Syringomyelia formed by epidural compression

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the epidural injection group. This “internal” comparison between the epidural and intradural injection groups implies that pure epidural compression in our experimental condition does not cause parenchymal changes in the cord.

Second, it should be noted that the present model exclusively causes dilation of the central canal and not cyst formation in the parenchyma—i.e., the model produces pure hydromyelias. This is different from most of the noncommunicating syringomyelia models which produce hydromyelia as well as intramedullary syringomyelia.13,20,24

Last, the timing of syrinx formation is delayed in the present model, thereby making it a “chronic” model of syringomyelia. The other noncommunicating syringomyelia models generate “acute” syringes within several days.

Comparison With Other Spinal Cord Compression Models

There have been other models of spinal cord compression, such as with tumor cell implantation,8,18 tightening of screws,1,26 insertion of plastic sheets or rubber,25 and inflation of balloons.15 These models may be categorized by the rate of onset and the duration of the compression. The tumor cell implantation model causes slowly escalating compression because it takes 10–20 days for the growing tumor to achieve critical size. In contrast, the balloon inflation model causes rapid and acute compression. The present model causes a less abrupt or “subacute” onset of compression because the kaolin solution that is used changes from paste to solid within an hour.

Regarding the duration of compression, previous models of balloon inflations or plastic sheet insertions sustain the compression for only a few hours to not more than a few days. More prolonged or chronic compression up to 25 weeks has been used in more recent studies. The present model, with 12 weeks of compression, may also be categorized as chronic. However, it should be noted that none of the previous compression models produced syringomyelia, regardless of speed of onset and chronicity of compression.

One recent rat model constructed to study cervical myelopathy used thin sheets of expanding polymer to cause sustained epidural compression at the C-5 and C-6 levels.12 The rats were observed for up to 25 weeks with no evidence of inflammation or demyelination as in our animals, but none had syringomyelia in the cervical model. The reason for this key difference from our model may be the location of the compression, i.e., cervical versus lumbar. The fluid dynamics within the spinal canal may be very different in various regions of the spinal column, and local compression presumably may result in region-specific cerebrospinal fluid flow disturbances. Also, whereas rats aged 5–6 weeks were used in the present study, the cervical model used 12- to 14-week-old rats, and the age difference may also influence fluid dynamics of the spinal cord. Further studies are needed to elucidate the mechanism.

Although ideally we would compare our results with results from other syringomyelia models, motor and lower urinary tract dysfunction have not been analyzed in detail in previous syringomyelia models, and we therefore compared our results with those derived from SCI models.

FIG. 8. Comparison of IHC results between animals that received epidural injection of kaolin, intradural injection of kaolin, and sham surgery. The first, second, and third columns are sections from rats that underwent sham surgery (A-1 to G-1), epidural injection of kaolin (A-2 to G-2), and intradural injection of kaolin (A-3 to G-3), respectively. The IHC stain for each row is as follows: A: H & E (morphology). B: GFAP (reactive astrocytes). C: NeuN (neurons). D: CC1 (oligodendrocytes). E: ED1 (macrophage or microglia). F: Caspase-3 (apoptosis). G: LFB (myelin). Bar = 200 µm. Other than the clear enlargement of the central canal (syringomyelia) seen in A-2, no difference is evident between the sham-operated group and the epidural injection group (first column, B-1 through G-1, vs second column, B-2 through G-2). H & E staining of intradural kaolin injection (A-3) shows a small central canal but extensive spongiform changes in the dorsal and ventral white matter. Also, an increased number of ED1-positive cells are seen throughout the white matter of the animal that received intradural injection of kaolin (E-3) compared with the sham-operated rat (E-1), suggesting an inflammatory process caused by the intradural kaolin. Patchy demyelination (G-3) is also observed in the animal with intradural injection. Figure is available in color online only.
The animals in our model tend to have milder initial motor and bladder dysfunction, with faster and more complete recovery, than those in SCI models. The neurological deficits seen in the early postoperative period should be interpreted as symptoms due to acute surgical trauma (but to a lesser degree than in SCI) rather than syringomyelia, as this model seems to be a “chronic” model of syringomyelia.

The interesting neurological trend in the study is that some of our rats suffered delayed onset of new neurological deficits. Of the rats that died unexpectedly 1 month or more after the operation, 3 had no deficits initially but developed late neurogenic bladder. Although their sudden demise precluded a new MRI and “emergent” postmortem examination of the spinal cord, progressive expansion of the syringomyelia may be speculated as one of the reasons for the delayed neurological deterioration. It is tempting to contemplate modifying this model in the future to study the long-term neurological consequences of progressive syringomyelia, but for the present study, our efforts were concentrated in producing syringomyelia.

