Experimental chronic compressive cervical myelopathy: effects of decompression

H. LOUIS HARKEY, M.D., OSSAMA AL-MEFTY, M.D., ISAM MARAWI, M.S., DUDLEY F. PEELER, PH.D., DUANE E. HAINES, PH.D., AND LON F. ALEXANDER, M.D.

Departments of Neurosurgery and Anatomy, University of Mississippi Medical Center, Jackson, Mississippi; and Department of Neurosurgery, University of Arkansas, Little Rock, Arkansas

Reports investigating the natural history of cervical spondylotic myelopathy (CSM) indicate that the disease process is benign and self-limiting; however, the preferred treatment remains controversial.4,21,24,28 Although there was some early resistance to surgical management, numerous decompressive procedures have been devised and advocated for CSM.8,31,33 When the outcomes of various surgical and conservative treatments have been analyzed and compared, many patients were found to have improved as a result of surgery; however, some remained unchanged or even deteriorated.1,5,9,12,23–25 Although debate continues on the best operative procedure to pursue, it is now generally accepted that CSM will, in many cases, improve with decompression and/or stabilization.

The authors of this study previously reported a canine model of chronic spinal cord compression that examined some of the questions on the pathophysiology of CSM. This model produced delayed onset of neurological deficits an average of 4 months after combined anterior and posterior compression of the cervical cord. Characteristic pathological findings consisting of large motor neuron loss, necrosis, and cavitation in the region of the anterolateral gray matter were identified at the level of greatest cord compression. A theory was proposed to explain the findings and suggest a possible pathophysiological mechanism.

Twelve dogs developed a delayed onset of neurological abnormalities from chronic cervical cord compression that was characteristic of myelopathy. The animals were divided into two groups and matched according to degree of neurological deficit. Six animals underwent decompression through removal of the anteriorly placed compressive device. Throughout the experiment, serial neurological examinations and somatosensory evoked potential studies were performed on each animal. Spinal cord blood flow measurements were obtained during each surgical procedure and at sacrifice. Magnetic resonance images were obtained after compression and before sacrifice.

All animals in the decompressed group showed significant neurological improvement after decompression; no spontaneous improvement in neurological function was seen in the compressed group. On pathological examination, irreversible changes including large motor neuron loss, necrosis, and cavitation were seen in four of the animals in the decompressed group and five in the compressed group.

Cervical spondylotic myelopathy in humans is known to respond to decompression; this study provides further evidence that this animal model for chronic compressive cervical myelopathy accurately reflects the disease process seen in humans.

KEY WORDS • cervical spondylosis • cervical myelopathy • spinal cord compression • spinal cord blood flow • somatosensory evoked potentials • histopathology • dog
De compression in experimental myelopathy

### Materials and Methods

#### Animal Selection

We studied 12 mongrel dogs that had developed neurological signs of myelopathy from subclinical chronic spinal cord compression. A posterior Teflon washer and anterior Teflon screw produced an average of 29% canal stenosis in the dogs, as previously described. The dogs were divided into two groups of six and matched according to the degree of neurological deficit. Four animals in each group had moderate deficits and two had mild deficits. Animals with moderate deficits developed abnormalities in withdrawal reflex, placing reactions, and voluntary gait relatively early in the study period, and these abnormalities tended to worsen progressively. Animals with mild neurological deficits had less severe functional abnormalities that appeared later in the study period. No animal had severe deficits such as complete quadriplegia or incontinence. There was no difference in the degree of spinal cord compression between the compressed and decompressed groups. Six animals from the original study, four sham-operated animals, and two compressed animals that did not develop neurological deficit were excluded from this report.

Throughout the study, the subjects were maintained under normal caging conditions in the central laboratory animal facility under the care and supervision of a veterinarian, according to the Institutional Animal Care and Use Guidelines. At the end of the experiment, all dogs were sacrificed while under general anesthesia, with an average survival period of 62 weeks (range 44–77 weeks).

