Case report

Hereditary neuropathy with liability to pressure palsies

D M W Dharmakeerthi[1], **D Sirisena**[2]

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Case presentation

A 68-year-old male presented with sudden onset weakness of right upper limb while reading a newspaper after lunch. The weakness did not progress or improve over next couple of hours. A day later a neurologist was consulted. The neurological examination revealed that there was a marked finger drop (power 2/5 MRC scale) and mild wrist drop (4/5 MRC scale). When the patient was asked to extend the wrist, there was a radial deviation of hand. Rest of the examination revealed slight reduction of power in finger abduction (4/5 Canterbury and Kent criteria) bilaterally and thumb abduction (4/5 MRC scale) bilaterally. Reflexes were diminished globally. Sensory examination revealed reduced pin prick and poor two point discrimination in both median and ulnar nerve distribution bilaterally, but sparing radial distribution.

Electro-diagnostic testing performed 3 days after initial presentation showed many abnormalities (Table). Nerve conduction tests were performed using "Nicolet Viking Quest" EMG machine. Hand temperature was 32° centigrade and foot temperature was 30° centigrade. To summarize, these abnormalities included right posterior interosseous nerve lesion with active denervation, right severe (4/6 Kent and Canterbury score) carpal tunnel syndrome, left moderate (3/6 Kent and Canterbury score) carpal tunnel syndrome, bilateral ulnar neuropathy at

Table. Results of nerve conduction and electromyography

Sensory nerve conduction

Nerve and site	*Peak latency*	*Amplitude*	*Segment*	*Latency difference*	*Distance*	*Conduction velocity*
Radial.R Forearm	2.1 ms	17 uV	Anatomical snuff box-Forearm	1.5 ms	110 mm	52 m/s
Median.R Digit III (long finger)	4.2 ms	5 uV	Wrist-Digit III (long finger)	3.5 ms	140 mm	40 m/s
Ulnar.R	3.4 ms	3 uV	R2-B2	2.6 ms	140 mm	53.8 m/s
Median.L Digit III (long finger)	4.4 ms	6 uV	Wrist-Digit III (long finger)	3.7 ms	140 mm	37.8 m/s
Ulnar.L	3.2 ms	2 uV	R2-B2	2.4 ms	140 mm	58.3 m/s
Radial.L Forearm	2.3 ms	20 uV	Anatomical snuff box-Forearm	1.7 ms	120 mm	52 m/s
Sural.L Lower leg	ms	0 uV	Ankle-Lower leg	ms	140 mm	m/s
Superficial peroneal.L Lower leg	ms	0 uV	Ankle-Lower leg	ms	140 mm	m/s

[1]*Department of Clinical Neurophysiology,* [2]*Department of Neurology, General Hospital Kurunegala, Sri Lanka.*

Motor nerve conduction						
Nerve and site	*Latency*	*Amplitude*	*Segment*	*Latency difference*	*Distance*	*Conduction velocity*
Ulnar.R						
Wrist	3.3 ms	4.1 mV	Abductor digiti minimi (manus)-Wrist	3.3 ms	80 mm	m/s
Below elbow	7.9 ms	4.0 mV	Wrist-Below elbow	4.6 ms	230 mm	50 m/s
Above elbow	10.8 ms	2.6 mV	Below elbow - Above elbow	2.9 ms	100 mm	34 m/s
Axilla	12.4 ms	2.6 mV	Above elbow-Axilla	1.6 ms	100 mm	63 m/s
Median.R						
Wrist	5.5 ms	8.5 mV	Abductor pollicis brevis-Wrist	5.5 ms	80 mm	m/s
Elbow	10.9 ms	6.7 mV	Wrist-Elbow	5.4 ms	250 mm	46 m/s
Median.L						
Wrist	5.0 ms	4.3 mV	Abductor pollicis brevis-Wrist	5.0 ms	80 mm	m/s
Elbow	10.6 ms	5.9 mV	Wrist-Elbow	5.6 ms	250 mm	44.6 m/s
Ulnar.L						
Wrist	3.1 ms	4.5 mV	Abductor digiti minimi (manus)-Wrist	3.3 ms	mm	m/s
Below elbow	7.6 ms	3.9 mV	Wrist-Below elbow	4.3 ms	230 mm	53.4 m/s
Above elbow	10.6 ms	3.4 mV	Below elbow - Above elbow	3.0 ms	100 mm	33.3 m/s
Axilla	12.2 ms	3.3 mV	Above elbow-Axilla	1.6 ms	100 mm	63 m/s
Peroneal.R						
Ankle	6.3 ms	0.6 mV	Extensor digitorum brevis-Ankle	6.3 ms	80 mm	m/s
Below Knee	14.4 ms	0.5 mV		8.1 ms	310 mm	38.0 m/s
Pop fossa	18.2 ms	0.5 mV	Abductor digiti minimi (manus)-Wrist	3.8 ms	100 mm	26.0 m/s
Peroneal.L						
Ankle	5.4 ms	1.4 mV	Extensor digitorum brevis-Ankle	5.4 ms	80 mm	m/s
Below Knee	12.7 ms	1.3 mV		7.3 ms	310 mm	42.0 m/s
Pop fossa	14.9 ms	1.3 mV	Abductor digiti minimi (manus)-Wrist	2.2 ms	100 mm	45.0 m/s
Tibial.R						
Ankle	5.6 ms	3.3 mV	Extensor digitorum brevis-Ankle	5.6 ms	80 mm	m/s
Below Knee	12.9 ms	3.1 mV		7.3 ms	340 mm	46.0 m/s

