Effects of omalizumab in Aspergillus-associated airway disease

The clinical spectrum of Aspergillus-associated airway diseases (AAAD) includes Aspergillus-induced asthma, allergic bronchopulmonary aspergillosis (ABPA) and bronchocentric granulomatosis. Corticosteroids are almost always used to suppress the immunological response to the fungal antigens. Although there are no evidence-based alternative treatment options besides steroids, the well-known adverse effects of these drugs have prompted clinicians to look beyond this standard practice and several cases of ABPA patients with very positive immunoglobulin E (IgE) levels were reported.3

We recruited 18 patients (13 women; mean age 49±17 years) with AAAD (2 of them had been previously diagnosed with cystic fibrosis) from 11 Spanish hospitals. All of them had been treated with omalizumab for at least 16 weeks and they were receiving inhaled corticosteroids (daily dose 1351±544 μg budesonide or its equivalent) and a long-acting β2 agonist at the moment of omalizumab initiation. Seventeen patients were being treated with oral corticosteroids at a median daily dose of 16 mg prednisone or its equivalent (IQR 6–28) and 10 with itraconazole. The mean number of albuterol puffs per day was 5.5 (range 1–8). Prior to omalizumab administration, IgE levels were (median [IQR]) 698 IU/ml (478–977) and the median absolute count of eosinophils in blood was 610 mm³ (317–1015). Sixteen of the 18 patients had CT-diagnosed bronchiectasis and fleeting pulmonary opacities were identified in 10 of them. All patients showed a delayed positive skin test for Aspergillus and 17 also developed an immediate response. Serum Aspergillus-specific IgE was found in all patients and precipitating antibodies in serum were observed in 10.

Omalizumab-treated patients were followed up for a median of 56 weeks (IQR, 28–42). The mean dose of omalizumab per week was 60±108 mg. No significant adverse effects were observed. The treatment was discontinued in five patients due to a lack of response and in another patient because of a positive test for pregnancy. The clinical and functional effects of omalizumab are summarised in table 1.

In this series, the largest reported to date, omalizumab has demonstrated a beneficial effect in reducing symptoms and exacerbations in a group of patients with AAAD. It also seems to improve pulmonary function even when oral corticosteroids were reduced or discontinued. Given the retrospective nature of this study and the small number of cases analysed, the results must be interpreted with caution. Although all patients met the criteria of ABPA proposed by Rosenberg,7 the differentiation between this entity and Aspergillus-induced asthma is problematic, so we decided to blanket them under the term ‘Aspergillus-associated airway disease’. While the pathogenesis of ABPA remains not fully understood, IgE has been advocated as a key pathogenic mechanism of the disease. Since the total serum IgE level is a marker of immunological activity in ABPA, the attenuation of the hyper-IgE response seems to be a reasonable target. Further studies are warranted to clarify the utility of omalizumab in AAAD, especially in ABPA.

Table 1 Functional and clinical outcomes following omalizumab therapy

<table>
<thead>
<tr>
<th>Pretreatment</th>
<th>Post-treatment</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁ (ml)</td>
<td>1360 (955–2200)</td>
<td>1850 (1270–2290)</td>
</tr>
<tr>
<td>FEV₁ (% predicted)</td>
<td>66% (39–73)</td>
<td>74% (70–84)</td>
</tr>
<tr>
<td>Annual rate of exacerbations</td>
<td>1 (1–4)</td>
<td>0 (0–1)</td>
</tr>
<tr>
<td>Daily symptoms (≥2 times per week)</td>
<td>15/18 patients (83%)</td>
<td>8/18 patients (44%)</td>
</tr>
<tr>
<td>Nocturnal symptoms (≥2 times per week)</td>
<td>15/18 patients (83%)</td>
<td>4/18 patients (22%)</td>
</tr>
<tr>
<td>Oral corticosteroids</td>
<td>17/18 patients (94%)</td>
<td>6/18 patients (33%)</td>
</tr>
<tr>
<td>Itraconazole</td>
<td>10/18 patients (55%)</td>
<td>3/18 patients (16%)</td>
</tr>
</tbody>
</table>

Results are expressed as median with range in brackets or as a percentage. The Wilcoxon test was used to evaluate any significant differences (p<0.05) between continuous variables and the χ² test was employed for comparison of categorical variables.

REFERENCES

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