Neurology Asia 2020; 25(3) : 399 – 401

Low back pain as a presenting symptom in GNE myopathy

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Abstract

GNE myopathy is a rare autosomal recessive early adult-onset myopathy with slow progression that preferentially affects the tibialis anterior muscles and commonly spares the quadriceps femoris muscles. It is caused by biallelic mutations in *GNE* gene encoding for a single protein with key enzymatic activities in sialic acid biosynthetic pathway. However, diagnosing GNE myopathy can be challenging due to its phenotypic variability. This is the report of a 35-year-old man with GNE myopathy who presented with a low back pain for four years. A lumbar magnetic resonance imaging showed atrophy of lumbar paraspinal muscles. GNE myopathy was confirmed by genetic analysis. This case is unique and broaden the early clinical spectrum of GNE myopathy.

Keywords: GNE myopathy, low back pain, paraspinal muscles

INTRODUCTION

GNE myopathy, also known as distal myopathy with rimmed vacuoles, Nonaka myopathy, or hereditary inclusion body myopathy, is an autosomal recessive early adult-onset myopathy with slow progression that preferentially affects the tibialis anterior muscles and commonly spares the quadriceps femoris muscles.[1,2] This disease is caused by mutations in the *GNE* gene encoding a bifunctional enzyme [uridine diphosphate-N-acetylglucosamine 2-epimerase and N-acetylmannosamine kinase] that catalyzes two rate-limiting reactions in cytosolic sialic acid synthesis.[3] There are now almost 150 known mutations associated with GNE myopathy, the vast majority of which are missense.[4]

Following the identification of the causative gene defect, patients with GNE myopathy characterized by unusual clinical presentations are increasingly recognized. Therefore, clinical diagnosis of GNE myopathy remains a challenge. This is the report of a patient with GNE myopathy who presented with a longstanding low back pain as a prominent and early feature of the disease.

CASE REPORT

A 35-year-old man presented with a low back pain for four years. It was experienced as dull and constant. The intensity ranged from mild to moderate. The pain did not radiate towards the lower limbs. Consultation with the orthopedic surgeon could not find any spinal lesions that might cause back pain. He was managed with conservative treatment including some procedures, but the pain was not relieved at all. He was referred to the tertiary hospital after lumbar MRI (Magnetic Resonance Imaging). There was no family history of neuromuscular disorders. He walked with his back leaning backwards and with both hands on his back. Neurologic examination showed weakness of dorsiflexion of ankles, extension of toes (Medical Research Council Grade 4), and abdominal muscles with normal hip extension, hip abduction, and knee extension. Ankle jerk was absent bilaterally. He has pes cavus. No other neurologic symptoms or signs were noted.

The chemical and serological laboratory data were unremarkable except for elevated creatine kinase (568 U/L). Nerve conduction studies showed only decreased amplitudes of compound muscle action potentials of the peroneal nerves. Except for that, the conduction velocities of motor and sensory nerves were within the normal limits. Needle electromyography revealed denervation potentials in the extensor digitorum brevis, tibialis anterior, gastrocnemius, first dorsal interossei, biceps brachii, and triceps brachii muscles with sparing the vastus lateralis muscles. Motor unit potential analysis showed

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Date of Submission: 14 February 2020, Date of Acceptance: 22 July 2020

small amplitudes, short duration, and polyphasic motor unit potentials. Early recruitments were noted in those denervated muscles. There were no insertional activities in the lumbar paraspinal muscles. MRI of the lumbar spine at the local clinic showed severe fatty infiltration of the lumbosacral paraspinal muscles with preserved psoas and thoracic paraspinal muscles (Figure 1). Given the age of onset, the level of creatine kinase, electrophysiological findings, and distribution of the involved muscles, a provisional diagnosis of GNE myopathy was made. PCR sequencing of *GNE* gene disclosed heterozygous variants c.[131G>C (exon 2)]; [1807G>C (exon 10)] (p.[Cys44Ser]; [Val603Leu]).

On follow up, he continued to be able to walk alone without aid, even two years after the initial diagnosis.

