INTERNAL MEDICINE

□ CASE REPORT □

# Thyrotoxicosis Presenting as Unilateral Drop Foot

Kenju Hara[1], Hajime Miyata[2], Takahide Motegi[1], Ken Shibano[1] and Hideaki Ishiguro[1]

## Abstract

Neuromuscular disorders associated with hyperthyroidism have several variations in their clinical phenotype, such as ophthalmopathy, periodic paralysis, and thyrotoxic myopathy. We herein report an unusual case of thyrotoxic myopathy presenting as unilateral drop foot. Histopathological examinations of the left tibialis anterior muscle showed marked variation in the fiber size, mild inflammatory cell infiltration, and necrotic and regenerated muscle fibers with predominantly type 1 fiber atrophy. Medical treatment with propylthiouracil resulted in complete improvement of the left drop foot. This case expands the phenotype of thyrotoxicosis and suggests that thyrotoxicosis be considered as a possible cause of unilateral drop foot.

**Key words:** drop foot, unilateral, hyperthyroidism, thyrotoxicosis, distal myopathy

**(Intern Med 56: 2053-2056, 2017)**
**(DOI: 10.2169/internalmedicine.56.8374)**

## Introduction

Neuromuscular disorders associated with hyperthyroidism have several different clinical phenotypes, such as ophthalmopathy, periodic paralysis, myasthenia gravis, and thyrotoxic myopathy (1). The incidence of muscular weakness is reported to be up to 82% in hyperthyroidism (2). Among the phenotypes above, the clinical symptoms of chronic thyrotoxic myopathy are usually characterized by progressive weakness of proximal muscles (2). Although some unusual cases of thyrotoxic myopathy mimicking distal myopathy have been reported (3-5), thyrotoxic myopathy presenting as unilateral drop foot has not been reported to date. We herein report a case of thyrotoxic myopathy presenting as unilateral drop foot.

## Case Report

A 19-year-old woman presented with a 2-month history of left drop foot. She had no family history of any neurological diseases, and her parents were not consanguineous. A general examination revealed sinus tachycardia (117 bpm) and a goiter without exophthalmos or tremor. A neurological examination revealed weakness of the left tibialis anterior muscle [(Medical Research Council (MRC) grade 1/5)] and calf muscles (MRC grade 4/5) without muscular atrophy. Other muscles of the left leg, including the iliopsoas, gluteus major, quadriceps, hamstrings, tibialis posterior, peroneus longs, extensor digitorum brevis, and flexor digitorum brevis, and the muscles described above of the right leg were of normal strength. She showed drop foot and steppage gait on her left side. The deep tendon reflex was absent in her left ankle.

Lumbar spine magnetic resonance imaging (MRI) did not show any specific findings such as disc herniation compressing the nerve root. Brain MRI did not show any abnormal findings either. Laboratory tests for thyroid functions showed an increased free tetraiodothyronine (T4) level of 6.98 ng/dL (normal: 0.9-1.7 ng/dL), an increased free triiodothyronine (T3) level of 21.88 pg/mL (normal: 2.3-4.3 pg/mL), and a decreased thyroid-stimulating hormone (TSH) level <0.005 μIU/mL (normal: 0.5-5.0 μIU/mL) accompanied by positivity for the TSH receptor antibody at 6.8 IU/L (upper limit 2.0 IU/L) and thyroid-stimulating antibody at 445% (upper limit 120%). Ultrasonography showed diffuse enlargement of the thyroid gland. The serum creatine kinase (CK) level was normal (110 mg/dL). Routine hematologic and biochemical tests otherwise showed normal findings, including serum potassium level. Nerve conduction studies of the left median, ulnar, peroneal, and sural nerves showed all normal findings (Table). Needle electromyography showed

[1]Department of Neurology, Akita Red Cross Hospital, Japan and [2]Department of Neuropathology, Research Institute for Brain and Blood Vessels - Akita, Japan
Received for publication October 6, 2016; Accepted for publication December 6, 2016
Correspondence to Dr. Kenju Hara, kenju_hara@akita-med.jrc.or.jp

**Table.** **Nerve Conduction Study.**

| | | DL (ms) | MCV (m/s) | CMAP (mV) | SCV (m/s) | SNAP (μV) |
|---|---|---|---|---|---|---|
| medain | L | 4.56 | 54.7 | 9.1/8.6 | 54.2 | 7.7 |
| ulnar | L | 2.31 | 60.2 | 12.8/12.1 | 60.2 | 7.3 |
| peroneal | R | 5.35 | 48.9 | 1.9/1.8 | | |
| | L | 5.55 | 47.8 | 2.0/1.9 | | |
| sural | R | | | | 42.9 | 8.5 |
| | L | | | | 42.6 | 5.3 |

