

LETTERS TO THE EDITOR

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Spinal nerve pathology in Guillain-Barré syndrome associated with COVID-19 infection

We very much enjoyed reading the article by Oguz-Akarsu and colleagues describing Guillain-Barré syndrome (GBS) in a coronavirus disease-2019 (COVID-19) patient with minimal systemic manifestations.¹ The patient was admitted with a 3-day history suggestive of GBS. We focused on the magnetic resonance imaging (MRI) study of the lumbar and cervical spines that, on short-tau inversion recovery (STIR) sequence, showed “asymmetrical thickening and hyperintensity of postganglionic roots supplying the brachial and lumbar plexuses.” This is a magnificent MRI demonstration of edema involving spinal nerves and their corresponding ventral rami.

Autopsy studies in early GBS (≤ 10 days after symptom onset) have revealed that the initial lesion is inflammatory edema, predominating where motor and sensory roots join to form the spinal nerve.² Our nerve ultrasonographic studies in early GBS have revealed

that prominent changes may also be present in the ventral rami of the cervical nerves (C5-C7), consisting of symmetrical or asymmetrical increase of cross-sectional areas and blurred boundaries, which correlate with endoneurial and epineurial inflammatory edema (Figure 1).³ Therefore, there is a good correlation between MRI/STIR, ultrasound, and pathological findings.

In early GBS, MRI imaging studies using postcontrast T1 sequences have regularly shown cauda equina nerve root enhancement.² Predominant involvement of intrathecal spinal roots and spinal nerves and their ventral rami is due to the greater permeability of the blood-nerve barrier in several important structures in the peripheral nervous system, including the spinal cord to root-nerve junction (spinal nerve), dorsal root ganglia, and neuromuscular junctions.^{4,5} These are areas not well-visualized with conventional imaging techniques.