Needle EMG examination

	Insertional	*Spontaneous activity*			*Volitional MUAPs*				
Muscle	*Insertional*	*Fibs*	*+ Wave*	*Fasc*	*Duration*	*Amplitude*	*Poly*	*Config*	*Recruitment*
1st dorsal interosseous.R	Normal	None	None	None	Normal	Sl. Incr	None	Normal	Reduced
Extensor indicis proprius.R	Normal	+2	+2	None	Sl. Incr.	Sl. Incr.	Few	Unstable	Reduced
Extensor digitorum communis.R	Normal	+2	+2	None	Sl. Incr.	Sl. Incr.	Few	Unstable	Reduced
Extensor carpi radialis longus.R	Normal	None	None	None	Normal	Normal	None	Normal	Normal
Brachioradialis.R	Normal	None	None	None	Normal	Normal	None	Normal	Normal
Extensor carpi ulnaris.R	Normal	+2	+1	None	Sl. Incr.	Sl. Incr.	Few	Unstable	Reduced
Flexor digitorum profundus, dig 4 & 5.R	Normal	None	None	None	Normal	Normal	None	Normal	Reduced
Triceps brachii.R	Normal	None	None	None	Normal	Normal	None	Normal	Normal
Tibialis Ant R	Normal	None	None	Gros.Inc	Gros. Inc	Many	Unstable	Reduced	
Tibialis post.R	Normal	None	None	None	Normal	Normal	None	Normal	

the elbow, left peroneal neuropathy at the fibular head. The overall electrodiagnostic impression was a predominantly demyelinating sensorimotor poly-neuropathy with multiple superimposed compression neuropathies which is more in keeping with hereditary neuropathy with liability to pressure palsies (HNPP).

On subsequent inquiry although the patient denied of clear episodes of previous weakness, he admitted to clumsiness of walking. His father had died of a stroke but there were no family history suggestive of focal mono neuropathies or generalized neuropathies. This is the usual scenario in HNPP where most of the patients go unnoticed. Therefore we decided to trace the family members to look for clinical signs (focal mono neuropathies, high arched feet etc.) and for electro-physiological evaluation.

He was conservatively managed with a plan for carpal tunnel decompression later. He was reviewed by the neurologist at four weeks and eight weeks and the power has improved 3/5 and 5/5 for finger extension and wrist extension respectively at 8 weeks.

Hereditary neuropathy with liability to pressure palsies

The discovery of HNPP is credited to Dutch neuropsychiatrist J.G.Y. de Jong in 1947 after his work with a family afflicted by numerous compressive neuropathies[1]. The disease has also been called potato-grubbing disease and tulip-bulb diggers palsy because of the compressive neuropathies resulting from these activities in people with HNPP[1]. The incidence is estimated at 16/100,000, although there may be more cases that are not diagnosed[2]. The hallmark of the disease is recurrent focal compression neuropathies, especially of the median, ulnar, and peroneal nerves, which tend to improve in hours to months[3]. Usually, onset of symptoms is between the ages of 10 and 30[4]. Interestingly, muscle wasting is sometimes observed in the absence of previous nerve palsy[5]. Also cases of brachial plexus involvement have been documented[6]. Subtle findings which may be present on

physical exam include a mild peripheral neuropathy, absent ankle reflexes (in 50-80%), and pes cavus foot deformities (in 20%)[7]. Patients suffering from possible entrapment neuropathies typically undergo electrodiagnostic testing. In HNPP patients, this testing will often reveal decreased sensory and motor conduction velocities across many of the aforementioned entrapment sites. In addition, prolonged distal motor nerve conduction latencies with slowed distal sensory nerve conduction velocities will demonstrate a peripheral neuropathy.

There are presently no universally accepted electrodiagnostic criteria for the diagnosis of HNPP. Studies by Gouider et al.[8] in 1995 and Mouton et al.[4] in 1999 demonstrated that diagnostic criteria of bilateral slowing of sensory and motor nerve conduction at the carpal tunnel with at least one abnormal parameter for motor conduction in one peroneal nerve is sufficient for diagnosis in patients with a family history. In 2001, Infante et al.[9] preferred sural nerve slowing and any two entrapments as criteria for diagnosis. HNPP_s electrodiagnostic profile is unique. Andersson et al.[10] in 2000 compared electrodiagnostic features of HNPP with diabetic polyneuropathy and chronic inflammatory neuropathy (CIDP), two diseases which have similar clinical presentations. He found HNPP patients to have more distal sensory nerve conduction velocity slowing and distal motor latency prolongation than patients with diabetic polyneuropathy or CIDP. Li et al.[11] in 2002 found HNPP distal sensory nerve conduction slowing to be a more diffuse process than the distal motor latency prolongation which has a predilection for certain nerves.

