

Severe rhabdomyolysis and acute renal failure in an adolescent with hypothyroidism

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SUMMARY: Çomak E, Koyun M, Kılıçarslan-Akkaya B, Bircan İ, Akman S. Severe rhabdomyolysis and acute renal failure in an adolescent with hypothyroidism. *Turk J Pediatr* 2011; 53: 586-589.

Hypothyroidism has been reported rarely as the cause of rhabdomyolysis in adults and children. We present here a non-compliant adolescent with a diagnosis of hypothyroidism who developed rhabdomyolysis and acute renal failure with no additional predisposing factor. A 13-year-old girl with a previous history of hypothyroidism due to thyroid hypoplasia presented with generalized myalgia, malaise, vomiting, and oliguria lasting for three days. Neurological examination revealed bilateral marked weakness and tenderness of muscles of both lower and upper extremities. Urine had bloody appearance and urine analysis 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, compatible with uncontrolled hypothyroidism. Renal function tests showed acute renal failure. Other causes of rhabdomyolysis such as muscular trauma, drugs, toxins, infections, vigorous exercise, and electrolyte abnormalities were excluded. Hemodialysis was administered for 24 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. One must be aware that rhabdomyolysis may develop in a non-compliant patient with hypothyroidism.

Key words: rhabdomyolysis, hypothyroidism, acute renal failure.

Rhabdomyolysis is a systemic metabolic disorder characterized by skeletal muscle necrosis that results in leakage of muscle cell constituents, e.g. myoglobin, into the blood. It is a rare condition with a clinical spectrum ranging from asymptomatic creatinine phosphokinase (CPK) elevation to severe acute renal failure (ARF). It may be due to trauma, vigorous exercise, various viral (influenza A and B, Coxsackievirus, Epstein-Barr virus, herpes simplex virus, parainfluenza, adenovirus, echovirus, human immunodeficiency virus [HIV], cytomegalovirus) and bacterial (leptospirosis, salmonella gastroenteritis) infections, certain drugs, electrolyte disturbances (hyponatremia, hypokalemia, hypocalcemia, hyperosmolar states), inflammatory myopathies, congenital deficiency of muscular enzymes, and endocrine disorders¹⁻⁷. Hypothyroidism has been reported rarely as the cause of rhabdomyolysis in both adults and children³⁻⁶. We present here a non-compliant adolescent

with a diagnosis of hypothyroidism who developed rhabdomyolysis and ARF with no additional predisposing factor.

Case Report

A 13-year-old girl presented with generalized myalgia, malaise, vomiting, oliguria, and red urine lasting for three days. Previous medical history revealed that three years ago she had been diagnosed as hypothyroidism due to thyroid hypoplasia during the investigation of mild motor-mental retardation; however, it was learned that she did not take L-thyroxine therapy regularly. She had no history of trauma, vigorous exercise, infection, or any other medication usage. Her physical examination revealed height of 151 cm (-1.39 SD) and weight of 32 kg (-2.9 SD). She was afebrile and had a normal heart rate (84 beats/min) and blood pressure (120/80 mmHg). There was periorbital and pretibial minimal edema; the

thyroid gland was non-palpable. Neurological examination revealed bilateral marked weakness and tenderness of muscles of both lower and upper extremities. Other systemic examination findings were unremarkable. Her urine was bloody in appearance and urine analysis showed blood reaction with dipstick test, but there were no erythrocytes on microscopic examination. Laboratory investigations were as follows: blood urea nitrogen (BUN) 57 mg/dl (7-18 mg/dl), creatinine 4.5 mg/dl (0.2-1.0 mg/dl), sodium 137 mEq/L (135-145 mEq/L), potassium 5.7 mEq/L (3.5-5.0 mEq/L), uric acid 8.3 mg/dl (2.7-5.7 mg/dl), phosphorus 7.6 mg/dl (2.9-5.4 mg/dl), total protein 6.6 g/dl (6.6-8.7 g/dl), albumin 2.7 g/dl (3.4-4.8 g/dl), CPK 12900 U/L (5-130 U/L), alanine aminotransferase (ALT) 1469 U/L (0-41 U/L), aspartate aminotransferase (AST) 1246 U/L (0-40 U/L), serum myoglobin >3000 ng/ml (25-58 ng/ml), thyroid stimulating hormone (TSH) 43.2 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. Anti-thyroglobulin and anti-microsomal antibodies were negative. Thyroid hypoplasia was detected on ultrasonography (thyroid volume: 1.83 ml; normal: 8.89 ± 2.8 ml)⁸. Renal biopsy revealed myoglobin casts in renal tubules, which was compatible with rhabdomyolysis (Fig. 1). Other causes resulting in rhabdomyolysis such as muscular trauma, drugs, toxins, vigorous exercise, and electrolyte abnormalities were excluded with history and laboratory investigations. Antibodies to cytomegalovirus, Epstein-Barr virus, parvovirus, influenza A and B viruses,

parainfluenza viruses types 1-4, respiratory syncytial virus, adenovirus, Coxsackievirus, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *Legionella pneumophila*, and *Leptospira* were all negative. Brucella and Salmonella agglutination tests were also negative.

We introduced intravenous infusion of 0.9% sodium chloride (NaCl), 20 ml/kg in the first hour, followed by 0.9% NaCl 3000 ml/m²/day. However, as she was anuric, intravenous hydration could be given only for 8 hours. As she had oligo-anuric ARF and hyperpotassemia, hemodialysis was started. Four weeks after beginning L-thyroxine, 100 µg/d, thyroid function tests normalized. Her muscle strength gradually improved; serum muscle enzyme levels returned to normal levels 4 weeks after starting the therapy. Urine output was observed and renal function tests recovered 4 weeks and 2 months after referral, respectively. Renal functions and serum CPK levels were normal during 15 months of follow-up with L-thyroxine therapy. The course of the main laboratory results is shown in Table I.

