

Hereditary Neuropathy with Liability to Pressure Palsies in a Turkish Patient (HNPP): A Rare Cause of Entrapment Neuropathies in Young Adults

Bir Hastada Basınca Duyarlı Herediter Nöropati: Genç Erişkinlerde Tuzak Nöropatisinin Nadir Bir Nedeni

ABSTRACT

Hereditary neuropathy with liability to pressure palsies (HNPP) is an autosomal dominant nerve disease usually caused by 1,5 Mb deletion on chromosome 17p11.2.2-p12, the region where the PMP-22 gene is located. The patients with HNPP usually have relapsing and remitting entrapment neuropathies due to compression. We present a 14-year-old male who had acute onset, right-sided ulnar nerve entrapment at the elbow. He had electrophysiological findings of bilateral ulnar nerve entrapments (more severe at the right side) at the elbow and bilateral median nerve entrapment at the wrist. Genetic tests of the patient demonstrated deletions in the 17p11.2 region. The patient underwent decompressive surgery for ulnar nerve entrapment at the elbow and completely recovered two months after the event. Although HNPP is extremely rare, it should be taken into consideration in young adults with entrapment neuropathies.

KEY WORDS: HNPP, Entrapment neuropathy, DNA analysis

ÖZ

Basınca duyarlı herediter nöropati PMP-22 geninin bulunduğu kromozom 17p11.2.2-p12'da 1,5 Mb'lık delesyonla ortaya çıkan otozomal dominant periferik sinir sistemini etkileyen bir hastalıktır. Bu hastalar kompresyon nedeniyle ataklar ve iyileşmeler şeklinde nöropatilerle seyrederek. Bu yazıda 14 yaşında erkek bir hastada akut dirsek seviyesinde ulnar tuzak nöropatisi olan bir hasta sunuldu. Hastanın elektrofizyolojik bulguları sağda daha belirgin dirsek seviyesinde bilateral ulnar, bilekte belirgin bilateral median tuzak nöropatisi ile uyumlu idi. Genetik testler sonunda 17p11.2 kromozomunda delesyon tespit edildi. Hastaya semptomatik olan dirsek seviyesindeki ulnar tuzak nöropatisi için dekompresif cerrahi uygulandı, iki ay sonra tamamen semptomları düzeldi. Basınca duyarlı tuzak nöropatisi nadir görülmekle birlikte tuzak nöropatisi olan genç erişkinlerde ayrıca tanıda akılda tutulmalıdır.

ANAHTAR SÖZCÜKLER: HNPP, Tuzak nöropati, DNA analizi

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INTRODUCTION

Hereditary neuropathy with liability to pressure palsies (HNPP) is a rare autosomal dominant neuromuscular disease usually caused by a deletion in the gene coding for the peripheral nerve myelin protein 22 (5,4). HNPP is characterized with recurrent acute peripheral nerve lesions at entrapment sites (10). It is a benign disease with complete recovery in most cases (5,10). The patients usually have relapsing and remitting entrapment neuropathy due to pressure that normal nerves easily tolerate. It is known that HNPP increases the sensitivity of peripheral nerves to pressure and may be associated with symptoms at multiple anatomic entrapment sites (5,4). Electrophysiological studies show an underlying generalized neuropathy with moderate slowing of conduction velocities, predominant over nerve entrapment sites (10). Tomacula, focal thickening of myelin sheaths, may be seen in histopathological studies and HNPP is usually caused by deletion of a 1.5 megabase pair segment of chromosome 17p11.2 or rarely mutations resulting in a functional loss of peripheral myelin protein 22 gene (1).

We present a fourteen-year-old male with HNPP who developed right-sided ulnar nerve entrapment at the elbow.

CASE

A fourteen-year-old male was referred for numbness and pain in his right arm and hand. The patient described one month of numbness involving his right fourth and fifth digits, accompanied by pain in the right elbow. There was no history of elbow trauma. Sensory loss was present in the fifth and splitting the fourth finger, and extended just proximal to the distal wrist crease. There was slight weakness of the abductor digiti minimi and interossei muscles on the right. Reflexes were normal and no tenderness of the ulnar nerve in the groove was found.

In electrophysiological studies; the right ulnar nerve compound muscle action potential (CMAP) recording from the abductor digiti minimi muscle showed a marked decrease in motor amplitude obtained above the elbow when compared with the values below the elbow (above the elbow: 3,8 millivolt, below the elbow: 8,4 millivolt). The conduction velocities of bilateral ulnar motor nerves in the forearm were normal, but the conduction

velocities around the elbow were found markedly reduced, especially in the right side (right: 22 m/sec, left: 34 m/sec). Bilateral ulnar F responses were prolonged. The amplitude of the right ulnar sensory nerve action potential (SNAP) was reduced and the conduction velocity was slightly reduced. The amplitude of the left ulnar SNAP was just below the normal range. Bilateral median nerve motor studies showed normal CMAP amplitudes and slightly prolonged distal motor latencies. Bilateral median sensory response to digit 2 showed reduced amplitude, prolonged onset latency and reduced conduction velocities. The other nerve conduction studies performed from the upper and lower extremities were found to be normal. Our patient had right-sided ulnar nerve entrapment at the elbow which was electrophysiologically and clinically confirmed, and he also had asymptomatic left-sided ulnar nerve entrapment at the elbow and bilateral median nerve entrapment at the wrists.

