Anaphylactic Reactions With 3 Nonrelated Drugs (Gadoteridol, Paclitaxel, Bevacizumab) in a Patient With Severe Comorbidities

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Key words: Anaphylaxis. Chemotherapy. Monoclonal antibodies. Excipients. Multiple drug hypersensitivity syndrome.

Multiple drug hypersensitivity syndrome (MDHS) confirmed by a positive allergy study is unusual. The few cases reported in the literature mainly involve delayed reactions, while immediate IgE-mediated cases are exceptional [1]. We report a case of MDHS where all episodes were immediate reactions.

The patient was a 66-year-old woman with high-grade ovarian and fallopian tube carcinoma, high blood pressure, and ankylosing spondylitis treated with prednisone 5 mg and an angiotensin II receptor blocker. She had no history of allergic diseases. Immediately after the first administration of gadoteridol during magnetic resonance imaging, she experienced anaphylactic shock (skin and respiratory involvement, hypotension, Glasgow score 3) requiring admission to the intensive care unit.

One month later, after an infusion of 5 mL of paclitaxel during her first chemotherapy cycle, she experienced immediate, severe anaphylaxis (skin and digestive involvement, hypotension) requiring antihistamines, corticosteroids, intravenous fluid, and oxygen treatment. The remaining drugs (carboplatin and bevacizumab) were administered the following day without complications.

During the second chemotherapy cycle, she experienced a new anaphylactic episode 3 minutes after starting the bevacizumab infusion. This consisted of facial erythema, itching palmar erythema, abdominal pain, nausea/vomiting, and dyspnea (baseline SaO₂, 88%). She recovered after receiving antihistamines, corticosteroids, and oxygen treatment. The patient tolerated carboplatin the following day.

We carried out an allergy work-up including basal serum tryptase (4 μg/L), total IgE (44 IU/mL), skin prick tests (SPTs) to aeroallergens and hazelnut (negative), and skin tests to gadoteric acid, gadoteridol, paclitaxel, and bevacizumab, which were positive for gadoteridol in the SPT and paclitaxel in the intradermal test (IDT) (Table).

Because paclitaxel was the most effective option for the patient’s carcinoma, desensitization with premedication (corticosteroids and antihistamines) was programmed. Two minutes after starting the first step at the first session (calculated dose administered, 1.7 µg), the patient presented an anaphylactic episode with skin, digestive, and respiratory involvement requiring epinephrine. Serum tryptase increased to 22.8 µg/L at 2 hours after onset of symptoms, with a subsequent decrease to 3.39 µg/L in 24 hours.

Paclitaxel was discontinued after a risk-benefit analysis by the oncologist and allergist. The oncologist scheduled an alternative chemotherapy regimen with gemcitabine and carboplatin, which was administered in 6 cycles without complications, followed by surgery. The carcinoma went into remission.

In an attempt to find an explanation for these 4 episodes of severe anaphylaxis, we first considered the possibility of a clonal mast cell activation disorder as an underlying cause. We calculated the Spanish Network on Mastocytosis

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**Table. Skin Tests to Drugs and Excipients**

<table>
<thead>
<tr>
<th></th>
<th>SPT 1/10</th>
<th>SPT 1/1</th>
<th>IDT 1/1000</th>
<th>IDT 1/100</th>
<th>IDT 1/10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gadoteric acid (279.3 mg/mL)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Gadoteridol (279.3 mg/mL)</td>
<td>+ (6-mm wheal)</td>
<td>NP</td>
<td>NP</td>
<td>NP</td>
<td>NP</td>
</tr>
<tr>
<td>Paclitaxel (6 mg/mL)</td>
<td>NP</td>
<td>–</td>
<td>NP</td>
<td>–</td>
<td>+ (8-mm wheal)</td>
</tr>
<tr>
<td>Bevacizumab (25 mg/mL)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Polyethylene glycol 1500 (0.5 g/mL)</td>
<td>NP</td>
<td>–</td>
<td>NP</td>
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<tr>
<td>Polyethylene glycol 3350 (0.5 g/mL)</td>
<td>NP</td>
<td>–</td>
<td>NP</td>
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<tr>
<td>Polyethylene glycol 4000 (0.5 g/mL)</td>
<td>NP</td>
<td>–</td>
<td>NP</td>
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</tr>
<tr>
<td>Polysorbate 80 (1 g/mL)</td>
<td>NP</td>
<td>–</td>
<td>NP</td>
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</tbody>
</table>

