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Contrast Enhancement in Spinal Nerve Roots: An Experimental Study

Canh Nguyen, Victor M. Haughton, Khang-Cheng Ho, Howard S. An, Joel B. Myklebust, Toru Hasegawa, Rongming Xu, and Joseph M. Harb

PURPOSE: To examine histopathologically the endothelium of contrast-enhancing spinal nerve roots. **METHODS:** In five adult baboons, chronic compression of the left S-1 spinal nerve root sufficient to produce a change in the evoked potential was produced by means of a suture tied around the nerve. The animals were studied with MR at 8 and 16 days after nerve compression and then killed for histopathologic and electron microscopic studies. Histopathologic changes in the nerve roots demonstrating contrast enhancement were described. **RESULTS:** In all compressed spinal nerves, contrast enhancement was observed. Histopathologically, wallerian degeneration of the root and inflammation and disruption of the endothelium of capillaries in the spinal nerve were evident. **CONCLUSIONS:** Degenerative changes in the nerve root and the capillary endothelium of a lumbar spinal nerve are associated with contrast enhancement.

Index terms: Spine, magnetic resonance; Nerves, spinal; Animal studies

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Contrast enhancement in lumbar spinal nerve roots has been seen variably in patients with spinal stenosis, herniated disks, or previous laminectomy (1-5). It is thought by some investigators to signify radiculopathy and a disruption of the normal blood-nerve endothelial barrier (6). The enhancement in spinal nerve roots secondary to nerve root compression typically extends from the point of compression to the cauda equina, probably because the extravasated contrast medium diffusing proximally through the nerve root meets a barrier at the Obersteiner-Redlich zone, the sharply defined and irregular transition region between nerve roots and spinal cord (6). The enhancement secondary to an injury of the nerve root is more intense than the faint generalized enhancement of nerve roots seen in about 50% of persons (6);

this enhancement is more conspicuous with a dose of 0.3 mmol/kg than with a dose of 0.1 mmol/kg (7). Whether the enhancement occurs because of a fibrotic reaction to the compression of the arachnoid, as one investigator speculated (7), or represents demyelination, edema, or inflammation in the nerve root, as has been found histopathologically in some cases of nerve root compression, is uncertain. Therefore we studied histopathologically nerve roots demonstrating contrast enhancement produced experimentally by chronic compression.

Materials and Methods

Five adult baboons used in tissue cardiac transplant studies and scheduled to be killed were used in the experiments. The animals had no medications, no recent surgery, and no known medical problems. Under general (halothane) anesthesia, the animals had a left hemilaminectomy at L-7 to S-1. The left S-1 nerve root sheath was identified. An electrode array consisting of three in-line 2-mm platinum disks spaced 4 mm apart was inserted through the laminectomy defect into the posterior epidural space 5 cm cephalad to the laminectomy site. A similar electrode array was placed on the S-1 nerve distal to the dorsal root ganglion. The distal electrode was stimulated with current pulses of 0.25 to 1.0 mA at 5 Hz. The stimulus was increased until a muscle response was observed in the leg. The evoked potential from the proximal electrode array was recorded with an evoked-potential monitor

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(model 5200A, Cadwell). An average of 10 responses was used. A 2.0 silk suture was placed around the S-1 nerve root 1 to 2 mm distal to the level of the dorsal root ganglion and tightened around the nerve while evoked potentials were monitored. The silk suture was continuously tightened until the evoked-potential amplitude diminished by 50%, and then the suture was knotted to prevent any change in tension. Hemostasis was rechecked and bleeding controlled with thermocoagulation, gelfoam, or gentle compression. Surgical debris was removed by irrigation and suction. The laminectomy defect was closed in layers. Cefazolin sodium (Kefzol) (1 g/d intramuscularly) was given for 4 days prophylactically. Buprenorphine hydrochloride (Buprenex, 0.3 mg/kg) was given for analgesia for 4 days. The animals were monitored closely for evidence of infection, surgical complication, or neurologic deficit.

MR of the spine was performed at 8 and 16 days after surgery on a 1.5-T imager equipped with a 3-in coil of our own design. T1-weighted images were obtained in axial and sagittal planes with the following parameters: 600/20/2 (repetition time/echo time/excitations), 10-cm field

of view, 256 × 256 matrix, and 3-mm section thickness. Images were repeated at 2 and 15 minutes after the bolus injection of 0.3 mmol/kg of gadopentetate dimeglumine (Berlex Labs, Secaucus, NJ) in axial, coronal, and sagittal planes. The precontrast and postcontrast images were compared for evidence of contrast enhancement.

