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Two cases of thyrotoxicosis with severe myalgia as early presentation

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Abstract

Myalgia is rare in acquired muscle diseases other than inflammatory myopathies. Thyrotoxic myopathy is usually painless. We reported here two patients with acute onset of thyrotoxicosis presenting with severe myalgia and mild proximal weakness. No other etiologies responsible for the myalgia was identified. The symptoms resolved in parallel with the achievement of euthyroidism, supporting hyperthyroidism as the cause of myalgia. Painless myopathy was well known to be related to hyperthyroidism, but the myalgia is scarcely reported. We summarized the previous literatures to elucidate the thyroid hormone effect on the muscle, such as increased energy expenditure in hyperthyroidism. We hypothesized that the myalgia is related to the muscle injury by the energy failure during an acute onset of thyrotoxicosis.

Keywords: Hyperthyroidism, thyrotoxicosis, myalgia, myopathy, Graves' disease, painful myopathy

INTRODUCTION

Myalgia is rare in acquired muscle diseases other than inflammatory myopathies.[1] Thyrotoxic myopathy is usually painless. Here, we reported two patients with hyperthyroidism, presented with painful myopathy.

CASE REPORT

Patient 1

A previously healthy 41-year-old male developed severe muscle pain in the bilateral thighs for 2 weeks. The pain became much more severe when moving legs, leading to difficulty in walking up and down stairs. He had no paresthesia, muscle twitches, tea-colored urine, or heat/cold intolerance. He lost 5 kilograms in the past 2 months.

Neurological examination revealed no visible muscle twitches and no muscle atrophy. There was mild weakness (MRC muscle scale: 4+) in the proximal part of four limbs. Muscle tenderness was found in multiple areas, including bilateral arms, buttock, and thighs. Sensory function was normal. Tendon reflex examination failed to reveal hyperreflexia or hyporeflexia. He was then admitted for further work-up.

The results of routine blood test on admission were normal, including creatine kinase (CK) of 37 U/L (normal 30-223 U/L). The electromyography (EMG) was normal. To investigate the underlying etiology for the acquired myopathies, endocrine functions and autoimmune disease screening were arranged. It revealed elevated T4 level (1.91 ng/dL; normal 0.70-1.48) and low TSH level (<0.0038 uIU/mL; normal 0.35-4.94), indicating a primary hyperthyroidism. He also had elevated anti-TPO antibodies level (298.47 IU/mL; normal <5.61), normal anti-thyroglobulin Ab (< 3.00 IU/mL; normal <14.4) and positive anti-TSH receptor antibodies in the blood. Findings of thyroid echogram revealed hypoechoic pattern with no goiters, compatible with the diagnosis of Graves' disease. Concomitant relative primary adrenal insufficiency (ACTH: 224 pg/mL; normal 7.4-57.3, morning cortisol: 4.8 ug/dL; normal 3.7-19.4) was also discovered with positive ACTH stimulation test. However, the cortisol levels returned to normal after the hyperthyroidism improved. This transient primary adrenal insufficiency was thought to be secondary to hyperthyroidism by our endocrinologist.

The patient received carbimazole and propranolol for hyperthyroidism. One month later, he gained 3 kilograms. His muscle pain and muscle weakness completely disappeared. His blood T4 level decreased to 1.08 ng/dL. (Figure 1).

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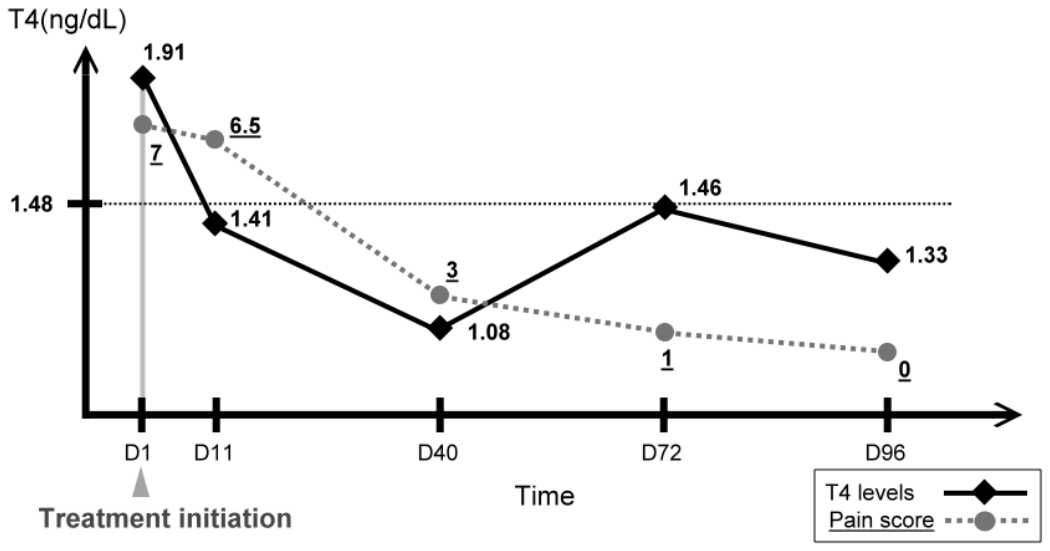