R: right, L: left, DL:distal latency, MCV: motor conduction velocity, CMAP: compound muscle action potential, SCV: sensory conduction velocity, SNAP: sensory nerve action potential

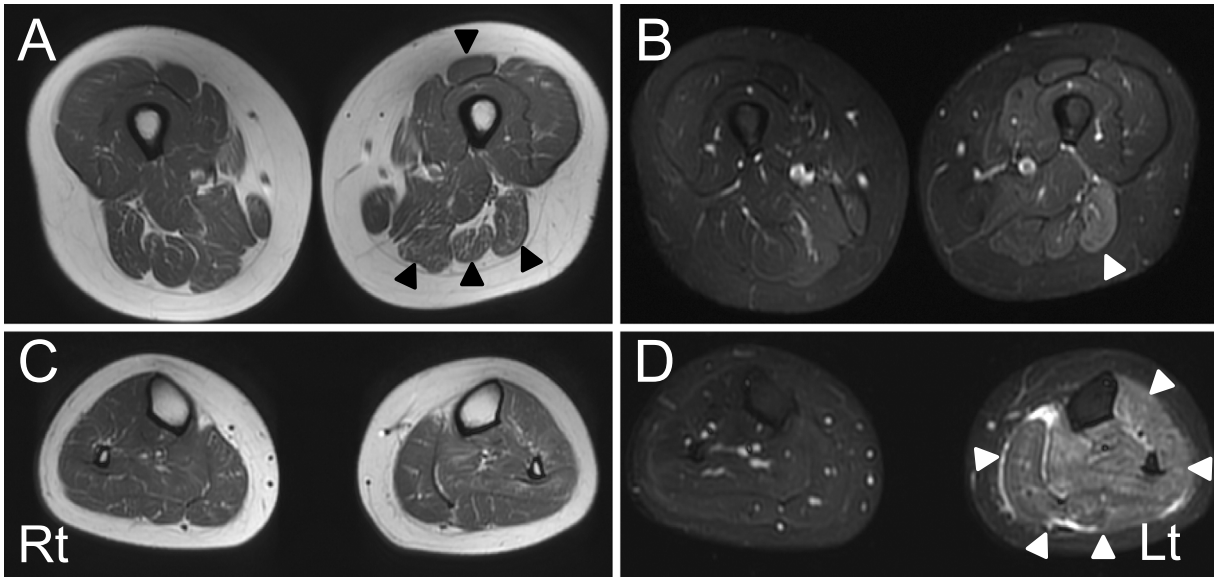


**Figure 1.** **MRI of the lower extremities. (A) T1-weighted image of femoral muscles shows muscle atrophy of the left sartorius, biceps femoris, semimembranosus, and semitendinosus (arrowheads). (B) Fat suppression image of femoral muscles shows hyperintense signals in the left biceps femoris muscle (arrowhead). (C) T1-weighted image of the calf muscles shows no muscle atrophy. (D) Fat suppression image shows diffuse hyperintense signals in both the anterior and posterior compartments of the left lower leg muscles.**

short-duration polyphasic motor unit potentials with early recruitment and complex repetitive discharges in the left tibialis anterior muscle, suggesting a myopathic pattern. Fat suppression MRI revealed mild muscle atrophy of the left sartorius, biceps femoris, semimembranosus, and semitendinosus accompanied by slightly hyperintense signals (Fig. 1A and B), and diffuse hyperintense signals in both the anterior and posterior compartments of the left lower leg muscles (Fig. 1C and D).

A muscle biopsy of the left tibialis anterior muscle was performed. A histopathological analysis revealed a marked variations in the fiber size and mild inflammatory cell infiltration, scattered necrotic and regenerated muscle fibers, and pyknotic nuclear clumps (Fig. 2A, B and C). Type 1 fiber-dominant atrophy with mild fiber type grouping was observed (Fig. 2D). There were no specific structures such as rimmed vacuoles or ragged-red fibers.

For the treatment of hyperthyroidism, propylthiouracil (300 mg/day) was administered orally. After 2 months, the patient's serum free T4 and T3 levels decreased to 2.18 ng/dL and 4.9 pg/mL, respectively, and the left drop foot completely disappeared. Follow-up MRI revealed the attenuation of diffuse hyper-intense signals in the left lower leg muscles.