Abbreviations: IDT, intradermal test; NP, not performed; SPT, skin prick test.
Infusion reactions to bevacizumab are rare (<6.1%) [7,9]. The first case of anaphylaxis due to bevacizumab was recently reported [9]; the present case is the second to date. Patients with cancer and chronic inflammatory diseases treated with monoclonal antibodies and antineoplastic agents are susceptible to immediate reactions to their drugs [7]. The reactions may be due to mechanisms other than those included in the classic Gell and Coombs classification of hypersensitivity reactions. Consequently, it has been suggested that different underlying endotypes/phenotypes might be involved in the development of immediate reactions to these agents [7,10].

In summary, we report a case of MDHS with 3 nonrelated drugs presenting as immediate anaphylaxis.

Studies that explain susceptibility to developing MDHS are lacking. It is necessary to investigate and clarify the predisposing mechanisms of this rare condition, which exceptionally involves immediate reactions.

Funding

The authors declared that no funding was received for the present study.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

References

Severe Perioperative Anaphylaxis due to Allergy to the Sugammadex-Rocuronium Complex

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doi: 10.18176/jiaci.0730

Key words: Sugammadex. Rocuronium. Neuromuscular blocking drug. Anaphylaxis. Perioperative allergy.


Perioperative anaphylaxis is a life-threatening hypersensitivity reaction that can develop during surgery. Of the many drugs involved in these allergic reactions, neuromuscular blocking drugs (NMBDs) are the most frequent type [1].

We report the case of a 71-year-old woman with no relevant previous medical history who underwent vascular surgery with general anesthesia for varicose veins in her lower left leg. Propofol, fentanyl, sevoflurane, rocuronium, and lidocaine were administered during the procedure, with no complications. When surgery had finished, sugammadex was used to reverse neuromuscular blockade, and the patient was given acetaminophen and dexketoprofen for analgesia. Severe symptoms suggesting anaphylactic shock developed immediately and progressed to cardiopulmonary arrest. Cardiopulmonary resuscitation and symptomatic treatment were applied, with a full recovery after a few minutes. Her serum tryptase level was 55.9 μg/L during this reaction and 67.9 μg/L 2 hours later.

The patient's informed consent was obtained before starting the study 30 days after the episode. Negative results were obtained (specific IgE levels) for suxamethonium, chlorhexidine, and latex (ImmunoCAP, Thermo Fisher Scientific). The basal serum tryptase level was 8 μg/L. Prick tests with latex and chlorhexidine yielded negative results. Prick tests (PT) and intradermal tests (IDT) with commercially available formulations of the involved drugs [2] were also negative: propofol (PT at 10 mg/mL, and IDT at 1 mg/mL), fentanyl (PT at 0.05 mg/mL, IDT at 0.005 mg/mL), and lidocaine (PT at 10 mg/mL, IDT at 1 mg/mL). Skin tests with sugammadex and rocuronium separately were carried out according to Garvey et al [3], with negative results for both sugammadex (PT at 100 mg/mL; IDT at 10 mg/mL) and rocuronium (PT at 10 mg/mL; IDT at 0.05 mg/mL).

We then performed skin tests with a mixture of sugammadex and rocuronium (SR-M) (1 cc of sugammadex [100 mg/mL] and rocuronium [10 mg/mL]) according to Garvey et al [3], with negative results. The patient was managed with desensitization to sugammadex and rocuronium with no further reactions.

References


Manuscript received March 15, 2021; accepted for publication June 28, 2021.

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