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The Atalstin 1 mutation related hereditary sensory neuropathy

Jae-Chan Koo M.D., Kang-Hyeok Kim M.D., Han-Young Jung M.D., Kyung-Lim Joa M.D., Chang-Hwan Kim M.D., Myeong-Ok Kim M.D. Department of Physical & Rehabilitation Medicine, College of Medicine, Inha University, Incheon, Republic of Korea.

Introduction

Hereditary sensory neuropathy (HSN) is a rare genetic disorder characterized by progressive sensory loss, primarily affecting the distal parts of the limbs. It may be caused by mutations in several genes, such as SPTLC1, SPTLC2, RAB7, and Atlastin 1 (ATL1) gene. While ATL1 mutation have been reported more commonly associated with hereditary spastic paraplegia type 3A (SPG3A), emerging evidence suggests that certain ATL1 variants may also result in an HSN phenotype. We report a case of a sensory neuropathy with ALT1 gene mutation, with detailed clinical and electrophysiologic features.

Case

A 5-year-old male was referred to the outpatient clinic with primary complaints of tingling sensation in his fingers and toes that had been ongoing for several months. Patient was born at full term with a birth weight of 3.3 kg. He had no significant medical history and did not experience any trauma to the hands or feet. His developmental milestones were within normal limits. There was no family history of similar symptom. Physical examination revealed no definite motor weakness in all limbs, while sensory examination revealed tingling sensations at the distal ends of all fingers bilaterally and at the tips of the first and second toes on both feet. Deep tendon reflexes were normal, and no signs of spasticity were observed. One week later, we performed laboratory test, brain imaging to evaluate possible pathology. Laboratory tests were all normal. Brain magnetic resonance imaging with venography and diffusion-weighted imaging showed no abnormal findings (Fig. 1). Neurophysiologic testing revealed abnormal findings in sensory nerve conduction velocities in all limbs, and absent F waves in bilateral peroneal nerves (Table 1). Based on these findings, a hereditary or idiopathic sensory neuropathy was primarily suspected. However, other differential diagnoses, including early-onset Charcot–Marie–Tooth disease and acquired peripheral neuropathies were also considered. To differentiate among these possible etiologies and to identify an underlying genetic cause, next-generation sequencing (NGS) was performed. It revealed a splice site mutation, c.35-3C>T, was detected. This variant was classified as a variant of uncertain significance; however, it was considered potentially relevant in the context of the patient's clinical and electrophysiological findings. Further family genetic testing and follow-up evaluations are planned.

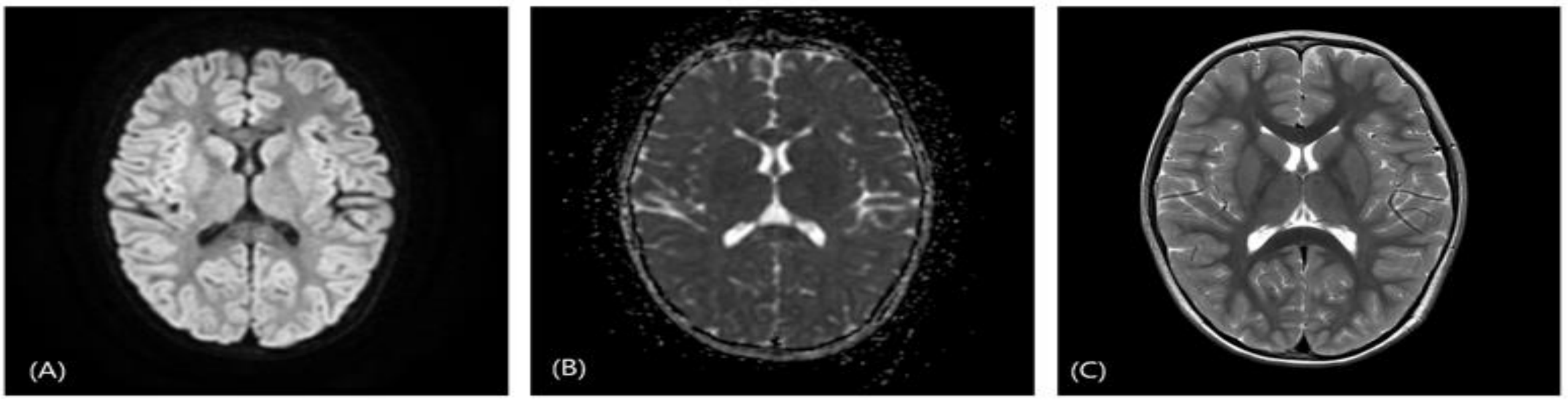

Figure 1. (A), (B), (C) Brain magnetic resonance image shows no abnormal findings.

Motor nerve conduction study								
	Right				Left			
	Latency (ms)	Amplitude (mV)	Conduction velocity (m/s)	F wave (ms)	Latency (ms)	Amplitude (mV)	Conduction velocity (m/s)	F wave (ms)
Median	2.42/5.06	5.3/5.6	52.9	16.8	2.10/4.77	6.8/6.8	52.5	18.3
Ulnar	2.00/4.40	6.6/6.9	58.4	18.3	1.85/4.31	8.1/7.1	56.9	16.1
Peroneal	2.33/6.58	3.3/3.2	45.9	Not evoked	2.44/6.69	2.1/2.2	45.9	Not evoked*
Tibial	2.06/7.21	15.8/8.4	45.7	27.9	2.23/7.06	16.8/16.1	48.6	28.0
Sensory nerve conduction study								
	Right				Left			
	Latency (ms)	Amplitude (uV)	Conduction velocity (m/s)		Latency (ms)	Amplitude (uV)	Conduction velocity (m/s)	
Median	2.52*	47.9	39.7*		2.56*	42.3	39.0*	
Ulnar	2.06*	39.7	38.8*		2.08*	38.8	38.4*	
Sural	1.83*	12.8	38.2*		2.42*	14.4	33.1*	
Peroneal	2.17*	10.5	36.9*		2.13*	7.8	37.6*	

Table 1. Nerve Conduction Study findings of both upper and lower extremities in this case.

Conclusion

This case reports a case of HSN associated with an ATL1 gene mutation. Nerve conduction studies and NGS are recommended to rule out overlapping neurological disorders. Therefore, clinicians should be aware that pediatric patients presenting with peripheral sensory symptoms of unknown etiology may have neurological abnormalities. And although the pathogenicity of this variant (c.35-3C>T) remains unclear, this case allows us to consider ATL1 variants as an unexplained pediatric sensory neurological abnormality.