Rituximab-associated interstitial pneumonitis

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Learning Objectives

1. Maintain a high index of suspicion for rituximab-associated interstitial pneumonitis.
2. List the differential diagnosis for bilateral ground glass opacities in a patient receiving rituximab.
3. Recognize the importance to rule out infection when considering rituximab as a cause of pneumonitis.

Discussion

- CT chest demonstrated a bilateral ground glass opacities and BAL showed a lymphohistiocytic alveolitis, consistent with rituximab-associated interstitial pneumonitis. Given his negative diagnostic work-up for alternate etiologies, and the suggestive time course, we presumed that his dyspnea and hypoxemia were due to rituximab-associated interstitial pneumonitis.
- Transbronchial or open lung biopsy may be used to confirm the diagnosis and identify the subtype of interstitial lung disease, but may not be practical in the clinical setting.
- Once the diagnosis of rituximab-associated interstitial pneumonitis is made, it poses a complex clinical dilemma regarding the continuation of rituximab containing therapy. Cautious intent for a malignant tumor must be balanced against the morbidity associated with pulmonary toxicity.

Table 2. Lymphocytic cellular pattern of bronchoalveolar lavage

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Definition</th>
<th>Cellularity</th>
<th>Lymphocytes</th>
<th>Mononuclears</th>
<th>Macrophages</th>
<th>Eosinophils</th>
<th>Neutrophils</th>
</tr>
</thead>
<tbody>
<tr>
<td>B-cell lymphoma</td>
<td>Lymphocytic predominant (usually &gt;25%)</td>
<td>&gt;25%</td>
<td>50%</td>
<td>40%</td>
<td>0%</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>Hodgkin lymphoma</td>
<td>Lymphocytic predominance (Lymphocytes = 50%, monocytes = 35%, histiocytes = 15%)</td>
<td>&gt;25%</td>
<td>50%</td>
<td>40%</td>
<td>0%</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>Diffuse b-cell lymphoma</td>
<td>Lymphocytic predominant (Lymphocytes &gt;50%, monocytes = 35%, histiocytes = 15%)</td>
<td>&gt;25%</td>
<td>50%</td>
<td>40%</td>
<td>0%</td>
<td>0%</td>
<td></td>
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</tbody>
</table>

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Background
- Rituximab is a monoclonal anti-CD20 antibody, widely used in various hematologic malignancies and autoimmune diseases, as a single agent or in combination.
- Pulmonary toxicity due to rituximab is reported to be 8.4% in non-Hodgkin lymphoma.
- Pathogenesis is unknown

Clinical Features
- The most common symptoms at presentation included dyspnea (81%), fever (72%), and cough (62%).
- CT chest typically shows diffuse interstitial pulmonary opacities
- Less severe respiratory effects include cough, bronchospasm, sinusitis and rinitis

Diagnosis
- Bilateral pulmonary opacities following exposure to Rituximab, in the absence of an alternative explanation.
- Bronchoalveolar lavage (BAL) is critical to rule out infectious etiologies.
- Lung biopsy is helpful to confirm the diagnosis and subclassify the parenchymal change, but is not often practical.

Treatment
- Withhold Rituximab
- A rapid response to systemic glucocorticoids is typical

References: