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Case Report

Hereditary spastic paraplegia accompanied by motor axonal polyneuropathy: A case report

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Abstract

Background and aims: Hereditary spastic paraplegia (HSP) encompass a diverse set of uncommon neurodegenerative conditions characterized by stiffness in the lower limbs resulting from the degeneration of the corticospinal tract. Although the primary pathology in HSP involves the degeneration of the long motor axons in the corticospinal tracts, which are responsible for voluntary muscle control, there may be associated features of peripheral neuropathy.

Case Presentation: We report a 26-year-old lady who was referred to us with progressive spastic gait abnormality. She underwent electrodiagnostic evaluation, and a neurogenic pattern, especially in distal muscles, was observed.

Results: Neurologic examination revealed muscle weakness, spasticity, and deep tendon reflexes in all limbs without sensory symptoms or ataxia. Along with the patient's history and physical examination, complicated HSP associated with motor axonal neuropathy was suggested.

Conclusion: This case highlights the importance of a comprehensive evaluation, combining clinical examination and electrodiagnostic studies, in understanding the intricate manifestations of neurogenetic disorders.

Keywords: Hereditary spastic paraplegia, Motor axonal polyneuropathy, Neurophysiology

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Introduction

Hereditary spastic paraplegia (HSP) represents an uncommon genetic neurodegenerative condition marked by gradually advancing stiffness and diminished strength in the lower limbs, stemming from the length-based breakdown of axons within the corticospinal tract and posterior columns (1). Its prevalence is 0.1–9.6 per 100 000 individuals worldwide (2). It has four inheritance patterns: autosomal dominant, autosomal recessive, mitochondrial, and X-linked inheritance patterns (3). Based on clinical presentation, it is classified into uncomplicated (or pure) and complicated (or complex) forms. Pure HSP is characterized by bilateral progressive lower-extremity spastic weakness, positive Babinski, hyperreflexia, and gait disturbances (4). The complex form is characterized by a range of neurological and non-neurological signs and symptoms, including cerebellar signs, peripheral neuropathy, seizures, intellectual disability, ataxia, and visual defects (5). HSP is diagnosed mainly by neurological exam and testing to rule out other disorders. However, due to the heterogeneous nature of HSP, genetic testing has emerged as a crucial element in clinical evaluations and diagnoses (6). The association of HSP with motor axon and peripheral neuropathy is quite rare.

A research investigation revealed that mutations in the SPG3A gene, associated with HSP, can be correlated with axonal sensory-motor neuropathy (7).

Given that the coexistence of motor axonal polyneuropathy is an infrequent complication of HSP, a case of HSP accompanied by motor axonal polyneuropathy will be presented. It aims to shed light on the uncommon association of HSP with motor axonal polyneuropathy, emphasizing the importance of considering such atypical presentations in diagnosing patients with HSP. The patient provided consent to participate in this presentation.

Case Presentation

Due to progressive walking difficulty, a 26-year-old Persian female patient has been referred to our clinic in the Electrodiagnostic Department of Amin Hospital, Isfahan, Iran.

She declared that when she was 15 years old, after experiencing emotional stress, her gait disturbance began. According to the patient and her mother, it manifested as a toe-walking gait. There have been no other complaints, such as blurred vision, speech disturbance, difficulty in swallowing, or signs and symptoms indicative of a cerebellar stroke at that time. At the age of 18, she had undergone Achilles tendon lengthening, but no improvement in gait was observed and the condition progressed even further.

There were no similar complaints from her family

members and relatives. Additionally, her family history was negative for any genetic disease. The parents were non-relatives.

There was no complaint of stiffness in upper limbs, craniobulbar symptoms, sensory symptoms, incoordination, seizures, and cognitive impairment. She had no complaints of urinary and bowel dysfunction and visual or hearing loss. The dexterity of the hands was normal. The patient was delivered via cesarean section, and her developmental milestones and general health have been normal until the appearance of the current symptoms.

In the physical examination, a scissor-like spastic gait was observed, accompanied by atrophy in the gastrocnemius muscles and pes cavus. She was able to walk independently and without any assistive device.

Motor examination showed lower limb power of 4/5 and upper limb power of 5/5. Sensory examination, including light touch and proprioception, were normal. Stretch tendon reflexes in both upper and lower limbs were hyperactive, associated with clonus (graded as 4+). Plantar responses were extensor. Superficial abdominal reflex was normal. There were no signs of incoordination, and Romberg's test was negative. Fasciculation was not observed. All paraclinical investigations, including conventional magnetic resonance imaging (MRI) and computed tomography (CT) scans of the brain and routine blood chemistry tests, were normal. Further investigation has not been done because of financial issues.

Electrodiagnostic evaluation was conducted using the standard techniques and reference values. Surface electrodes were utilized for recording and stimulation in the nerve conduction study. Additionally, electromyography (EMG) was performed using a concentric needle electrode.

