Elevated Systemic Inflammatory Mediators in Pediatric Traumatic Spinal Cord Injury

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Nothing to Disclose
Introduction

- Knowledge about biological responses and potential biomarkers after traumatic SCI in the pediatric population is limited
  - limits therapeutic development

- Inflammatory responses → double-edged sword in pre-clinical models
  - Necessary for wound healing and known to benefit axonal regeneration
  - Exacerbate neuronal loss & induce secondary damage

- Growing number of studies investigating inflammatory responses and systemic biomarkers in adults with traumatic SCI
  - Inflammatory mediators are elevated acutely after SCI in the CSF and sera
  - Subset of inflammatory factors may correlate with injury severity and functional recovery
  - Inflammation persists chronically → increased medical consequences and limits potential for functional recovery by blocking neurorehabilitation
• Pediatric traumatic SCI → relatively rare
  • ~ 1300 US children annually

• Gaps in Knowledge:
  • Lack of published data focusing on inflammatory responses to SCI in pediatric patients
  • Lack of a standard of care clinical tool to determine injury severity in all ages of children (gold standard ISNCSCI neurological exam used in adults is unreliable in younger children)

• Need to Develop:
  • Biomarkers that indicate Injury Severity in all ages of children
  • Better understanding of inflammatory and other biological responses that may lead to development of novel treatment strategies
Objective

Single institution, pilot study to determine if circulating inflammatory mediators are elevated in pediatric patients with SCI as compared to non-injured controls.
Methods

- Prospective identification of pediatric traumatic SCI patients at ACS-Level 1 pediatric trauma center (n= 5)

- November 2016- April 2019

- Identification of age-matched healthy controls (n = 4)

- Measurement of select inflammatory mediators from discarded clinical serum samples
Results

Control and SCI subjects are well-matched in age.
<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Sex</th>
<th>Trauma Mechanism</th>
<th>Injury</th>
</tr>
</thead>
<tbody>
<tr>
<td>17.6</td>
<td>M</td>
<td>Sports injury</td>
<td>L1 burst fx; cord compression</td>
</tr>
<tr>
<td>17.8</td>
<td>M</td>
<td>2nd Story Fall</td>
<td>multiple compression fractures of T &amp; L-spine with retropulsion; ligamentous injury; epidural hematoma with compromise of the thecal sac</td>
</tr>
<tr>
<td>14.0</td>
<td>M</td>
<td>Hit by falling tree branch</td>
<td>cervical and thoracic compression fractures with retropulsion; ligamentous injury; epidural hematoma; moderate spinal canal narrowing with deformity of the spinal cord</td>
</tr>
<tr>
<td>7.3</td>
<td>M</td>
<td>Fall from standing Arrest at park</td>
<td>congenital c-spine deformity causing cord injury at C2 and C4</td>
</tr>
<tr>
<td>14.0</td>
<td>F</td>
<td>Pedestrian Struck*</td>
<td>fx of C6-T1; cervical ligamentous injury; epidural hematoma; cord injury at C6-C7</td>
</tr>
</tbody>
</table>

* polytrauma
Inflammatory Markers are Elevated in Pediatric SCI Patients

<table>
<thead>
<tr>
<th></th>
<th>Uninjured Controls</th>
<th>SCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-6 (pg/mL)</td>
<td>Undetectable</td>
<td>15.3 ± 19.4</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>1.4 ± 2.7</td>
<td>8.4 ± 6.6</td>
</tr>
<tr>
<td>MIF (pg/mL)</td>
<td>2604 ± 3621</td>
<td>3824 ± 3034</td>
</tr>
</tbody>
</table>
## Participants with higher CRP required OR for SCI Treatment

<table>
<thead>
<tr>
<th>Patient</th>
<th>CRP (mg/L)</th>
<th>OR Required</th>
<th>Neurologic Exam</th>
<th>Disposition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>13.4</td>
<td>Yes</td>
<td>left psoas muscle weakness; left L1 dermatome numbness</td>
<td>Home PT</td>
</tr>
<tr>
<td>2</td>
<td>1.65</td>
<td>No</td>
<td>left thigh sensory deficit</td>
<td>Inpatient Psych with PT</td>
</tr>
<tr>
<td>3</td>
<td>0.808</td>
<td>No</td>
<td>intact exam</td>
<td>Home PT</td>
</tr>
<tr>
<td>4</td>
<td>13.14</td>
<td>Yes</td>
<td>four extremity weakness; clonus some improvement prior to D/C</td>
<td>Rehabilitation facility</td>
</tr>
<tr>
<td>5</td>
<td>13.18</td>
<td>Yes</td>
<td>no movement in B/L LE, + hyperreflexia improved to toe wiggling prior to D/C</td>
<td>Rehabilitation facility</td>
</tr>
</tbody>
</table>

PT: physical therapy; B/L LE: bilateral lower extremity
Conclusions

• In this small pilot study, inflammatory mediators were increased acutely after pediatric SCI.

• Possible correlation with injury severity
  • Higher CRP levels seen in patients with worse exam and requiring OR

• Larger sample size and prospective serum collection are needed to further verify and further elucidate these conclusions.
Future Directions

• Additional pilot study patients at single institution

• **Multi-institutional study to verify and extend this pilot study**
  • Larger sample sizes
  • Establish a timeline for these inflammatory mediators

• Long term goal: Determine any correlations in inflammatory makers with functional outcomes to determine a prognostic marker for pediatric SCI
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