Vascular and neural pathology of lumbosacral spinal stenosis

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During a study of the intrinsic vasculature of the lumbosacral spinal nerve roots in cadavers, a typical case of spinal stenosis was encountered. A review of the antemortem anamnesis revealed that this patient had had an intermittent claudication of the cauda equina. Investigation of the concomitant vascular and histopathological alterations of the affected nerve roots suggested that the claudication may have resulted from ectopic nerve impulse discharges elicited by rapid changes in the blood supply following exertion. The unexpectedly slight apparent neural deficit relative to observed root damage may be attributed to a neuronal plasticity within the spinal cord that permitted functional compensations to develop during the slow acquisition of the chronic nerve root pathology.

KEY WORDS cauda equina spinal stenosis spinal nerve root intermittent claudication spinal nerve root arteries

The term "claudication" is derived from the Latin verb claudicare which means "to limp" or "to be lame." It can be applied to any form of lameness, but conventional usage combines it with the adjective "intermittent" to designate a discomfort in the lower extremities that is exacerbated by exercise and relieved by rest. The condition may be symptomatic of a direct vascular insufficiency to the leg musculature due to an occlusive arteriopathy, or it may be neurogenic. Dejerine 4 first used the term in 1911 to describe neurogenic symptoms produced by a cord ischemia, and Blau and Logue 1 later applied it to dysfunction resulting from compression of the cauda equina. The neurocompressive phenomena associated with degenerative spinal stenosis can give rise to a broad spectrum of symptom complexes, of which intermittent claudication may be but one of the manifestations. Yet Wakamatsu 21 has reported that this symptom occurs in 88% of cases of spinal stenosis involving degenerative spondylolisthesis at or above the L4–5 intervertebral level. Despite the fact that an episodic neuroischemia is generally regarded as responsible for cauda equina intermittent claudication, there have been very few investigations concerning the neural and/or vascular changes within the involved spinal nerve roots. This may be explained partly by the lack of a true lumbosacral cauda equina in readily available experimental quadrupeds, and the chronicity such experimentation would require to adequately simulate the slow pathogenesis evident in many human cases.

It was therefore rather fortunate that, in the course of cadaver studies of the normal intrinsic vasculature of spinal nerve roots, we found a typical case exhibiting the chronic effects of spinal stenosis upon the cauda equina. This specimen provided immediate comparative reference for the neurovascular and histopathological changes consequent to this condition. Equally important was the availability of a sufficiently detailed antemortem medical history that afforded an unprecedented opportunity to compare the symptoms with the actual underlying morphological pathology. Thus, this case provides a basis of a reasonable hypothesis for the clinical manifestations of cauda equina intermittent claudication, in the light of recent data concerning the nutrition of spinal nerve roots.

Case Report

This 83-year-old Caucasian male complained of leg pain, primarily in the right lower extremity, for a period of 5 years. This pain was aggravated by walking, and limited his ambulation to a distance of approximately 100 m ("about a block"). Cessation of walking for a few minutes was accompanied by sufficient pain reduction to allow him to again proceed. There was no record of
a major back injury or prolonged episode of low-back pain. His medical history indicated that he had suffered a congestive heart disease for about 10 years, which had led to several hospital admissions. As the more life-threatening nature of the heart condition became the primary focus of medical concern, it was natural that no operative measures to reduce the leg pain were then considered. The patient became addicted to a non-opiate analgesic and was a laxative abuser due to chronic constipation. Despite the pain, he remained ambulatory up to his last hospital admission, and showed no sign of foot drop or urinary incontinence. Physical examination revealed equivocal knee jerks and bilaterally absent ankle jerks. No marked sensory loss or muscle atrophy in the lower extremities was noted, and a straight-leg raising test was not conducted. The pain eventually became persistent on recumbency in the hospital and, due to exacerbation of the congestive heart failure, he died 3 weeks after his final admission. As he had donated his body to the medical school for anatomic study, it was intra-arterially embalmed within 24 hours after death.