The animals were killed with an overdose of barbiturate at 16 days. A complete laminectomy from T-12 to S-4 was performed with blunt and sharp dissection. The spinal nerves were sectioned distal to the dorsal root ganglion at each level, and the dural sac and spinal cord were transected at T-12. The lumbar dural sac was lifted from the spinal canal and placed in 10% buffered formalin for light-microscopic studies. In two specimens, biopsy of the S-1 spinal nerve proximal to the suture was done before fixation of the entire spinal cord and cauda equina, and the biopsied specimens were fixed in 2.5% glutaral in cacodylate buffer for electron microscopic study. Thirty days later the fixed cauda equina specimens were embedded in paraffin, sectioned, stained with hematoxylin and eosin, luxol fast blue, or Bodian stain, and examined by light microscopy. One sample for electron microscopy was processed

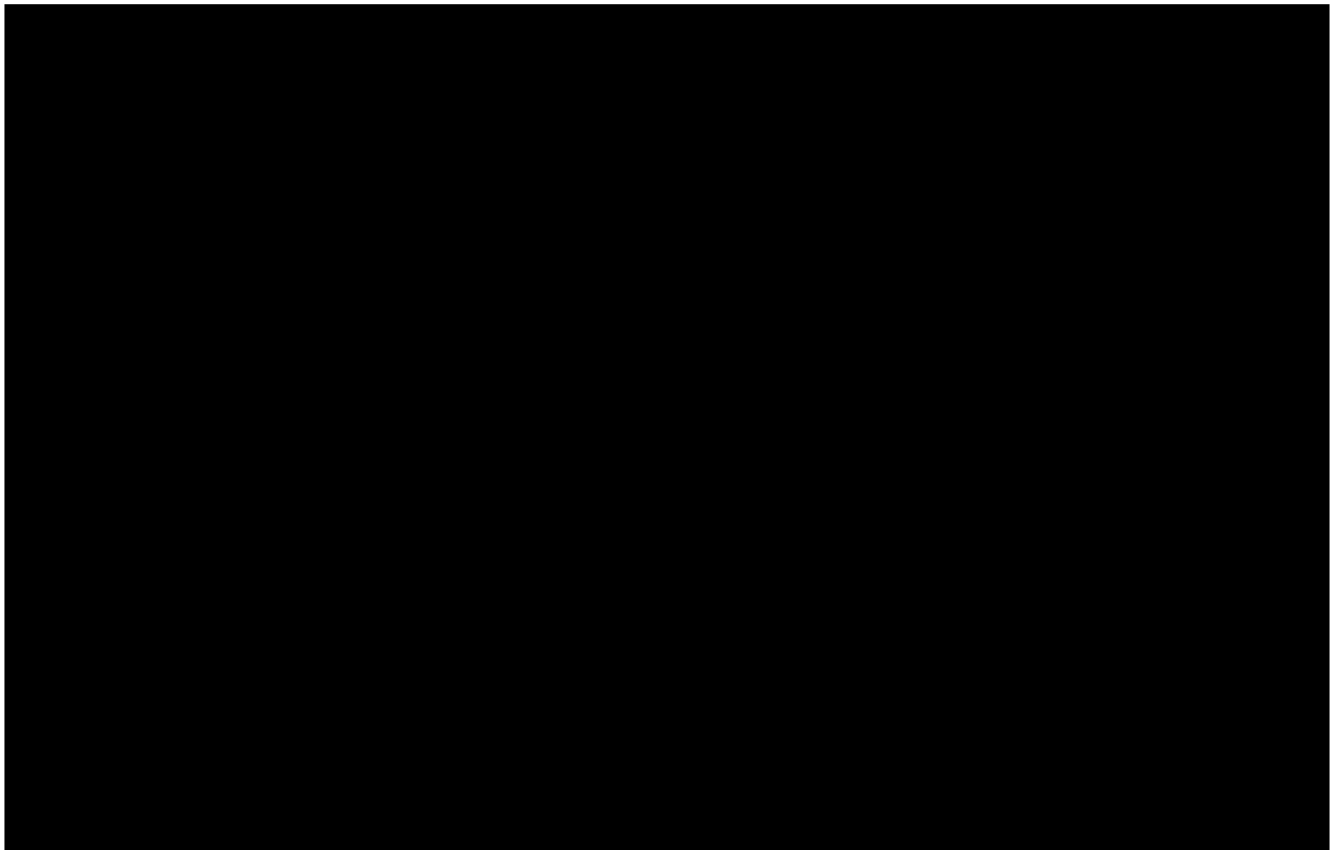


Fig 1. Axial (A-D) and sagittal (E) MR images 2 minutes after injection of the contrast medium show enhancement of a spinal nerve (arrow) that has been compressed by a suture.

At the level of the ganglion comparison of the image before (A) and after (B) gadopentetate dimeglumine administration show enhancement of the spinal nerve root.

C and D, The enhancement is detected cephalad to the ganglion.

E, It is not as well shown in sagittal images.

and embedded with techniques previously described (8, 9).

Results

All animals survived the surgical procedures without evidence of weakness or abnormal activity. In each animal, contrast enhancement and histopathologic changes were evident on the left S-1 spinal nerve root.

MR images were obtained at 8 days and at 16 days. Enhancement in the left S-1 spinal nerve root was observed in each animal at 2 and 15 minutes after injection (Fig 1). The intensity of enhancement varied little from animal to animal or from 2 to 15 minutes. The enhancement was visible in the axial images between the L-7/S-1 level and the L-4 level. In coronal and sagittal images, the enhancement was less effectively demonstrated.

