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Editorial

Nerve ultrasound: Unravelling the different patterns of nerve enlargement in CIDP subtypes

Nerve ultrasound has gained prominence as a complementary tool to electrophysiological tests in evaluating neuromuscular disorders including immune-mediated neuropathies such as chronic inflammatory demyelinating polyneuropathy (CIDP). In the recent revised CIDP guidelines by the European Academy of Neurology/Peripheral Nerve Society (EAN/PNS), the Task Force included sonographic detection of enlarged nerves as a supporting criterion in the diagnosis of CIDP (Van den Bergh et al., 2021). This is based on numerous studies supporting the enlargement of nerves in up to 90 % of patients with CIDP (Niu et al., 2023). However, CIDP is not a homogeneous disease and as acknowledged in the current guidelines, patients with CIDP have various clinical subtypes. These include typical, distal, multifocal, focal, pure motor, and pure sensory forms of CIDP, each with distinct clinical and electrophysiological characteristics. However, there have been few studies that have explored the patterns of nerve enlargement on ultrasound in the different CIDP subtypes.

In the current issue of *Clinical Neurophysiology Practice*, Yoshikawa and colleagues conducted an ultrasound study of patients with different CIDP subtypes, comparing them to another chronic immune-mediated neuropathy, multifocal motor neuropathy (MMN) (Yoshikawa et al., 2023). In this retrospective study, the authors investigated 39 patients with chronic immune-mediated neuropathies, comprising of 14 typical CIDP, 7 multifocal CIDP, 4 distal CIDP and 14 MMN. The study involved measuring the cross-sectional areas (CSA) of the median and ulnar nerves at four pre-defined sites (wrist, forearm, elbow and upper arm) and calculating the ratios at the wrist-to-forearm and elbow-to-upper arm, referred to as wrist-to-forearm index (WFI) and elbow-to upper arm index (EUI) respectively. In addition, the authors determined the intranerve CSA variability (INCV) which represents the difference between the maximum and minimum CSA of each nerve. Despite the small number of patients, the authors detected significant nerve enlargements at the intermediate or non-entrapment nerve segments (forearm and midarm) of their multifocal CIDP cohort. The number of patients studied is too small to draw firm conclusions and may have contributed to the lack of correlation with disease duration or treatment. Two of the seven patients had higher CSA recordings that could be considered outliers. However, the authors acknowledged this limitation but postulated that this might in fact be a characteristic of multifocal CIDP. Certainly, their findings merit further study in larger cohorts. Correspondingly, the WFI and EUI were significantly lower whereas the INCV was significantly higher in multifocal CIDP compared to the other CIDP subtypes and MMN. Others have reported similar findings including regional, non-homogenous, and homogenous enlargement in CIDP patients (Grimm et al., 2016), as well as predominantly proximal and non-entrapment site nerve enlargement (Jang et al., 2014).

Multifocal CIDP is considered a variant of CIDP that can be distinguished by a specific set of clinical features. It is characterised by muscle weakness and sensory loss in a multifocal pattern, usually asymmetric with predominant upper limb involvement. The electrophysiological findings in multifocal CIDP have typically reported the presence of conduction block, primarily in the intermediate nerve trunk. This is in contrast to typical CIDP, where there is preferential involvement of distal nerve terminals and nerve roots, often associated with anatomical deficiencies of the blood-nerve barrier (Kuwabara et al., 2015). These findings could be in keeping with the reported sonographic findings in the study by Yoshikawa et al., which detected nerve enlargement at intermediate nerve segments, potentially correlating with conduction block. However, the authors were not able to provide the corresponding electrophysiological values, further limiting the conclusions that could be drawn.

Importantly, Yoshikawa and colleagues were able to compare their findings to ultrasound findings in patients with MMN, an important differential diagnosis in this group of patients. The distribution of lesions observed in multifocal CIDP shares similarities to those in MMN, despite the presumed differences in their underlying pathophysiology. In MMN, nerve ultrasound studies have found that nerve enlargement does not necessarily correspond to sites of conduction block (Beekman et al., 2005; Kerasnoudis et al., 2014). Instead, focal nerve enlargement was detected at sites without conduction block and also in nerves that were normal on electrophysiological testing (Beekman et al., 2005). These findings were in contrast to ultrasound findings in multifocal CIDP, where focal nerve enlargement tended to be at the nerve trunk, although not always correlating with electrophysiology (Grimm et al., 2016; Goedee et al., 2017; Kerasnoudis et al., 2015).

There is merit in further studies to elucidate these contradictory findings and gain a better understanding of the underlying pathophysiology of the two conditions. In CIDP, the nerve enlargement that is seen on ultrasound has been attributed to various patholog-

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ical processes, including nerve oedema, acute inflammation, Schwann cell proliferation due to recurrent demyelination and remyelination, and fibrotic changes in the interstitial tissue (Niu et al., 2023). Conduction block can be a consequence of severe demyelination but can also be due to dysfunction of voltage-gated sodium channels in the nodal and paranodal regions. Whilst the process of demyelination and remyelination contributes to increased nerve CSA, dysfunction of ion channels typically does not (Niu et al., 2023). This might explain the differences seen in the ultrasound findings between the different subtypes of chronic immune-mediated neuropathies.

