glomerular hyperfiltration, direct kidney injury, and proteinuria, and results in increased oxidative stress contributing to progression of chronic kidney injury [3]. Physiological effects of hypothyroidism often occur together with fluid and electrolyte imbalance, and particularly with hyponatremia. Although the underlying cause of hypothyroidism is not clear in case of AKI, the major factor considered is reduced GFR associated with hypodynamic circulation and reduction in plasma flow. Hypothyroidism reduces cardiac output with its negative chronotropic and inotropic effects, and it increases systemic and renal vascular resistance resulting in intrarenal vasoconstriction. Therefore it adversely affects renal hemodynamics [5–7], and results in a reduced GFR. Hypothyroidism results in hyponatremia due to reduced free water clearance and reduced sodium reabsorption, and contributes development of proteinuria by increasing glomerular capillary permeability [4,8]. Presence of proteinuria contributes to a reduction in GFR [8]. Clinical presentation of our patient was consistent with the aforementioned data, and she had moderate hyponatremia and proteinuria at the nephrotic level. We do not have any facilities in our center to differentiate glomerular and tubular proteinuria, however renal biopsy of the patient did not reveal any glomerular pathologies that could explain proteinuria.

A significant correlation was reported between TSH and serum creatinine concentrations, and it was reported that worse is the thyroid dysfunction, higher is the risk for developing kidney injury [9]. A significant improvement was observed in GFR after thyroid hormone replacement in patients with hypothyroidism and chronic kidney disease [10]. Mooraki et al. reported that serum creatinine concentration returned to normal after administration of levothyroxine for 6–12 weeks, in four patients with hypothyroidism and AKI [11]. In our case, serum creatinine concentration on admission was 7.6 mg/dl, but it decreased to 1.2 mg/dl 2 months after starting levothyroxine therapy.

There are scarce reports in the literature concerning presence of AKI secondary to hypothyroidism-induced rhabdomyolysis [12,13]. Rhabdomyolysis causes a reversible increase in serum creatinine concentration. Demonstrating an increased CK is the gold standard test in rhabdomyolysis. However, rhabdomyolysis was not evident in our case, and muscle enzymes were in normal limits. Renal biopsy may reveal histopathological changes in presence of hypothyroidism, including a thickened glomerular basal membrane, deposition of thyroglobulin in glomerular basal membrane, and dilation of mesangial matrix, which contribute to reduced GFR [14]. However in our case, light and electron microscopic examinations of renal biopsy did not show any thickening in glomerular or tubular basal membranes, or extracellular deposition of any amorphous material having the characteristics of thyroglobulin.

We do not have enough evidence to determine the time needed for development of renal dysfunction after hypothyroidism, or reversibility of renal functions after adequate hormone replacement. In a case report, it was stated that although hypothyroidism improved after thyroid hormone replacement, renal functions did not return to normal [15]. However, most publications reported that renal functions returned to normal after adequate thyroid hormone replacement. It is not known whether a long-lasting, untreated hypothyroidism would result in
chronic kidney injury.

Despite all this information, thyroid functions are usually overlooked while evaluating the patients with renal dysfunction. Both nephrologists and endocrinologists should remember that hypothyroidism is an important factor in the etiology of AKI.

In conclusion, renal dysfunction and hypothyroidism are frequently associated, and hypothyroidism should not be overlooked as the cause of reversible kidney injury since it is easy to treat, and there is almost complete response to treatment in terms of renal failure.

Conflict of interest: None declared.

4 References