Hereditary neuropathy with liability to pressure palsies

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ABSTRACT

Hereditary neuropathy with liability to pressure palsies (HNPP) is a disease that presents with recurrent reversible episodes of neurapraxia that occur typically after trivial trauma. It is an autosomal dominant, demyelinating neuropathy. A 20-year-old man presented with left ulnar nerve palsy after a fall. He had reduced two-point discrimination over his left ulnar nerve distribution, with mild clawing of the ring and little fingers, and accompanying weakness of the first dorsal interrosseus and abductor digiti minimi of grade four power. His Froment's sign was also positive. Careful clinical examination and appropriate tests, including electromyography and genetic testing, confirmed the diagnosis of HNPP. This case report is presented to promote awareness and recognition of this disease in the local and regional context.

Keywords: demyelinating neuropathy, hereditary neuropathy, neurapraxia, pressure palsies.

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INTRODUCTION

Hereditary neuropathy with liability to pressure palsies (HNPP) is an autosomal dominantly-inherited disorder that is characterised by focal and recurrent episodes of sensorimotor deficits typically after trivial neural compression injuries. It rarely manifests itself before the age of 20 years. This disorder presents with acute episodes of weakness and paraesthesia arising in a defined territory of a nerve trunk. Ultrastructurally, HNPP is characterised by sausage-like multi-focal thickenings of the myelin sheath[1]. The genetic defect in most HNPP patients is a 1.5 Mb deletion on chromosome 17p11.2 which contains the peripheral myelin protein 22 (PMP-22) gene. This produces a dosage effect of this gene[2].

CASE REPORT

A 20-year-old Eurasian man who was undergoing his National Service in the Singapore Armed Forces was referred to our clinic for ulnar nerve palsy after falling on the left elbow at standing height. He was found to be of good health and was certified fit for combat training prior to his enlistment in the armed forces. There was no pain or swelling of his left elbow, but he developed numbness over the ulnar aspect of his left hand, with reduced grip strength. There was no medical history of diabetes mellitus, thyroid disease or alcohol dependence. The symptoms did not resolve after one month and he was subsequently referred to our hospital for further management.

On examination, he had reduced two-point discrimination over the left ulnar nerve distribution, with mild clawing of the ring and little fingers. There was accompanying weakness of the first dorsal interrosseus and abductor digiti minimi of grade four power according to the Medical Research Council (MRC) scale. His Froment's sign was also positive. The left elbow had no swelling or lump, and range of movement was full. He had no other peripheral nerve abnormality on physical examination and his right elbow was clinically normal. His gait was normal and he did not have any pes cavus.

On further questioning, there was a previous episode of left foot drop a few years ago after minor trauma. The deficit lasted three months, and he eventually recovered fully. His father also had a history of left wrist drop, which had resolved. Radiological investigations of his left elbow were normal. An electromyograph was performed for the patient, which showed left ulnar neuropathy at the elbow joint and left carpal tunnel syndrome. Further examination revealed slowing in the tibial nerve. DNA analysis by real-time quantitative polymerase chain reaction (PCR) technique demonstrated PMP-22 deletion, which confirmed the diagnosis of HNPP.

DISCUSSION

HNPP was probably first described by De Long[3]

in 1947, when he described a family with three generations who suffered from recurrent peroneal neuropathy after digging for potatoes. Today, HNPP is still sporadically reported but its awareness among physicians and surgeons may be under-appreciated. Clinically, patients typically present with peripheral neuropathy affecting the distal nerves such as peroneal (35%), ulnar (20%) and radial (8%), with the superficial nerves being more commonly involved than the deep nerves[5,6]. There may be up to 20% of patients with brachial plexus impairment[7,8]. The symptoms typically occur almost immediately after minor trauma and do not progress. The prognosis is usually good, with complete recovery in most cases.