#### Neurological Testing

During the study period, neurological testing was performed approximately biweekly. Spinal cord blood flow (SCBF) was measured by a modified hydrogen clearance technique during each surgical procedure and before sacrifice. Cortical somatosensory evoked potentials (SSEPs) were recorded during each surgical procedure and on at least a monthly basis until sacrifice. The SSEP data for the decompressed group were assessed for changes in latency and amplitude of the first negative (N1) and second positive (P2) peaks and changes in the relationship between these two peaks. An MR image was obtained in all animals at least 24 weeks postcompression, and repeat imaging was obtained in all decompressed animals and four compressed animals before sacrifice.

#### Histopathological Study

Following sacrifice, the cervical spinal cords were preserved and sectioned for histological staining. Sample sections were obtained at the level of compression, two segments above the level of compression, and one segment below the level of compression. The tissue sections were stained with hematoxylin and eosin, Luxol fast blue–cresyl violet, and a modified Weil stain. The tissue was also impregnated using the selective silver method, which was a modification of the Fink and Heimer technique. The sections were examined for evidence of anterior horn cell loss, demyelination, axonal degeneration, necrosis, caviation, and abnormal vasculature. This study methodology has been published in greater detail.

#### Surgical Decompression

Six subjects comprising the decompressed group underwent a decompression procedure an average of 45 weeks (range 37–50 weeks) following the initial compression procedure. Each animal was prepared for the decompression operation in the same fashion as for the compression operation. The old dorsal wound was reopened and the previous laminotomy was located. A contralateral laminotomy was performed and SCBF was recorded. The wound was temporarily closed and the animal was turned supine; the previous ventral incision was reopened to expose the anterior spine, the Teflon screw was removed, the anterior incision was then closed, and the animal was again turned prone for a second recording of SCBF. Somatosensory evoked potentials were obtained at the outset of the surgical procedure, before and after each blood flow measurement, after decompressive removal of the screw, and immediately after surgery was completed. The dorsal incision was then closed and the animal was transferred to the recovery area.

#### Results

### Neurological Findings

All animals in both groups were neurologically normal at the outset of the study but developed neurological deficits in a delayed fashion during the study period. The degree of neurological deficit varied from moderate to mild, and the distribution of neurological deficits was similar for each group.

Table 1 illustrates the effect of decompression on neurological deficit, MR images, and histopathology. All six animals in the decompression group improved dramatically after decompression. Neurological improvements were first noticed between 2 and 5 weeks after decompression; the recovery of function was gradual and, in four animals, function eventually returned to normal. One animal improved to a very mild unilateral deficit, and one improved but was left with a significant unilateral deficit that corresponded to a large caviation on one side of the cord.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Onset of Myelopathy (wks)</th>
<th>Degree of ND</th>
<th>MR Findings Before Decomp</th>
<th>Onset of NI After Decomp (wks)</th>
<th>Residual ND</th>
<th>MR Findings After Decomp</th>
<th>Pathology</th>
</tr>
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<tbody>
<tr>
<td>7</td>
<td>32</td>
<td>mod</td>
<td>low SI (cav)</td>
<td>2</td>
<td>mild</td>
<td>low SI (cav)</td>
<td>macrocyt</td>
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<td>8</td>
<td>22</td>
<td>mod</td>
<td>normal</td>
<td>5</td>
<td>mild</td>
<td>normal</td>
<td>normal</td>
</tr>
<tr>
<td>9</td>
<td>36</td>
<td>mild</td>
<td>high SI</td>
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<td>no change</td>
<td>mild LMNCL, microcyt</td>
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<tr>
<td>10</td>
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<td>mod</td>
<td>high SI</td>
<td>3</td>
<td>none</td>
<td>decreased SI</td>
<td>mild LMNCL</td>
</tr>
<tr>
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<td>high SI</td>
<td>4</td>
<td>none</td>
<td>decreased SI</td>
<td>normal</td>
</tr>
</tbody>
</table>

* MR = magnetic resonance; ND = neurological deficit; comp = decompression; NI = neurological improvement; mod = moderate; SI = signal intensity; cav = caviation; LMNCL = large motor neuron cell loss.

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The order of improvement tended to be recovery from withdrawal reflex, gait disturbance, hopping, and placing abnormality, which is a reverse of the progression of onset. None of the compressed group showed any spontaneous improvement in neurological function, and some progressively worsened.

