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Letter to the Editor

Paraspinal amyotrophy in *DNM-2*-related centronuclear myopathy

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Dear Editor,

Centronuclear myopathy (CNM) is a rare congenital myopathy characterized by the morphological feature of centrally located nuclei in a large number of muscle fibers. CNM is related to several causative genes: dynamin 2 (*DNM2*), myotubularin (*MTM1*), amphiphysin 2 (*BIN1*), and ryanodine receptor 1 (*RYR1*) [1]. *DNM2*-related CNM (*DNM2*-CNM) is an autosomal-dominant inherited disease that accounts for about 50% of CNM cases [1]. Although *DNM2*-CNM has shown a variety of clinical manifestations, from severe neonatal onset to mild adult onset, most patients present with slowly progressive muscle weakness in the distal or sometimes proximal limbs, ptosis, ophthalmoplegia, and facial weakness [2–4]. Muscle imaging, computed tomography (CT) and magnetic resonance imaging (MRI), studies have clearly shown relatively diffuse involvement in the lower leg muscles, but a selective pattern of involvement in posterior compartment muscles like gastrocnemius, soleus, biceps femoris, and semimembranosus [3–5]. Proximal limb girdle and paraspinal muscles could be affected clinically. However, no reports have evaluated muscle involvements other than of the upper and lower extremities using CT or MRI. Herein, we report a case of CNM with a *DNM2* mutation (p.E650 K) that demonstrated marked erector spinae muscle atrophy on CT.

1. Case report

A 50-year-old Japanese man noticed grip weakness in his 20s. He presented with a 5-year history of lumbar pain, flexed posture, easy fatigability, and slow progression of foot weakness. He had only brother and no children. No family history of neuromuscular disorders was elicited and parents had nonconsanguineous marriage. On admission, he showed mild camptocormia but no head drop. Neurological examination showed mild grip weakness and slight muscle weakness and atrophy in the distal lower extremities. He showed no weakness of the neck flexor and extensor strength. He also exhibited pes cavus due to plantar muscle atrophy (Fig. 1a). However, the patient was independent in terms of daily activities. He did not have ptosis or ophthalmoplegia. Serum creatine kinase level was 150 IU/L. Sensory and motor conduction study revealed normal latency, velocities, and amplitude of the evoked potentials, and electromyography revealed low-amplitude, short duration, polyphasic motor unit potentials with early recruitment in four limbs. Muscle CT showed marked fat replacement in the posterior compartment of the lower extremities (biceps femoris, semitendinosus, semimembranosus, gastrocnemius and soleus), while the quadriceps femoris and adductor magnus muscles were less affected (Fig. 1b,c). Muscle CT also demonstrated severe involvement of the erector spinae muscles (iliocostalis, longissimus and spinalis) (Fig. 1e–g), and moderate atrophy and fatty changes were observed in the gluteus maximus (Fig. 1g). Hematoxylin and eosin staining of a muscle biopsy from the quadriceps femoris showed nuclear centralization in 60% of fibers (Fig. 1d), and radial distributions of sarcoplasmic strands were observed on NADH-TR (data not shown). Genetic analysis identified heterozygous c.1948G > A (p.E650 K) mutation in the *DNM2* GTPase effector domain, representing a previously reported mutation [6].

2. Discussion

We report a case of DNM2-CNM in a patient who exhibited marked paraspinal amyotrophy on CT and showed a mutation in the GTPase effector domain (GED) of *DNM2*. Muscle CT in this case showed severe atrophy in the posterior compartment of the lower extremities (biceps femoris, semitendinosus, semimembranosus, gastrocnemius and soleus), and this selective pattern of muscle involvement was compatible with the findings of previous reports [3–5]. Our case also revealed a characteristic feature of marked paraspinal amyotrophy. No previous reports have described the appearance of paraspinal muscles on CT or MRI. However, since some cases showed muscle atrophy in the gluteus maximus [5], marked atrophy in not only the posterior compartment of the lower extremities, but also the trunk could offer a valuable feature for the diagnosis of *DNM2*-CNM.

DNM2 is one of the large GTPases that play a role in endocytosis and membrane trafficking. DNM2 is a 100-kDa multidomain protein, comprising an N-terminal GTPase domain, a middle domain (MD), a pleckstrin homology (PH) domain, a GED, and a C-terminal proline-rich domain (PRD). The majority of *DNM2*-CNM mutations are located in

Abbreviations: CNM, Centronuclear myopathy; CT, computed tomography; *DNM2*, dynamin 2; GED, GTPase effector domain; MD, middle domain; MRI, magnetic resonance imaging; PH, pleckstrin homology; PRD, proline-rich domain

