Case Report

Acute Kidney Injury After Thyroid Hormone Withdrawal in an Adolescent with Papillary Thyroid Carcinoma

Short Title: Thyroid Carcinoma and Acute Kidney Injury

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What is already known on this topic?
Differennated thyroid cancer is the most common type of thyroid cancer in children. The standard surgical treatment is total thyroidectomy. Radioactive iodine (RAI) therapy is indicated for patients with pulmonary metastases or small-volume, unresectable residual cervical disease. During RAI therapy, having TSH above 30 mIU/mL facilitates uptake. It can usually be achieved by thyroid hormone withdrawal (THW) for ≥14 days in children.

What this study adds?
Patients who have undergone thyroidectomy may experience creatine kinase (CK) elevation and acute kidney injury may occur as a result of THW prior to RAI treatment. Kidney function tests and CK levels should be assessed in cases with THW and dehydration should be prevented.

Abstract
Objectives: We report a patient with papillary thyroid carcinoma (PTC) who developed acute kidney injury (AKI) and elevated creatine kinase (CK) after thyroid hormone withdrawal (THW) prior to radiiodine therapy.

Case presentation: A 12-year-old female patient who had undergone total thyroidectomy for PTC one year ago presented with leg pain for the past 2 days. Following THW 3 weeks ago, the case had received 70 mCi radioiodine treatment 6 days ago. Serum creatinine (1.53 mg/dL, normal range [NR]: 0.3-1.1), aspartate aminotransferase (102 IU/L, NR: 0-40) and CK (3451 IU/L, NR: 26-174) levels were elevated. Thyrotropin level was elevated (>100 µIU/mL, NR: 0.51-4.3), and free T4 level was decreased (0.05 ng/dL, NR: 0.98-1.63). Serum creatinine and CK levels decreased after intravenous hydration and levothyroxine treatment.

Conclusion: In PTC cases with thyroidectomy, kidney function and CK elevation should be assessed after THW and dehydration should be prevented.

Keywords: Papillary Thyroid Carcinoma, Thyroid Hormone Withdrawal, Rhabdomyolysis, Acute Kidney Injury, Radioactive Iodine Therapy

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Introduction
Differennated thyroid cancer (DTC) is the most common thyroid cancer in children. A previous history of radiotherapy used in treatment regimens for other malignancies is a risk factor for the development of thyroid cancer (1). Less than 2% of thyroid cancers develop in childhood (2). Thyroid cancer is most common in females aged between 15 and 19 years in the pediatric and adolescent population (1,2). Papillary thyroid carcinoma (Bc) is a subtype of DTC, accounts for 90% of pediatric cases. At the time of diagnosis, approximately 50% of children with PTC have a cervical lymph node metastasis (1).

Total thyroidectomy is the standard surgical approach for pediatric DTC due to the higher frequency of bilateral or multifocal involvement in children compared to adults (3). In cases with central cervical lymph node involvement, central lymph node dissection should be performed along with total thyroidectomy (2). Radioactive iodine (RAI) therapy is indicated for patients with pulmonary metastases or small-volume, unresectable residual cervical disease (2,3). During RAI therapy, having thyrotropin (TSH) levels above 30 mIU/mL facilitates uptake. It can usually be achieved by thyroid hormone withdrawal (THW) for ≥14 days in children (3).

In patients with DTC, short-term hypothyroidism during THW causes an increase in serum creatinine levels of approximately 30%. Thyroid hormones have direct and indirect effects on the cardiovascular system and the hemodynamic conditions in the kidney. The decrease in cardiac output and increase in peripheral resistance seen in hypothyroidism decreased renal blood flow. Decreased renal perfusion and glomerular filtration rate (GFR) lead to decreased water excretion and increased creatinine levels (4).