**Somatosensory Evoked Potentials**

Because of several technical and biological factors that produced variability in the data, only trends in the latencies and amplitudes of the SSEPs could be correlated with changes in neurological function. The N1 to P2 amplitude difference tended to decrease at the time, or before, neurological deficits appeared and to increase with, or before, recovery from the deficits. The N1 to P2 latency failed to parallel the improvement in neurological function following the decompression; all six subjects showed recovery in function, but only two of six demonstrated recovery of the latency scores.

**Spinal Cord Blood Flow**

An analysis of variance (ANOVA) with repeated measures was conducted to assess differences at the time of precompressive, postcompressive, and final SCBF measurements in both groups. Blood flow measures obtained before and after decompression in the decompressed group were not included in the ANOVA. There was no significant difference between compressed and decompressed blood flow changes overall, but the interaction was significant (p < 0.015) (Fig. 1).

**Imaging Data**

One animal in each group initially had normal MR images after compression. High-intensity signal abnormalities were seen within the cord substance on five of the compressed and five of the decompressed animals (Fig. 2). In addition, low-signal intensity lesions corresponding to gross cavitation were seen in one dog in each group (Fig. 3). On repeat MR imaging, the signal intensity and size of lesions decreased in three of the decompressed animals; similar decreases were seen in two animals in the compressed group. None of the abnormal MR images showed complete resolution of the lesions on follow up or worsening of intramedullary lesions.

**Histopathological Study**

Five dogs in the compressed group had pathological abnormalities at sacrifice, including large motor neuron cell loss, edema, necrosis, and cavitation. One compressed animal had frank cavitation, one had only mild, large motor neuron cell loss, and three had motor neuron cell loss, edema, and necrosis. Of the decompressed animals, three had motor neuron cell loss, necrosis, and cavitation. The cavitation in two of these subjects was large (Figs. 4

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**Fig. 1.** Graph depicting mean spinal cord blood flow by group. Values were obtained in the compressed group and decompressed group prior to compression (pre-comp), immediately after compression (post-comp), and at sacrifice (final). Values were also obtained in the decompressed group immediately before decompression (pre-decomp) and immediately after decompression (post-decomp). There was no significant difference between compressed and decompressed blood flow changes overall, but the interaction was significant (p < 0.015). Vertical bars indicate standard errors.

**Fig. 2.** Axial magnetic resonance images (TR 800 msec, TE 20 msec) showing the C-5 vertebral level in Case 11 (decompressed). Upper: The Teflon screw (s) and a high-intensity signal lesion (arrow) is seen in the anterior lateral region of the spinal cord. Lower: The screw has been removed (h), showing a persistent high-intensity signal lesion (arrow).
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and 5). One animal had mild, large motor neuron cell loss only, and two had no pathological abnormalities (Fig. 6).

There was no striking evidence of white matter demyelination or axonal degeneration at the level of compression or in more caudal sections, except in those animals with large areas of cavitation. In animals with cavitation of the gray matter, slight degrees of demyelination appeared in the ventral funiculus or in the dorsal part of the lateral funiculus. The lack of frank demyelination, as seen in the myelin-stained sections, was further corroborated by the corresponding lack of degenerated axons in the silver-impregnated sections. Also, there was no difference in the degree of demyelination or axonal degeneration seen between groups.

Discussion

The benefits of surgical decompression through laminectomy for CSM have long been recognized. 7,9,26,31,34 Clinical studies evaluating the effectiveness of anterior decompression have also shown significant neurological improvement in CSM. 18,29 Although comparative studies have been performed, controversy still remains on the superiority of anterior and posterior decompressive techniques. 5,15,16 Experimental decompression of the spinal cord by laminectomy has been shown to reverse declining neurological function in cats with posteriorly placed masses but failed to reverse deficits in the presence of anteriorly placed masses. 3 In this study, all the decompressed animals showed improvement in neurological function following removal of the anterior screw.
provements were apparent at the first postoperative evaluation and were progressive thereafter. In addition, functional recovery mirrored the functional loss seen during chronic compression, with the most recent deficits improving first. These findings are in accordance with outcomes in humans following anterior decompression for CSM.

