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Case Report

The Clinical Investigator

Exercise-induced myalgia in hypothyroidism

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Summary. Recurrent rhabdomyolysis is very uncommon in hypothyroid myopathy. A 30-year-old woman is reported, who presented with exercise-induced myalgias and high levels of serum creatine kinase but no muscle weakness. Muscle biopsy showed signs of a recurrent rhabdomyolysis. Hypothyroidism was diagnosed by serum hormone levels. The myopathy rapidly improved with thyroxine treatment.

Key words: Hypothyroidism – Myalgia – Myopathy – Rhabdomyolysis

Myopathy is a widely recognized complication of hypothyroidism, with an estimated incidence of 30–80% in patients with myxedema [2, 6, 7]. Generally the severity of the myopathy parallels the duration and degree of the hypothyroidism. Common symptoms are proximal muscle weakness and elevated levels of the serum creatine kinase (CK). Muscle biopsies often reveal no abnormality or show only mild and nonspecific changes. Histological changes include type 1 fiber predominance, type 2 fiber atrophy, and increased numbers of central nuclei. Ultrastructural changes include excessive amounts of glycogen, lipid accumulations, abnormal mitochondria, dilated sarcoplasmic reticulum, and focal myofibrillar degeneration [2, 6, 7]. Magnetic resonance spectroscopy of hypothyroid muscle shows low intracellular pH in resting muscle and delayed glycogen breakdown in exercising muscle [8]. Rhabdomyolysis is a uncommon sign of hypothyroid myopathy; three cases of rhabdomyolysis caused by hypothyroidism have been reported in the literature [3–5].

We present a case showing exercise-induced myalgias and high CK levels as an early sign of hypothyroidism but not the common signs of hypothyroid myopathy. The muscle biopsy showed recurrent rhabdomyolysis.

Abbreviation: CK = creatine kinase

Case report

A 30-year-old woman presented with exercise-induced myalgias in her lower limbs existing for several months. At rest there was no muscle pain or weakness. The patient also noted slight periorbital edema, a hoarse voice, tiredness, and gain of weight. Neither she nor her family had any prior history of thyroid disease, neuromuscular or autoimmune disorders.

Physical examination showed no muscle atrophy, hypertrophy, or paresis. The calves were painful if pressed. The relaxation time of deep tendon reflexes was slow. The thyroid gland was not palpable. The results of other general and neurological examinations were unremarkable. Laboratory investigation was remarkable for a CK of 2130 U/l (normal, 10–80 U/l), persistent for 3 months, thyroid-stimulating hormone of 158 μU/ml (normal, 0.4–4 μU/ml), and triiodothyronine of 15 ng/dl (normal, 80–180 ng/dl), free thyroxine was not found. Antibodies to thyroid microsomes were positive. Ultrasound imaging showed a small and hypodense thyroid gland. Electromyographic examination showed some polyphasic, short-duration and small-amplitude motor unit potentials with early recruitment in the tibialis anterior and medial gastrognemius muscles. Only single positive waves as pathological spontaneous activity were seen.

Muscle biopsy findings

An open biopsy of the right medial gastrocnemius muscle was obtained. Specimens were prepared and stained according to standard procedures for light and electron microscopic examinations [1]. As confirmed by light microscopic criteria, most of the muscle fibers were of normal structure and configuration; a slight increase in the variability of fiber size was seen without any changes in the fiber type distribution. Connective tissue and vasculature appeared normal. No inflammatory infiltrates were seen, but disseminated regressive and

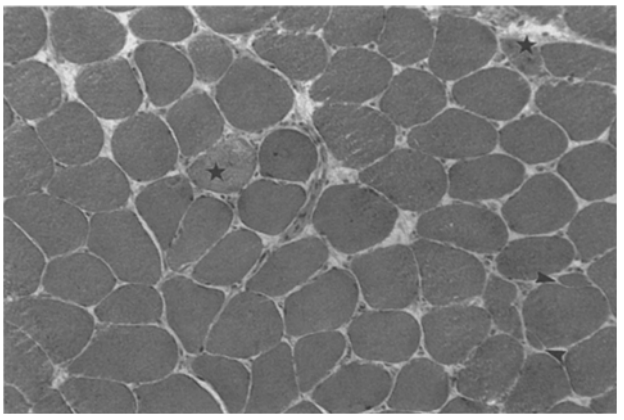

Fig. 1. Transverse section of the medial gastrocnemius muscle. Most of the fibers show normal configuration. *Stars*, fiber necrosis; *arrows*, fiber splitting. H&E ×100

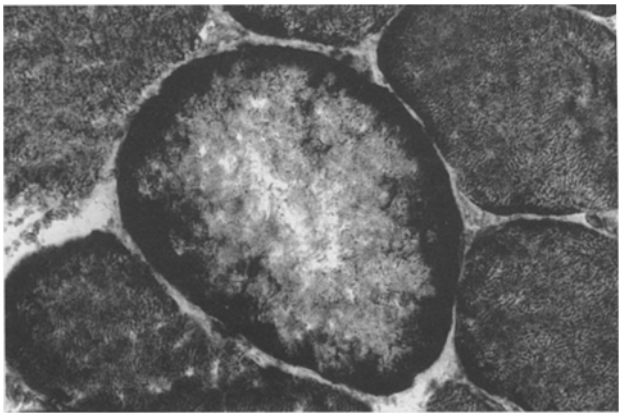

Fig. 2. Subsarcolemmal accumulation of mitochondrial enzyme activity. NADH tetrazolium reductase ×400