DISCUSSION

The atrophy of lumbosacral paraspinal muscles was likely to be the cause of the low back pain, and the unique walking posture in this patient was helpful to direct the investigations towards genetic investigation. Another noteworthy feature is that the reason for the delay in diagnosis was that it has long been thought that mild weakness in the lower limbs was usually caused by lumbosacral radiculopathy along with a low back pain. However, the patient's unique lordotic gait was due to spinal muscle weakness. Lordosis can lead to excess pressure on the spine, causing muscle pain and discomfort. When the spine curves abnormally, the muscles get pulled in different directions, resulting in muscle tightening or spasm.

Recently, muscle MRI has been demonstrated to be helpful in a number of myopathies, especially hereditary myopathies. It can provide added value when correlated with clinical phenotype, be a guide for genetic testing, and demonstrate longitudinal changes of muscle disease.[5] MRI in the myopathy has been focused on the pelvis, thigh, and calf muscles, but this case emphasizes the value of assessing lumbar paraspinal muscles on MRI because of their striking features in the early stage of GNE myopathy. Given the pathophysiology of the disease, recent clinical trials have evaluated the use of sialic acid or ManNAc (N-Acetyl-D-mannosamine; a precursor of sialic acid) in patients with GNE myopathy, as well as early gene therapy trials. Now that there are therapies under investigation, it is critical that a timely and accurate diagnosis is made in patients with GNE myopathy.[4]

Among the symptoms or signs of large enrolled patients with GNE myopathy in Asia[6,7], low back pain or atrophy of the lumbar paraspinal muscles is very unusual but may be important in some patients.[8-10] Atrophy of lumbar paraspinal muscles should be considered to be one of the early clinical features of GNE myopathy.

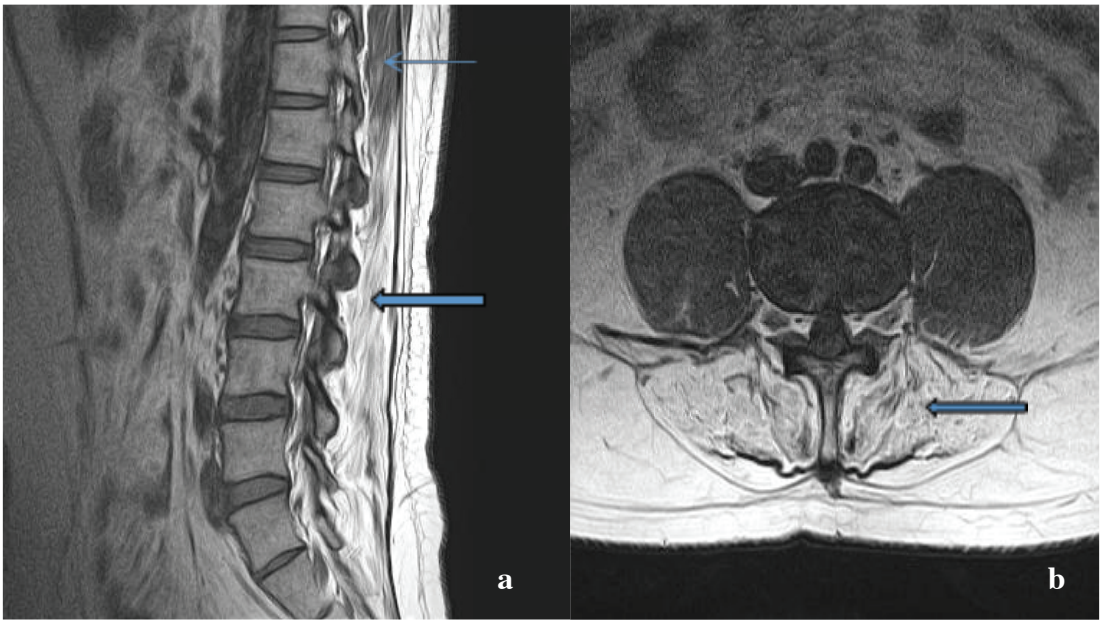

Figure 1. Sagittal (a) and axial (b) T_1 weighted MRI of the lumbar spine demonstrating severe atrophy of the lumbar paraspinal muscles (thick arrows) and preserved thoracic paraspinal muscles (thin arrow).

DISCLOSURE

Conflict of interest: None

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