It is a condition of surgical importance, especially during intraoperative patient positioning. It is also of relevance to orthopaedic patients who are typically subjected to traction, or splinting, all of which may cause various peripheral nerve palsies in these patients. Treatment is symptomatic and is aimed at preventing nerve compression. Electrophysiological findings in HNPP are usually characterisic[9]. Nerve conduction velocities are generally slightly reduced with prolonged distal motor latencies. This can happen in clinically unaffected as well as symptomatic nerves. Compound muscle action potential amplitudes are also reduced[10]. This has been suggested to be due to the inability to maintain myelin stability in such patients.

Histologically, the characteristic finding is multifocal sausage-shaped thickening (tomaculae) of peripheral myelin sheaths[1]. Other findings include hypo- and hypermyelination, myelin sheath irregularities and even nodes of Ranvier distortions[10]. Genetically, the disease is caused by the functional loss of one allele of the peripheral myelin protein 22 (PMP-22) gene[11]. The loss is most often from a 1.5 Mb deletion on chromosome 17p11.2-p12, the region where the PMP-22 gene is located. There is an unequal crossing-over event that can generate either a duplication leading to Charcot-Marie-Tooth disease type 1A (CMT1A) or a deletion resulting in HNPP.

DNA analysis is now part of the diagnostic work-up for suspected HNPP patients. It is less invasive than a histological biopsy for confirmation. As HNPP is inherited in an autosomal dominant manner, genetic counselling is important for index cases and their families. For the parents of a proband, approximately 80% of individuals with HNPP have inherited the gene mutation from an affected parent. Approximately 20% of affected individuals have a de novo mutation[12]. Although HNPP has been well-described in genetic and neurological literature and is essentially a benign disease with almost full recovery of neuropathy in most instances, this is believed to be the first described case in local literature. It is hoped that this report will help promote awareness and recognition of this entity among local and regional healthcare practitioners. Such heightened awareness will help reduce chances of inappropriate surgical exploration, enhance proper genetic counselling and ensure perioperative preventive measures.

REFERENCES

1. Behse F, Buchthal F, Carlsen F, Knappeis GG. Hereditary neuropathy with liability to pressure palsies. Electrophysiological and histopathological aspects. Brain 1972; 95:777-94.
2. Schenone A, Nobbio L, Mandich P, et al. Underexpression of messenger RNA for peripheral myelin protein 22 in hereditary neuropathy with liability to pressure palsies. Neurology 1997; 48:445-9.
3. Koehler PJ. Hereditary neuropathy with liability to pressure palsies: the first publication (1947). Neurology 2003; 60:1211-3.
4. Bradley WG, Madrid R, Thrush DC, Campbell MJ. Recurrent brachial plexus neuropathy. Brain 1975; 98:381-98.
5. Meier C, Moll C. Hereditary neuropathy with liability to pressure palsies. Report of two families and review of the literature. J Neurol 1982; 228:73-95.
6. Gorke W. Clinical and electroneuromyographical findings in hereditary neuropathy with liability to pressure palsies. Neuropadiatrie 1974; 5:358-68.
7. Mouton P, Tardieu S, Gouider R, et al. Spectrum of clinical and electrophysiologic features in HNPP patients with the 17p11.2 deletion. Neurology 1999; 52:1440-6.
8. Orstavik K, Skard Heier M, Young P, Stogbauer F. Brachial plexus involvement as the only expression of hereditary neuropathy with liability to pressure palsies. Muscle Nerve 2001; 24:1093-6.
9. Andersson PB, Yuen E, Parko K, So YT. Electrodiagnostic features of hereditary neuropathy with liability to pressure palsies. Neurology 2000; 54:40-4.
10. Van den Neucker K, Vanderstraeten G. Hereditary compression neuropathy. Report of a family. Electromyogr Clin Neurophysiol 1990; 30:509-12.
11. Chance PF, Alderson MK, Leppig KA, et al. DNA deletion associated with hereditary neuropathy with liability to pressure palsies. Cell 1993; 72:143-51.
12. Infante J, Garcia A, Combarros O, et al. Diagnostic strategy for familial and sporadic cases of neuropathy associated with 17p11.2 deletion. Muscle Nerve 2001; 24:1149-55.