Severe pulmonary complications after initial treatment with rituximab for the Asian-variant of intravascular lymphoma

Rituximab improves response to treatment and outcome for patients with CD20⁺ B-cell lymphoma. However, it is suggested that patients with this subtype of lymphoma are monitored carefully for possible drug reactions during the use of rituximab.

Table 1. Clinical and Laboratory features at presentation of three patients with Asian-variant of intravascular lymphoma.

<table>
<thead>
<tr>
<th>Case</th>
<th>Age/sex</th>
<th>Fever*</th>
<th>Respiratory symptoms</th>
<th>Marrow involved</th>
<th>HPS</th>
<th>Other Organ involved</th>
<th>Hb (g/dL)</th>
<th>Platelet (10⁹/L)</th>
<th>WBC (10⁹/L)</th>
<th>PMN/Lymph%</th>
<th>Lymphom cells</th>
<th>LDH** (U/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>77/M</td>
<td>+</td>
<td>–</td>
<td>+</td>
<td>+</td>
<td>–</td>
<td>8.7</td>
<td>127</td>
<td>4.65</td>
<td>52.5</td>
<td>26.3</td>
<td>–</td>
</tr>
<tr>
<td>2</td>
<td>79/M</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Adrenal gland</td>
<td>9.4</td>
<td>66</td>
<td>2.69</td>
<td>63.0</td>
<td>12.0</td>
<td>1267</td>
</tr>
<tr>
<td>3</td>
<td>54/F</td>
<td>–</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>–</td>
<td>8.1</td>
<td>156</td>
<td>10.36</td>
<td>68.1</td>
<td>15.6</td>
<td>4838</td>
</tr>
</tbody>
</table>

M: male; F: female; HPS: hemophagocytosis in bone marrow aspiration; PMN: polymorphonuclear leukocyte, including segmented and band forms of neutrophil; Lym: lymphocyte. * Secondary to hemophagocytosis, not infection. **Normal range of LDH: 230 - 460 in our institution.
throcytes and necrotic neutrophils suggestive of acute capillaritis.

Figure 2. High-resolution computed tomography (HRCT) of the chest and histopathology of the lung biopsy tissue of case n. 2 after rituximab administration. The HRCT (upper) showed ground-glass opacity and consolidation associated with reticulation in both lungs as well as moderate bilateral pleural effusions. The diagnostic impression was interstitial pneumonitis. The histopathological examination (lower) showed pulmonary hemorrhage with an intra-alveolar proteinaceous exudate containing erythrocytes and necrotic neutrophils suggestive of acute capillaritis.

during treatment. Reports of respiratory distress syndrome after rituximab infusion in patients with lymphoma are rare; most such events have been associated with the use of this monoclonal antibody in chronic lymphocytic leukemia. All three AIVL patients reported in this study developed severe pulmonary complications soon after rituximab infusion, indicating an association specific to this lymphoma variant. The pulmonary complications did not appear to be an allergic reaction to rituximab as repeated administration of the same drug in the two surviving patients did not reproduce the adverse response. Previous studies of patients with IVL-associated hemophagocytosis have revealed elevation of several cytokines that could be key factors in a systemic inflammatory response syndrome. Furthermore, elevations of inflammatory cytokines, such as tumor necrosis factor-α and interleukin-6, have also been reported during rituximab infusion. It appears probable, therefore, that rapid clearance of intravascular lymphoma cells after rituximab in AIVL cases may lead to further increases in already-elevated pro-inflammatory cytokines. Additionally, the intravascular lymphoma cells may occlude vessels, resulting in vessel wall damage and increased permeability.

The combination of an overwhelming elevation of cytokines and a damaged vascular barrier may result in severe systemic inflammatory response and acute respiratory distress.

In spite of the adverse effect, rituximab was a highly effective treatment for AIVL in our presented Taiwanese patients, confirming the findings in another reported case of IVL. However, because of the potential risk of pulmonary distress syndrome after rituximab infusion as initial treatment for AIVL, the use of the drug for this subtype of lymphoma is recommended only after reduction of the tumor burden by systemic chemotherapy.

References