**Postmortem Study**

**Preparation of Specimen**

In common with the other anatomic cadavers used in the nerve root vascularization study, a rachitomy was performed to remove the laminae from T-6 to L-5, with additional exposure of the sacral spinal canal. The dura was freed as far laterally as the spinal ganglia, and the lower thoracic cord and cauda equina with their intact dural covering were removed. The acidity of the embalming fluid which would prematurely polymerize the injection medium was neutralized by soaking the extirpated specimen in a 1.5% solution of sodium bicarbonate for 12 hours. The ventral dura was then slit longitudinally to expose the anterior spinal artery. Cannulation of this artery in the region of its junction with the large medullary artery permitted an injection of the injection medium was neutralized by soaking the extirpated specimen in a 1.5% solution of sodium bicarbonate for 12 hours. The ventral dura was then slit longitudinally to expose the anterior spinal artery. Cannulation of this artery in the region of its junction with the large medullary artery permitted an injection of the lumbosacral cord and its root with a 1:1:1 mixture of latex, distilled water, and India ink. After a period of 2 hours, in which the intravascular pressures of the injected medium were allowed to equalize, the specimen was refixed in 10% formalin for 24 hours and prepared for micro- and macrophotography. Segments of roots and cord were then prepared for clearing and transillumination in an 11:2 mixture of tricresyl and tributyl phosphate. Details of the above procedures are provided in a previous publication.17

Sections for light microscopy were embedded in paraffin and visualized with Masson's trichrome stain, while segments for scanning electron microscopy were critical-point dried and gold-coated to 400 A. In several roots the venous side of the circulation could be demonstrated by immersing the specimens in a 2% solution of hydrogen peroxide. The peroxides in the formed elements of the venous blood liberated the free oxygen and temporarily inflated the venous channels.

**Postmortem Observations**

During the rachitomy, an extensive hypertrophy of the L4--5 facet joints was noted. Elevation of the dura revealed a spondylolisthesis of approximately 25% at the same level, and a lateral radiogram was taken (Fig. 1A). Examination of the excised specimen showed that the spinal stenosis produced a marked circumferential constriction of the dura between the thecal extensions of the L-4 and L-5 roots (Fig. 1B). On exposure of the contained cauda equina, it was noted that all the roots were also very constricted at this point and bound to each other and to the tightened dura by pia-arachnoid adhesions (Fig. 1C). The right L-5 dorsal and ventral nerve roots were isolated and photographed to show that they were constricted to less than 25% of their original diameter; the hypertrophic pia-arachnoid is shown still attached to the lesion (Fig. 2A). Figure 2B shows the right S-1 dorsal nerve root and its area of constriction. This specimen was cleared and transilluminated to reveal that the major longitudinal radicular arteries, although very convergent and straightened, still demonstrated a functional continuity (Fig. 2C). It may be noted, however, that the coiled arterial "pigtails" that periodically occur throughout the arterial circulation in a normal root are much accentuated on either side of the lesion but are absent in the constriction. The radicular venous system proved to be much more affected by the compression since the veins in the region were reduced in number, collapsed, and showed a grossly visible congestion proximal to the lesion. Within the same nerve root cephalad to the lesion, conspicuous arteriovenous anastomoses appeared better developed than in a normal root (Fig. 2D).

The histological sections showed a variety of neural changes. There was an obvious loss in the number of neurons, especially among the large-caliber fibers. Numerous empty axons and various degrees of demyelination with some presumably regenerated small fibers were discerned, and visible non-neural changes included pia-arachnoid adhesions, interstitial fibrosis, and thick-walled congested veins (Fig. 3). In the sections distal to the lesion, myelin bubble formation, an accepted indication of chronic demyelination, was noted. The arteriovenous anastomoses showed an epithelioid cell arrangement in their intima that may indicate a chemosensitive type of luminal control which could be independent of external innervation. Scanning electron microscopy of the sectioned ends of the lesioned root corroborated the pathological changes observed in the histological sections (Fig. 4).

