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# The Neurophysiologic Frequency of Hereditary Neuropathy with Liability to Pressure Palsy in Entrapment Neuropathies

## *Ailesel Basınca Duyarlılık Nöropatisi Hastalığının Tuzak Nöropatili Hastalarda Elektrofizyolojik Tanı Sıklığı*

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### Summary

**Objective:** Hereditary neuropathy with liability to pressure palsy (HNPP) needs to be differentiated from entrapment neuropathies due to differences in the treatment management.

**Materials and Methods:** Among 5075 patients with entrapment neuropathy, we retrospectively evaluated the neurophysiologic results of 20 patients with three or more entrapments.

**Results:** Ten patients were diagnosed as having HNPP according to their genetic or nerve biopsy results; eight (80%) had bilateral Carpal tunnel syndrome, nine (90%) had bilateral ulnar entrapment neuropathy, eight (80%) had bilateral median and ulnar entrapment together; and three (30%) had one-sided peroneal neuropathy.

**Conclusion:** Our data suggest that analyzing the neurophysiologic studies and keeping HNPP in mind are essential to characterize underdiagnosed patients with HNPP referred for entrapment neuropathy.

**Keywords:** Hereditary neuropathy with liability to pressure palsy, entrapment neuropathy, peripheral myelin protein 22

### Öz

**Amaç:** Ailesel basınca duyarlılık nöropatisi (ABDN) tanısı diğer tuzak nöropatilerden tedavi yaklaşımlarındaki farklılıkları açısından ayrılmalıdır.

**Gereç ve Yöntem:** 5075 elektrofizyolojik olarak tuzak nöropatisi tanısı konulan hastalar arasından, üç ve üçün üzerinde çoklu tuzak nöropatisi olan 20 hastanın elektrofizyolojik bilgileri geriye dönük olarak incelendi.

**Bulgular:** Bu hastalar arasından on hastaya genetik veya biyopsi sonucuna göre ABDN tanısı konuldu. Tanı konulan sekiz (%80) hastada bilateral Karpal tünel sendromu, sekiz hastada (%80) bilateral ulnar sinir tuzaklanması, dokuz (%90) hastada hem bilateral medyan, hem de bilateral ulnar sinir tuzaklanması birlikte bulunmaktaydı. Üç (%30) ise tek taraflı peroneal sinir tuzaklanması bulunmaktaydı.

**Sonuç:** Sonuçlarımız nörofizyolojik çalışma analizinin ve ABDN tanısının akılda tutulmasının nörofizyolojik olarak ABDN hastalarını, tuzaklanma nöropatisi için danışılan hastalardan ayrılmasına yardımcı olduğunu göstermektedir.

**Anahtar Kelimeler:** Ailesel basınca dirençlilik nöropatisi, tuzaklanma nöropatisi, periferik miyelin protein 22

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## Introduction

Hereditary neuropathy with liability to pressure palsy (HNPP) is an autosomal dominant disease characterized by recurrent, non-painful, sensory or motor dysfunction, usually after a minor trauma. It usually presents with entrapment neuropathy symptoms in the second or third decade of life (1). Eighty-five percent of cases occur as a result of deletion in chromosome 17p11.2, which encodes peripheral myelin protein 22 (PMP22), and is duplicated in Charcot-Marie-Tooth neuropathy type 1A (2,3). Point mutations in PMP22 can also rarely cause HNPP (4). PMP22 is a myelin component and is thought to have a functional task rather than structural task (5). HNPP can also be sporadic besides being hereditary (6). Electrophysiologic findings are symptoms of multiple entrapment neuropathies and distal latency prolongation superimposed on moderate neuropathy findings with mild conduction slowdowns (7). In this study, the diagnostic frequency and characteristics of HNPP in patients who were diagnosed as having multiple entrapment neuropathy/nerve compression in electromyography (EMG) laboratory are discussed.