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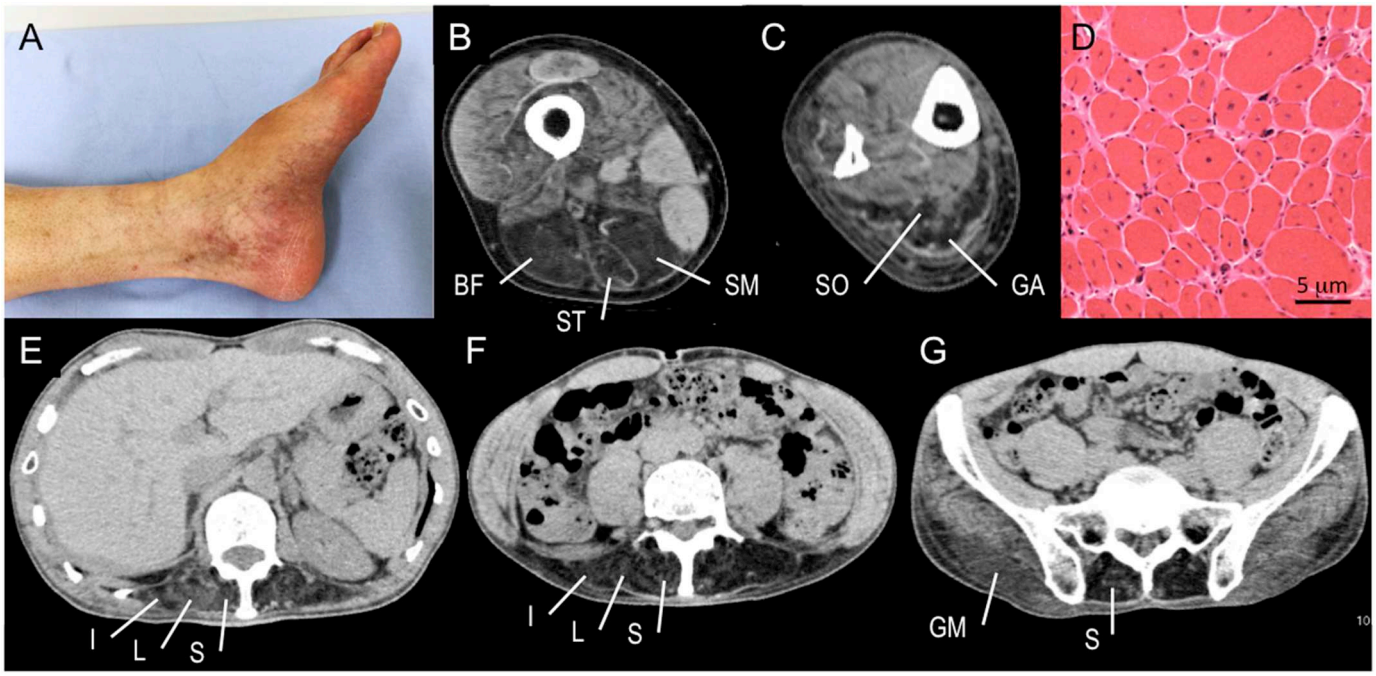

Fig. 1. Clinical and pathological findings and muscle CT images.
a: Patient presents pes cavus. b,c: Muscle CT reveals marked fat replacement in the posterior compartment of the lower extremities: biceps femoris (BF), semitendinosus (ST), semimembranosus (SM), gastrocnemius (GA) and soleus (SO). d: Hematoxylin-eosin stain of muscle biopsy shows numerous centronuclear fibers. e-g: Muscle CT shows severe involvement in erector spinae muscles: iliocostalis (I), longissimus (L) and spinalis (S), and moderate atrophy and fatty changes in the gluteus maximus (GM).

the MD and PH domains, while mutations in the PH domain lead to more serious clinical manifestations [6]. Our case showed slowly progressive moderate myopathy compatible with the clinical features of a previously reported case with the same GED mutation [6]. This GED mutation leads to relatively mild clinical features compared to those of CNM patients with the two majority mutations in the MD and PH domains. In addition, the marked paraspinal atrophy may represent a unique feature of *DNM2*-CNM harboring the GED mutation.

In the previous studies, *DNM2*-CNM patients frequently showed ptosis and ophthalmoplegia [1–3]. However, the patient in our case revealed neither symptom. A previous study indicated that ptosis and ophthalmoplegia are comparatively rare among Japanese patients, and ethnic background or genetic factors may contribute this finding [6].

3. Conclusions

Marked paraspinal amyotrophy on CT or MRI may be a characteristic feature of *DNM2*-CNM. The selective involvement of the erector spinae muscles and posterior compartment of the lower extremities could offer a valuable feature for the diagnosis of *DNM2*-CNM.

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Ethics approval and consent to participate

The authors declare that ethics approval was not required for this case report.

Declaration of Competing Interest

The authors declare that they have no competing interests.

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