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Case report

An elderly-onset limb girdle muscular dystrophy type 1B (LGMD1B) with pseudo-hypertrophy of paraspinal muscles

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Abstract

Mutations in *LMNA*, encoding A-type lamins, lead to diverse disorders, collectively called "laminopathies," which affect the striated muscle, cardiac muscle, adipose tissue, skin, peripheral nerve, and premature aging. We describe a patient with limb-girdle muscular dystrophy type 1B (LGMD1B) carrying a heterozygous p.Arg377His mutation in *LMNA*, in whom skeletal muscle symptom onset was at the age of 65 years. Her weakness started at the erector spinae muscles, which showed marked pseudo-hypertrophy even at the age of 72 years. Her first episode of syncope was at 44 years; however, aberrant cardiac conduction was not revealed until 60 years. The p.Arg377His mutation has been previously reported in several familial *LMNA*-associated myopathies, most of which showed muscle weakness before the 6th decade. This is the first report of pseudo-hypertrophy of paravertebral muscles in *LMNA*-associated myopathies. The pseudo-hypertrophy of paravertebral muscles and the elderly-onset of muscle weakness make this case unique and reportable.

Keywords: LMNA; Laminopathy; Limb-girdle muscular dystrophy type 1B; Pseudo-hypertrophy; Late-onset

1. Introduction

Laminopathies, disorders caused by mutations in the *LMNA* gene, exhibit extremely diverse phenotypes [1,2]. *LMNA* encodes A-type lamins, which are major constituents of the nuclear lamina and are expressed in all post-mitotic cells. The first *LMNA* mutation was identified in a family with Emery–Dreifuss muscular dystrophy 2 (EDMD2) [3] and thereafter seen in many other disorders, including dilated cardiomyopathy (DCM), conduction defect (CD), limb-girdle muscular dystrophy type 1B (LGMD1B), *LMNA*-related congenital muscular dystrophy (L-CMD), Charcot–Marie–Tooth disease (CMT), lipodystrophy, restrictive dermopathy, and progeria syndrome [1,2]. More than 400 mutations in *LMNA* have been identified (http://www.umd.be/LMNA/).

Clinical onset of *LMNA*-associated myopathies is usually before the mid-thirties. In a large cohort study, 60% of patients with muscle weakness had onset before the age of 20 years, and only 15% of patients had onset after the age of 40 years [4]. In both LGMD1B and EDMD2, the cardiac muscle is frequently involved. While the distribution of the affected skeletal muscles sometimes overlaps in LGMD1B and EDMD2, the involvement of paravertebral muscles is more frequent in EDMD2 than in LGMD1B (40% vs. 20%) [4] and early contracture is the characteristic feature of EDMD2. In L-CMD, the involvement of axial muscles reached up to 60% [4]. Although calf pseudo-hypertrophy and paravertebral atrophy are sometimes reported, pseudo-hypertrophy of paravertebral muscles had not been reported.

We report a very-late-onset LGMD1B patient harboring a heterozygous mutation (c.1130G > A, p.Arg377His) in *LMNA* with marked paraspinal pseudo-hypertrophy.

2. Case report

The patient was a 72-year-old Japanese female with hyperlordosis and weakness of the limbs. Her developmental milestones were normal. She experienced the first episode of syncope at 44 years and thereafter fainted once in several years. Although electrocardiography was frequently performed by her attending physician, abnormalities were not detected until she

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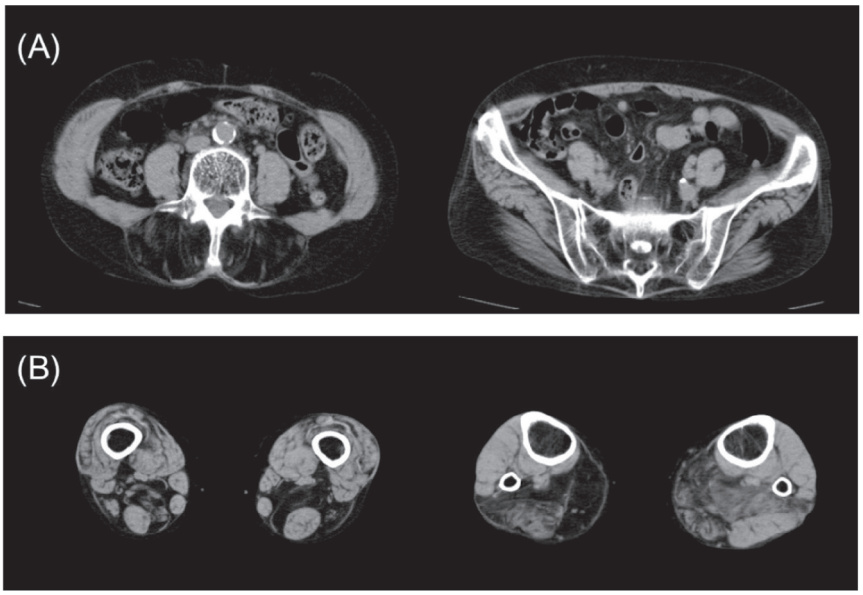

