http://dx.doi.org/10.5607/en.2013.22.3.232
Exp Neurobiol. 2013 Sep;22(3):232-234.
pISSN 1226-2560 • eISSN 2093-8144

Case Report

Experimental Neurobiology

A Case of Thyrotoxic Myopathy with Extreme Type 2 Fiber Predominance

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In hyperthyroidism, many patients had neuromuscular symptoms and clinical weakness correlated with free thyroxine (T4) concentrations. The common clinical symptoms of chronic thyrotoxic myopathy were characterized by progressive weakness in proximal muscles and atrophy. A 55-year old woman was visited our hospital with two years of progressive weakness of both legs. Physical examination showed diffuse enlargement of the thyroid gland, muscle atrophy and tachycardia. Motor examination showed proximal weakness in both legs. Serum creatine phosphokinase was normal and electromyography showed a myopathic pattern. Serum thyroxine (T4) was greatly increased and serum thyroid stimulating hormone was very low. Muscle biopsy showed mild atrophic change and type 2 fiber predominance. The patient's symptoms were improved during treatment with methimazole. Herein we report a case of thyrotoxic myopathy with extreme type 2 fiber predominance histologically.

Key words: thyrotoxic myopathy, hyperthyroidism, type 2 fiber

INTRODUCTION

The muscle diseases of hyperthyroidism were recognized and include exophthalmic opthalmoplegia, thyrotoxic myopathy, myasthenia gravis and periodic paralysis [1]. In hyperthyroidism, 67% patients had neuromuscular symptoms, 62% patients had clinical weakness in at least one muscle group that correlated with free thyroxine (T4) concentrations [2]. The clinical symptoms of chronic thyrotoxic myopathy are characterized by progressive weakness in proximal muscles, atrophy and wasting. Bulbar or respiratory muscle symptoms are rare [3]. The mechanism of thyrotoxic myopathy is unclear. In general, electromyographic abnormalities are non-specific and routine histopathological examination shows non-specific changes in muscle biopsy and some patients have an increased frequency of type 2 fibers [4]. However, only few cases of thyrotoxic myopathy with extreme dominance of type 2 fibers in muscle histological finding have been reported [5]. In this report, we present the case of a patient with chronic thyrotoxic myopathy with extreme type 2 fiber (fast twitch) predominance in histological findings.

CASE REPORT

A 55-year-old woman was admitted to our hospital with two years of progressive weakness of both legs. Initially, she had difficulty in climbing stairs and rising from a chair, but she felt no problem when she walked on flatland. Both legs weakness was progressed and she lifted up her both legs when going up stairs and walking on flatland at three months before visiting our clinic. Over the previous 1 year she had lost 2 kg in weight and become

Received August 24, 2013, Revised August 31, 2013,
Accepted August 31, 2013

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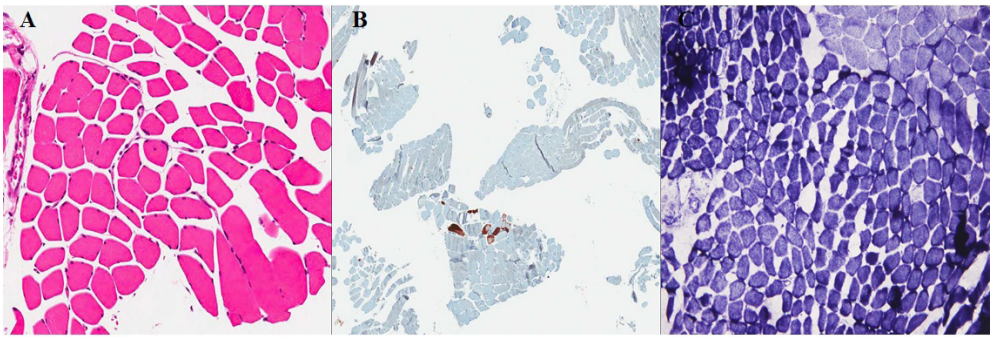

Fig. 1. Histological and histochemical studies of vastus lateralis muscle. (A) Mild atrophic myofibers are observed. No inflammatory change and vascular change is present (H&E, ×200). (B) NADH-TR stain shows Type II fiber predominance or grouping (NADH-TR, ×200). (C) COX-2 stain shows Type II myofiber predominance (COX-2, ×200).

increasingly nervous, vulnerable to heat and shortness of breath on exertion. She had noticed tremor of the outstretched fingers and hyperhidrosis over the previous four months. However, there were no weakness of upper extremities, sensory symptom, myalgia, dysarthria and dysphagia. Physical examination revealed a mild degree of bilateral exophthalmos and diffuse enlargement of thyroid gland. The arterial blood pressure was 189/93 and the pulse was regular tachycardia and the frequency 118 per minute. Motor examination showed proximal muscle atrophy with MRC grade 4/5 in proximal limbs and grade 4+/5 in distal limbs. She showed Gower sign when trying to stand up from squatting but toe gait and heel gait were intact. Motor power of both upper extremities was normal and deep tendon reflexes were normal. Cranial nerve examination was intact and there was no sensory loss. No fasciculation or myotonic reactions were present.

