White blood cell counts, alcoholism, and cirrhosis in pneumococcal pneumonia

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Background

The white blood cell (WBC) count is generally expected to rise in response to infection. However, up to 25% of patients hospitalized for pneumococcal pneumonia and up to 38% hospitalized for community acquired pneumonia (CAP) have a normal WBC count at the time of admission.

A low WBC count has been associated, albeit not consistently, with poor outcomes in pneumococcal pneumonia, and there is even less consensus about the prognostic value of very high WBC counts in this disease. Alcoholism has been commonly associated with pneumococcal pneumonia and has been said to be responsible for leukopenia.

To our knowledge, no previous study has systematically evaluated the prognostic significance of leukopenia, leukocytosis and increased early forms (bandemia) in a single cohort of patients with pneumococcal pneumonia or has reported on the association of these factors with alcohol ingestion. We now present the results of such a study.

Methods

Study design:

Patients with pneumococcal pneumonia were selected from a database of all patients with pneumococcal infections seen at the Michael E. DeBakey VA Medical Center between 2000 and 2013.

Patients had either proven pneumococcal pneumonia (clinical picture of pneumonia and isolation of \textit{S. pneumoniae} from a normally sterile site) or presumptive pneumococcal pneumonia (clinical picture of pneumonia and consistent gram stained or sputum culture yielding predominant \textit{S. pneumoniae}).

Initial WBC count and differential, history of alcohol abuse or cirrhosis, and date of death were extracted from the medical record. Patients with leukemia or medication-induced neutropenia were excluded, but patients with cirrhosis, HIV infection or other immunocompromising conditions were not.

Statistics:

Differences across groups were compared using the Chi-square test for categorical variables and the unpaired t-tests or Kruskal-Wallis test for continuous variables as appropriate. Survival at 7 days and 30 days for different groups of WBC were compared by Kaplan-Meier methodology. Univariate and multivariate Cox proportional-hazards models were used to determine the contribution of potential risk factors to risk of death. Results were reported as hazard ratios.

Results

Table 1. Factors associated with increased 7- or 30-day mortality

<table>
<thead>
<tr>
<th>WBC</th>
<th># of patients</th>
<th>Mortality 7-day</th>
<th>Mortality 30-day</th>
<th>Hazard Ratio</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6,000</td>
<td>49</td>
<td>18.4%</td>
<td>30.6%</td>
<td>5.66</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>6,000-10,000</td>
<td>85</td>
<td>5.9%</td>
<td>8.2%</td>
<td>1.49</td>
<td>0.50</td>
</tr>
<tr>
<td>10,000-25,000</td>
<td>307</td>
<td>3.3%</td>
<td>11.1% (reference)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;25,000</td>
<td>40</td>
<td>12.5%</td>
<td>12.5%</td>
<td>3.94</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Immature forms

- <10%: 412 (3.3% | 12.4% | (reference) |
- >10%: 69 (10.1% | 14.5% | 3.59 | 0.23 |

Bacteremia

- 164 (9.3% | 15.2% | 2.08 | 0.06 |

Alcohol Abuse

- 105 (8.8% | 13.3% | 1.80 | 0.22 |

Cirrhosis

- 27 (14.8% | 18.5% | 3.11 | 0.048 |

Key Findings

- WBC counts <6,000 or >25,000 correlated significantly with increased 7-day mortality.
- Elevated immature forms (>10%) were not associated with increased mortality.
- Neither alcohol abuse nor a normal WBC (6,000-10,000) poor prognostic factors in our population, in contrast with previous reports.
- Of the patients with culture data, 38% were bacteremic, and these patients had an increased risk of dying within 7 days of admission.
- Patients with WBC < 6,000 were significantly more likely to be bacteremic than patients with normal or elevated WBC counts.
- Neither alcohol abuse nor cirrhosis was associated with WBC <6,000.

Conclusions

- A low or very high WBC count is a poor prognostic factor.
- Low WBC is not due to alcohol intake and resultant bone marrow suppression, as previously hypothesized.
- We suggest the following alternative mechanisms:
  - Acute infection stimulates the release of TNF-α, IL-6, IL-8, G-CSF, and CXCL-12, and subsequent mobilization of mature PMNs and immature forms from the bone marrow [1, 2].
  - Infection also stimulates release of E-selectin [2], which triggers the complement cascade and activates vascular endothelium, causing intravascular leukostasis and capillary plugging by mature PMNs [3-5].
- The balance of these factors and the host’s response result in an increase in immature forms and a decrease in mature neutrophils with an overall low WBC count in some patients during the acute phase of infection.

Table 2. Rate of bacteremia

<table>
<thead>
<tr>
<th>WBC count</th>
<th>Number of patients (% of total)</th>
<th>Number cultured (% of total)</th>
<th>Bacteremia (% of total)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6,000</td>
<td>49 (10.2%)</td>
<td>41 (9.6%)</td>
<td>23 (54.8%)</td>
<td>0.012</td>
</tr>
<tr>
<td>6,000-10,000</td>
<td>85 (17.7%)</td>
<td>73 (17.1%)</td>
<td>20 (27.8%)</td>
<td>--</td>
</tr>
<tr>
<td>10,000-25,000</td>
<td>307 (63.8%)</td>
<td>277 (64.7%)</td>
<td>106 (38.3%)</td>
<td>--</td>
</tr>
<tr>
<td>&gt;25,000</td>
<td>40 (8.3%)</td>
<td>37 (8.6%)</td>
<td>15 (40.5%)</td>
<td>0.585</td>
</tr>
</tbody>
</table>

References