The normal range for T4 levels in our laboratory is 0.70-1.48 ng/dL. The underlined numbers are the documented pain score using the visual analogue scale.

Figure 1. The Patient 1's pain score decreased in accordance to thyroid hormone levels.

Patient 2

A 27-year-old female has had nontoxic thyroid goiter and bilateral hand action tremor since her teens. Three months prior to admission, she developed fatigue and weakness in legs. One month later, muscle pain in bilateral arms, thighs, and calves supervened. Her symptoms worsened gradually. She could not climb or descend stairs or raise her arm above the shoulder. She had no weight loss, numbness, fever, or tea-colored urine. She was diagnosed to have polymyositis by a clinic. However, she was found to have no elevated serum muscle enzymes, and she was then admitted for further work-up.

Physical examination on admission showed a grade 2 goiter. Neurological examination revealed no muscle atrophy but generalized muscle tenderness was found in the proximal muscles. There was also weakness (MRC muscle scale: 4+) of the neck and proximal four limbs with positive Gower's sign. Sensory function was normal. The deep tendon reflexes were also normal.

Routine blood test on admission revealed no significant abnormalities. The blood CK level was normal (37 U/L). EMG showed short-duration, low-amplitude polyphasic waves in right biceps brachii muscle and right rectus femoris muscle. On investigation of the underlying etiology for her acquired myopathy, abnormal results in thyroid test were found: high free T4 level (2.15 ng/dL) and low TSH level (<0.0038 uIU/mL), positive anti-TSH receptor Ab, high anti-TPO Ab (23.35 IU/mL) and high anti-thyroglobulin Ab (378.41 IU/mL). Thyroid echogram showed hypoechoic gland with nodularity change. A diagnosis of Graves' disease was made.

For hyperthyroidism, she was given methimazole and propranolol, and low dose prednisolone. One month later, she reported much improvement in muscle pain and weakness.

DISCUSSION

In contrast to patients with chronic hyperthyroidism having painless myopathy, our patients had no obvious hyperthyroidism symptoms until myalgia appeared. The acute rise of thyroid hormone seems playing a role in myalgia. Although some studies proposed muscle pain as a possible symptom of thyrotoxic myopathy[2], but case reports elaborating this connection were scarce[3,4] and no mechanism is elucidated. Thyroid hormone influences the muscle physiology and profile by affecting different genes expression. (Table 1). Increased thyroid hormone in hyperthyroidism, therefore, would promote a shift from slow-twitch to fast-twitch fibers, shorten contraction-relaxation cycles, increase energy consumption and production, and decrease ATP production efficiency. We hypothesize that an acute rise in thyroid hormone would result in rapid increase in energy expenditure, leading to energy failure of fast-twitch fibers, and then muscle injury[5,6],

Table 1: Gene expressions and muscle physiology changes associated with hyperthyroidism

Protein	Genes	TH effect	Alterations in muscle physiology
MHCβ	*MYH7*	↓	Shift slow-twitch fibers towards fast-twitch forms[7]
MHC1, MHC2, MHC4	*MYH1, MYH2, MYH4*	↑	Shift slow-twitch fibers towards fast-twitch forms[7]
Calcium-transporting ATPase	*SERCA1*	↑	Increase Ca^{2+} storage in SR Increase ATP consumption Shortened contraction-relaxation cycle[8]
Uncoupling protein 1	*UCP1*	↑	Decrease energy production efficiency Increase mitochondrial uncoupling Increase energy expenditure in the form of heat[9]
Na-K-ATPase	-[a]	↑	Increase ATP consumption

MHC: Myosin heavy chain; SR: Sarcoplasmic reticulum.
[a]: Alterations related to up-regulated membrane translocation.[10]

resulting in myalgia and fatigability.

In conclusion, we reported two patients with myalgia as the early symptom of acute hyperthyroidism. Acute hyperthyroidism should be included in the differential diagnosis of patients with painful myopathy, normal deep tendon reflex, and normal blood CK level.

DISCLOSURE

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