The following laboratory test showed normal results: complete blood cell count, hemoglobin, C- reactive protein, erythrocyte sedimentation rate, serum electrolyte, calcium, urinalysis, blood urea nitrogen, creatinine, chest x-ray and liver function test. Serum creatine phosphokinase (CPK), lactate dehydrogenase (LDH), fluorescent antinuclear antibody (FANA) and rheumatoid factor were also normal. She was diagnosed with hyperthyroidism by thyroid function studies which showed free T4 9.02 (0.7-1.8 ng/dl), T3 680 (87-184 ng/dl) and thyroid stimulating hormone (TSH) 0.05 (0.4-4.1 μIU/ml). In thyroid autoantibodies studies, TSH receptor antibody 31.69 (0-1 IU/L) and antithyroid microsomal antibody 1,478 (0-60 U/ml) were increased. Tc-99m thyroid scan showed diffuse enlargement with evenly increased uptake (40.8%).

Electromyography showed motor unit potentials of reduced amplitude and short duration (30%) in left vastus lateralis, tibialis anterior, peroneous longus and gastrocnemius muscles with early recruitment, but no spontaneous activity. These findings suggested a myopathic pattern. Muscle specimens were obtained from the vastus lateralis. Sections were stained with the modified Gomori trichrome and processed for the nicotinamide adenine dinucleotide-tetrazolium reductase (NADH-TR) reaction. Muscle fiber typing was done using the pH 9.4 myofibrillar adenosine triphosphatase (ATPase) reaction and cytochrome C oxidase (COX-2) immunohistochemistry staining. When examined by light microscopy and electron microscopy, size of myofibers was slightly variable and there were a few atrophic myofibers. There were no inflammatory infiltrates or blood vessel abnormalities (Fig. 1A). There was extreme predominance of type 2 fibers (fast twitch) in the analysis of NADH-TR reaction, ATPase reaction and COX-2 immunohistochemistry staining (Fig. 1B, C).

For treatment of hyperthyroidism and thyrotoxic myopathy, methimazole 15 mg/day was administered orally. After 1 month, hands tremor, shortness of breath, nervous and weakness of both legs were improved. She has continued methimazole treatment presently.

DISCUSSION

The thyroid diseases such as hypothyroidism and hyperthyroidism may cause neuromuscular diseases. Hypothyrodism is associated with clinical features of myopathy with proximal muscle weakness, mononeuropathy and sensorimotor polyneuropathy in 79%. Hyperthyroidism can cause of myopathy, myasthenia gravis and polyneuropathy in 67% [2, 4]. Severe muscle weakness and atrophy were first reported by Graves and von Basedow. The incidence of various degrees of muscular weakness was reported up to 82% in hyperthyroidism [4, 6]. Myopathy commonly occurs in hyperthyroidism. Initial symptoms related to a chronic proximal myopathy are difficulty in climbing stairs, rising from a chair, or washing hair. The weakness of bulbar or respiratory muscles is rare symptoms. Distal muscles may also be affected infrequently [1, 4, 7]. Serum creatine kinase and myoglobin concentrations in most of patients are normal despite muscle wasting and do not correlated with muscular weakness [1, 2]. Electromyographic findings are non-specific and there is no spontaneous electrical activity. Histopathological examination shows various findings,which include normal, non-specific structural alteration and type 2

fiber (fast twitch) predominance [4-6]. Previously, experimental changes of thyroid status affected phenotype of skeletal muscle fibers in rats by quantifying the changes in ATPase activity. In this result, hyperthyroidism produced similar changes with fibers atrophy and conversion of fibers from type 1 (slow twitch) to type 2 (fast twitch) [8]. The pathogenesis of muscle dysfunction in thyrotoxicosis is unclear. The development of thyrotoxic myopathy is probably a direct effect of elevated level of circulating thyroid hormones. Thyroxine (freeT4) induces disturbance of oxidative phosphorylation which leads to muscle dysfunction. Thyroid hormones increase lysosomal activity and release of amino acid by proteolysis of muscle fibers. Thyroid hormones act with biogenic amines at plasma membrane receptor sites to promote activation of membrane bounded adenyl cyclase system and increased cyclic adenosine monophosphate (AMP) may induce cellular metabolism and produce a hypermetabolic condition [1, 4, 8]. The muscle atrophy is due to increased protein catabolism by effect of thyroid hormones [4, 9]. The weakness in hyperthyroidism probably also results from factors including reduced membrane excitability and lower power of contraction due to an increase in the rate of relaxation [5]. In hyperthyroidism, muscles may show abnormal glucose tolerance and decreased intracellular water, potassium, creatine, creatine phosphate, and several enzymes including creatine phosphokinase [4, 5, 8]. Elevated thyroxine level can induce different metabolism in skeletal muscles and may change ratio of type 1 (slow twitch) and type2 fiber (fast twitch). The muscle weakness improved in 79% of the patients within an average treatment time of 6.9 months. After 1 year 21% of the patients had complaints of weakness, treatment of the hyperthyroidism results in nearly full recovery from muscle weakness.

To date, patients with hyperthyroidism have been to have variable muscular diseases. However, there were few case reports on thyrotoxic myopathy with type 2 fiber predominance in histologic findings. And there is no report showed extreme type 2 predominance. Thus, we report the first case of thyrotoxic myopathy with extreme predominance of type 2 fiber (fast twitch) histologically. We propose that thyrotoxic myopathy with type 2 fibers develops because increased thyroxine hormones may induce different metabolism in skeletal muscles.

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