**Discussion**

The neurological symptoms of a given degree of nerve root compression may vary widely depending on whether the compression is suddenly or chronically developed. In the case presented here, the degree of static neural compression was remarkable and must
FIG. 1. A: Lateral radiogram of the lumbar spine of an 83-year-old anatomic cadaver showing L4–5 spondylolisthesis in excess of 25% (arrows). The vertebral displacement plus facet joint hypertrophy produced a marked spinal stenosis. No neural arch components are seen here, as they were removed to expose the cord prior to discovery of the condition. B: Photograph of the extirpated cord showing the extent of the external constriction of the dura between the thecal extensions of the L-4 and L-5 nerve roots. C: The ventrally slit dura shows considerable constriction of all lumbosacral nerve roots inferior to L-4. The anterior spinal artery had been injected at the T-10 level and latex-India ink medium can be seen in the radicular arteries.

have been acquired over a period in excess of the 5 years of reported claudication. It was recalled that one of the authors, when first examining the drastically attenuated roots of the freshly dissected cauda equina, commented that this individual must have been very nearly if not completely paralyzed in the musculature supplied by the roots of the lumbosacral plexus caudal to L-4. Yet the medical record showed that he was quite ambulatory at the time of his last hospital admission and without footdrop! It must be surmised then that the reduced number of neurons that survived the constrictive pressure still represented, or slowly reacquired, the wide range of spinal and muscular associations necessary for the highly coordinated activity of ambulation. This assumption is supported by the observations of Goldberger and Murray,9,14 who noted that the immediate loss of neuronal function following experimental partial hemisection of the spinal cord14 and selected root deafferentation7 in cats was eventually partially recovered through the establishment of new neuronal associations.

There is little doubt that in the case presented here much neuromuscular strength had been lost, but at dissection the overall musculature of the lower extremities appeared bilaterally symmetrical and without focal neurosegmental areas of atrophy, and sphincter involvement was not reported. In contrast, the rapidly developing nerve root compressions that are usually associated with disc protrusions are characterized by more suddenly incapacitating neurological deficits, even though the roots may show a much lesser degree of attenuation.

There is consensus in the literature that the symptoms of intermittent claudication are related to a temporary but recurring inadequacy in the vascular nutrition in some part of the cauda equina that results from the increased demands of exercise. That muscular exertion increases the vascular requirements in the functionally associated elements of the nervous system has been well demonstrated in the classic work of Blau and Rushworth.2 They showed that, when a single hindlimb of a mouse was exercised, the blood vessels became visibly dilated in the ipsilateral half of the involved area of the spinal cord and its nerve roots.
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A focal point compression, unless involving one of the medullary feeder arteries variably located with the lumbosacral roots, evidently does not extensively compromise the radicular vascular nutrition proximal or distal to the lesion. Parke, et al., have shown that, although the longitudinal radicular arteries display a continuous system of vessels, the functional vascular flow is provided from both the proximal and distal ends of the roots. Thus, the arterial flow to root tissue quite close to both the proximal and distal sides of a focal point of pressure may be independently maintained, and the true ischemia is therefore quite localized. Nevertheless, as emphasized by the early work of Denny-Brown and Brenner, who studied compressed segments of peripheral nerve, the ultimate neuronal pathology of nerve compression short of frank mechanical injury is due to nutritional deprivation of the fibers. They also noted that a given degree and time of compression produced a variable effect, and explained the survival of some fibers by their proximity to the few vascular channels that were more resistant to compressive occlusion than the others. These observations appear to be supported by our analysis of the chronically compressed segment of the spinal nerve roots. As noted in the cleared root specimen (Fig. 2C), the injection medium demonstrated the continuity of the major longitudinal arterial channels but failed to show finer branches within the region of constriction.

The observations of Evans have further implicated the role of relative hypoxia in the production of claudication symptoms. In one of his four cases, he found no disc lesion, but an adhesive arachnoiditis apparently constricted the roots of the cauda equina, and the resulting claudication was eventually relieved by the surgical breaking of these adhesions. Prior to the operation, however, he measured the extent of exercise required to induce the symptoms ("claudication time") and found it was shortened when the patient breathed an atmosphere of reduced oxygen. It was concluded that during exercise the oxygen tension within the interstices of the nerve roots would be lowered if a simultaneous increase in the vascular supply was prevented. When the blood supply was allowed to return to these hypoxic roots, the larger myelinated fibers adjacent to the vessels became better oxygenated and began to discharge simultaneously, causing paresthesias and "pseudocramp." This idea of ectopic impulse generation in sensitized fibers has been favored by many authors as an explanation for neuralgias.

