A Chronic Model of Syringomyelia by Epidural Compression of the Lumbar Spinal Cord in Rats

Ji Yeoun Lee¹, Sangjoon Chong¹, Saet Pyoul Kim¹, Ji Hoon Phi¹, Seung-Ki Kim¹, Sun Ha Paek², Kyu-Chang Wang¹

¹Division of Pediatric Neurosurgery
Seoul National University Children’s Hospital, Seoul National University
²Department of Neurosurgery
Seoul National University Hospital, Seoul National University

No disclosures to be made.
Syringomyelia and lumbosacral spinal dysraphism

- Syringomyelia accompanied in 20 ~ 30% of occult spinal dysraphisms of the lumbosacral region.
  - Distinct from those caused by Chiari malformation, trauma or arachnoiditis
  - Treatment: Direct manipulation of the syrinx vs Lipoma resection and/or untethering
  - Transient increase in the syringomyelia after untethering (--- spontaneous resolution) vs Syringomyelia in retethering
Animal Models?

- Communicating type
- Noncommunicating type: trauma, inflammation
Study objective

- Novel animal model recapitulating the “mass effect” of lumbosacral lipomas
  - Lumbar region
  - Compression of the cord
  - Noninflammatory → Epidural
  - Chronic duration

1. Establishment of a novel animal model (SD rats)
2. Detailed description of the animal model
   1. Neurobehavioral results
   2. MRI: 9.4 T animal MR scanner (Agilent 9.4T/160AS; Agilent Technologies, CA, USA)
   3. IHC

All procedures were approved by the Institutional Animal Care and Use Committee of Seoul National University Hospital (IACUC NO.12–2005–006–9).
1. Establishment of a novel animal model

Matters to be settled....

- Step 1: Compressing material
  - Gelfoam
  - Adhesive glue
  - Kaolin

- Step 2: Mode of compression
  - Epidural injection
  - L1 – L5 total laminectomy
  - L1 & L5 partial laminectomy

- Step 3: Duration of compression
  - 4 weeks
  - 8 weeks
  - 12 weeks

through pilot studies
1. Establishment of a novel animal model

Established Model

A

Established procedure

Anesthesia (Rat) → L1 and L5 partial laminectomy → Epidural injection of 1:1 kaolin with needle → closure → MRI, neurobehavioral test → Sacrifice (12 weeks later)

B

L1 Laminectomy

L5 Laminectomy

Kaolin Injection
2. Detailed description of the animal model

Syringomyelia

A. Proportion of syringomyelia (+) samples
34 out of 40 rats (85%)
* All true hydromyelia cases

B. Central canal – spinal cord ratio (b / a)
sham group: 0.008
syringomyelia group: 0.071

\[ p\text{-value} < 0.05 \]
2. Detailed description of the animal model

**Neurobehavioral outcome**

1. **Motor**
   Initial motor deficit: 28%
   Improvement: 5 weeks

2. **Urinary dysfunction**
   Initial urinary dysfunction: 33%
   Improvement: 2 weeks
2. Detailed description of the animal model

Serial MRI images of syringomyelia formation.

MRI images of syringomyelia at 3 months

Rats with no syringomyelia on MRI
## Immunohistochemistry

### 2. Detailed description of the animal model

<table>
<thead>
<tr>
<th></th>
<th>Syringomyelia (Epidural injection)</th>
<th>Intradural injection</th>
<th>Sham</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Morphology (H &amp; E)</strong></td>
<td>Enlarged central canal, otherwise normal</td>
<td>Spongiform changes in the white matter</td>
<td>normal</td>
</tr>
<tr>
<td><strong>Extent of astrogliosis (GFAP)</strong></td>
<td>No difference from sham</td>
<td>No difference from sham</td>
<td>Scanty GFAP positive astrocytes in the white and grey matter</td>
</tr>
<tr>
<td><strong>Neuronal loss (NeuN)</strong></td>
<td>No difference from sham</td>
<td>No difference from sham</td>
<td>Neurons in the grey matter</td>
</tr>
<tr>
<td><strong>Oligodendrocyte (CC1)</strong></td>
<td>No difference from sham</td>
<td>No difference from sham</td>
<td>Distributed throughout white and grey matter</td>
</tr>
<tr>
<td><strong>Macrophage infiltration (ED1)</strong></td>
<td>No difference from sham</td>
<td><strong>Much increased in the white matter</strong></td>
<td>Very few</td>
</tr>
<tr>
<td><strong>Apoptosis (Caspase-3)</strong></td>
<td>No difference from sham</td>
<td>No difference from sham</td>
<td>Scattered throughout the white and grey matter</td>
</tr>
<tr>
<td><strong>Demyelination (LFB)</strong></td>
<td>No difference from sham</td>
<td><strong>Patchy demyelination</strong></td>
<td>No demyelination</td>
</tr>
</tbody>
</table>

B : GFAP, C : NeuN, D : CC1, E : ED1, F : Caspase-3, G : LFB
Summary

1. A novel model of syringomyelia by epidural compression of lumbar spinal cord was established.

2. Different from previous noncommunicating syringomyelia models
   1. Noninflammatory
   2. Central canal dilatation
   3. Chronic
Thank you for your attention