CASE REPORT

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Multiple tendon transfer for a case of radial nerve palsy in hereditary neuropathy with liability to pressure palsy

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ABSTRACT

Hereditary neuropathy with liability to pressure palsy (HNPP) is a rare autosomal dominant disease characterized by focal, recurrent, demyelinating peripheral neuropathies. It is caused by deletions of the gene encoding for peripheral myelin protein 22 (PMP22) on chromosome 17. While it may range widely, the most common clinical presentation is an acute, focal mononeuropathy with numbness or muscle weakness after trauma or compression. Diagnostic tools include electrophysiological studies, genetic tests and nerve biopsies. There is no standard surgical or pharmacological treatment. The course of the disease is usually benign, with spontaneous improvement after most episodes of peripheral nerve palsy. HNPP is best managed by early detection, preventative measures, and subsequent treatment of symptoms. According to the medical literature, operative treatment was undertaken in few cases and limited to decompression of the nerve at the classic entrapment sites of the carpal or cubital tunnels. We present a case of multiple tendon transfer (pronator teres to extensor carpi radialis brevis and flexor carpi radialis to extensor digitorum communis) with a two-year follow-up in a 24-year-old woman with HNPP who was affected by irreversible radial nerve palsy, and conclude with a review of the medical literature related to the disease.

Keywords: hereditary neuropathy with liability to pressure palsies (HNPP), hereditary sensory and motor neuropathy, radial neuropathy, radial nerve, tendon transfer

Abbreviations:
HNPP: hereditary neuropathy with liability to pressure palsy
PMP22: peripheral myelin protein 22

INTRODUCTION

Hereditary neuropathy with liability to pressure palsy (HNPP, OMIM number 162500), first described by De Jong in 1947,[1] is an autosomal dominant disorder characterized by focal, recurrent, demyelinating peripheral neuropathies.

There are few studies describing patients who needed to undergo surgery for HNPP. Grossman et al[2] presented the case of a 38-year-old woman who had a good recovery after bilateral carpal

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and cubital tunnel release for sensorimotor neuropathy resistant to conservative treatment. Both Taggart et al[3] and Çelik et al[4] showed a history of decompressive surgery for ulnar entrapment at the elbow. Lazar et al[5] performed anterior ulnar transposition at the elbow in 2 adult male patients with excellent outcomes. We report a successful case of multiple tendon transfer for prolonged partial radial nerve palsy in a patient who was diagnosed with HNPP.

CASE REPORT

A 24-year-old woman unintentionally fell asleep in a bathtub for 2 hours, resting against her right arm. After this extended period of immobilization and pressure, she was unable to extend the wrist, fingers and thumb of her right hand. She was gradually able to extend her wrist and thumb, but the middle and ring finger extension remained weak (manual muscle test, grade 1). With symptoms unimproved 2 years after onset, she underwent electrophysiological and imaging studies. The nerve conduction study revealed a low compound muscle action potential (CMAP) amplitude of the right radial nerve, while motor conduction velocities of the radial, median, and ulnar nerves were normal. Elbow and cervical magnetic resonance imaging (MRI) showed no abnormal findings. However, given her inability to extend the middle and ring fingers coupled with a poor wrist extension, she was referred to our department (Fig. 1).

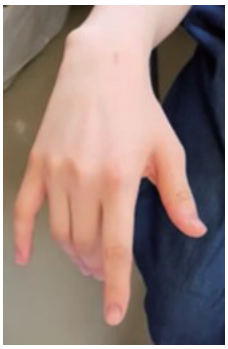

Fig. 1 Wrist and finger extension before surgery

Physiotherapy and vitamin B12 treatment were undertaken at the previous hospital, but the partial radial nerve palsy remained recalcitrant. In reviewing her family medical history, we learned that her grandmother had undefined motor disorders. Suspecting the likelihood that an inherited condition could be involved, we administered a genetic test. This confirmed that the patient lacked the peripheral myelin protein 22 (PMP22) gene and indicated HNPP. So, two and a half years after the onset of symptoms, we performed a surgical reconstruction for the fingers and the wrist extension.

We transferred the pronator teres to extensor carpi radialis brevis and flexor carpi radialis to extensor digitorum communis. The operation was done without a tourniquet, a function of the special attention required to avoid impingement or compression. Rehabilitation started after

