Usefulness of Omalizumab in Rapid Drug Desensitization in Patients With Severe Anaphylaxis Induced by Carboplatin: Open Questions

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Carboplatin is an effective and well-tolerated chemotherapeutic agent used as first-line and subsequent treatment for ovarian cancer. Hypersensitivity reactions to chemotherapy have increased in frequency in the last 20 years, thus preventing the use of first-line therapies and causing a negative impact on patient survival and quality of life [1,2].

Omalizumab is a recombinant humanized anti-IgE monoclonal antibody approved for the treatment of severe allergic asthma and recurrent chronic idiopathic urticaria. It has been studied as an add-on therapy in food allergy, oral immunotherapy for food allergy, atopic dermatitis, idiopathic anaphylaxis, and mastocytosis [3].

We present 2 cases of severe anaphylaxis to carboplatin in which omalizumab was used to prevent reactions during rapid drug desensitization (RDD).

The first patient was a 57-year-old woman diagnosed with ovarian adenocarcinoma who had initially been treated with 6 cycles of carboplatin and paclitaxel without complications. A local recurrence developed 1 year later, and the patient started carboplatin and gemcitabine. During the second cycle of carboplatin (eighth exposure), she developed palmar pruritus and generalized erythematous rash that resolved with dextchlorpheniramine and methylprednisolone. With the following cycle (ninth exposure), she developed palmar pruritus, generalized erythematous rash, nausea, and vomiting and reported a sense of impending doom. Her blood pressure was 60/30 mmHg and her heart rate was 40 bpm. She was treated with intravenous dextchlorpheniramine, methylprednisolone, and intramuscular adrenaline. She also had epigastric pain radiating to the back, with ST segment
erythema to a generalized rash only once. All the reactions resolved with intravenous antihistamines and corticosteroids, and the patient was able to finish the 4 cycles.

RDD enables safe readministration of a drug to which a patient has become allergic. The procedure is usually safe and effective, although there is an inherent risk of a severe or even fatal anaphylactic reaction when a medication to which a patient had presented a severe hypersensitivity reaction is reintroduced [1]. Both patients presented severe life-threatening reactions with serious cardiovascular involvement. We recommended a 16-step desensitization with carboplatin in an intensive care unit. However, both patients and their oncologists refused the drug owing to the severity of the previous reactions. Given that carboplatin is the most appropriate drug in patients with ovarian cancer, we decided to administer omalizumab as an adjuvant treatment in order to diminish the risk of a severe reaction during RDD. One patient tolerated RDD without experiencing a reaction, and the other presented mild skin reactions. We do not know whether they would have tolerated the RDD if omalizumab had not been administered as an adjuvant.

To our knowledge, there are only 6 publications on the beneficial effect of omalizumab as an adjuvant in drug desensitization protocols: 1 case report with insulin [4], 12 patients with aspirin [5,6], and 3 cases with chemotherapeutic agents [7-9]. The Table summarizes the latter 3 cases, together with the 2 cases we report.

Omalizumab dosing in allergic asthma is based on the patient’s weight and total IgE, whereas in urticaria a 300-mg dose is given. All the patients desensitized to aspirin with add-on omalizumab had asthma, and the dose was calculated as for the asthma indication and administered every 2-4 weeks for 16 weeks prior to desensitization [5,6]. However, when clinicians consider using omalizumab as an adjuvant in RDD to chemotherapy, they do not know what dose to administer and cannot pretreat patients for several months, because continuing

<table>
<thead>
<tr>
<th>Authors</th>
<th>Cases</th>
<th>Patient</th>
<th>Drug</th>
<th>Symptoms</th>
<th>Dose of Omalizumab</th>
<th>No. of Doses of Omalizumab Before RDD</th>
<th>No. of RDD Cycles</th>
<th>Tolerance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cahill et al [8]</td>
<td>1</td>
<td>68 y (sex not specified)</td>
<td>Oxaliplatin</td>
<td>Anaphylaxis</td>
<td>150 mg/2 wk</td>
<td>2 doses</td>
<td>4</td>
<td>Mild reaction</td>
</tr>
<tr>
<td>Ojaimi et al [7]</td>
<td>1</td>
<td>Female 63 y</td>
<td>Carboplatin</td>
<td>Anaphylaxis</td>
<td>300 mg/2 wk</td>
<td>3 doses</td>
<td>4</td>
<td>No reaction</td>
</tr>
<tr>
<td>Prieto et al [9]</td>
<td>1</td>
<td>Female 61 y</td>
<td>Oxaliplatin</td>
<td>Anaphylaxis</td>
<td>300 mg/2 wk</td>
<td>1 dose</td>
<td>6</td>
<td>No reaction</td>
</tr>
<tr>
<td>Sánchez-Morillas et al</td>
<td>2</td>
<td>Female 57 y</td>
<td>Carboplatin</td>
<td>Anaphylaxis</td>
<td>300 mg once. After 7 d, 150 mg/2 wk</td>
<td>2 doses</td>
<td>6</td>
<td>No reaction</td>
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<td></td>
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<td>Carboplatin</td>
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Abbreviations: RDD, rapid drug desensitization.

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with the chemotherapy regimen is more urgent. Consequently, the dose given is decided arbitrarily.

In all the cases reported in the Table, omalizumab was administered every 2 weeks, albeit at variable doses. Ojaimi et al [7] and Prieto-García et al [9] administered 300 mg, whereas Cahill et al [8] administered 150 mg. We administered 300 mg followed 7 days later by 150 mg/2 wk. The patients described by Ojaimi et al and Prieto-García et al and patient #1 in the present report tolerated all RDD cycles with omalizumab without reactions. In contrast, the patient reported by Cahill et al and patient #2 in the present report experienced mild reactions. While more data are needed, it seems that the 300-mg dose is more effective than the 150-mg dose. The number of doses of omalizumab administered before RDD varies from 1 to 3.

In the light of currently available data, we suggest that omalizumab 300 mg given every 2 weeks, and with at least 1 dose given before starting RDD, enables patients with severe anaphylaxis to platinum drugs to receive them safely. Adding omalizumab increases the treatment cost of gynecological cancer, although when platinum-based treatment is avoided, the second-line chemotherapy agents seem to be associated with reduced survival [2].

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Conflicts of Interest

Dr. Sánchez-Morillas reports personal fees from the Sociedad Madrid-Castilla La Mancha de Alergología e Inmunología Clínica, ALK, and Stallergenes.

Dr. Casado Herráez reports participating on advisory boards for Pharmamar, Lilly, Merck (MSD), EISAI, and Roche International and receiving consultancy fees from Pharmamar, Roche, and Lilly.

Dr. Rubio Pérez declares that she has no conflicts of interest.

Dr. Robledo Echarren reports personal fees from Sociedad Madrid-Castilla La Mancha de Alergología e Inmunología Clínica and GSK.

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Dr. Vázquez Cortés reports personal fees from Novartis, Diater, SanofiAventis, and Sociedad Madrid-Castilla La Mancha de Alergología e Inmunología Clínica.

Dr. Cerecedo reports consultancy fees from Diater, Leti, ALK, and Stallergenes outside the submitted work and personal fees from Sociedad Madrid-Castilla La Mancha de Alergología e Inmunología Clínica, and grants from the Spanish Government (ISCIII). Dr. Cerecedo holds a patent (PCT/ES2014/070634).

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