## Materials and Methods

The medical records of patients who were electrophysiologically diagnosed as having entrapment neuropathy-nerve compression in the EMG unit in Hacettepe University Hospital between 2003 and 2013 were screened retrospectively. Nerve conduction studies (NCSs) were performed using bipolar Ag-AgCl surface electrodes with electrical stimulation through the skin. Motor NSCs were performed over median, ulnar (below elbow to wrist, above elbow to below elbow segments), tibial and peroneal (below fibular head to ankle, popliteal fossa to below fibular head) nerves, and sensory NCSs were performed over ulnar, median (2nd digit to wrist, palm to wrist segments) and sural nerves using an orthodromic method. Patients with three or more entrapment neuropathies by motor and sensory NCSs also underwent evaluation of sensory and motor nerves of both upper and lower extremities. Needle EMG studies were performed in patients with findings of entrapment neuropathy/nerve compression or polyneuropathy. Nerve conduction and needle EMG studies of patients were carried out using a Medtronic Keypoint (Denmark A/S) EMG device.

Patients meeting the criteria of three or more peripheral entrapment neuropathy/nerve compression were selected from a database of electrophysiologic recording reports and included in the study. Of these patients, patients with polyneuropathy due to diabetes mellitus and chronic renal failure, and patients meeting the diagnostic criteria of chronic inflammatory demyelinating polyneuropathy were excluded. The clinical, electrophysiologic and other laboratory parameters of patients with electrophysiologically-diagnosed HNPP (8) were analyzed retrospectively.

## Results

### Patients

Entrapment neuropathy/nerve compression was diagnosed electrophysiologically in 5075 patients between 2003 and 2013. Of these patients, 3920 (77.2%) patients had median nerve compression at the wrist level (in the carpal tunnel), 910 (17.9%) had ulnar nerve compression at the elbow level, and 98 (1.9%) had peroneal nerve compression at the knee segment. Concomitant median and ulnar nerve compression findings were detected in 210 (4.1%) patients. Of 3920 patients, three or more entrapment neuropathy with polyneuropathy findings were detected in twenty (0.39%) patients and a electrophysiologic diagnosis of HNNP was considered. The diagnosis of HNNP was confirmed through biopsy or genetic research in ten (0.19%) patients.

Of patients diagnosed as having HNNP, seven (70%) were male and three (30%) were female. The mean age was 21.4±7.03 years (range, 13-30 years). Six (30%) patients had a family history for HNNP as repeated entrapment neuropathies. PMP22 gene deletion was detected in nine (36%) patients. Three (15%) patients underwent nerve biopsy examination. The diagnosis was confirmed with both gene deletion and biopsy examination results in two (10%) patients. The demographic and electrophysiologic characteristics of the patients are presented in Table 1 (8).

Table 1. The demographic and electrophysiologic characteristics of patients

| Patient | Age | Sex | Family history | PMP22 | Sural nerve biopsy | Electrophysiologic entrapment region | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | Median | Ulnar | Peroneal |
| 1 | 25 | M | + | + | | Bilateral | Bilateral | |
| 2 | 21 | M | _ | + | | Bilateral | Bilateral | |
| 3 | 28 | F | + | + | + | Bilateral | Bilateral | |
| 4 | 15 | M | + | + | | Bilateral | Bilateral | Right |
| 5 | 34 | M | + | + | + | Bilateral | Bilateral | |
| 6 | 17 | F | + | + | | Bilateral | Bilateral | |
| 7 | 30 | M | _ | + | | Left | Bilateral | |
| 8 | 13 | M | _ | + | | Bilateral | Bilateral | Right |
| 9 | 14 | M | _ | + | | Bilateral | Bilateral | |
| 10 | 17 | F | + | _ | + | Right | Right | Left |

F: Female, M: Male, PMP22: Peripheral myelin protein 22

### Electrophysiologic Findings

The electrophysiologic diagnosis of entrapment neuropathy/nerve compression was made with findings of segmental demyelination in specified regions in the form of motor and sensory nerve conduction velocity slowdowns, distal latency prolongation or motor conduction block. Of the ten patients, eight (80%) had bilateral median nerve entrapment at the wrist segment (Carpal tunnel syndrome), nine (90%) had bilateral ulnar nerve entrapment at the elbow segment, and three (30%) patients had unilateral peroneal nerve entrapment neuropathy. Eight (80%) patients had bilateral concomitant median and ulnar entrapment neuropathies. Three (30%) patients had concomitant median, ulnar and peroneal nerve entrapment neuropathies. Bilateral peroneal nerve entrapment neuropathy was not observed in any patients. Polyneuropathy findings were present in nine (90%) patients.