Discussion

The patient presented here had rhabdomyolysis due to hypothyroidism with poor drug compliance. She had been definitively diagnosed as hypothyroidism previously; the clinical manifestations occurred after stopping L-thyroxine. 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. The exact cause of rhabdomyolysis in hypothyroidism remains unclear; however, it

Table I. Main Laboratory Results on Admission and During the Follow-Up

	0 day	8 th day	18 th day	4 th wk	5 th wk	9 th wk	13 th wk
CPK (5-130 U/L)	12900	5608	494	134	102	75	58
Myoglobin (25-58 ng/ml)	>3000	2035	597	305	129	28.7	27.2
Serum creatinine (mg/dl) (0.2- 1.0 mg/dl)	4.5	3.8	2.1	4.4	2.9	1.05	0.89
AST (0-40 U/L)	1246	120	45	23	15	15	-
ALT (0-41 U/L)	1469	508	91	5	4	7	10
TSH (0.4 - 4.8 uIU/ml)	43.2	21.3	38.6	2.7	2.8	0.27	0.02
Free T3 (1.57-4.71 pg/ml).	0.69	0.95	1.88	1.7	2.14	2.45	6.02
Free T4 (0.85-1.78 ng/dl)	0.72	0.91	1.04	1.77	2.34	1.91	2.26

0 day: On admission. wk: Weeks. CPK: Creatine phosphokinase. AST: Aspartate aminotransferase. ALT: Alanine aminotransferase. TSH: Thyroid stimulating hormone. T3: Triiodothyronine. T4: Thyroxine.

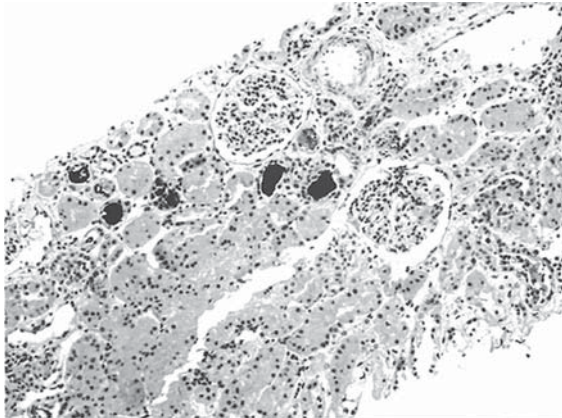


Fig. 1. Renal biopsy showing myoglobin casts in renal tubules (Myoglobin stain, x 20).

was suggested that impaired glycogenolysis or impaired mitochondrial oxidative metabolism in hypothyroidism may be responsible for rhabdomyolysis⁹. An autoimmune mechanism could also be possible, as has been described for Graves' disease¹⁰. Gunther et al.⁵ reported rhabdomyolysis and delayed gross-motor development in a 23-month-old toddler due to acquired autoimmune hypothyroidism, which recovered after thyroid replacement. Galli-Tsinopoulou et al.⁶ reported a 10-year-old girl with hypothyroidism due to autoimmune thyroiditis who developed rhabdomyolysis, pericardial effusion, ARF, and acquired von Willebrand disease, which was cured by thyroid replacement therapy. Sekine et al.⁴ reported a 61-year-old woman with hypothyroidism for seven years who developed rhabdomyolysis and ARF after strenuous walking.

Rhabdomyolysis has a clinical spectrum ranging from asymptomatic CPK elevation to acute tubular necrosis. ARF is the most severe and life-threatening condition of rhabdomyolysis. Its frequency ranges from 5% to 45% in pediatric cases with rhabdomyolysis⁷. The exact cause of ARF in rhabdomyolysis is not known but may be attributable to vasoconstriction/hypoperfusion, renal tubular dysfunction/cast formation, and/or myoglobin-induced tubular cytotoxicity^{1,7}. The cell injury in rhabdomyolysis may be due to direct injury to the cell membrane, muscle cell hypoxia leading to depletion of ATP or electrolyte disturbance disrupting the sodium-potassium pump². Serum CPK levels are the most sensitive marker of muscle injury. It was reported that the risk of ARF is high when serum

CPK level is >5000 U/L¹. The CPK level of our patient, who had ARF, was 12900 U/L, consistent with this data. Hepatic dysfunction may occur because of proteases released from injured muscle cells in one-fourth of cases with rhabdomyolysis¹¹. In our patient, ALT and AST were 1622 and 999 U/L, respectively, which recovered after appropriate therapy. Renal biopsy is not mandatory in the definite diagnosis of rhabdomyolysis. We performed renal biopsy to exclude any comorbidities leading to ARF. In a previous report, myoglobin could be removed by hemodialysis using high-flux dialyzers¹². Fortunately, high-flux dialyzer could be obtained for the present patient. Hemodialysis with high-flux dialyzer was administered in order to correct the increased myoglobin, hypervolemia and hyperkalemia in the patient with oligo-anuric ARF.

Rhabdomyolysis due to hypothyroidism is very rare, especially in children. To our knowledge, there are only two reports in the literature (5,6). One must be aware that rhabdomyolysis may develop in a non-compliant patient with hypothyroidism. Further, we recommend considering hypothyroidism in cases with rhabdomyolysis when the etiology is unknown.

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