Histopathologic analysis revealed slight to moderate degeneration of the left S-1 nerve root characterized by degeneration and loss of axons and myelin sheaths and slight proliferation of Schwann cells and endoneurial cells. Marked inflammatory cell infiltration of nerve fibers was evident in the S-1 nerve root near the compression. The inflammatory cells consisted mostly of round cells except in the vicinity of the suture, where eosinophil, foreign body giant cells, and slight focal fibrosis were noted. The dorsal root ganglia were less severely affected than the nerve. The vascular channels in the nerve were congested in comparison with the uncompressed ones. No pathologic changes were noted in either the untreated spinal nerves or the spinal cord.

Electron microscopy showed abnormalities in the capillaries characterized by fragmentation and duplication of the basal lamina (Fig 2). The electron microscopic sections did not show disruption or widening of the lateral interdigitations in the capillary endothelium.

Discussion

The findings suggest that contrast enhancement secondary to nerve root compression is related to degenerative changes in the nerve root and its capillary endothelium. Concentric compression of a spinal nerve was sufficient in this study to cause contrast enhancement of the spinal nerve on MR examination, and to cause vascular engorgement, nerve root degenera-

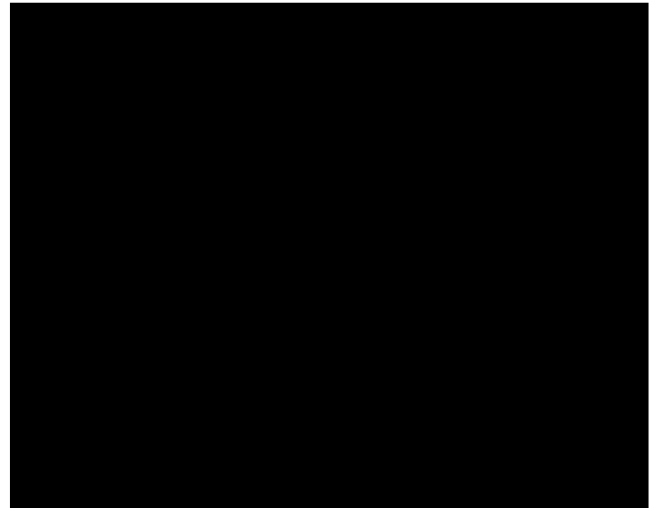


Fig 2. Electron micrograph of the same S-1 spinal nerve (sampled in a different region) shows fragmentation and duplication of the basal lamina in a capillary (*short arrows*). The lateral interdigitations between cells (*long arrows*) appear normal.

tion, and disruption in the basement membrane in the endothelium of the blood vessels in the nerve root. The changes in the basement membrane may increase the permeability of the vessel to contrast media. Widening of the tight junctions and lateral interdigitations between endothelial cells, which characterize some conditions with a leaky endothelial barrier, was not found in this study.

Contrast-enhancing spinal nerve roots were studied histopathologically in an experimental animal model because nerve root biopsies are not usually justified in clinical cases of enhancing nerve roots. Because the pathophysiologic process of contrast enhancement is unknown, we used compression, which may cause ischemia, edema, inflammation, and/or degeneration. The previous experimental procedures in the baboons did not affect the spine or healing mechanisms. An experimental technique was devised to compress the spinal nerve sufficiently to cause a detectable physiologic impairment. The compression by a suture completely surrounding the nerve may not simulate the compression that occurs clinically from a herniated disk. In other studies we have found enhancement in canine spinal nerves that were transiently compressed for 60 to 120 seconds at laminectomy (C. Nguyen and V. Haughton, unpublished results). The MR imaging technique used a higher-than-average dose of contrast medium (0.3 mmol/kg). Detection of nerve root enhancement is qualitatively the same with

the 0.1-mmol/kg dose used routinely in spine imaging (7).

Enhancement in spinal nerves has been observed clinically in spines previously operated on (2, 3), in cases of arachnoiditis (4), and in herniated intervertebral disks (1, 2, 10). The enhancement has been considered "a marker for active neural pathology" (3), although it does not have a specific clinical correlation or prognostic significance (6). In previous reports, histologic studies of enhancing spinal nerves have not been obtained. Histologic studies of degenerating peripheral nerves have shown associated changes in vascular permeability (9). Edema and degeneration have been found in spinal nerves in patients with sciatica and disk herniation (11–13). Vascular engorgement (14, 15) (Lane JI et al, presented at the 31st Annual Meeting of the American Society of Neuroradiology, 1993) may play a role in some cases of enhancement.

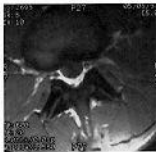
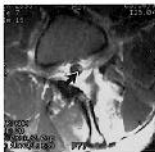
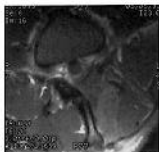
The significance of the present study is that histologic changes suggesting increased vascular permeability and congestion may occur secondary to nerve root compression. Contrast enhancement observed in spinal nerves in patients may be caused by vascular changes in the spinal nerve root.

Acknowledgments

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