Finally, whereas HNPP should be considered in patients with multiple entrapment neuropathies, an electrodiagnostic study by Sander et al.[12] in 2005 of patients with multiple surgically treated entrapment neuropathies demonstrated the low prevalence of the disease.

While molecular genetic testing is the most reliable tool for diagnosis[4 13], it's availability is limited in most of the regions. Therefore electrodiagnostic examination is widely available and reliable method for screening HNPP.

The disease is an autosomal dominant condition caused by a defect at chromosome 17p11.2 that results in abnormal peripheral myelin protein 22. In approximately 80% of cases, the defect is a 1.5 Mb deletion, whereas the other 20% has a point mutation. Both the deletion and point mutation are detectable by a variety of sophisticated genetic tests[7]. Interestingly, a 1.5- Mb duplication at the same locus as the deletion produces Charcot-Marie-Tooth 1A which shares some clinical and histologic features with HNPP. The two diseases are thought to be reciprocal products of the same unequal crossover[2]. Studies have reported that the deletion and point mutation percentages may vary considerably by ethnicity[14].

HNPP nerves have characteristic histopathologic features. It is understood that peripheral myelin protein 22 is responsible for producing compact and stable myelin sheets around large and small myelinated nerve fibers. However, the abnormal peripheral myelin protein 22 present in HNPP results in paradoxically thickened myelin sheaths in the large myelinated fibers[15]. These thickenings are focal, amounting to segmental hypermyelination and appear in teased fiber preparations as sausage-like expansions of myelinated fibers called tomaculae (Figure 1).

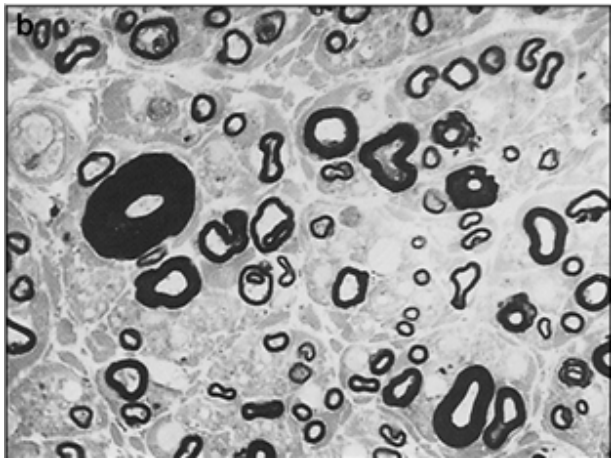

Figure 1. This low-power magnification photomicrograph of an axial section of a nerve shows scattered large myelinated fibers that have thickened myelin sheaths representing tomaculae (reprinted from Pathology of Peripheral Nerves, 2001, page 116, Chap 7, J.M. Schroeder, Figure 101a, copyright Springer, Heidelberg, with kind permission of Springer Science and Business Media).

The term tomaculous neuropathy describes this condition which is present in diseases including HNPP, CMT, CIDP, IgM paraproteinemia, HNA, and Dejerine-Sottas[8]. The abnormal peripheral myelin in HNPP nerves also increases susceptibility to injury by compression, resulting in the reduction of conduction velocities associated with compression neuropathies[16,17]. The effects of trauma may also induce degeneration of the myelin sheaths with subsequent remyelination, resulting in hypertrophic nerves with the classic onion-bulb features of demyelinating diseases. In many cases, the effects of the compression are short-lived and relatively reversible. In some chronic cases, the muscles innervated by damaged nerves (in this case, those of the left hand from chronic carpal tunnel syndrome) are likely to show

evidence of denervation and atrophy. Historically, HNPP tomaculae and onion-bulbing have been observed with sural nerve biopsy, but biopsies are now rarely performed because of the utility of genetic testing[18].

Prevention of compression neuropathies such as carpal tunnel syndrome, ulnar neuropathy, and peroneal neuropathy includes activity modification and protective padding. Activity modification such as avoiding repetitive hand movements and minimizing time spent leaning on elbows, crossing legs, and kneeling can be combined with protective elbow and knee pads[7]. When compressive symptoms develop, orthoses such as wrist splints and ankle-foot orthoses may be utilized transiently for relief of carpel tunnel symptoms and foot drop, respectively. Full recovery in hours to months occurs in the majority of episodes as in our patient, whereas incomplete recovery is somewhat common but rarely debilitating. Incomplete recovery correlates with a history of prolonged focal compression. Controversy exists as to the benefit of surgical decompression. Typically, carpal tunnel release is of little benefit, and ulnar nerve transposition at the elbow may worsen symptoms. However, in cases with severe symptoms, debility, and/or deformity, surgical intervention should be considered on an individual basis.

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