The hypothesis that chemically and/or mechanically distressed nerve fibers are a source of ectopic impulses is well supported. Howe, et al., and Devor and Bernstein have noted that chronically injured nerve root fibers, regenerating axons, and even the healthy dorsal root ganglion are all very mechanosensitive, and will generate prolonged repetitive discharges under extraneous stimuli. The hypersensitivity of demyelinated spinal nerve root fibers to chemical stimuli has been shown by Devor, et al.

The excitability of neuronal processes regarding var-

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**Fig. 2.** A: Isolated right L-5 dorsal and ventral roots showing hypertrophy of the pia-arachnoid (PA) in the region of the constrictive lesion (between arrows). The roots in the area of stenosis were bound to each other and the dura by an adhesive arachnoiditis. B: The isolated right S-1 dorsal root has been cleaned of redundant pia-arachnoid to show the extent of irreversible chronic root compression. Note that the diameter has been reduced to less than 25% of the original root dimensions. Measure in centimeters. C: Photograph of the cleared and transilluminated specimen shown in B (above). Surprisingly, most of the longitudinal radicular arteries maintained their continuity during the slowly developing compression. The pronounced compensatory coils (CC) are more exaggerated adjacent to the lesion. This is believed to compensate for the immobilization of the root at the point of the lesion which would produce extra tension during flexion-extension of the lumbar vertebrae. D: A section of the right S-1 dorsal root proximal to the lesion that has been treated with hydrogen peroxide to inflate the veins (V). Note the large-bore arteriovenous anastomoses (AVA) that permitted the medium to pass from the injected radicular arteries (RA) to the veins. The intraradicular branches (IRB) of the vasculature that passed between adjacent roots are shown.
FIG. 3. A: Photomicrograph of a paraffin-embedded section of the right S-1 dorsal root about 1 mm proximal to the narrowest part of the lesion. There is a complete lack of large myelinated fibers, but degenerating/regenerating small fibers are present. The interstices between the fascicles appear edematous, and the large vein (V) was congested. Masson's trichrome, bar = 20 μm. B: Photomicrograph of a paraffin-embedded section of normal lumbar dorsal root for comparative reference to the pathological section shown in A (above). Note the number of large myelinated fibers and the profusion of normal small fibers of various degrees of myelination. Masson's trichrome, bar = 20 μm.

Fig. 4. A: Scanning electron micrograph of a cut end of the compressed right S-1 dorsal root near the region of maximum constriction. The major longitudinal arteries are easily identified by the solidified latex medium within their lumina. Few veins (V) showed any continuity through the lesioned area as they are more readily collapsed by the chronic compression. Demyelination, nerve fiber degeneration, and interstitial fibrosis give the area a solidified amorphous appearance. Erythrocytes appear as small spherules on the cut surface and, being consistently 7 μm in diameter, provide a comparative size scale. Note the hypertrophic pia-arachnoid around the larger superficial arteries (A). B: Scanning electron micrograph of a sectioned end of normal human lumbosacral dorsal nerve root showing the typical arrangement of myelinated nerve fibers and their relationship to healthy capillaries (C) and connective tissue.

In their blood supply has been demonstrated by Nathan. He found that Group A fibers showed an initial excitability that caused a tingling sensation shortly after vascular occlusion, but that this gradually decreased. However, restoration of the blood supply to the ischemic area gave evidence of extreme excitability that caused fasciculation, paresthesias, and pseudo-cramp, according to the type of fibers involved.

