

Adolescent with Hypothyroidism Induced Rhabdomyolysis and Acute Kidney Injury

Mohamed Hamed Abbas*, Ayman Maher Nagib, Mahmoud Mohamed Khaled and Ahmed Farouk Donia

Department of Dialysis and Transplantation, The Urology Nephrology Center, Mansoura University, Egypt

Abstract

Objectives: Rhabdomyolysis is a potentially life-threatening syndrome. Hypothyroid patients may present with myopathy and mild elevation of CK levels; however, overt rhabdomyolysis is extremely rare, and few cases have been described. Hypothyroidism should be considered in patients presenting with renal impairment associated with rhabdomyolysis.

Case report: A 24-year-old young man with accidentally discovered hypothyroidism on admission presented with generalized myalgia, profound proximal muscle weakness of the bilateral lower extremities, anuria, vomiting and dark colored urine lasting for three days. Neurological examination revealed bilateral marked weakness and tenderness of muscles of both lower and upper extremities. Urine had dark red appearance and urinalysis showed blood reaction with dipstick test, but there were no erythrocytes on microscopic examination. Serum creatine phosphokinase and myoglobin levels were elevated. Thyroid stimulating hormone (TSH) levels were high, and Free Thyroxine (T4) and Triiodothyronine (T3) levels were low, renal function tests showed acute kidney injury. Other causes of rhabdomyolysis such as muscular trauma, drugs, toxins, infections, vigorous exercise, and electrolyte abnormalities were excluded. Hemodialysis was administered for five sessions. After L-thyroxine therapy, thyroid function tests normalized, muscle strength improved, serum muscle enzyme levels returned to normal levels, and renal function tests recovered.

Conclusion: Hypothyroidism should be considered in patients presenting with renal impairment associated with rhabdomyolysis.

Keywords: Acute kidney injury; Rhabdomyolysis; Hypothyroidism

Introduction

Rhabdomyolysis is a potentially life-threatening syndrome characterized by muscle necrosis and the release of intracellular muscle contents into the circulation. The etiology of rhabdomyolysis can be classified into traumatic and nontraumatic causes. The latter is associated with alcohol and drug abuse, seizures, strenuous exercise, muscle hypoperfusion, hyperthermia, electrolyte disturbances, diabetic coma, severe infection and hypothyroidism, among others [1]. Nontraumatic rhabdomyolysis is elusive; it often occurs without symptoms and is diagnosed when creatine kinase (CK) levels are elevated in the initial stages of the disease. Acute kidney injury (AKI) and severe electrolyte derangements are life threatening, and are accompanied by extreme elevations in CK levels [2]. Hypothyroid patients may present with myopathy and mild elevation of CK levels; however, overt rhabdomyolysis is extremely rare, and few cases have been described [3]. Hypothyroidism should be considered in patients presenting with renal impairment associated with rhabdomyolysis and emphasize that the causes of hypothyroidism warrant further investigation [4]. We report a rare presentation of AKI secondary to hypothyroidism-induced rhabdomyolysis.

Case Report

A 24-year-old young man presented with generalized myalgia, profound proximal muscle weakness of the bilateral lower extremities, anuria, vomiting and dark colored urine lasting for three days. Previous medical history revealed bronchial asthma with family history of Diabetes mellitus, hypertension and hypothyroidism with irrelevant surgical history and no special habits of medical importance. His physical examination revealed height of 180 cm (+1.39 SD) and weight of 96 kg (+2.9 SD). He was afebrile and had a normal heart rate (80 beats/min) and blood pressure (130/90 mmHg). There was a mild pretibial pitting edema; Neurological examination revealed bilateral marked weakness and tenderness of muscles of both lower and upper

extremities. Other systemic examination findings were unremarkable. His urine was dark red in appearance and urine analysis showed blood reaction with dipstick test, but there were no erythrocytes on microscopic examination.

Laboratory investigations were as follows: Serum creatinine 13 mg/dl (0.2–1.0 mg/dl), sodium 130 mEq/L (135–145 mEq/L), potassium 4.1 mEq/L (3.5–5.0 mEq/L), uric acid 13.1 mg/dl (2.7–5.7 mg/dl), phosphorus 6.6 mg/dl (2.9–5.4 mg/dl), total protein 7.1 g/dl (6.6–8.7 g/dl), albumin 3.6 g/dl (3.4–4.8 g/dl), Creatine phosphokinase (CPK) 40,000 U/L (5–130 U/L), Lactate dehydrogenase (LDH) 1919 U/L alanine aminotransferase (ALT) 133 U/L (0–41 U/L), aspartate aminotransferase (AST) 225 U/L (0–40 U/L), serum myoglobin >3000 ng/ml (25–58 ng/ml), Urine myoglobin 481 mg/dl, thyroid stimulating hormone (TSH) 16.08 uIU/ml (0.4–4.8 uIU/ml), free thyroxine T4 0.72 ng/dl (0.85–1.78 ng/dl), and free triiodothyronine T3 0.69 pg/ml (1.57–4.71 pg/ml). Hemoglobin, white blood cell and platelet counts were in normal ranges. Antinuclear antibodies (ANA), Anti-double-stranded DNA (Anti-dsDNA), Anti Jo 1 antibodies were negative. Hepatitis C virus Antibodies (HCV Ab), hepatitis B surface antigen (HBsAg) and human immunodeficiency virus (HIV) IgM and IgG were negative. Thyroid ultrasonography revealed normal shape, size and echo pattern of both lobes with multiple minute hypoechoic nodules.

