CASE REPORT

Rhabdomyolysis: a rare complication of Hashimoto's thyroiditis precipitated by statin therapy

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SUMMARY

Hashimoto's thyroiditis (HT) or chronic lymphocytic thyroiditis is the most common form of primary hypothyroidism. Muscular manifestations like weakness, pain, stiffness and elevated muscle enzymes have been noticed in hypothyroidism. Statins are also known to cause myositis and rhabdomyolysis. This is a case of a middle-aged man, on statin therapy, who presented with severe muscle aches and pain and was found to have rhabdomyolysis. Further evaluation revealed an underlying HT as the culprit for his condition. He was managed with intravenous fluids and levothyroxine along with cessation of statins, following which he improved.

BACKGROUND

Rhabdomyolysis is characterised by muscular necrosis and the release of intracellular muscle components like creatine kinase (CK), myoglobin, lactate dehydrogenase (LDH), aldolase, aspartate aminotransferase and potassium into the circulation.[1] This can result in limb weakness, myalgia, swelling and passing of dark-coloured urine in the absence of haematuria. Myoglobinuria may be present. Hashimoto's thyroiditis (HT) is an autoimmune form of primary hypothyroidism, where the thyroid gland is destroyed following attacks by the immune system. Musculoskeletal symptoms like proximal muscle weakness, pain or cramps have been associated with hypothyroidism.[2] Statins, used in the treatment of dyslipidaemia, can cause myositis and rhabdomyolysis.[3] Since both hypothyroidism and statins can cause rhabdomyolysis, this case projects the importance of assessing the thyroid status of a patient before starting him on statin therapy for dyslipidaemia.

CASE PRESENTATION

A 54-year-old man, accountant by occupation, presented with complaints of severe muscle aches and pains for the past 2 months. He also gave history of passing dark-coloured urine. About 1-month ago he had visited a local doctor with complaints of fatigue. His blood tests showed normal fasting and post prandial glucose (104 and 132 mg/dL, respectively) and total cholesterol of 264 mg/dL. Thyroid profile was not done. He was started on atorvastatin (20 mg at night). His symptoms aggravated over the past 1 month and was now associated with severe muscle pain. He was told to have fibromyalgia and was given pregabalin. He did not have any symptoms like cold intolerance, dry skin, weight gain, pedal oedema or constipation.

On presentation, he was conscious, oriented and afebrile. He was overweight (weight 80 kg and height 173 cm), with a body mass index of 26.72 kg/m^2. He had a hoarse voice, mild facial puffiness and mild pedal oedema. There was no obvious neck swelling. His pulse rate was 60/minute and blood pressure 140/90 mm Hg. Neurologically, his deep tendon reflexes were very sluggish, but there was no muscle weakness, stiffness or hypertrophy. Other systemic examinations were normal.

INVESTIGATION

His blood investigations showed anaemia with haemoglobin (Hb) 11.2 g/dL (13–16), deranged renal function with urea 49 mg/dL (10– 40) and creatinine 2.97 mg/dL (0.9–1.3) and elevated liver enzymes serum glutamic oxaloacetic transaminase 113 U/L (0–35) and serum glutamic pyruvic transaminase 62 U/L (0–45). Serum electrolytes, calcium, phosphorus, magnesium and HbA1c were normal. His fasting lipid profile showed triglycerides 365 mg/dL (<150), low-density lipoprotein 203 mg/dL (<130), high-density lipoprotein 24 mg/dL (40–60) and very-low-density lipoprotein 46 mg/dL (6–38). Peripheral smear revealed microcytic anaemia. Sinus bradycardia with low voltage complexes were seen on ECG but echocardiography was normal. Troponin I and antinuclear antibody profile were negative. Ultrasound abdomen revealed moderate fatty liver and chest X-ray was normal. His CK and LDH levels were elevated, 5369 U/L (24–190) and 649 U/L (114–240), respectively. Urine examination did not show any pus cells, myoglobinuria or haematuria. His thyroid profile was suggestive of HT with thyroid-stimulating hormone 394 µIU/mL (0.40–4.20), T3 24.6 ng/dL (40–181) and T4 0.69 µg/dL (4.60–10.50), and positive antithyroid peroxidase antibody of 6257 U/mL (<35). Ultrasound of neck was consistent with thyroiditis.

TREATMENT

He was managed with aggressive intravenous fluid administration. Atorvastatin was withheld, and oral levothyroxine 300 μg was given as initial bolus dose followed by 125 μg once daily.

OUTCOME AND FOLLOW-UP

By day 3 of admission, his creatinine levels had started normalising. Electromyography and muscle biopsy were not done as the patient had improved

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symptomatically. He was discharged on day 7 of admission with a normal creatinine value, and advised levothyroxine 125 μg once daily. On follow-up after 1 month, the patient was asymptomatic and his blood reports showed a normal haemogram, thyroid profile, liver and renal functions, and CK levels.

DISCUSSION

Hypothyroidism is well associated with musculoskeletal problems including myopathy. It has been estimated that about one-third of patients with hypothyroidism present with proximal muscle weakness, stiffness, pain or cramps. Diabetes mellitus, liver and renal disease, alcoholism and old age are some of the risk factors for developing hypothyroid myopathy. Rhabdomyolysis due to hypothyroidism is a rare scenario and can be precipitated by exercise, trauma and drugs like statins or alcohol.[4 5]

The spectrum of manifestations in rhabdomyolysis extends from asymptomatic elevations in serum muscle enzymes to acute kidney injury. Trauma is the most common aetiology. Non-traumatic causes include heat exposure, electrolyte imbalance, seizures, endocrine disorders, infections and heavy exercise.[1 6]

Various hypotheses have been proposed with regard to the cause of rhabdomyolysis in hypothyroidism. These include induction of insulin-resistant state, impaired mitochondrial oxidative metabolism and decreased muscle carnitine levels, including autoimmune mechanism.[7–9] Thyroxine deficiency leads to abnormal glycogenolysis, mitochondrial oxidative metabolism and triglyceride turnover. This in turn results in impaired muscle function by causing a transition of fast-twitching type 2 muscle fibres to slow-twitching type 1 fibres, low myosin ATPase activity and low ATP turnover in the skeletal muscles.[10]

Statins are 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors used in the treatment of dyslipidaemia. Rhabdomyolysis is an uncommon adverse effect with statin therapy. Risk factors which predispose to develop statin-induced rhabdomyolysis include old age, frailty or low body mass index, female sex, hypertension, hypothyroidism, polypharmacy and alcohol.[11] Several factors like liver and renal impairments, hypothyroidism and diabetes can also lead to exacerbation of the situation. Drugs like macrolides, antifungals and cyclosporine can elevate the serum levels of statins and thereby increase the risk of rhabdomyolysis.[3] A literature search showed that statin-induced rhabdomyolysis was also common among men and in people >45 years of age. The incidence was higher among simvaststin and atorvastatin users, especially when combined with drugs like fibrates or fusidic acid.[12]

The patient being discussed had symptoms of fatigue initially. Following the initiation of statin therapy for dyslipidaemia, his symptoms worsened to severe muscle aches and pains. On evaluation, he was found to have rhabdomyolysis due to HT which was precipitated by statin therapy. Hypothyroidism-induced rhabdomyolysis is a rare scenario.

Learning points

- Hypothyroidism can lead to rhabdomyolysis.
- Statins can also cause or precipitate rhabdomyolysis.
- Assessment of thyroid status is necessary in all cases of dyslipidaemia before starting statin therapy.

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