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● *Original Contribution*

DIFFERENT PATTERNS OF NERVE ENLARGEMENT IN POLYNEUROPATHY SUBTYPES AS DETECTED BY ULTRASONOGRAPHY

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Abstract—The purpose of our study was to examine how the pathologic type of polyneuropathy affects nerve size as assessed by high-resolution ultrasonography with a 15 MHz transducer. Cross-sectional area (CSA) of the C5–C7 nerve roots and several upper and lower limb nerves at multiple sites was measured in 38 patients with acquired diffuse sensorimotor demyelinating or axonal polyneuropathy and in 34 healthy control subjects. Significant differences were found among the groups for all nerve and root segments: Both types of polyneuropathy are characterized by nerve enlargement in comparison to controls, but in different patterns. In demyelinating polyneuropathies, an additional degree of nerve thickening appears in proximal upper limb nerves and cervical nerve roots compared with axonal polyneuropathies. With respect to the other nerves, a similar degree of nerve enlargement was observed in both patient groups. These results highlight that ultrasonography may be a complementary tool in differentiating polyneuropathies. (E-mail: erika.scheidl@gmail.com) © **2014 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Axonal polyneuropathy, Cross-sectional area, Demyelinating polyneuropathy.**

INTRODUCTION

High-resolution ultrasonography (HRUS) is a tool that is increasingly being used to investigate superficial peripheral nerves, as it allows the precise structural analysis and quantitative measurement of nerves. Morphologic parameters collected by ultrasound, such as cross-sectional area (CSA) measured on transverse scans and anteroposterior diameter measured on longitudinal scans, constitute useful information complementary to electrophysiological data. High-resolution ultrasonography is especially helpful in the diagnosis of entrapment neuropathies, traumatic peripheral nerve injuries and tumors of the peripheral nerves (Bayrak et al., 2007; Bayrak et al., 2010; Beekman and Visser 2004a, 2004b; Beekman et al. 2004; Hobbson-Webb et al. 2012; Peer 2008; Visser et al., 2008; Yoon et al., 2008). However, only few reports are available on the use of peripheral nerve ultrasound in polyneuropathies. Previous studies described diffuse and/or multifocal enlargement of certain peripheral nerves and the brachial plexus in some hereditary and acquired demyelinating polyneuropathies, such as Charcot-Marie-Tooth type 1, hereditary neuropathy with liability to pressure palsies, chronic inflammatory demyelinating polyneuropathy (CIDP), Guillain-Barré syndrome (GBS), multifocal motor neuropathy and multifocal acquired demyelinating sensory and motor neuropathy (Beekman 2005; Beekman and Visser 2002; Cartwright et al. 2009; Imamura et al. 2009; Jang et al. 2012; Kerasnoudis 2012, 2013; Martinoli et al. 2002; Matsuoka et al. 2004; Rayabally et al. 2012; Scheidl et al. 2012; Sugimoto et al., 2013; Taniguchi et al. 2000; Zaidman et al. 2009). Little is known about nerve size changes in axonal polyneuropathies. According to some authors, nerve enlargement is more characteristic of demyelinating than axonal polyneuropathies (Rayabally 2012; Zaidman 2009). The preferential involvement of the nerve roots and brachial plexus in CIDP has been shown in some magnetic resonance and ultrasound studies (Crino et al. 1993; Matsuoka et al. 2004; Midroni et al. 1999); however, data are still scarce. Furthermore, diagnosis may be difficult in the early stages of some immune-mediated polyneuropathies (CIDP and subtypes), whereas early treatment is crucial to

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avoid long-term disability in these disorders. Our goal was to explore the use of ultrasonography in polyneuropathy to assess whether a systematic evaluation of peripheral nerves by ultrasound provides information complementary to electrophysiological data, with special emphasis on immune-mediated demyelinating polyneuropathies.

Systematic ultrasonographic assessment of both upper and lower limb nerves, including pure sensory nerves, in polyneuropathies is lacking. We decided to examine a reliable nerve size parameter, cross-sectional area (CSA) as measured by high-resolution ultrasound at multiple sites of upper limb nerves, in the brachial plexus and in lower limb nerves, in patients with diffuse acquired sensorimotor demyelinating and axonal polyneuropathies and in healthy subjects, to see how the pathologic nature of polyneuropathy affects nerve size.

