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Comparison of clinical, electrophysiological, sonographic and MRI features in CIDP☆,☆☆

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ABSTRACT

Introduction: We investigated the applicability of nerve ultrasound and magnetic resonance imaging (MRI) in chronic inflammatory demyelinating polyneuropathy (CIDP).
Methods: We systematically examined several nerves with ultrasound and the lumbar roots and tibial nerve in the popliteal fossa of nine CIDP patients with MRI additionally to the nerve conduction studies.
Results: Patients with overall disability sum score (ODSS) 2–3 were characterised by normal fascicular structure in MRI and ultrasound. Patients with higher ODSS showed isolated enlarged fascicles and increased cross sectional area (CSA) of the peripheral nerves and of the diameter of the cauda equina and L5 root, whereas two of them showed atrophic fascicles in both imaging techniques.
Conclusions: Nerve ultrasound and MRI findings show the same morphological fascicle alterations in peripheral nerves in correlation to ODSS. Nerve ultrasound as an affordable tool, easy and quick to perform, could replace MRI in daily routine for monitoring peripheral nerve morphology.

1. Introduction

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a clinically heterogeneous, sensorimotor neuropathy evolving as a monophasic, relapsing or progressive disorder [1]. Immune-mediated inflammation and neurodegeneration is considered to play a central role in the pathogenesis of this disease, although the precise mechanisms remain unclear [2,3].

Electrophysiology remains the gold standard to assess the extent of nerve damage. However, at a later stage of the disease, or in severe cases, the loss of F-waves, compound muscle action potentials (cMAPs) and sensory nerve action potentials (sNAPs) may hinder the assessment of the nerve damage. In order to dissect morphological abnormalities of the peripheral nerves, different imaging techniques, such as nerve ultrasound and MRI, were introduced. MRI techniques were the first to show the distinctive pattern of peripheral nerve hypertrophy [4–7] and nerve ultrasound followed as a practical, affordable and effective method to detect morphological nerve alterations in different forms of peripheral neuropathy [8–11]. However, the pathophysiological background and the diagnostic and prognostic value of these morphological nerve alterations still remain unclear. To the authors' knowledge, the correlation between these two methods and clinical findings in CIDP has not been referred in the literature until now.

The primary objective of this study was to systematically evaluate the usefulness of ultrasound and MRI in assessing the morphological peripheral nerve pathology in CIDP.

2. Methods

2.1. Subjects and patients

The local university ethics committee approved our study protocol and all CIDP patients signed informed consent. Nine patients aged over 18 years, fulfilling the diagnostic criteria of CIDP and with severity distributed along the INCAT (inflammatory neuropathy cause and treatment) validated overall disability sum score (ODSS) scale (Table 1), were recruited over a period of 6 months in the study. For the diagnosis of definite CIDP we used the diagnostic criteria proposed from the Joint Task Force of the European Federation of Neurological Societies and the Peripheral Nerve Society. According to these criteria, the clinical

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Table 1
Clinical data of the nine CIDP patients. Abbreviations: F: female, M: male, IVIG: intravenous immunoglobulins, MRI: magnetic resonance imaging, NCS: nerve conduction studies.

Clinical data						
Nr	Age Gender	Disease duration (years)	CSF protein (mg/l)	ODSS	IVIG dosage	Additional treatment (dosage)
1	53 F	2	471	2	1 g/kg/8 weeks	–
2	55 F	9	695	2	1 g/kg/6 weeks	–
3	68 M	5	726	3	1 g/kg/4 weeks	–
4	61 M	5	834	4	1 g/kg/4 weeks	Cyclophosphamide (600 mg/m^2/6 weeks)
5	43 M	5	630	4	1 g/kg/4 weeks	Azathioprin (2 mg/kg/day)
6	45 F	3	830	4	1 g/kg/4 weeks	Azathioprin (2 mg/kg/day)
7	63 M	6	963	5	1 g/kg/4 weeks	Cyclophosphamide (660 mg/m^2/6 weeks)
8	64 M	1	748	5	1 g/kg/4 weeks	Mycophenolate mofetil 1500 mg/day
9	43 F	8	500	7	1 g/kg/4 weeks	Cyclophosphamide (660 mg/m^2/6 weeks)

criterion and at least one of the electrodiagnostic criteria, which represent pathology in at least two peripheral nerves, should be fulfilled for a definite CIDP [12].

