

# MORC2 p.R252W Mutant Axonal Charcot–Marie–Tooth Disease Causes Peripheral Neuropathies and Pathological Myofiber Destruction

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## To the Editor

We present a case of a 32-year-old woman who presented with lower extremity weakness ongoing for 7 years. Her father had similar symptoms. The patient's physical examination reports showed atrophy and weakness of the distal limb muscles, and electromyography results suggested neurogenic damage. A biopsy of the patient's left sural nerve tissue was performed. Toluidine blue staining revealed a severe reduction in the density of myelinated nerve fibers in the nerve bundle, with no medullary-like structures, suggesting peripheral neuropathy. The patient's serum creatine kinase was 515.0 U/L (upper limit of normal 200 U/L), and her magnetic resonance imaging scans showed muscle edema in the anterior and posterior compartments of the lower extremities. The serial sectioning of the left gastrocnemius muscle demonstrated pathological myofiber destruction and the target fibers. Hematoxylin and eosin staining showed target fibers and inflammatory cell infiltration around some myofibers accompanied by obvious myofiber degeneration and necrosis. Nicotinamide adenine dinucleotide dehydrogenase-tetrazolium reductase staining showed obvious prominent fibers. Immunohistochemistry staining indicated partial degeneration of necrotic myofibers with CD68 (+). Disorganized and broken myogenic fibers and abnormal mitochondrial aggregation were observed under the transmission electron microscope (Figures 1 and 2).

The MORC2 c.754C>T(p.R252W) mutation was detected by gene analysis, which led to a diagnosis of Axonal Charcot-Marie-Tooth disease type 2Z(CMT2Z). Low-dose methylprednisolone tablets and an energy supplement were given to the patient. The patient's serum creatine kinase decreased to 220 U/L 3 months later. After 6 months, the muscle strength of both the patient's hands gradually decreased without affecting her quality of life.

CMT2Z comprises a clinically and genetically heterogeneous group of disorders affecting the motor and sensory neurons in the peripheral nervous system.<sup>1</sup> The microorchidia family CW-type zinc finger 2 (MORC2) has been newly identified as a causative gene of CMT type 2Z in 2016.<sup>2</sup> Our patient exhibited remarkable

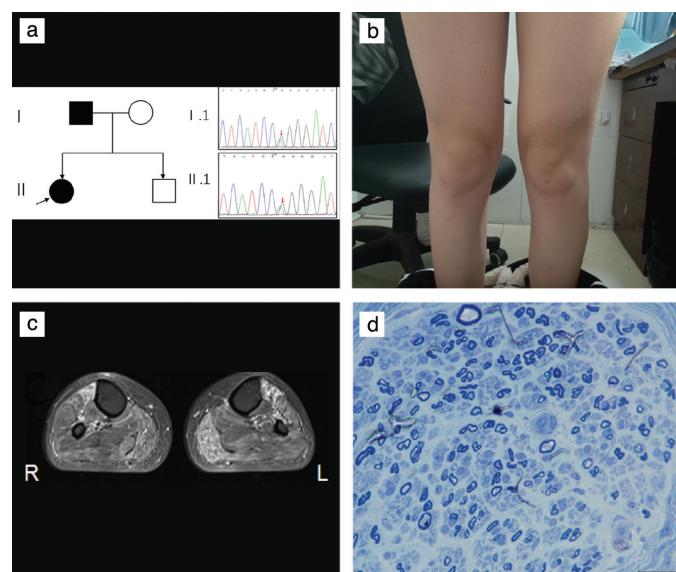


FIG. 1. Clinical findings of the patient. a-d: Pedigree of individuals with CMT2Z carrying the MORC2 c.754C>T(p.R252W) mutation and sequencing chromatograms (a); Photographs of the patient showing distal muscular dystrophy of bilateral lower extremities (b); Short-tau inversion recovery of MRI scans of the patient showed muscle edema in the anterior and posterior compartment of the lower extremities (c); Pathology of Sural nerve showed the density of myelinated nerve fibers was reduced severely (d, Toluidine Blue Staining,  $\times 1000$ )



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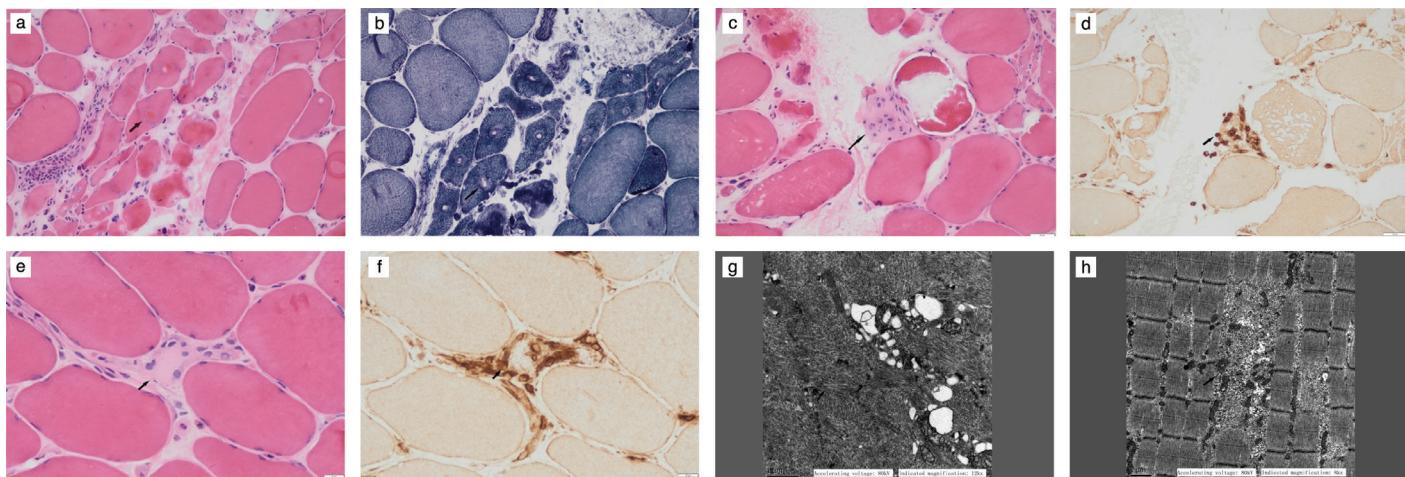
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**FIG. 2.** Pathological findings of the patient's left gastrocnemius muscle.a-h: Hematoxylin and eosin (H&E) staining and NADH-TR staining showed target fiber, respectively (a, b, Black Arrow,  $\times 200$ );H&E staining showed degenerated and necrotic myofibers (c, Black Arrow,  $\times 200$ ; e, Black Arrow,  $\times 400$ ); Immunohistochemical staining showed CD68 positive in necrotic muscle fibers (d, Black Arrow,  $\times 200$ ; f, Black Arrow,  $\times 400$ );Transmission electron microscope axial scanning showed myofibers became irregular (g, Black Arrow,  $\times 12000$ ); Longitudinal scanning showed myofiber destruction and abnormal mitochondrial aggregation (h, Black Arrow,  $\times 8000$ )

pathological myofiber destruction distinct from that previously reported in CMT2Z, which greatly expands the knowledge of CMT2Z.

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