Cerebrospinal Fluid Cytokine and Chemokine Patterns in Central Nervous System Infections, Hemorrhage and Neoplasms

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**Cerebrospinal Fluid Cytokine and Chemokine Patterns in Central Nervous System Infections, Hemorrhage and Neoplasms**

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### ABSTRACT

Cytokines and chemokines are soluble proteins that act as regulators of cellular functions throughout the body. Cytokines and chemokines released in the setting of various CNS disorders appear in the CSF compartment where detection of their levels can provide insights into pathogenic processes such as neuroinflammation. We utilized the miPore HTCSArray to perform multiplexed immunoassays on CSF from a variety of central nervous system (CNS) infections, hemorrhage, and neoplasms. Many CNS infections and hemorrhage are associated with increased levels of cytokines and chemokines. In general, these levels are more elevated in infectious conditions compared to hemorrhage or tumor cases. CSF from a chronic HPeV3 infection, EV68 encephalitis was associated with increased CSF levels of additional cytokines; CCLX1, IL-4 and IL-7.

There is a general elevation of chemokine/cytokine profiles may be the most immediate parameter to disease processes; however, they are affected by various factors such as disease time course, organism burden, and test parameters. For instance, in up to 30% of cases of suspected viral meningoencephalitis, no definite virus is identified. By studying the cytokine/chemokine profiles of various infections, these patterns may be able to provide insight into the type of infectious agent involved in such cases. Additionally, since many CNS infections are not histologically analyzed during active infections, chemokine/cytokine profiles may be the most immediate parameter available to gain insight into the particular, pathogenic agent acts on the brain. Csf cytokine/chemokine analysis provides an incredible wealth of information which may help narrow differential diagnosis, understand disease pathophysiology, and—with further studies—help predict clinical course and disease outcome.

Because of its relationship to the critical structures of the central nervous system (CNS), the cerebrospinal fluid (CSF) compartment reflects the current state of the CNS, especially in neurological diseases. When pathogens invade the CNS, the inflammatory cascade begins upon the expression of pro- and anti-inflammatory chemokines and cytokines, which become detectable in the CSF. Because viruses and bacterial pathogens utilize various mechanisms to elicit host response, the patterns of chemokines and cytokines released during these various infections are different. A variety of cells including monocytes/microglial cells play a role in initiating, coordinating, and regulating the innate response to infectious agents and other stimuli via expression of a variety of chemokines/chemokines.

Routine laboratory testing of the CSF (cell counts, microbiology, etc.) are essential in the initial evaluation of certain disease processes; however, they are affected by various factors such as disease time course, organism burden, and test parameters. For instance, in up to 30% of cases of suspected viral meningoencephalitis, no definite virus is identified. By studying the cytokine/chemokine profiles of various infections, these patterns may be able to provide insight into the type of infectious agent involved in such cases. Additionally, since many CNS infections are not histologically analyzed during active infections, chemokine/cytokine profiles may be the most immediate parameter available to gain insight into the particular, pathogenic agent acts on the brain. Csf cytokine/chemokine analysis provides an incredible wealth of information which may help narrow differential diagnosis, understand disease pathophysiology, and—with further studies—help predict clinical course and disease outcome.

### RESULTS

<table>
<thead>
<tr>
<th>Cytokine/Chemokine</th>
<th>Lyme (n=1)</th>
<th>TB (n=2)</th>
<th>Strep (n=1)</th>
<th>EV (n=2)</th>
<th>HPeV3 (n=1)</th>
<th>SAH (n=1)</th>
<th>Control (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GRO/CXCL1</td>
<td>2,000</td>
<td>1,000</td>
<td>4,000</td>
<td>?</td>
<td>51,409</td>
<td>6,830</td>
<td>4,600</td>
</tr>
<tr>
<td>IP-10</td>
<td>10,000</td>
<td>27,000</td>
<td>2,000</td>
<td>40,000</td>
<td>23,075</td>
<td>10,000</td>
<td>3,674</td>
</tr>
<tr>
<td>MCP-1</td>
<td>1,200</td>
<td>1,400</td>
<td>1,800</td>
<td>90</td>
<td>352</td>
<td>20</td>
<td>13</td>
</tr>
<tr>
<td>IL-6</td>
<td>17</td>
<td>6</td>
<td>8</td>
<td>200</td>
<td>45</td>
<td>250</td>
<td>1276</td>
</tr>
<tr>
<td>IL-8</td>
<td>60</td>
<td>2,600</td>
<td>3,700</td>
<td>260</td>
<td>45</td>
<td>20,000</td>
<td>10,500</td>
</tr>
<tr>
<td>IL-10</td>
<td>8</td>
<td>8</td>
<td>10</td>
<td>3</td>
<td>2</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>VEGF</td>
<td>2,412</td>
<td>682</td>
<td>1,180</td>
<td>28</td>
<td>25</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>PGE2</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

### CONCLUSIONS

1. Cytokine/chemokine profiles are different in various CNS disease processes.
2. Cytokine/chemokine profiles may be useful in determining the nature of the inflammatory process, especially in the setting of inconclusive microbiology tests.
3. In the context of a pro-inflammatory state, very low levels of MDC/CCL22 may represent a distinct pro-inflammatory response, possibly related to deficient anti-inflammatory mechanisms.
4. With further studies, CSF cytokine/chemokine profiles will provide more information, including predictions regarding clinical course and disease outcome.