Somatosensory Evoked Potentials

As a result of wide variability, electrophysiological measurements failed to reliably predict or reflect the changes in neurological function in either group; the limitations of SSEP in CSM have been recognized in previous animal and clinical studies. The failure of SSEP to precisely correlate with neurological function may have resulted from the variability in individual SSEP recording sessions. Alternatively, persistently abnormal SSEP parameters may also reflect subtle abnormalities in function that could not be detected by neurological examination.

Spinal Cord Blood Flow

There were no meaningful, statistically significant differences in mean blood flow measures. In future studies using this model, a more updated and reliable method of measuring local SCBF may provide better data.

Histopathological Findings

The pathological findings in both groups were consistent with those seen in previous studies of experimental cord compression. The abnormalities were seen primarily in the ventral and intermediate gray matter, with relative sparing of the long tracts of white matter. In the milder cases, large motor neurons were lost at the level of compression. In more severe cases, there was additional demyelination and an overall reduction in the size of the anterior intermediate gray matter. In the most severe cases, necrosis and cavitation occurred in the anterior gray matter, intermediate gray matter, and adjacent white matter.

The pathological changes were consistent with increasing degrees of ischemic insult to the spinal cord. Intermittent increases in compression of the spinal cord associated with cervical flexion and extension produces brief but repeated disruption of microvascular blood flow. Because large motor neurons are most vulnerable to ischemia, one would expect them to be the first cells affected. As the ischemic episodes persist, more cells are affected, including less vulnerable cells. The ultimate outcome is necrosis and cavitation. The long tracts of the spinal cord, being more resistant to ischemia, are the last to be affected.

Overall, the pathological changes were less severe in the decompressed group than in the compressed group: the spinal cords in the compressed group were compromised for approximately 6 months more than the decompressed group. At sacrifice, most of the animals that had not undergone decompression had significant pathological abnormalities consistent with a greater overall ischemic insult.

The decompressed group polarized with respect to pathological changes: half had significant and irreversible changes and half had either no abnormalities or very mild ones. Large motor neuron dropout, necrosis, and cavitation are irreversible processes that would not be expected to change after decompression; however, dysfunctional neurons still capable of repair could recover if the ischemic insults were terminated through decompression. Other reversible processes such as edema and demyelination could also improve after decompression.

A positive correlation between the degree of neurological deficit and the severity of pathological abnormalities existed in all of the animals. The compressed animals clustered toward moderate neurological and pathological deficits whereas the decompressed animals tended toward mild neurological and pathological abnormalities. However, three animals in the decompressed group had large motor neuron cell loss, necrosis, and cavitation with either mild neurological deficits or none. These animals had irreversible pathological changes that would not be expected to improve with decompression. The improvement in neurological function seen in the decompressed animals with persistent pathological abnormalities must result from recovery of dysfunctional cells that have not suffered irreversible damage. Because demyelination was not a significant factor in any of the animals in this study, improvement in neurological function must represent a recovery of function at the neuronal level.

Conclusions

It is generally agreed that the best chance of influencing the natural history of CSM is through early surgical intervention. A number of reports show a better surgical outcome if symptoms have been present less than 1 year. The results of this study suggest a pathophysiological mechanism that explains this phenomenon. Neurological improvement seen in the decompressed group supports the theory of CSM pathogenesis previously proposed. Removing the anteriorly placed screw increases the reserve space within the spinal canal and eliminates the intermittent pinching effect on the spinal cord associated with neck mobility. In the absence of the intermittent tissue hypoxia in the watershed area that accompanies intermittent cord compression, the pathological process is terminated and healing may occur. The dramatic improvement in neurological function after decompression must result from the restoration of normal function on a physiological basis, as necrosis and anterior horn cell loss are irreversible processes that persist despite decompression.

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Manuscript received April 13, 1994. Accepted in final form August 8, 1994.

This study was supported in part by National Institutes of Health Grant 2 S07 RRO5386 at the University of Mississippi Medical Center, and by Department of Veterans Affairs Research Advisory Group Grant 151C4 at the Veterans Administration Hospital, Jackson, Mississippi.

Address reprint requests to: H. Louis Harkey, M.D., Department of Neurosurgery, University of Mississippi Medical Center, 2500 North State Street, Jackson, Mississippi 39216–4505.