***Corresponding author:** Mohamed Hamed Abbas, The Urology Nephrology Center, Mansoura University, Egypt, Fax: 0020502263717; Email: dr_hamed_414@yahoo.com

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	0 day	1 st day	2 nd day	3 rd day	4 th day	5 th day	6 th day	7 th day	8 th day	9 th day	10 th day	11 th day	12 th day	13 th day	14 th day	15 th day	4 th wk
S.Cr (mg/dl)	13	12	9	10	12	14	10	8.7	6.5	5.2	4.1	3.1	2.4	1.9	1.5	1	1
CPK (U/L)	40.000	22092	6902	6316	6046	4040	3093	2234	1860	-	-	-	-	-	-	-	219
LDH (U/L)	1919	621	608	576	626	598	544	509	300	-	-	-	-	-	-	-	-

0 day: on admission; Wk: Weeks; CPK: Creatine Phosphokinase; S.Cr: Serum Creatinine; LDH: Lactate Dehydrogenase.

Table 1: Main laboratory results on admission and during the follow-up.

Renal ultrasonography revealed increased echogenicity with normal size, shape and corticomedullary differentiation of both kidneys. Other causes resulting in rhabdomyolysis such as muscular trauma, drugs, toxins, vigorous exercise, and electrolyte abnormalities were excluded with history and laboratory investigations.

The patient managed by introduced intravenous infusion of 0.9% sodium chloride (NaCl), and 130 meq/L of sodium bicarbonate via an intravenous line separate from that used for the isotonic saline infusion. However, as he had oligo-anuric AKI and, hemodialysis was started for five daily sessions without ultrafiltration. Urine output was observed, his muscle strength gradually improved; renal functions and serum CPK returned to normal levels within 2 weeks after starting the therapy. Four weeks after beginning L-thyroxine, 100 µg/d, and thyroid function tests normalized. The course of the main laboratory results is shown in Table 1.

Discussion

Our patient presented on admission with acute kidney injury and rhabdomyolysis due to first discovered hypothyroidism. He fulfilled the following Acute Kidney Injury Network proposed diagnostic criteria for AKI: an abrupt (within 48 hours) reduction in kidney function defined by an absolute increase in serum creatinine of ≥ 26.4 µmol/l (0.3 mg/dl), a $\geq 50\%$ increase in serum creatinine (1.5-fold from baseline), or a reduction in urine output (<0.5 ml/kg/h for >6 h). The diagnosis of rhabdomyolysis was primarily based upon the presence of muscle injury and elevated levels of CK, lactate dehydrogenase (LDH), and plasma and/or urine myoglobin. The recovery of clinical signs and renal functions after thyroxine replacement therapy and the lack of other etiologic agents causing rhabdomyolysis suggested that hypothyroidism was the cause of rhabdomyolysis in the present patient.

Until now, AKI secondary to hypothyroidism-induced rhabdomyolysis has rarely been reported. Hypothyroidism is an uncommon, nontraumatic cause of rhabdomyolysis, the exact etiology of which remains unclear. Thyroid hormone deficiency in glycogenolysis and mitochondrial oxidative metabolism has been proposed as a possible explanation [5]. Çomak et al. [6] reported a 13-year-old girl with rhabdomyolysis due to hypothyroidism with poor drug compliance. Cai and Tang [4] retrospectively analyzed five cases of AKI secondary to hypothyroidism-induced rhabdomyolysis. An autoimmune mechanism could also be possible, as has been described for Graves' disease [7]. Gunther et al. [8] reported rhabdomyolysis and delayed gross-motor development in a 23-month-old toddler due to acquired autoimmune hypothyroidism, which recovered after thyroid replacement. Sekine et al. [9] reported a 61-year-old woman with hypothyroidism for seven years who developed rhabdomyolysis and ARF after strenuous walking.

Patients with very severe and longstanding hypothyroidism are more likely to develop concurrent complications, such as muscle injury inducing rhabdomyolysis, which is implicated as a significant cause of AKI. Although the exact mechanisms by which rhabdomyolysis impairs glomerular filtration rate (GFR) are unclear. Some evidence suggests that the mechanisms of renal damage may include: 1) intrarenal

vasoconstriction and ischemia; 2) direct and indirect ischemic tubule injury; and 3) tubular obstruction. Hypothyroidism may aggravate renal ischemia, as hypothyroidism exerts some hemodynamic effects for reducing cardiac output, increasing systemic and renal vascular resistance, and reducing GFR [10]. Hepatic dysfunction may occur because of proteases released from injured muscle cells in one-fourth of cases with rhabdomyolysis [11]. In our patient, ALT and AST were 133 and 225 U/L, respectively, which recovered after appropriate therapy. Renal biopsy not performed as it is not mandatory in the definite diagnosis of rhabdomyolysis [6]. Nontraumatic rhabdomyolysis due to hypothyroidism is clinically obscure, although patients may be asymptomatic for an extended period, the disease can later present at a serious stage, therefore; it is essential to attenuate the severity of rhabdomyolysis by early detection of the underlying cause and comorbid conditions and by prompt therapeutic management. Active thyroid hormone replacement therapy and blood purification are imperative [4].

Conclusion

Hypothyroidism should be considered in patients presenting with renal impairment associated with rhabdomyolysis.

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