Pathogenetic Mechanism of Syringomyelia Formation

Multiple hypotheses have been postulated to explain the genesis of syringomyelia. The oldest hypothesis is the “water-hammer theory” proposed by Gardner, followed by William’s “suck effect theory” and Oldfield’s “piston theory,” but these hypotheses are focused on abnormal CSF flow dynamics at the craniovertebral junction, particularly in association with a Chiari malformation. More recently, Greitz proposed a “unified” theory of “intramedullary pulse pressure,” which would provide an explanation for syringomyelia regardless of the underlying etiology. He stated that the syrinx is formed by fluid distension of the cord brought about by a relative increase in the pulse pressure within the central canal of the spinal cord relative to the CSF pulse pressure in the nearby subarachnoid space. According to the Bernoulli principle, the CSF pulse pressure in the subarachnoid space is decreased when the subarachnoid space is narrowed (in various situations causing partial or total obstruction of the space, such as Chiari malformation, arachnoiditis, or tumor) and subsequently the velocity of CSF flowing through the narrowed portion is increased. In our model, the kaolin material causes total obstruction of the lumbar subarachnoid space, and the result may be seen as a model of fixed and total obstruction of subarachnoid space in a fairly long segment of the spinal cord, most similar to the case of spinal tumors. However, because the CSF pulse pressure originates from the pressure wave of CSF displaced from the head during arterial pulsations, as postulated by Greitz, the compliance of the thecal sac “dampens the systolic pulse wave as it propagates down the spinal canal.” Therefore, in the case of spine tethering at more caudal regions, he suggests that flexion movement would be an additional cause of mechanical distension and traction of the spinal cord. Still, as discussed earlier with respect to contrasting results in syringomyelia formation in the chronic epidural compression of cervical and lumbar regions, unrevealed differences in the fluid dynamics according to the proximity to the craniocervical junction may be playing a critical role in the pathophysiology of syringomyelia in the present model. Therefore, further elucidation of the pathogenetic mechanism of the present animal model may reveal other specific elements of syringomyelia.

Association With Occult Spinal Dysraphism

Thoracolumbar syringomyelia is frequently seen in association with large lumbosacral lipomas and is occasionally seen in association with simple tethering from a thickened filum. The deleterious effect on the spinal cord for most lipomas is likely due more to the tethering than to the compression by the fat mass, and it could be beneficial for a “complete” animal model to investigate whether the traction itself independent of the mass compression could cause syrinx formation. However, constructing a tethering model in rat was technically not feasible because of the fragility of the spinal cord and filum terminale. The present model recapitulates only the compressive aspect of the pathophysiology of lumbosacral lipoma, not the role played by the tethering. In a previous model simulating cord tethering, 5.0 grams of traction was applied for 10 minutes to the filum of guinea pigs; the filum was then fixed to the sacrum with cyanoacrylate. Electrophysiological and morphological evaluation done 10 days after the surgical procedures revealed defective motor and sensory conduction, as well as edema and damage to the neurofilaments, axons, and myelin sheath. However, syrin-
Syringomyelia was not observed, possibly because the model was an acute one.

Limitations and Future Directions

There are several limitations in this model. First, inasmuch as this model was initially designed to address the mechanisms by which lumbosacral lipomas cause syrinx formation, it only partially accomplishes its mission. Only the compressive effect on the spinal cord is simulated, not the tethering component. Furthermore, the epidural location of the compression does not quite match the intradural site of lipomas. Also, the compression was done at the most caudal portion of the spinal cord, thereby eliminating the possibility of syrinx formation caudal to the compression site. Second, the lack of correlation between progressive expansion of the syrinx and symptomatic deterioration is puzzling. This discrepancy may be artifactual, perhaps due to a lack of good assessment tools. A more thorough and quantitative assessment of urinary function and more reliable methods of sensory evaluation with longer observation periods might detect subtle changes in neurological status. The limited number of animals with MRI evaluation is another weakness in terms of our data set. Because the goal of the study was to establish a new animal model, serial imaging was also done as a “pilot” trial. In the future, we hope that more extensive imaging can be incorporated into the study design—with serial imaging being performed in more animals and possibly with all of the animals undergoing at least one postoperative MRI study.

Third, our low yield of syringomyelia (68%) is disturbing. In part this is due to the high early mortality rate of 20%, which should be correctable through improvements in anesthesia and postoperative care. Also, our technique of producing adequate epidural compression could be improved, to examine cases with insufficient mass effect and consequently negative results.

Nevertheless, this study has established a novel animal model of syringomyelia caused by epidural compression of the spinal cord, resembling one aspect of the pathogenic mechanism of lumbosacral lipomas or spinal tumors. It can serve as the platform for evaluating the pathophysiology of syringomyelia as well as the CSF hydrodynamics in the spinal canal. We hope that further studies to elucidate the possibility of new diagnostic measures and treatment modalities will be based on the model.

Conclusions

A novel animal model of syringomyelia was established by inducing epidural compression of the lumbosacral spinal cord using highly concentrated kaolin solution and allowing 12 weeks for syrinx development. The exclusive enlargement of the central canal cephalad to the compression site was observed on MRI and postmortem histological examination of the spinal cord. No evidence of inflammation in the spinal cord surrounding the syrinx was found in H&E studies, differentiating the present model from previous models of noncommunicating syringomyelia. Future studies on the pathogenetic mechanism and therapeutic strategies for the established model are being considered.

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References


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