2.2. Nerve conduction studies and electromyography

All patients with CIDP interested in participating in this study underwent nerve conduction studies of the sural, tibial and fibular nerves on both sides and electromyography of the anterior tibial muscle to detect spontaneous activity (positive sharp waves and fibrillation potentials).

All the nerve conduction studies (NCS) were performed from a board certified neurologist (M.-S. Y.) with the use of a Medtronic 4 canal electromyography (EMG) Device (Medtronic, Meerbusch, Germany). All testing was done while maintaining the skin temperature at 36 °C. As reference values we used the ones proposed from Stöhr et al. [13].

Electromyographical recording of spontaneous activity was performed in 2 insertion sites for the anterior tibial muscle and at 5 directions for each insertion site (total of 10 directions). Spontaneous activity was defined as + if present in 1–3/10 directions, ++ if present in 4–6/10 and +++ if present in 7–10/10 directions.

2.3. Ultrasound examination

Ultrasonography was performed at the same day with the NCS from one neurologist (K.P.) with at least 3 years of neuromuscular ultrasound experience. All ultrasound studies have been performed with the use of an Aplio® XG ultrasound system (Toshiba Medicals, Tochigi, Japan). For the superficial nerves of the lower extremities (fibular nerve at the fibula head, tibial nerve at the ankle, sural nerve) an 18-MHz linear array transducer was used, and for the deeper nerves (tibial and fibular in popliteal fossa) a 12-MHz linear array transducer was used. The transducer was always kept perpendicular to the nerves to avert anisotropy. No additional force was applied other than the weight of the transducer and the extremities were kept in the neutral position to avoid causing any artificial nerve deformity. Cross sectional area measurements were performed at the inner border of the thin hyperechoic epineural rim by the continuous tracing technique and the average values were calculated after serially measuring three times.

All peripheral nerves of the lower extremities were measured bilaterally in all subjects and patients at the following sites: tibial nerve in the popliteal fossa and at the ankle, fibular nerve at the fibular head and in the popliteal fossa and sural nerve (between the lateral and medial head of the gastrocnemius muscle). As reference values we used the ones published by Kerasnoudis et al. [14].

2.4. MRI technique, image interpretation and MRI outcome measures

MRI examinations were performed 2 weeks after the NCS and ultrasound examinations utilizing a 3 T scanner (Skyra, Siemens Healthcare, Erlangen, Germany). MRI examinations consisted of sagittal and axial T2 weighted images with and without spatial fat saturation (TR 7130-7230, TE 96 ms, slice thickness 2,5 mm) through the popliteal fossa of the clinically most affected lower extremity. Additionally T2 weighted sequences of the lumbar spine in axial, coronal and sagittal orientation were acquired (TR 4470, TE 98, slice thickness 3 mm).

Original MRI films were independently reviewed by a neuroradiologist (MS), blinded to clinical and ultrasound results. The presence or absence of lumbar nerve root enlargement was assessed in the intrathecal, intraforaminal, and extraforaminal segments of the roots and the maximum diameter of root L5 was measured in the intraforaminal segment. Nerve roots were considered normal if the diameter was less than 3 mm and an enlargement of cauda equina was diagnosed if more than 50% of the lumbar roots were enlarged [4,15].

The tibial nerve in the popliteal fossa was evaluated quantitatively (maximal cross sectional area in mm^2) and qualitatively as: N: normal structure of the fascicles, E: enlarged fascicles, A: atrophic fascicles.

In order to acquire reference values of the cross sectional area of the tibial nerve in the popliteal fossa, we sampled individuals from our database, who had an MRI examination in the same MRI tomogram because of knee pain. These control individuals did not have any signs of peripheral neuropathy and they were matched with respect to sex and age for the CIDP patients. Then, we randomly sampled the final control patients from the candidate patients without replacement. Two control patients were sampled for each patient with CIDP. Eventually, 18 control patients were enrolled (9 women and 9 men; mean age ± SD (min–max) was 50 ± 9 years (20–61)) and the mean cross sectional area ± (2SD) (min–max) was 16.3 ± 10,2 mm^2 (8–26).

2.5. Statistics

Statistical comparison of groups was performed with the help of Student's t test using SPSS 17.0 for Windows. All reference values for ultrasound, MRI and NCS are given in squared brackets in the tables as mean ± 2SD.

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