METHODS

Patients

Our prospective study was approved by the Institutional Ethics Committee of Semmelweis University. Patients gave written informed consent. Between April and October 2011, 38 patients with the clinical diagnosis of acquired diffuse symmetric polyneuropathy were recruited. Diagnosis was based on the signs and symptoms of the disease and electrophysiological workup at our laboratory. Thirty-four healthy controls were also investigated by ultrasonography. Control subjects were recruited from hospital staff and patients from the general neurologic department. None of the control subjects had symptoms or signs as assessed by physical examination suggestive of polyneuropathy or systemic diseases potentially associated with polyneuropathy, nor any history of neuromuscular disease. They provided oral informed consent.

Patients were classified into the following categories based on electrophysiological criteria: diffuse sensorimotor axonal (n = 26) and diffuse sensorimotor primary demyelinating (n = 12) polyneuropathies. Within the latter group, 9 patients were diagnosed with CIDP and 3 patients with demyelinating polyneuropathy of other origin. In patients with axonal polyneuropathies, underlying conditions included diabetes mellitus (n = 11), uremia (n = 1), chronic alcoholism (n = 5), vitamin B_{12} deficiency (n = 2), chemotherapy (n = 2) and unknown origin (n = 5). Patients with hereditary polyneuropathy and patients with acquired polyneuropathy presenting in the form of multiple mononeuropathy were excluded from the study. Demographic data, including age, gender, height and weight, were collected and are summarized in Table 1.

Electrophysiological workup

Electrophysiological studies were performed in all patients using a Viking electromyography device manufactured by CareFusion (Med-Pro Hungary Kft., Budapest, Hungary) and included median and ulnar nerve motor and sensory nerve conduction studies and F-wave studies, peroneal and tibial nerve motor nerve conduction studies and F-wave studies, sural sensory nerve conduction study and concentric needle electromyography of at least two muscles (generally abductor digiti minimi and tibial anterior muscles), according to standard techniques (England et al. 2009; Kimura 1989). The left side was examined in all patients. Additional tests were performed in patients in whom additional nerves were needed to fully meet the diagnostic criteria of demyelinating polyneuropathies (in 4 of 9 patients with CIDP, the tibial nerve and median nerve and F-waves on the right side were also examined, and in 2 of these 9 patients, femoral nerves were also measured). Axonal and primary demyelinating polyneuropathy was diagnosed using standard criteria (Sander 2003; Tankisi et al. 2005). Reference values for nerve conduction studies were normal data collected earlier and established for our electromyography laboratory based on serial studies performed within our laboratory. These are used in routine daily practice in our laboratory; the mean ± 2.5 SD (standard deviation) was used for limits of normality.

Ultrasonography

For ultrasound examinations, a Philips HD15 XE Pure Wave ultrasound device (Hun-Med Kft., Budapest, Hungary) with small part imaging software and 15-MHz 3-cm linear array transducer was used. XRES and SonoCT (compound imaging) software were turned on to improve image quality. The dynamic range setting was 50 dB. The time interval between ultrasound and electrophysiological investigation did not exceed 10 d. Ultrasonographic examinations were performed by one of the authors who is a neurologist and was blinded to clinical and electrophysiological data. Nerve size measurements were also performed on one side because of the diffuse and symmetric nature of the polyneuropathy. These measurements were made on the same side subjected to the electrophysiological examination, which, in all patients, was the left side. On transverse scan, the CSA of the following upper limb nerves was measured: cervical nerve roots (C5–C7) immediately after their exit from the cervical foramina; the median nerve on the mid-upper arm, on the distal third of the forearm (just above the pronator quadratus muscle) and at the wrist (at the level of the pisiform bone); the ulnar nerve on the mid-upper arm, at the elbow (in the condylar groove at the level of the medial epicondyle) and on the mid-forearm; the radial nerve at the mid-upper arm (at the level of the spiral groove); and the superficial radial nerve 7–8 cm proximal to the styloid process of the radius. On the lower limbs, the CSA of the peroneal nerve