

Phenotype HNPP (Hereditary Neuropathy With Liability to Pressure Palsies) Induced by Medical Procedures

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Abstract

The phenotype HNPP (hereditary neuropathy with liability to pressure palsies) is caused by heterozygous deletion of the *PMP22* gene. HNPP is clinically characterized by asymmetric focal sensory loss and muscle weakness. Reports of HNPP have been rare.

In this article, we report the case of an asymptomatic woman with the HNPP mutation. After undergoing total knee arthroplasty, she developed a footdrop with prolonged recovery. We concluded (a) that the HNPP mutation may carry a high risk for certain surgical procedures not expected to cause neurologic deficits in normal patients and (b) that humans with the HNPP mutation can be asymptomatic. Lack of symptoms can contribute to underrecognition of the disease.

PMP22 is a tetra-span membrane protein primarily expressed in myelinating Schwann cells. Heterozygous deletion of the *PMP22* gene (1 copy) causes HNPP (hereditary neuropathy with liability to pressure palsies).¹ Interestingly, a reciprocal genetic disorder with 3 copies of human *PMP22* causes the most common inherited neuropathy, Charcot-Marie-Tooth disease type 1A (CMT1A).^{2,3} As the reciprocal mutations occur at initiation of gestation, it is expected that HNPP and CMT1A have a similar prevalence. However, studies have shown HNPP prevalence of 2 to 5 cases per 100,000, far below the CMT1A prevalence of 1:5000.⁴ This finding prompted speculation that many patients with HNPP may be undiagnosed because of the subtlety of the phenotypes.⁵

Patients with HNPP typically present with focal sensory loss and muscle

weakness related to mechanical stress–induced failure of action potential propagation.^{6,7} In this article, we report the case of an asymptomatic woman with the HNPP mutation. Her focal neurologic deficits occurred only after total knee arthroplasty (TKA), which in healthy patients is not expected to induce focal sensory and motor symptoms. The patient provided written informed consent for print and electronic publication of this case report.

Case Report

The patient, a healthy 57-year-old woman, had a normal developmental history. For decades, she had practiced ballet without any physical difficulties. She underwent left TKA and woke up with a footdrop on the left side. The left foot was less sensitive to temperature. Ankle strength returned 2 months later. There was no family history of HNPP.

The patient was examined by a local neurologist, who found steppage gait, weak ankle dorsiflexion (4 on Medical Research Council scale), and diminished touch on the lateral aspect of the left leg. Deep tendon reflexes were present in the arms but not the legs.

Table. Nerve Conduction Study Data on Patient With Reported Case of Footdrop on Left Side^a

	Motor Nerves			Sensory Nerves		
	DL, ms	Amp, mV	CV, m/s	DL, ms	Amp, μ V	CV, m/s
First Case						
Peroneal	6.1	0.8	N/A	—	—	—
Sural	—	—	—	3.8	11.2	42.9
Norm	≤ 6.0	≥ 2.5		≤ 4.0	≥ 5.0	≥ 39.0
Tibial	6.7	0.7	N/A	—	—	—
Median	13.1	4.0	44.8	NR	—	—
Norm	≤ 4.5	≥ 4.0	≥ 50.0	≤ 4.0	≥ 20.0	≥ 50.0
Ulnar	3.9	7.8	32.8	5.4	14.4	32.7
Norm	≤ 3.5	≥ 6.0	≥ 50.0	≤ 3.5	≥ 10.0	≥ 50.0

Abbreviations: Amp, amplitude; CV, conduction velocity; DL, distal latency; norm, normative value; N/A, not applicable; NR, nonresponsive.
^aAbnormal values in bold.

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A nerve conduction study (NCS) performed after the footdrop revealed prolonged distal latency and decreased amplitude in the left peroneal and tibial nerves. The left sural nerve was normal. Needle electromyogram revealed denervation changes in the muscles innervated by the left peroneal nerve (Table). In addition, we also performed an NCS on the arm (Table), which was unaffected by the surgical procedure. This NCS revealed severely prolonged distal latency across the left wrist in the median nerve and focal slowing of conduction velocity of the ulnar nerve across the left elbow. These changes provide evidence of asymptomatic carpal tunnel syndrome and ulnar nerve entrapment, typical electrophysiologic abnormalities of HNPP.⁸

As there was no explanation for the footdrop from the surgery, we had a DNA test performed (Athena Diagnostics). This test identified a heterozygous deletion of chromosome 17p12 containing the PMP22 gene, the HNPP mutation.

Discussion

This case had several important features. First, though the patient developed an electrophysiologic phenotype of HNPP, she was completely asymptomatic clinically and very athletic before her medical procedure. She would not have been diagnosed with HNPP if her clinical deficits had not been induced by TKA. Therefore, the prevalence of HNPP is likely underestimated. Second, for patients with the HNPP mutation, there may be serious neurologic consequences of certain medical procedures. The diagnosis of HNPP should be pursued if there is no explanation from the medical procedure per se. In addition, patients with a family history of HNPP should be carefully evaluated before any procedure that may put them at risk for severe peripheral nerve damage, and they should be counseled regarding the risks. It is important to determine the prevalence of HNPP among patients who develop footdrop after knee arthroplasty, as this information could potentially be used to revise ideas about the etiology of peripheral nerve complications of knee arthroplasty. We now describe possible revisions of these ideas.

Footdrop is a rare complication of TKA. Retrospective studies have found its incidence ranging from 0.3% to 1.3%.⁹⁻¹¹ The investigators in those studies postulated 3 main causes for peroneal nerve palsy. First, traction may put pressure on the peroneal nerve during normalization of the mechanical axis of a valgus knee. Our patient did not have a valgus knee. Second, epidural hematoma by anesthetic procedure may compress the spinal roots. Our patient received general anesthesia during the

procedure; epidural or spinal anesthesia was not used. Third, postoperative dressing may compress the nerve. Our patient did not develop any signs of constrictive dressing, such as inordinate pain, which can be relieved by removing the dressing, and swelling of the leg distal to the dressing. Therefore, her footdrop likely was not a complication of surgery.

This case demonstrates how a patient with undiagnosed HNPP can manifest the HNPP phenotype only after undergoing a particular surgical procedure. HNPP is unfamiliar to most orthopedic surgeons.

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