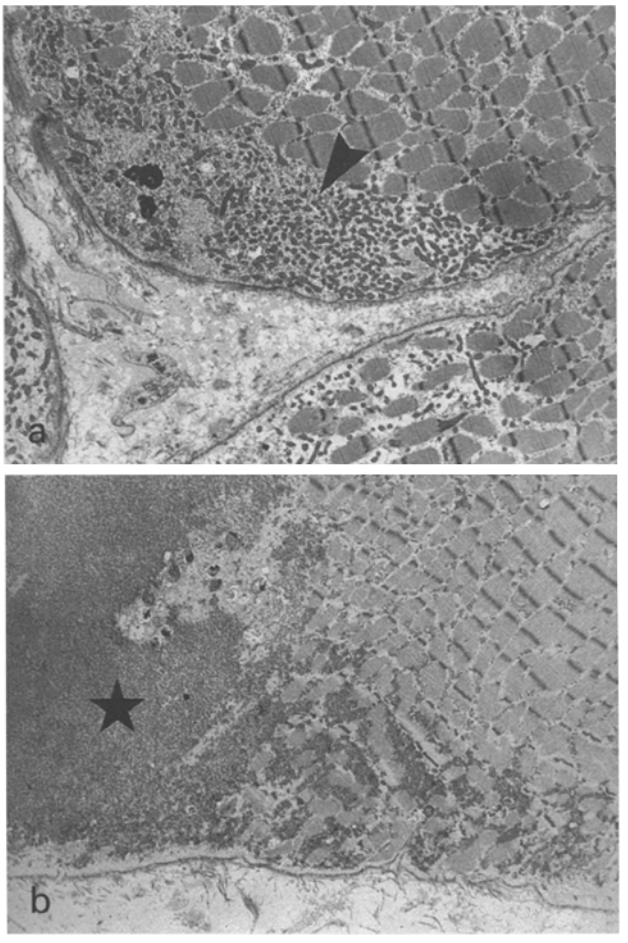

Fig. 3. a Subsarcolemmal accumulation of mitochondria (*arrow*). **b** Non-lysosomal-bound glycogen (*star*). Electron microscope ×10000

regenerative fiber changes were found. Additional single-fiber necrosis, macrophages, proliferating satellite cells, and fiber splitting were detected (Fig. 1). In some fibers a subsarcolemmal accumulation of material positive on periodic acid-Schiff's reaction and a slightly increased mitochondrial enzyme activity was found (Fig. 2). The myophosphorylase reaction showed a positive result. The histological diagnosis was a recurrent rhabdomyolysis. Electron microscopic examination also showed an elevated amount of subsarcolemmal, not lysosomal-bound glycogen and an increase in regularly configurated mitochondria in single fibers (Fig. 3). A metabolic or mitochondrial myopathy was not confirmed.

Clinical course

The patient was placed on levothyroxine, starting with 50 µg and increasing to 150 µg daily. After 1 week of therapy the patient felt remarkably improved, muscle pain was absent, and the CK fell to 1000 U/l. On follow-up examination after 6 months, the patient had no muscular complaints, and thyroid hormone levels and CK (20 U/l) were normal.

Discussion

In this case the clinical symptoms – exercise-induced myalgia – together with the laboratory and myopathological findings (elevation of CK and muscle fiber necrosis) indicated recurrent rhabdomyolysis.

Exercise-induced myalgias and recurrent rhabdomyolysis are uncommon signs of hypothyroid myopathy [2, 6, 7]. Three cases of rhabdomyolysis caused by hypothyroidism have been reported in the literature [3–5]. In all cases rhabdomyolysis complicates long-term myxedema and is not an

early sign of hypothyroidism. Rhabdomyolysis is seen more often in toxic or metabolic myopathies, for example, McArdle's disease (myophosphorylase deficiency). Even the morphological examinations of the case revealed some similarities to metabolic muscle disorders – a subsarcolemmal accumulation of glycogen and mitochondria. A possible explanation for these parallels could be offered by magnetic resonance spectroscopy of hypothyroid muscle. A delayed glycogen breakdown and a change in proton handling in hypothyroid muscle have been suggested [8]. The reason, why in this case a recurrent rhabdomyolysis, however in the majority of reported cases a proximal myopathy with muscular weakness results from this metabolic disorder, remains unclear.

The diagnosis of hypothyroid myopathy should not be missed because of its therapeutic and prognostic consequences, even if there are only slight classical signs of hypothyroidism, as in this case. Exercise-induced myalgia may be an early clinical symptom of hypothyroid myopathy.

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