## Discussion

Unilateral drop foot is characterized by weakness of the dorsiflexor muscles of a single foot, and this usually arises from peripheral neuropathy, such as peroneal nerve damage or lumbar radiculopathy (6). Our patient was unlikely to have had those peripheral neuropathies because she had no history of mechanical external knee compression, and both lumbar MRI and a nerve conduction study of the left peroneal nerve showed no abnormalities. However, this patient did present with histopathologically nonspecific myopathic changes in the biopsied muscles along with hyperthyroidism, and her drop foot was completely improved by only

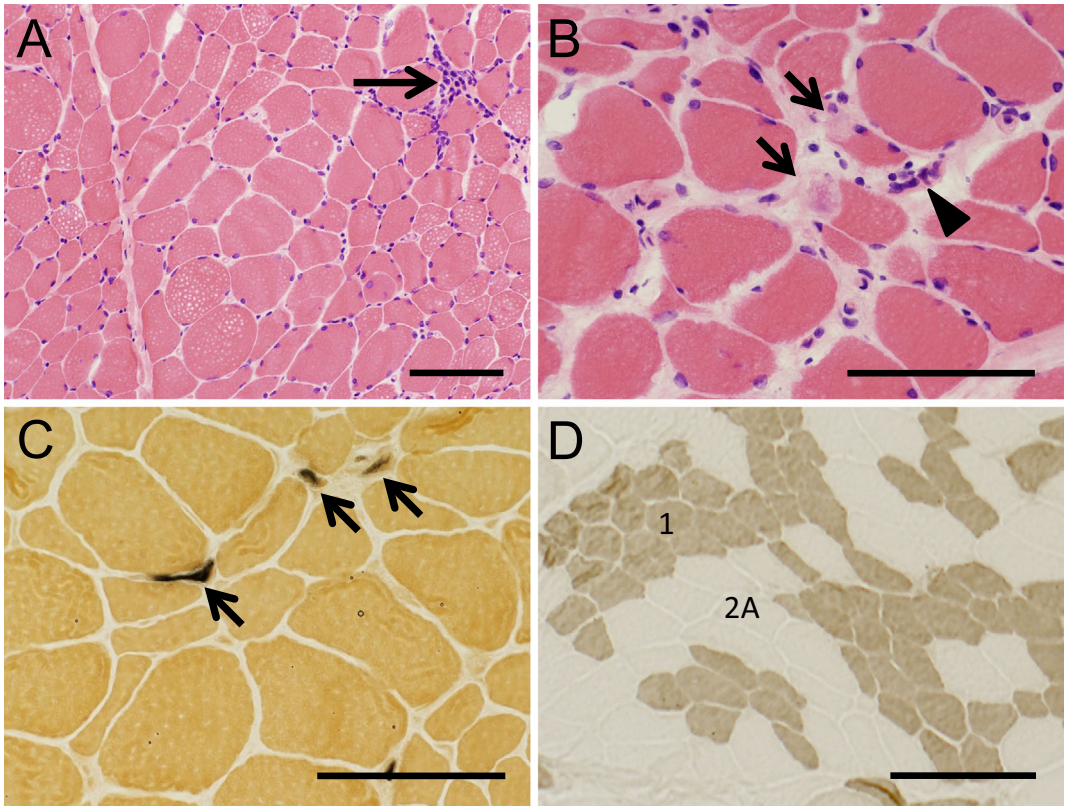


**Figure 2.** **Histopathological findings of the left tibialis anterior muscle. (A) Hematoxylin and Eosin staining section shows marked variations in the fiber size and focal mild inflammatory cell infiltration (arrow). (B) Necrotic fibers (arrows) and pyknotic nuclear clumps (arrowhead). (C) ALP stained section shows regenerated fibers (arrows). (D) ATPase (pH 4.6) stained section shows type 1 fiber-dominant atrophy with mild fiber type grouping. The bars in all panels indicate 100 μm.**

treatment with an anti-hyperthyroid drug. Given these findings, we consider this a case of thyrotoxic myopathy.

The distal muscle weakness and marked laterality of muscle involvement on MRI in this patient were unusual, as thyrotoxic myopathy is generally characterized by symmetrical weakness in proximal muscles. Ramsay reported that 18.5% of 54 patients with thyrotoxicosis showed involvement of both proximal and distal muscles (7). Some unusual cases of thyrotoxic myopathy mimicking distal myopathy have also been reported (3-5). Tsuchiya et al. described a case of chronic thyrotoxic myopathy resembling distal myopathy with rimmed vacuoles (3). Their patient showed steppage gait with muscle weakness and atrophy in four extremities, particularly prominently in the extensor muscles of the lower leg and in the flexor muscles of the thigh (3). Mild laterality of muscle involvement on computed tomography (CT) was also observed in their patient. The distribution of muscular weakness of the leg in their patient and the histopathological findings of the biopsied muscle resemble those of our patient. Although unilateral involvement of the lower leg was not observed in their patient, we cannot exclude the possibility that our patient was examined in the early stage before she developed bilateral leg muscle weakness.