The symptomatology related to permanent histopathological changes resulting from chronic compression, and the episodic phenomena characteristic of claudication should be regarded as separate manifestations. Most reports concerning intermittent claudication of cauda equina origin correctly describe the complaint only in terms of pain and/or paresthesias, but some authors have included weakness as part of the symptom complex. We contend that the cyclic pain and/or paresthesias of claudication are most likely due to a neuronal hyperexcitability that may occur with or without focal-point compressions responsible for fiber hypoconductivity and/or destruction indicated by weakness.

The case presented here showed extensive neuropathology throughout the cross sections of the lesioned roots that included quantitative loss of nerve fibers, especially of the large myelinated type, with a mixture of degenerating and regenerating fibers (Fig. 3A) in addition to adhesive changes of the pia-arachnoid. However, we believe these findings do not qualitatively differ from the root pathologies described by Lindblom and Rexed from cadavers with disc protrusions that did not necessarily produce the symptoms of claudica-
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ation. Simple compression alone is most likely responsible for the more constant sciatica and motor deficits associated with single root compression. The pain characteristic of cauda equina claudication is in general diffuse, often non-neurosegmental, and uniquely episodic. Therefore, to establish a reasonable explanation for the symptoms of neurogenic intermittent claudication, a set of common neurophysiological and morphological characteristics that are evident in most cases must be determined.

Perusal of the literature revealed two conditions that appear to be associated with most reported cases of cauda equina claudication. The first concerns the vertebral level of the causal extraneural lesions. At present this association is inexplicable, but almost all of the cases showing intermittent claudication involve spinal lesions at or above the L4–5 intervertebral level. It is noteworthy that stenoses resulting from spondylolistheses at the L4–5 level, which are mostly of the degenerative type, produce a high incidence of claudication, whereas the L5–S1 spondylolistheses, which are preponderantly of the spondylolytic or so-called "congenital" type, seldom cause the intermittent symptoms.

The second factor consistently associated with lumbosacral nerve roots involved in intermittent claudication is some mechanism by which the cerebrospinal fluid (CSF) is prevented from freely perfusing the root tissues. A simple stenotic confinement of a section of the cauda equina may be sufficient, but in most cases it appears to involve an adhesive pia-arachnoiditis.

In order to appreciate the significance of such a CSF barrier, some recent findings concerning nerve root metabolism should be reviewed. As emphasized by Parke and Watanabe, the nerve root is a tract of the central nervous system (CNS) and as such its intrinsic vascular arrangements and connective tissue coverings more closely resemble those of the CNS than those of peripheral nerves. The vasa radiculorum show a sparser pattern of vascular distributions than do the peripheral vasa nervorum. Because the flexion-extension biomechanics of the spinal column continually stretch and relax the lumbosacral nerve roots, the radicular vessels show a compensating series of coils or "pigtails" (Fig. 2C and D) to relieve vascular stresses. Also, as in the CNS, the major venous channels do not course with the arteries, but tend to be larger, fewer in number, and more centrally placed in the tissue. Of particular significance was the frequent distribution of relatively large arteriovenous anastomotic shunts along the course of the root (Fig. 2D). Unlike peripheral nerves, the roots do not possess a thick epineurium and perineurium, but are bound in much thinner extensions of the spinal pia-arachnoid. These layers are very fenestrated and, particularly in the outer root sheath, show an open meshed lacework of collagen fibers. The importance of these structural characteristics became evident with the recent studies of root metabolism performed by Ryde-
and their associated venules, it is now postulated that the shunts and veins may respond to the chemical imbalances accumulating in the root tissue proximal and distal to the lesioned area, and through a responsive dilation allow a much greater blood flow to reach the sensitized areas on either side of the lesion. This then provides the blood flow restoration that Nathan and Evans held responsible for the generation of ectopic impulses that produce pain/paresthesia and pseudo-cramps. With cessation of exertion, the diminished neuronal metabolism and slow percolation of CSF re-establish the symptom’s reduced state, and the cycle may be reactivated on further exertion.

It must be emphasized that, although the above concept is partially based on new direct morphological observations, the physiological aspects have been inferred from indirect evidence and thus await experimental verification. To date, however, it appears to be the only hypothesis that supports a neuroischemic basis for cauda equina intermittent claudication and also explains the paradoxical timing of the symptoms.

**References**

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