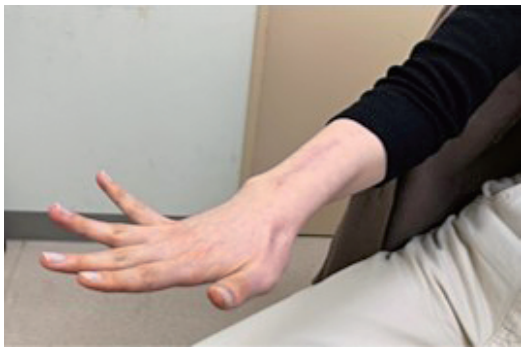

Fig. 2 Wrist and finger extension at two-year follow-up

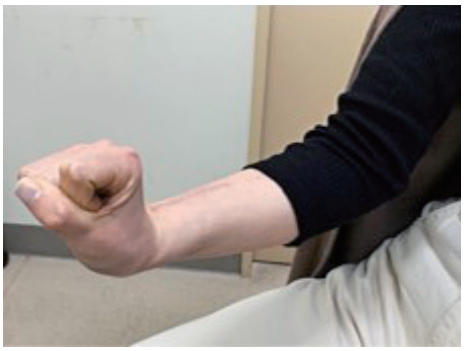

Fig. 3 Active wrist extension to 70° at two-year follow-up

3 weeks of immobilization. The patient had a good recovery without post-surgical complications. We advised her on preventative measures to take in her daily life after surgery, foremost among them being to avoid physical postures that elevate the risk of excessively compressing or stretching peripheral nerves.

At the two-year follow-up, the patient had a complete active extension of all fingers (Fig. 2) and had recovered an active wrist extension of 70° (Fig. 3). The grip strength of her right hand improved from 14 kg preoperatively to 19 kg. The NRS-pain score was 0/10. The result on Hand20, a patient-rated outcome measure, improved from 67 preoperatively to 24.

She was satisfied with the surgical treatment, postoperative rehabilitation, and final outcome. In fact, the experience inspired her to leave her factory job and begin studying to become an occupational therapist.

DISCUSSION

Hereditary neuropathy with liability to pressure palsy is a rare disease characterized by focal, recurrent, demyelinating peripheral neuropathies. Two studies reported a prevalence of 7.2 per 100,000 in Northern England and 16 per 100,000 in Southwest Finland, respectively.[6,7] Sporadic cases due to de novo mutations accounted for 21% of affected individuals in a study of 14 HNPP families.[8]

While HNPP symptoms can occur at any age, the initial manifestation is usually experienced during the second or third decade of one's life. HNPP has a wide-ranging clinical presentation.[9] It can vary from clinical silence in asymptomatic gene carriers to episodic debilitating palsies in others. The most common history is an acute, focal mononeuropathy, with numbness and sensory loss and/or muscle weakness.[10,11] Most palsies are the result of nerve entrapment due to compression or negligible traumas—like pressure during sleep, prolonged immobilization,[12] and exercise—but they may also be caused by temperature changes[13] or medical procedures.[12,14] The nerves commonly involved are the median nerve at the wrist, ulnar nerve at the elbow, peroneal nerve at the knee, and brachial plexus nerves at the shoulder.[1,9] Muscle atrophy and decreased deep tendon reflexes can also be associated with HNPP.

Although they occur less frequently, patients may also have acute or chronic polyneuropathies. Sometimes secondary orthopedic deformities such as pes cavus or scapular winging are present.[9,15] The duration of symptoms varies from days to months. Orthoses may be required in cases of prolonged palsies. Nevertheless, the prognoses are good and surgical interventions are rarely needed.

Particular onset and trigger events without obvious diagnoses are occasionally reported. For example, Perugula et al[15] documented the case of a 19-year-old army recruit who developed an acute 4-limb polyneuropathy 1 day after vigorous exercise and 2 weeks after having been administered an influenza vaccination. Also, Li et al[16] presented a case report of HNPP accompanied by type 2 diabetes mellitus and psoriasis.

Kalfakis et al[17] described the case of a 37-year-old man suffering from non-Hodgkin lymphoma who is the first known person to manifest HNPP after treatment with vincristine. The sensory impairment of face and trunk with a late onset has also been observed.[18] Chen et al[13] reported a history of slight bilateral hearing loss associated with numbness in the right foot of a 46-year-old man. Rarely, onset can be fulminant—with multifocal motor and sensory loss and acute denervation—requiring a long time to recover.[19]

The pediatric clinical patterns are less clear and difficult to identify. Bar et al[20] presented 3 cases in children: cramps and slight amyotrophy of hand muscles with paresthesia in the region

of the ulnar nerve due to intensive piano practice, distal muscle weakness of hands and feet, and fluctuating paresthesia of bilateral upper limbs. Onset in another pediatric case was indicated by calf hypertrophy and bilateral Babinski signs with normal electrophysiological findings during toddlerhood, although a diagnosis was not reached until 5 years later.[21]

Although HNPP is generally considered a pain-free condition,[9] Beales et al[22] reported that, in a cohort of 43 participants with a genetically established diagnosis of HNPP, 32 (74%) had persistent pain. Of those, 24 likely had neuropathic pain and 27 central sensitization.