Electrodiagnostic tests were conducted on this patient, yielding the following outcome:

1. Sensory nerve action potentials (SNAP) were normal.
2. Nerve conduction velocity (NCV) of compound muscle action potentials (CMAP) was within the lower limit of normal except for the tibial nerve, which was below the normal lower limit (right tibial NVC = 37 and left tibial NCV = 38m/s).
3. EMG in all tested muscles, as shown in Table 1, had a neurogenic pattern and revealed evidence of partial denervation and reinnervation, especially in distal muscles.
4. The F waves and H reflexes were within the normal range.

Regarding electrodiagnostic findings and patient examination, early onset HSP associated with motor axonal neuropathy was considered.

Discussion

HSP is a clinically and genetically heterogeneous disease. It typically presents with spasticity in lower limbs and difficulty in walking (8). Clinically, it is divided into pure and complicated forms (4).

We describe a patient who presented with a gradually developing spastic walking difficulty, typically starting at around 15 years of age. Electrodiagnostic investigations unveiled a neurogenic pattern in EMG, particularly severe in distal muscles, suggesting a motor axonal neuropathy associated with early onset HSP.

A mutation in the SPG3A gene has been reported by Fusco et al, which caused the association of motor axonal neuropathy with spastic paraplegia in a 4-year-old girl. The results of neurophysiological studies in their case were consistent with pure motor neuropathy (9).

Various diseases can be considered as part of the differential diagnosis of HSP. One common condition that can mimic HSP is cerebral palsy. We ruled out it due to the normal perinatal history and brain MRI. Furthermore, metabolic disorders resembling HSP clinically, such as amino acid deficiencies, insufficient vitamin B12 or vitamin E levels, and inherited neuropathies, were ruled out.

Another neurological disorder that may exhibit clinical features overlapping with HSP is primary lateral sclerosis

Table 1. EMG summary

Muscle	Nerve	Roots	Spontaneous					MUAP			Recruitment
			IA	Fib	PSW	Fasc	H.F.	Amp	Dur.	PPP	Pattern
L. Gastrocnemius (medial head)	Tibial	S1-S2	2+	2+	3+	None	None	2+	2+	3+	Reduced
L. Tibialis anterior	Deep peroneal (fibular)	L4-L5	N	None	None	None	None	N	N	1+	Normal
L. Peroneus longus	Peroneal	L5-S1	+1	None	None	None	None	N	2+	2+	Normal
L. Vastus medialis	Femoral	L2-L4	N	None	None	None	None	N	2+	2+	Normal
R. Vastus medialis	Femoral	L2-L4	N	None	None	None	None	N	2+	2+	Normal
R. Gastrocnemius (medial head)	Tibial	S1-S2	2+	2+	3+	None	None	N	2+	3+	Normal
R. Tibialis anterior	Deep peroneal (fibular)	L4-L5	N	None	None	None	None	N	N	1+	Normal
R. Peroneus longus	Peroneal	L5-S1	N	None	None	None	None	N	2+	2+	Normal
L. First dorsal interosseous	Ulnar	C8-T1	N	None	None	None	None	N	N	N	Normal
L. Flexor carpi radialis	Median	C6-C7	N	None	None	None	None	N	N	N	Normal
L. Biceps brachii	Musculocutaneous	C5-C6	N	None	None	None	None	N	N	N	Normal

IA, Insertional Activity; Fib, Fibrillations; PSW, Positive Sharp Waves; Fasc, Fasciculations; H.F., High Frequency (Discharge; Amp, Amplitude; Dur., Duration; PPP, Polyphasic Potentials; MUAP, Motor Unit Action Potential

(PLS). Differentiating between PLS and HSP is challenging in patients with upper motor neuron presentations in adulthood. However, symptoms affecting the arms and bulbar area, which are rare in pure HSP, may indicate a potential diagnosis of PLS (10). In our case, the presence of HSP appears more plausible. Moreover, specific clinical features, including an onset age younger than 35, have been identified as valid criteria for distinguishing between PLS and HSP (11). These features align more closely with HSP in the presented case.

Dyck and Lambert outlined a type of hereditary motor and sensory polyneuropathy (HMSN) linked to HSP, categorizing it as "HMSN type V". It is characterized by spastic paraplegia, and patients typically experience difficulties in walking during the first or second decade of life (12).

Distinguishing between HMSN V and complex types of HSP is currently difficult, and there are no established clinical or electrophysiological diagnostic criteria at present. However, this disease was also excluded due to the absence of clinical and confirmed electrodiagnostic evidence of sensory involvement.

According to a previous study, tibial nerves were more frequently impaired than ulnar nerves, indicating a more significant impact on the longer motor axons in the legs (13). Likewise, in our case, the NCV of the tibial nerve was more affected than that of other tested nerves.

Conclusion

In conclusion, it is essential to remember that although uncommon, certain individuals with HSP may display electrophysiological indications of peripheral motor neuropathy. The combination of motor axonal neuropathy alongside HSP may form a unique syndrome. As a result, further investigations are required to define the characteristics of this condition.

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Authors' Contribution

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Competing Interests

None.

Ethical Approval

The present study was approved by Research Ethics Committee of Isfahan University of Medical Sciences (IR.ARI.MUI.REC.1403.023).

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