Hypothyroidism may lead to rhabdomyolysis. The diagnosis of rhabdomyolysis is based on medical history and laboratory findings. For the diagnosis of rhabdomyolysis, the serum creatine kinase (CK) level should be greater than 5 times the upper limit of normal or greater than 1000 U/L and the serum myoglobin >150 ng/mL. Acute kidney injury (AKI) is a common and serious complication of rhabdomyolysis. It has been reported that 13%-46% of patients with rhabdomyolysis develop AKI. Rhabdomyolysis causes kidney damage due to fluid sequestration in injured skeletal muscle, activation of the renin-angiotensin system and sympathetic nervous system, antiuretic hormone release, and renal vasoconstriction. Acute kidney injury is thought to be the result of salt and water retention and tubular damage due to myoglobin-induced oxidative damage (5).

We report a patient with PTC who developed AKI and elevated CK after THW prior to RAI therapy.

Case Report
A 12-year-old female patient who had undergone total thyroidectomy and cervical lymph node dissection for PTC one year ago presented with leg pain for the past 2 days. She had received L-thyroxine and cholecalciferol treatment for iatrogenic hypothyroidism after the operation. Following THW for 3 weeks, she received 70 mCi radiiodine treatment 6 days ago. No infections, metabolic disorders, or recent medication use were noted in her medical history. Physical examination revealed tenderness in the thigh muscles without other symptoms.
In hypothyroidism, reduced cardiac output leads to reduced renal blood flow and prerenal AKI (3). When muscle cells break down, they release myoglobin into the bloodstream and in cases of significant muscle damage, the kidneys may struggle to handle the increased load of myoglobin. High concentrations of myoglobin in the kidneys can lead to acute tubular necrosis the combination of the direct toxic effects of myoglobin and the obstruction of renal tubules (5). On the other hand, kidney function is important for iodine excretion (3). Adequate hydration is required to increase 131I clearance which can be hazardous for the renal tubules if clearance is decreased. Therefore, if necessary, additional super-thrive care with stool softeners, laxatives, and antidepressants may be considered to increase 131I clearance (3). In addition, the effect of 131I on the renal tubules has been associated with early complications of RAI therapy. These include radiation thyroiditis, xerostomia, ocular dryness, taste changes, sialadenitis, nausea, and vomiting which may increase the degree of dehydration (1,3). We speculate that AKI may be due to tubular damage associated with rhabdomyolysis as a result of THW and possible 131I toxicity due to dehydration (9,13).

The main goal in the management of rhabdomyolysis is the preservation of kidney function and prevention of AKI. Early recognition is important to prevent AKI, and treatment consists of aggressive intravenous fluid resuscitation with correction of electrolyte abnormalities. Adjunctive therapies including the urinary alkalization of urine, diuretics, and continuous renal replacement therapy have been discussed; but the benefits of these treatment modalities are controversial (5). Increased serum creatinine and CK levels can be reversed together with thyroid replacement therapy and intravenous fluid resuscitation (9).

Data on the use of recombinant human thyrotropin (rhTSH) in children are limited. It is reported that rhTSH is clinically safe and provides adequate TSH stimulation in children with differentiated thyroid cancer (14). However, its use is recommended in adults with endogenous TSH deficiency (14). Despite this, rhTSH treatment causes a significant transient decrease in transient kidney function by reducing GFR, rhTSH injection is recommended for the preparation of RAI therapy (9).

**Conclusion**

Complications of short-term THW include cognitive, cardiovascular, affective, renal clearance, and lipid abnormalities. A significant complication of rhabdomyolism is rhabdomyolysis and associated AKI. Kidney function and CK level should be assessed in cases of AKI. Recombinant human TSH can be used in selected patients instead of THW, despite insufficient evidence from the use in the pediatric and adolescent population.

**Ethics**

**Informed Consent:** Informed consent was obtained from the parents of the patient for publication of this case report.

**Acknowledgment:** The authors have no conflicts of interest to declare.

**References**


Figure 1. Serum creatinine, CK and AST levels of the patient decreased dramatically after thyroid hormone and intravenous fluid replacements

(CK: Creatine kinase, AST: Aspartate aminotransferase, hr: hour)