Histopathology of thyrotoxic myopathy generally shows nonspecific myopathic changes and type 2 fiber-dominant atrophy (2, 7, 8). Since type 1 fiber-dominant atrophy with mild fiber type grouping was also observed in this patient, it is possible that thyrotoxic peripheral neuropathy (9) with myopathy affected the type 1 fiber predominance.

It is intriguing that muscle weakness was predominantly involved in tibialis anterior muscle despite diffuse MRI findings in the lower leg. Since MRI findings reflecting inflammatory changes (10) are frequently observed in asymptomatic muscle groups in polymyositis (11), chronic subclinical inflammation may be detected on MRI in cases of thyrotoxic myopathy. Ramsay showed that extensor muscles were twice as commonly affected as flexors in thyrotoxic myopathy (7). Extensor muscles are known to have a higher proportion of red fibers than white (12), and red muscles have a much greater number of mitochondria than white muscles (13). Previous studies have shown that excessive thyroid hormones can lead to the impairment of mitochondrial energy metabolism in skeletal muscles by driving both coupled oxidative phosphorylation and uncoupled respiration (14, 15). Therefore, we speculate that excessive thyroid hormones predominantly affect mitochondria-rich extensor muscles, such as the tibialis anterior muscle.

In summary, we reported the first case of thyrotoxic myopathy presenting as unilateral drop foot. Thyrotoxicosis should be considered as a potential cause of unilateral drop

foot.

**The authors state that they have no Conflict of Interest (COI).**

## *References*


1. Kammer GM, Hamilton CR Jr. Acute bulbar muscle dysfunction and hyperthyroidism. A study of four cases and review of the literature. Am J Med **56**: 464-470, 1974.
2. Ruff RL, Weissmann J. Endocrine myopathies. Neurol Clin **6**: 575-592, 1988.
3. Tsuchiya I, Sahashi K, Ibi T, et al. Chronic thyrotoxic myopathy resembling the distal myopathy with rimmed vacuoles--a case report. Rinsho Shinkeigaku **27**: 223-227, 1987 (in Japanese).
4. Puvanendran K, Cheah JS, Naganathan N, et al. Thyrotoxic myopathy: a clinical and quantitative analytic electromyographic study. J Neurol Sci **42**: 441-451, 1979.
5. Korényi-Both A, Korényi-Both I, Kayes BC. Thyrotoxic myopathy. Pathomorphological observations of human material and experimentally induced thyrotoxicosis in rats. Acta Neuropathol **53**: 237-248, 1981.
6. Oh SJ. Clinical electromyography-nerve conduction studies. 3rd ed. Lippincott Williams & Wilkins, Philadelphia, 2003: 666-672.
7. Ramsay ID. Muscle dysfunction in hyperthyroidism. Lancet **2**: 931-934, 1966.
8. Wiles CM, Young A, Jones DA, et al. Muscle relaxation rate, fibre-type composition and energy turnover in hyper- and hypothyroid patients. Clin Sci (Lond) **57**: 375-384, 1979.
9. Feibel JH, Campa JF. Thyrotoxic neuropathy (Basedow's paraplegia). J Neurol Neurosurg Psychiatry **39**: 491-497, 1976.
10. Hernandez RJ, Keim DR, Chenevert TL, et al. Fat-suppressed MR imaging of myositis. Radiology **182**: 217-219, 1992.
11. O'Connell MJ, Powell T, Brennan D, et al. Whole-body MR imaging in the diagnosis of polymyositis. AJR Am J Roentgenol **179**: 967-971, 2002.
12. Adams RD, Denny-Brown D, Pearson CM. Diseases of Muscle. London, 1999.
13. Lawrie RA. The relation of energy-rich phosphate in muscle to myoglobin and to cytochrome-oxidase activity. Biochem J **55**: 305-309, 1953.
14. Hoch FL. Biochemical actions of thyroid hormones. Physiol Rev **42**: 605-673, 1962.
15. Harper ME, Seifert EL. Thyroid hormone effects on mitochondrial energetics. Thyroid **18**: 145-156, 2008.