The use of nerve CSA alone may not adequately capture the non-homogenous nerve enlargement that is typical of inflammatory neuropathies. There are other reported scoring systems that might offer more robust evidence in these settings. This includes internerve CSA variability (Padua et al., 2012), side-to-side difference ratio of the INCV (Kerasnoudis et al., 2013), nerve ultrasound protocol (Kerasnoudis et al., 2016), homogeneity score and regional nerve enlargement index (Grimm et al., 2016). There are also emerging ultrasound parameters that may be useful in assessing disease activity such as nerve echogenicity, vascularity, elastography and individual fascicle size.

There are also differences in the treatment responses between CIDP subtypes (Kuwabara et al., 2015). In the study by Kuwabara and colleagues, corticosteroids appear to have similar efficacy in patients with typical CIDP and multifocal CIDP (83 % vs. 72 %). However, the response to intravenous immunoglobulin (IVIG) (87 % vs. 38 %) and plasmapheresis (81 % vs. 17 %) was notably poorer in multifocal CIDP. The long-term outcome also differed with typical CIDP patients exhibiting a remission rate of 55 % compared to 33 % in multifocal CIDP patients. A high percentage (40 %) of patients with multifocal CIDP also appeared to be severely disabled. Thus, early recognition of the different CIDP subtypes is crucial to avoid delays in instituting appropriate therapeutic intervention. For this, nerve ultrasound appears to show promise as an adjunct to clinical features and electrophysiology in differentiating between the subtypes of CIDP.

Declarations of interest

None.

References

Beekman, R., van den Berg, L.H., Franssen, H., Visser, L.H., van Asseldonk, J.T., Wokke, J.H., 2005. Ultrasonography shows extensive nerve enlargements in multifocal motor neuropathy. Neurology 65, 305–307.
Goedee, H.S., van der Pol, W.L., van Asseldonk, J.-T.-H., Franssen, H., Notermans, N.C., Vrancken, A.J.F.E., et al, 2017. Diagnostic value of sonography in treatment-naive chronic inflammatory neuropathies. Neurology 88, 143–151.
Grimm, A., Vittore, D., Schubert, V., Lipski, C., Heiling, B., Décard, B.F., et al, 2016. Ultrasound pattern sum score, homogeneity score and regional nerve enlargement index for differentiation of demyelinating inflammatory and hereditary neuropathies. Clin Neurophysiol 127, 2618–2624.
Jang, J.H., Cho, C.S., Yang, K.S., Seok, H.Y., Kim, B.J., 2014. Pattern analysis of nerve enlargement using ultrasonography in chronic inflammatory demyelinating polyneuropathy. Clin Neurophysiol 125, 1893–2189.
Kerasnoudis, A., Klasing, A., Behrendt, V., Gold, R., Yoon, M.S., 2013. Intra- and internerve cross-sectional area variability: New ultrasound measures. Muscle Nerve 47, 146–147.
Kerasnoudis, A., Pitarokoili, K., Behrendt, V., Gold, R., Yoon, M.S., 2014. Multifocal motor neuropathy: correlation of nerve ultrasound, electrophysiological and clinical findings. J Peripher Nerv Syst 19, 165–174.
Kerasnoudis, A., Pitarokoili, K., Gold, R., Yoon, M.-S., 2015. Bochum ultrasound score allows distinction of chronic inflammatory from multifocal acquired demyelinating polyneuropathies. J Neurol Sci 348, 211–215.
Kerasnoudis, A., Pitarokoili, K., Haghikia, A., Gold, R., Yoon, M.-S., 2016. Nerve ultrasound protocol in differentiating chronic immune-mediated neuropathies. Muscle Nerve 54, 864–871.
Kuwabara, S., Isose, S., Mori, M., Mitsuma, S., Sawai, S., Beppu, M., et al, 2015. Different electrophysiological profiles and treatment response in 'typical' and 'atypical' chronic inflammatory demyelinating polyneuropathy. J Neurol Neurosurg Psychiatry 86, 105–109.
Niu, J., Zhang, L., Hu, N., Cui, L., Liu, M., 2023. The distribution pattern of nerve enlargement in clinical subtypes of chronic inflammatory demyelinating polyneuropathy. J Neuroimaging, 1–11.
Padua, L., Martinoli, C., Pazzaglia, C., Lucchetta, M., Granata, G., Erra, C., et al, 2012. Intra- and internerve cross-sectional area variability: new ultrasound measures. Muscle Nerve 45, 730–733.
Van den Bergh, P.Y.K., van Doorn, P.A., Hadden, R.D.M., Avau, B., Vankrunkelsven, P., Allen, J.A., et al, 2021. European Academy of Neurology/Peripheral Nerve Society guideline on diagnosis and treatment of chronic inflammatory demyelinating polyradiculoneuropathy: report of a joint Task Force-Second revision. Eur J Neurol 28, 3556–3583.
Yoshikawa, M., Sekiguchi, K., Suehiro, H., Watanabe, S., Noda, Y., Hara, H., et al, 2023. Nerve enlargement differs among chronic inflammatory demyelinating polyradiculoneuropathy subtypes and multifocal motor neuropathy. Clin Neurophysiol Pract. this issue.

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