Paraspinal amyotrophy in DNM-2-related centronuclear myopathy

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Case report

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Abstract

Background Dynamin 2-related centronuclear myopathy (DNM2-CNM) is a rare congenital myopathy, and clinically, slowly progressive muscle weakness in the distal or proximal limbs, calf muscle atrophy, and pes cavus are features that are highly suggestive of DNM2-CNM. We experienced a case of DNM2-CNM who exhibited marked paraspinal amyotrophy on CT and showed a mutation in the GTPase effector domain (GED) of DNM2. Case presentation A 50-year-old man presented with a 5-year history of lumbar pain and slow progression of foot weakness. He showed bilateral pes cavus. Electromyography revealed a myopathic pattern, and nerve condition velocities and amplitudes were normal. Muscle CT showed marked fat replacement in the posterior compartment of the lower extremities, and also demonstrated severe involvement of the erector spinae muscles. Muscle biopsy from quadriceps femoris showed nuclear centralization in the majority of fibers. Sequence analysis of Dynamin 2 (DNM-2) demonstrated heterozygous c.1948G>A (p.E650 K) mutation compatible with the diagnosis of DNM2-CNM. Conclusions This case suggests that marked paraspinal amyotrophy 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.

Background

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 proximal limbs, ptosis, ophthalmoplegia, and facial weakness [2,3]. 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 [2-4]. 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.

Case Presentation

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. No family history of neuromuscular disorders was elicited. On admission, neurological examination showed slight muscle weakness and atrophy in the distal lower extremities. 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. Electromyography revealed a myopathic

pattern without neuropathic signs, and nerve condition velocities and amplitudes were normal. 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. d), 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 [5].

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 [2-4]. 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 [4], 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 the MD and PH domains, while mutations in the PH domain lead to more serious clinical manifestations [5]. Our case showed slowly progressive moderate myopathy compatible with the clinical features of a previously reported case with the same GED mutation [5]. 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 [1,2]. 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 [5].

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.

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

Declarations

Ethics approval and consent to participate

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

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Availability of data and materials

The dataset supporting the conclusion of this article is included within the article.

Competing interest

The authors declare that they have no competing interests.

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None.

Authors' contributions

KK and HN examined and wrote the manuscript. KU performed the analyses. IN performed the pathological and gene analyses. SA helped to draft the manuscript. All authors read and approved the final manuscript.

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Figures

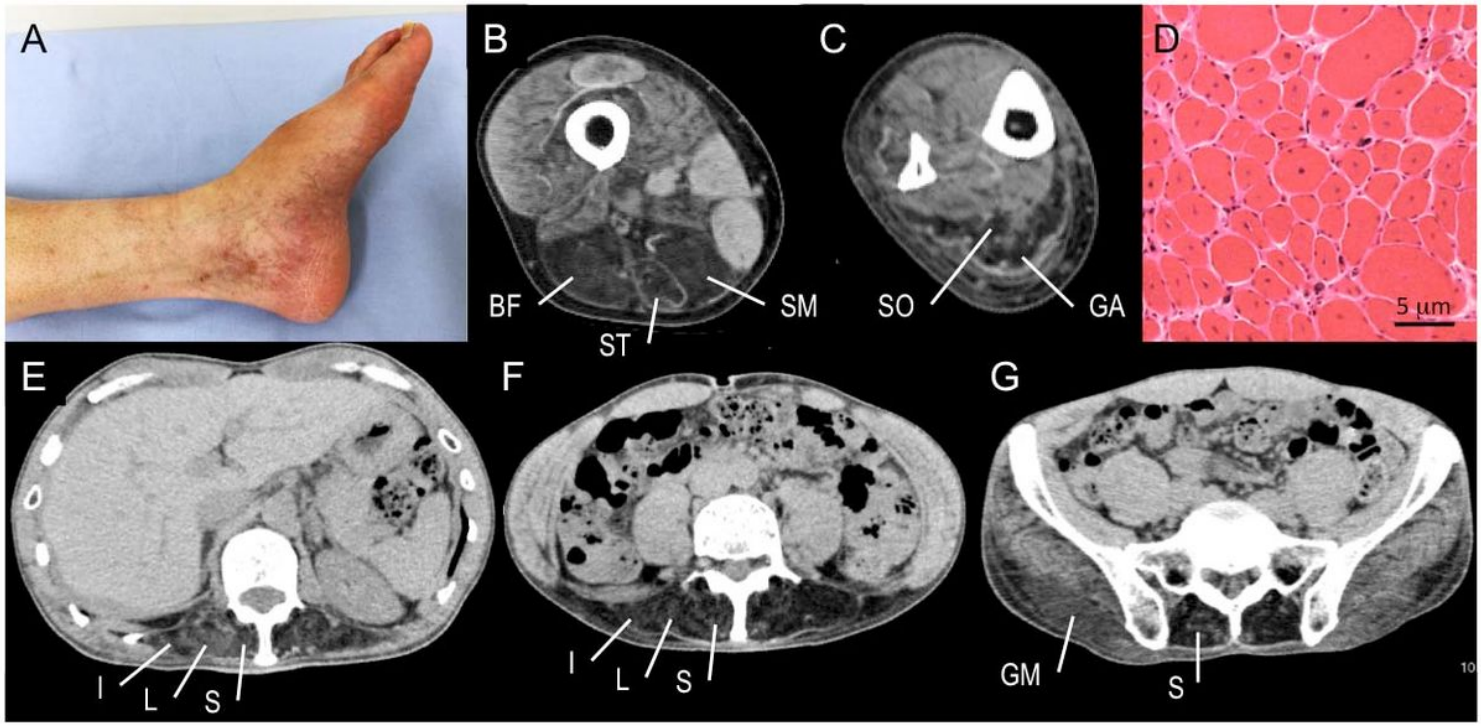

Figure 1

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).

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