The clinical and electrophysiological findings of our case were typical of HNPP, and the DNA tests showed deletions in the 17p11.2 region. The patient underwent surgical decompression of the ulnar nerve before the genetic test was performed and he was totally asymptomatic two months after the surgery.

DISCUSSION

The first report of HNPP was published by De Long in 1947 (1). HNPP is usually seen after minor trauma and does not progress. The patients may typically present with peripheral neuropathy affecting the distal nerves such as peroneal (35%), ulnar (20%) and radial (8%) nerve (7). There may be up to 20% of patients with brachial plexus impairment (8). The prognosis is extremely good and complete or almost complete recovery within a few months after each event is typical. Moutan et al (8) reported that only 15% of patients with HNPP had significant residual weakness. Our patient also completely recovered two months after the event.

Electrophysiological findings in HNPP are usually characteristic. Electrophysiological studies demonstrate prolonged distal motor latencies, prolonged F wave latencies, mildly reduced motor and sensory conduction velocities, reduced amplitudes of sensory nerve action potentials and segmental slowing of conduction velocity at the usual entrapment sites (the median nerve at wrist,

the ulnar nerve at the elbow and the peroneal nerve at the fibular head segment) (6). Electrophysiological characteristics may be seen in clinically unaffected nerves and may be due to the inability to maintain myelin stability (10). Our patient had ulnar neuropathy at the symptomatic (more severe) and asymptomatic sides and he also two-sided median nerve neuropathies at the asymptomatic wrists.

The histopathological changes observed in the peripheral nerves of patients with HNPP include segmental demyelination, "sausage like" formations (tomacula in 56,4% of cases) and axonal loss (3). DNA analysis is the most important part of the diagnostic procedure for suspected HNPP patients. HNPP has an autosomal dominant transmission and genetic counseling is important. The disease is caused by the functional loss of one allele of the peripheral myelin protein 22 (PMP-22) gene (1). The loss is most often from a 1,5 Mb deletion on chromosome 17p11.2-2-p12, the region where the PMP-22 gene is located (1). Sporadic cases due to de novo deletions or asymptomatic carriers account for 21% of the patients with HNPP (2). Approximately 50% of deletion carriers are asymptomatic and do not display abnormal neurological findings on clinical examination (2). We showed the deletion on chromosome 17p11.2 in our patient.

Treatment is symptomatic and is aimed to prevent nerve compression. Rarely, some patients undergo surgery. Toggart and Allen (9) reported a case of ulnar nerve entrapment at the elbow due to HNPP, who underwent a surgical release operation. Our patient also underwent a surgical release operation, and he recovered completely two months after the surgery.

In conclusion, HNPP should be taken into consideration in young patients with recurrent

entrapment neuropathies such as median nerve neuropathy at the wrist, ulnar nerve entrapment at elbow and fibular nerve entrapment at fibular head. Although the treatment of HNPP is symptomatic, surgical procedures may accelerate the improvement.

REFERENCES

1. Chance PF, Alderson MK, Leppig KA, Lensch MW, Matsunami N, Smith B, Swanson PD, Odelberg SJ, Distche CM, Bird TD: DNA deletion associated with hereditary neuropathy with liability to pressure palsies. *Cell* 72:143-151, 1993
2. Infante J, Garcia A, Combarros O, Mateo JI, Berciano J, Sedano MJ: Diagnostic strategy for familial and sporadic cases of neuropathy associated with 17p11.2 deletion. *Muscle Nerve* 24: 1149-55, 2001
3. Kim SM, Chung KW, Choi BO, Yoon KW, Choi JY, Park KD, Sunwoo IN: Hereditary neuropathy with liability to pressure palsies (HNPP) patients of Korean ancestry with chromosome 17p11.2-p12 deletion. *Experimental and Molecular Medicine* 36: 28-35, 2004
4. Koc F, Guzel R, Benlidayi IC, Yerdelen D, Guzel I, Sarica Y: A rare genetic disorder in the differential diagnosis of the entrapment neuropathies: hereditary neuropathy with liability to pressure palsies. *J Clin Rheumatol* 12: 78-82, 2006
5. Koehler PJ: Hereditary neuropathy with liability to pressure palsies: the first publication *Neurology* 60: 1211-1213, 2003
6. Li J, Krajewski K, Shy ME, Lewis RA: Hereditary neuropathy with liability to pressure palsy. The electrophysiology fits the name. *Neurology* 58: 1769-1773, 2002
7. Meier C, Moll C: Hereditary neuropathy with liability to pressure palsies. Report of two families and review of the literature. *J Neurol* 228: 73-95, 1982
8. Mouton P, Tardieu S, Goider R, Birouk N, Maisonobe T, Dubourg O, Brice A, LeGuern E, Bouche P: Spectrum of clinical and electrophysiologic features in HNPP patients with the 17p11.2 deletion. *Neurology* 52: 1440-1446, 1999
9. Taggart TF, Allen TR: Surgical treatment of a tomaculous neuropathy. *J R Coll Surg Edinb* 46(4): 240-241, 2001
10. Verhagen WI, Gabreëls-Festen AA, van Wensen PJ, Joosten EM, Vingerhoets HM, Gabreëls FJ, de Graaf R: Hereditary neuropathy with liability to pressure palsies: a clinical, electrophysiological and morphological study. *J Neurol Sci* 116: 176-184, 1993