Rhabdomyolysis and Acute Renal Failure in a Patient with Hypothyroidism

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A 61-year-old woman developed rhabdomyolysis and acute renal failure after strenuous walking. She had been treated for seven years with levothyroxine (T4) for hypothyroidism. On admission, her thyroid function test revealed marked hypothyroidism, suggesting poor drug compliance. Electromyographic and muscle biopsy findings were compatible with hypothyroid myopathy. Other diseases that could cause rhabdomyolysis were excluded. Her renal function completely recovered with peritoneal dialysis, and thyroid function normalized with 100 μg/day of T4. The present case suggests that rhabdomyolysis could occur in patients with hypothyroidism, especially those with poor drug compliance, in combination with other aggravating factors such as exercise.

Key words: Hashimoto’s thyroiditis, hypothyroid myopathy

Introduction

Muscle disorders are frequently associated with hypothyroidism (1). Symptoms and signs of muscular abnormality are variable from mere elevation of serum enzymes of muscular origin (e.g. creatine kinase) to prominent muscular changes such as those seen in Hoffman’s syndrome (2). However, association of rhabdomyolysis with hypothyroidism is so rare that only 3 cases have been reported to date (3–5). From these previous case reports, it is unclear whether hypothyroid myopathy alone could lead to rhabdomyolysis or whether other pathogenetic factors play a primary role in the development of rhabdomyolysis.

We report a patient with treated hypothyroidism who developed acute renal failure due to rhabdomyolysis during the period of poor drug compliance. Our case suggests that hypothyroid myopathy, in combination with exercise, could lead to rhabdomyolysis.

Case Report

A 61-year-old woman was admitted to our hospital because of severe myalgia in the lower extremities and generalized muscle weakness. She had had a seven-year history of hypothyroidism due to Hashimoto’s thyroiditis. Her thyroid function was once normalized with 100 μg/day of T4, but the dose was increased to 200 μg/day five months before admission because of elevation in the serum thyroid-stimulating hormone (TSH) level. She had no other medication than T4. Her baseline serum creatinine level was 0.8 mg/dl and thyroid function measured two months before admission was normal. She had history of neither hypertension nor diabetes. Ten days before admission (June 20), she walked at a moderate speed for a couple of hours in rainy weather. The total distance she walked on that day was estimated to be less than 4 km. Shortly thereafter, she began to feel pain in both thighs and experienced a series of muscle cramps. Eight days before admission, she noticed dark-coloured urine three times, and her urine volume decreased gradually thereafter. Muscle weakness progressed and she finally became unable to walk.

Physical examination revealed a body temperature of 35.8°C, pulse rate of 50/min, and blood pressure of 186/90. No evidence of dehydration was found. Her consciousness was alert. A diffuse rubbery-firm goiter was palpable. Pitting edema was noted in the lower extremities. Neurological examination revealed marked proximal-dominant weakness and slight tenderness of
the muscles. No sensory disturbance was observed.

Urinalysis gave a (+++) test for orthotoluidine in the absence of microscopic hematuria. The blood urea nitrogen was 167 mg/dl, creatinine 10.0 mg/dl, sodium 136 mEq/l, potassium 7.6 mEq/l, chloride 99 mEq/l, total protein 7.0 g/dl, albumin 4.0 g/dl, and white blood cell count 6,200/mm³. Serum muscle enzymes were markedly elevated; CK 8,437 IU (normal 15–74), LDH 6,635 IU (230–445), GOT 398 IU (8–30). Urine and serum myoglobin levels were both over 500 ng/ml. Serum triiodothyronine level was 41 ng/dl (96–192), thyroxine (T₄) 2.1 μg/dl (4.7–12.3), free T₄ < 0.2 ng/dl (0.78–2.11), and TSH 110.4 μU/ml (2–10). Both serum anti-thyroglobulin antibody and anti-microsomal antibody were positive. Antinuclear antibody was negative.

Peritoneal dialysis was begun soon after admission and continued for a week. Replacement with T₄ was started at 50 μg/day and increased to 100 μg/day two weeks later, resulting in normalization of the thyroid function. The patient’s muscle power improved gradually and the serum muscle enzymes normalized over a 6-week period. Her serum creatinine decreased to 1.0 mg/dl at the time of discharge (Fig. 1).

Biopsy from the left quadriceps muscle was performed on the third day of admission. It revealed type II fiber group atrophy with angulated fibers. Neither inflammatory infiltrate nor fiber necrosis was observed (Fig. 2). Electromyogram showed a myopathic pattern with low amplitude, short duration and polyphasic motor unit potentials. Electromyogram performed one year later, when the thyroid function was maintained as normal, showed no abnormality.

**Discussion**

The present case presented rhabdomyolysis and acute renal failure during treatment of hypothyroidism. Diagnosis of rhabdomyolysis was made based on the severe myalgia, muscle weakness and marked elevation of serum CK, as well as remarkably high levels of urinary and serum myoglobin. As a cause of rhabdomyolysis, disorders such as collagen disease (e.g. polymyositis), ingestion of massive alcohol or other agents, infection, trauma, or congenital deficiency of muscular enzymes (6), were excluded. Although the electromyographic findings in hypothyroidism are extremely variable, normal and myopathic patterns (7) are usually observed. On muscle biopsy findings, selective atrophy of type II fibers has been reported in hypothyroidism (8). In thyroidectomized rats, there are prominent changes in muscle fiber type distribution, in which the characteristics of myofibrillar ATPase, myosin light chain and LDH shift to those typical of slow muscles (type I) (9). Therefore, the electromyographic and muscle biopsy findings seen in the present case were compatible with hypothyroid myopathy. Thus, the basic muscle disorder in this patient which lead to rhabdomyolysis was considered to be hypothyroid myopathy. Further, strenuous walking could be a precipitating factor of rhabdomyolysis.

Although it is well known that muscle disorders are
frequently associated with hypothyroidism, only 3 cases have been reported that developed rhabdomyolysis (3-5). In these reports, some precipitating factors are described such as hypoxemia or hypotension associated with myxedema coma (3), certain inflammatory reactions of the muscles (4), or vigorous exercise (5). The present case is similar to the last one in that both hypothyroidism and muscular exercise might have been involved in the development of rhabdomyolysis. However, the two cases differ in the severity of hypothyroidism and muscle exercise. In the previously reported case, the degree of exercise was so intense (playing basketball vigorously for 3 hours) that the excessive stress to the muscles could be the primary cause of rhabdomyolysis. In contrast, hypothyroidism was more severe and the exercise done before the episode of rhabdomyolysis was milder in the present case. Since abnormal carbohydrate, protein and lipid metabolism in muscles of hypothyroid patients have been reported (5, 10, 11), an increase in energy demand during exercise might increase the risk of rhabdomyolysis. Thus, it seems reasonable to speculate that patients with underlying hypothyroid myopathy might readily develop severe muscle damage even with relatively mild exercise.

It is no doubt that the drug compliance of our patient had been poor before admission, since her thyroid function was normalized finally with 100μg/day of T4. Thus, we should be aware that rhabdomyolysis could occur, although rarely, if drug compliance is poor in patients with hypothyroidism.

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References