Cerebrospinal fluid chimerism analysis in patients with neurological symptoms after allogeneic cell transplantation

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Neurological complications after allogeneic cell transplantation

Incidence  8%-42%   Central nervous system relapse 2.9%-11%

CSF Analysis

Gold standard method: cerebrospinal fluid (CSF) cytological analysis → Low sensitivity

Flow cytometry plus morphology → Improved sensitivity

CSF chimerism analysis → Few reports
Small patients series

Study population  50 patients (85 samples)

Exclusion criteria
CNS prophylaxis
Samples > 10 red blood cells/μL
Patients (n=50)

CSF Full donor chimerism (n=29)
  - CNS Relapse: 1
  - Viral meningitis: 5
  - Undetermined: 23

CSF Mixed chimerism (n=21)
  - CNS Relapse: 13
  - Viral meningitis: 2
  - Guillain-Barre syndrome: 1
  - Undetermined: 5

Cell Phenotype
CD3 +/- CD19
## Patient characteristics according chimerism status in CSF

<table>
<thead>
<tr>
<th></th>
<th>Patients with MC in CSF (n=21)</th>
<th>Patients with CC in CSF (n=29)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender Male/Female</strong></td>
<td>14/7</td>
<td>16/13</td>
</tr>
<tr>
<td><strong>Mean age at Tx (range)</strong></td>
<td>50 (21-75)</td>
<td>53 (22-75)</td>
</tr>
<tr>
<td><strong>Mean follow up in days (range)</strong></td>
<td>740 (82-2533)</td>
<td>929 (45-3501)</td>
</tr>
<tr>
<td><strong>Mean time to LP in days (range)</strong></td>
<td>341 (17-1388)</td>
<td>315 (19-3310)</td>
</tr>
<tr>
<td><strong>Remission status at Tx</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CR</td>
<td>12</td>
<td>15</td>
</tr>
<tr>
<td>Non-CR</td>
<td>9</td>
<td>14</td>
</tr>
<tr>
<td><strong>Initial diagnosis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AML</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>ALL</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>NHL</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>CLL</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Others</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td><strong>Conditioning regimen</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reduced Intensity</td>
<td>13</td>
<td>20</td>
</tr>
<tr>
<td>Standard</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td><strong>Acute GvHD</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 0-I</td>
<td>19</td>
<td>25</td>
</tr>
<tr>
<td>Grade II-IV</td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>
**Correlation analysis**

**Cell content-Recipient DNA**

- Spearman $r=0.324$
- All CSF MC patients

**FACS-Recipient DNA**

- Spearman $r=0.832$
- CNS relapsed patients
Agreement analysis: Bland-Altman

Fluctuations not dependent on the magnitude of measurement

Both methods may be used interchangeably
CNS relapse cell content. Chimerism analysis
Receiver-operating characteristics (ROC) of chimerism performance for CNS relapse

Sensitivity 89%
Specificity 85%
Cut off 17% Recipient DNA

AUC: 0.95
95% CI 0.87-1.03
p < 0.05
Progression-free survival

<table>
<thead>
<tr>
<th></th>
<th>Alive</th>
<th>Dead</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSF full donor CHM:</td>
<td>10</td>
<td>19</td>
</tr>
<tr>
<td>CSF mixed CHM:</td>
<td>4</td>
<td>17</td>
</tr>
</tbody>
</table>

Logrank p = 0.72
Conclusions

CSF chimerism analysis can be used as a complementary method in the diagnostics work-up.

CSF chimerism analysis and FACS can be used interchangeably for patients with CNS relapse.

ROC curve analysis shows that CSF chimerism is a reliable test for CNS relapse.
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