## Discussion

In our study, the electrophysiologic diagnostic frequency of HNNP in patients with detected entrapment neuropathy/nerve compression in the EMG laboratory was retrospectively analyzed. The diagnosis was confirmed in 50% of patients with electrophysiologically considered HNNP (three or more concomitant entrapment neuropathy findings and moderate polyneuropathy) through biopsy and genetic analysis. Although no comments can be made about patients without these examinations, the presence of segmental demyelination findings in more than three entrapment regions and underlying moderate polyneuropathic involvement suggest the diagnosis of HNNP with a high probability in these patients.

Regarding its prognosis and treatment, the diagnosis of HNNP requires a different approach from common isolated entrapment neuropathies. Therefore, we believe that it is appropriate to expand electrophysiologic studies in terms of HNNP in patients who are referred to the electrophysiology laboratory with a prediagnosis of entrapment neuropathy/nerve compression and in whom three or more nerve involvements are detected. This approach is necessary in terms of not overlooking the findings of both subclinical entrapment neuropathy and diffuse polyneuropathy. This gains more importance especially in patients who have no predisposing risk factors for entrapment neuropathy such as age, sex, occupation, and systemic disease.

Although genetic inheritance was mentioned in most HNNP cases, sporadic cases have also been reported (9). Acute clinical presentation is known to occur most commonly in the form of entrapment neuropathies at the ages of 2-3 years (1). The mean age of patients with HNNP in our series also supports literature. In this disease, electrophysiologically moderate demyelinating polyneuropathic involvement is known to be present as well as entrapment neuropathy (1,8,10). Polyneuropathy was also detected in nine of our patients. Brachial plexus involvement along with peripheral entrapment neuropathy is also a rarely reported electrophysiologic finding (11,12), but plexus involvement was not observed in our patients. Although the clinical presentation often occurs following minor trauma (13), electrophysiologic findings can also be found in unaffected nerves (8). It is also known that 10-15% of cases are asymptomatic (8). Behse was the first researcher to analyze and demonstrate the histopathologic features of the disease (14). The demonstration of tomacular ultrastructure with sausage-shaped swellings of the myelin in the focal paranodal region by isolation of the individual nerve fibers (teasing) in nerve biopsy is helpful in diagnosis. However, it is known that this finding is not specific for this disease, and that it can also be observed in Charcot-Marie-Tooth disease and Dejerine-Sottas phenotype (8). Although the prognosis is variable, recovery usually occurs spontaneously (15). There is no definitive treatment other than symptomatic treatment (15), and avoiding trauma and supportive treatment for entrapment symptoms are recommended. As the clinical symptoms are considered increase with surgery (15), surgical treatment is not recommended. Therefore, we think that it is important to recognize the clinical and electrophysiologic characteristics of HNNP in patients undergoing neuropsychological examination with entrapment neuropathy symptoms, and to refer these patients for further investigation.

### Ethics

Ethics Committee Approval: The study does not need ethics committee approval. The paper does not report on the use of experimental or new protocols. All data analyzed were collected as part of routine diagnosis and treatment.

Peer-review: Externally peer-reviewed.

### Authorship Contributions

Surgical and Medical Practices: Sevim Erdem Özdamar, Çağrı Mesut Temuçin, Gülay Nurlu, Concept: F. Gökçem Yıldız, Design: Çağrı Mesut Temuçin, Data Collection or Processing: F. Gökçem Yıldız, Analysis or Interpretation: F. Gökçem Yıldız, Çağrı Mesut Temuçin, Literature Search: F. Gökçem Yıldız, Çağrı Mesut Temuçin, Writing: F. Gökçem Yıldız.

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