Fig. 1. Muscle CT images. (A) Marked pseudo-hypertrophy of the paraspinal muscles was found in the transverse section of the trunk. The rectus abdominis muscle showed fatty degeneration, particularly in the upper part. Gluteal muscles were relatively spared. (B) Left: thigh; Right: lower leg. Some of the hamstrings and gastrocnemius showed marked fatty degeneration but muscle volume was preserved. On the other hand, the quadriceps femoris atrophied severely and showed fatty degeneration to a lesser extent than the flexor muscles.

was 60 years old. She experienced fatigue on exertion at 60 years, and sick sinus syndrome with a complete atrioventricular (AV) block was discovered for the first time. After a pacemaker was implanted, the syncope attacks and fatigue disappeared. At 65 years, her family pointed out that she had lordosis. It became hard for her to climb stairs, and she noticed slowly progressive weakness in her lower limbs at 70 years. At her first visit to our institution at the age of 72 years, her Medical Research Council (MRC) scale was 3−4 and 4−5 for the proximal lower and upper limbs, respectively. For example, the MRC scale of deltoid muscle was 4, biceps brachii 4+ , barchioradialis 4−, triceps 4, gluteus maximus 3−, quadriceps femoris 4+ , hamstrings 4, tibialis anterior 4+ , gastrocnemius 3+ . She could stand up on tiptoes, and Gowers' sign was negative. The MRC scale of neck and truncal extension muscle was 3. No prominent weakness was observed in the distal muscles. Joint contractures, rigid spine, lipodystrophy, and sensory disturbances were not present.

Computed tomography revealed severe fatty degeneration and pseudo-hypertrophy of paraspinal muscles from the thoracic to lumbar segments (Fig. 1A) and involvement of the muscles of the leg (Fig. 1B). Some of the hamstrings and calves showed severe fatty degeneration, and the quadriceps femoris showed severe atrophy and, to a lesser extent, fatty degeneration. The pelvic muscles were relatively spared.

Laboratory data as well as results of electromyographical and histopathological investigation indicated mild muscular disorder. The creatinine kinase (CK) value was 344 IU/L (normal <200 IU/L). Nerve conduction velocities were normal. Needle electromyography showed early recruitment and normal interference for biceps brachii, 1st interosseus dorsales, tibialis anterior, and lumbar paraspinal muscle. Insertion and resting potentials were normal. A muscle biopsy from the biceps brachii revealed mild myopathic changes with some atrophic

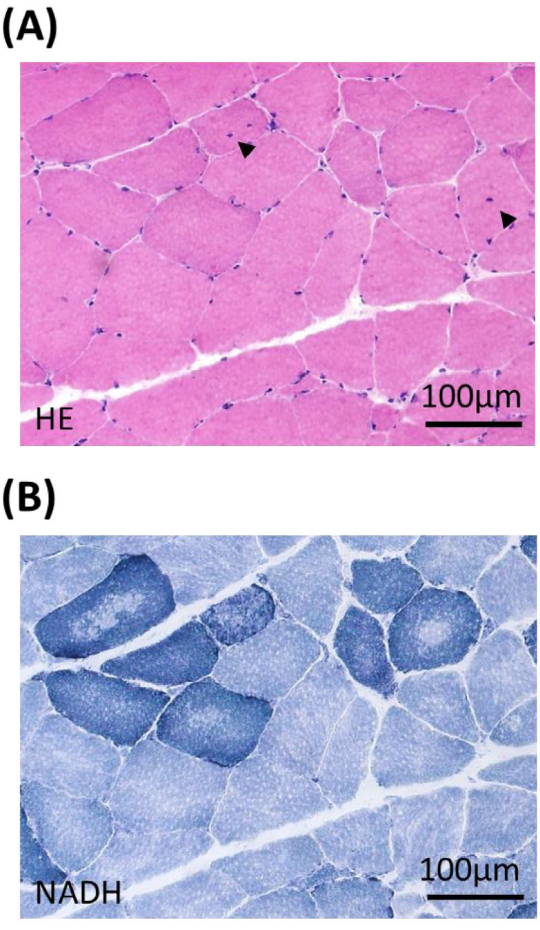

Fig. 2. Muscle biopsy from the biceps brachii of the index patient. (A) H&E stain reveals variation in fiber size, a few fibers with internal nuclei (arrowheads), and some atrophic fibers. (B) NADH-TR stain reveals fibers containing core-like structures, suggesting disorganized myofibrillar networks.