Etiologically, according to guidelines from the European Charcot-Marie-Tooth (CMT) Consortium, about 85–90% of those with clinical HNPP symptoms have a deletion of 1.5 Mb on chromosome 17p11.2 that contains the PMP22 gene.[23] In a large multicenter study by consortium members, of 156 unrelated HNPP patients, 84% had the deletion.[24] PMP22 encodes a 160 amino acid membrane-associated protein specifically expressed in Schwann cells and located in the compact portion of nerve myelin.[25] In a review article, Chance[9] suggested that PMP22 plays an important role in Schwann cell mitosis, adhesion, and axon myelination. In original studies, Chance et al[26,27] proposed that the approximately 1.5 Mb chromosomal deletion derives from a mechanism of unequal crossover leading to a haplo-insufficient genotype with only 50% of the normal expression of the PMP22 gene in peripheral Schwann cells.[28] In the remaining cases, Chance's review cited that HNPP is due to other rare mutations including base pair deletions, base pair insertions, or point mutations that induce expression of altered and nonfunctional PMP22.[9]

At present, genetic and electrophysiological tests together are essential to diagnose HNPP. The neurophysiological characteristics of HNPP have been known since 1964.[29] They include generalized demyelination with prolonged sensory and motor nerve conduction velocity in a bilateral generalized pattern and are found not only in symptomatic patients but also in clinically silent gene carriers.[9] Mouton et al[30] reported the primary diagnostic criteria to be a bilateral slowing of sensory and motor nerve conduction of the median nerve at the wrist with abnormal motor conduction in one peroneal nerve. On the other hand, nerve conduction blocks are typical at entrapment sites in symptomatic nerves. In our case, the nerve conduction study revealed a low CMAP amplitude of the right radial nerve but normal motor conduction velocity. During an extended period of immobilization and pressure such as our patient experienced by falling asleep in the bath, partial axonotmesis of the radial nerve might occur rather than demyelination.

Sausage-like structures called tomacula are the most typical histopathological feature in HNPP,[31] although they are not limited to it, as they are present in many other neuropathies.[32] They consist of focal thickening of the myelin sheath in both motor and sensory nerves first described from sural nerve biopsies.[31]

The role of ultrasound and MRI is still not completely defined. Currently they can be considered complementary tools that are potentially able to help during differential diagnostic pathway and nerve condition evaluations. Padua et al[33] conducted ultrasound examinations on 70 patients with peripheral neuropathies, 10 of whom had HNPP. An enlargement of a cross-sectional area of the ulnar nerve at each elbow was identified in all of the patients with HNPP, but clinical correlations were not investigated. A case series of 6 HNPP patients with ages of onset ranging between 14 and 46 years showed cervical and lumbar disc degeneration with physiological curvature changes in 4 of them, but clinical correlations of the MRI findings with neuropathies were not clear.[13] In our patient, an elbow MRI was taken 7 months after onset, followed by a cervical MRI one and a half years after onset. Findings failed to indicate a pathological basis for symptoms associated with HNPP. The radial nerve showed no abnormality such as swelling or hyperintensity. Further, no signal changes in the muscle innervated by the radial nerve were observed. The nerve might have been partially demyelinated; however, this is difficult to capture by MRI because the radial nerve is relatively thin. We reasoned that the muscle signal did not

change due to partial paralysis.

HNPP has no specific surgical or pharmacological treatment. It is best managed by early detection, preventative measures, and subsequent treatment of symptoms.[9] It is crucial to avoid overexertion, repetitive movements, and prolonged static joint positions such as crossing legs or sleeping with arms overhead. Splints to avoid excessive joint flexion and extension can be useful. A few case reports described patients who experienced significant improvements after steroid therapy for symptomatic HNPP.[34]

The course of the disease is generally benign.[9] Most cases reported in the literature showed results ranging from significant improvement to total recovery from episodes of peripheral nerve palsy. Recurrent focal neuropathies are a characteristic presentation of HNPP. Pareyson et al reported recurrence of palsy in 4 of 8 cases (50%).[35] Given that HNPP is a rare disease, most case series describing it are relatively small. Although the exact recurrence rate is not clear, HNPP is identified by repeated paralysis in most cases.

Good clinical and instrumental outcomes after surgical decompression are reported, without local relapse of the disease.[36] Although favorable results are expected to be obtained after decompression surgery for patients with symptomatic HNPP, preventive surgery of the median nerve at the wrist and ulnar nerve at the elbow for asymptomatic patients is not recommended.[36]

CONCLUSIONS

HNPP is a rare, debilitating pathology characterized by transient nerve palsies. Our patient did not recover from the initial right radial nerve palsy, so we resorted to surgery and obtained good results. Early diagnosis of the disease is fundamental to preserve the quality of life of patients with minor symptoms. In select cases, surgery can be useful to restore nerve conduction or, as we showed, wrist and finger function.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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