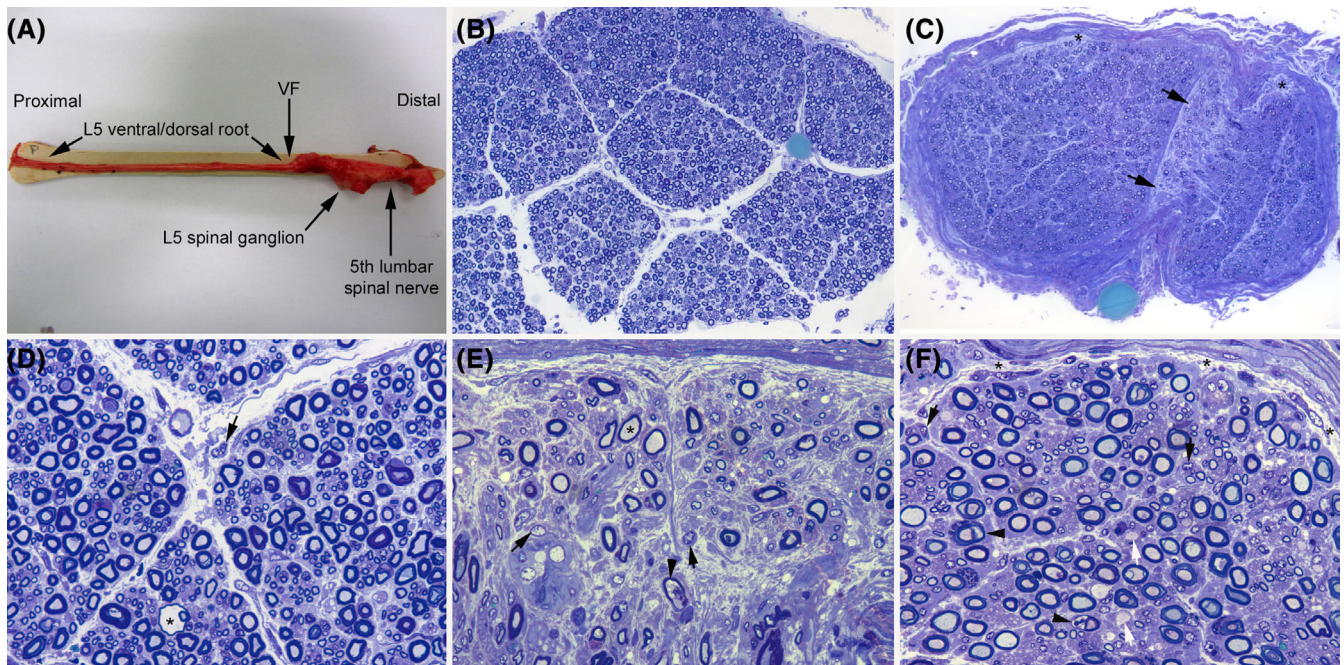


FIGURE 1 Pathological features in L5 spinal root, fifth lumbar nerve, and sciatic nerve in a severe GBS patient who died on day 9.³ A, Note the nerve enlargement as of the vertebral foramen (VF). B, Semithin cross-section of L5 ventral root showing no identifiable abnormalities. C, Semithin cross-section of the ventral ramus of the fifth lumbar nerve, illustrating widespread endoneurial edema that is more conspicuous in areas adjacent to the septum (arrows) and in subperineurial areas (asterisk), resulting in a spacing-out phenomenon giving the false impression of reduced density of myelinated fibers. D, High-power view of the L5 ventral root showing preservation of the density of myelinated fibers with occasional mononuclear cells (arrow) and a fiber exhibiting myelin vacuolization (asterisk). E, High-power view of the subseptum area indicated by the arrow in C. Note the presence of florid inflammatory edema with numerous mononuclear cells (arrows), fibers with inappropriately thin myelin sheaths (asterisk), and fibers exhibiting myelin vacuolation (arrowhead). F, Semithin section of sciatic nerve showing some demyelinated axons (white arrows), fibers with vacuolar degeneration (arrowheads), mononuclear cells (black arrows), and slight endoneurial edema more marked in subperineurial areas (asterisks). Overall, lesions clearly predominate in the ventral ramus of the fifth lumbar nerve

Variations of permeability between such areas are presumably important for the distribution of lesions caused by various toxic, immunological, or infectious agents, as with GBS.

Knowledge of the microscopic anatomy of the peripheral nervous system is essential for an adequate understanding of the pathogenic relevance of early pathological events in GBS.⁶ Spinal roots traverse the subarachnoid space covered by a lax multicellular root sheath derived from the arachnoid and penetrate the dura at the subarachnoid angle. At the subarachnoid angle, where motor and sensory roots join to form the spinal nerve, dura mater is in continuity with epineurium, whereas the arachnoid turns into perineurium. Therefore, intrathecal nerve roots are covered by an elastic root sheath, whereas spinal nerves and more distant nerve trunks out to their preterminal segments possess epi-perineurium that is relatively inelastic. Conceivably, initial inflammatory edema may be accommodated in intrathecal nerve roots that enlarge in size but without resulting in a significant increase in endoneurial fluid pressure (EFP). Conversely, in nerve trunks surrounded by epi-perineurium, such edema may cause a critical elevation of EFP that constricts transperineurial vessels by stretching the perineurium beyond the compliance limits, leading to ischemic conduction failure, and eventually to Wallerian-like degeneration.⁷ Although this phenomenon may occur in any segment of peripheral nerve trunks, MRI/STIR, ultrasound, and pathological studies indicate that spinal nerves are the hotspot in early GBS, thus explaining the high prevalence of electrophysiological changes pointing to pathology in proximal nerve segments (alteration of F waves as in the current patient).² In any case, inflammatory edema is also a histological feature of intermediate and preterminal nerve segments, a potential cause of partial conduction block, nerve inexcitability, or reversible conduction failure on serial studies.

In short, the MRI/STIR study in the report by Oguz-Akarsu et al¹ of cervical and lumbar spines in an early GBS patient illustrates that is a useful imaging technique for detecting the presence of edema in the spinal nerves and their ventral rami.

KEYWORDS

COVID-19 infection, endoneurial edema, Guillain-Barré syndrome, MRI, spinal nerve, STIR

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

ETHICAL PUBLICATION STATEMENT

We confirmed that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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Reply: "Spinal nerve pathology in Guillain-Barré syndrome associated with COVID-19 infection"

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We are pleased to see the correspondence from Berciano and Gallardo with regard to our paper published in *Muscle & Nerve*.^{1,2} We

would like to thank them for their interest and positive comments. They clearly mentioned the pathophysiologic mechanisms of