To the Editor: Charcot-Marie-Tooth disease (CMT) is a clinically and genetically heterogeneous inherited neuropathy, with Type 1A being the most common. CMT 1A is characterized by progressive weakness and atrophy of the distal limb muscles beginning in the peroneal group, mild distal sensory loss, diminished tendon reflexes, and slow nerve conduction velocity.[1] Spinal nerve root hypertrophy is a distinct sign of CMT 1A.[2] This sign can be detected on magnetic resonance images (MRI), but it is often overlooked. Instead, diagnosis of this disease is often made based on biopsy and genetic testing.

A 28-year-old woman was admitted to our neurology unit with a 2-year history of progressive lower extremity weakness accompanied with muscle atrophy. Two years before admission, she first experienced decreased strength in both lower limbs that was more severe on the right with mild foot drop. These symptoms progressed until the patient noticed decreased muscle mass of both lower extremities. Her father and elder sister had similar manifestations. Neurological examinations revealed level IV distal muscular atrophy in both upper extremities and left lower extremity, and level III muscular strength in her right lower extremity, with hyporeflexia of the bilateral tendon reflex. Bilateral calf (especially gastrocnemius), thenar, hypothenar, and first dorsal interosseous muscles showed atrophy. In addition, pes cavus was observed, and pain sensation of the distal lower limbs was mildly decreased. Cerebral spinal fluid (CSF) examination showed normal white blood cell count (1 × 10⁶/L) and protein level (360 mg/L, normal range: 150–450 mg/L). A nerve conduction study (NCS) showed uniformly reduced velocity and delayed latency in all four extremities. Compound muscle activation potential and sensory nerve action potential were grossly reduced, especially in the lower extremities. F wave was absent in the right tibial nerve. Needle electromyography showed motor unit potentials with prolonged duration and increased amplitude, indicating chronic denervation.

MRI of the spine revealed markedly hypertrophic cauda equina and nerve roots that almost completely filled the spinal canal in the cervical (C5–C7) and lumbar-sacral areas (L3–S3), and the thecal sac was mildly enhanced with gadolinium-diethylenetriamine pentaacetic acid in these areas [Figure 1]. Sural nerve biopsy revealed nerve demyelination, axonal degeneration, and an obvious loss of large myelinated fibers, accompanied by Schwann cell proliferation and onion bulb formation. Duplication of the peripheral myelin protein 22 gene was confirmed by a genetic sequence test. Therefore, the diagnosis of CMT 1A was established.

Enlargement of nerve roots, which is a distinct feature of hypertrophic neuropathy, has been frequently reported in neurofibromatosis and chronic inflammatory demyelinating polyneuropathy (CIDP).[3,4] This phenomenon can also be seen in CMT disease that caused by onion-bulb formation, but rare have been reported. Our case had been misdiagnosed with neurofibromatosis twice and with CIDP once at different local hospitals. Despite the many similarities between CMT 1A and neurofibromatosis, there are some major differences. First, in contrast to the smooth enlargement of nerve roots seen in CMT 1A, neurofibromatosis is characterized by nodular enlargement. Second, patients of neurofibromatosis often have typical skin manifestations of café au lait spots or Lisch nodules. Third, the lack of neural foramina erosion or widening on MRI helped us rule out the diagnosis of neurofibromatosis.

Nerve root hypertrophy is also present in CIDP. It is difficult to distinguish CMT 1A from CIDP basing on findings on MRI.

Address for correspondence: Dr. Li Yong Wu, Department of Neurology, Xuanwu Hospital, Capital Medical University, 45 Changchun Street, Beijing 100053, China E-Mail: wmywy@hotmail.com

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

© 2017 Chinese Medical Journal | Produced by Wolters Kluwer - Medknow

Received: 05-06-2017 Edited by: Li Min Chen
How to cite this article: An H, Li J, Wang LM, Cui B, Piao YS, Ren YJ, Chen H, Wang YP, Wu LY. A Rarely Concerned Magnetic Resonance Image Sign of Spinal Nerve Root Hypertrophy in Type 1A Charcot-Marie-Tooth Disease. Chin Med J 2017;130:2767-8.
alone. Uniformly reduced velocity and delayed latency in all four extremities on NCS examination are often observed in CMT 1A. In contrast, nonuniform abnormalities in nerve conduction tend to present in CIDP. In addition, protein-cell separation in CSF is supportive for the diagnosis of CIDP, but not usually seen in CMT 1A. The above-mentioned features do no progress consistently at different stages of these diseases, therefore, the differential diagnosis should remain broad and be based on clinical characteristics such as a family history, physical findings, CSF laboratories, appropriate imaging, and electrophysiological and pathological features. If necessary, genetic tests are needed.

Acknowledgment
We are grateful to the patient and her family for permission to publish this information.

Financial support and sponsorship
This work was supported by grants from the National Natural Science Foundation of China (No. 81470074 and No. 81401040), Clinical Fund from Beijing Municipal Science and Technology Committee (No. Z141107002514117), and Beijing Municipal Government Fund (No. PXM2017_026283_000002).

Conflicts of interest
There are no conflicts of interest.

References
1. Rui W, He L, Wei Z, Zhaoxia W, Yuehuan Z, Jing L, et al. Clinical and pathological variation of Charcot-Marie-Tooth 1A in a large Chinese cohort. Biomed Res Int 2017;2017:6481367-72. doi: 10.1155/2017/6481.
2. Liao JP, Waclawik AJ. Nerve root hypertrophy in CMT type 1A. Neurology 2004;62:783. doi: 10.1212/01.WNL.0000103234.32489.CA.
3. Shibuya K, Sugiyama A, Ito S, Misawa S, Sekiguchi Y, Mitsuma S, et al. Reconstruction magnetic resonance neurography in chronic inflammatory demyelinating polyneuropathy. Ann Neurol 2015;77:333-7. doi: 10.1002/ana.24314.
4. Pytel P, Rezania K, Soliven B, Frank J, Wollmann R. Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) with hypertrophic spinal radiculopathy mimicking neurofibromatosis. Acta Neuropathol 2003;105:185-8. doi: 10.1007/s00401-002-0616-7.

Figure 1: Spinal magnetic resonance images showed bilateral enlargement of nerve roots (S1–S3 levels). The widest point was about 1.2 cm. There were multiple abnormal cystic abnormal signals (yellow arrows) along the nerves (red arrows). (a and c) T₁-weighted images; (b and d) T₂-weighted images.