Desensitization Protocol to Trastuzumab in a Patient with Anaphylaxis and Stage IV Breast Cancer: A Case Report

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A surge in hypersensitivity reactions (HSRs) to monoclonal antibodies (mAb) has been observed, often preventing the use of first-line therapies for fear of inducing severe reactions [1]. Trastuzumab is approved for the treatment of metastatic breast cancer reducing recurrence and death by increasing pathological response rate and improving overall survival [2]. Rapid drug desensitization (RDD) is a safe and effective tool for the administration of first line therapy to patients allergic to their oncology treatment [1]. Allergic patients can receive their chemotherapy and biologics thanks to RDD, which ensures the same survival outcomes as standard first line therapy [3] and is cost-effective [4]. We found that no allergy or oncology society has yet published a specific guideline on drug desensitization to chemotherapy, and so many physicians might be unaware of this option and thus decide to stop first line treatment when is still effective.

A 50 year old female patient was diagnosed with stage IV Her2- positive breast cancer on October 2018 with metastasis to bone, liver and lungs. The oncology service indicated the first cycle of treatment with trastuzumab (6 mg/kg), docetaxel
(75 mg/m2) and zoledronic acid (4mg) with administration every 3 weeks. Twenty minutes after initiating the second cycle of trastuzumab the patient presented dyspnea, facial and palmar erythema, angioedema, blurred vision, hypotension, hypoxia and tachycardia. The infusion was suspended and she was treated with intravenous norepinephrine in the emergency room with resolution of anaphylaxis and referred to our allergy service for further evaluation. Skin tests were performed to docetaxel (1mg/1mL) with negative result. The following administration of docetaxel was treated as a high-risk drug provocation test, and this was negative, so hypersensitivity to docetaxel was ruled out [5]. Zoledronic acid had not been yet administered in the cycle so it was not tested. Trastuzumab skin prick test (21 mg/mL) and intradermal tests (0.21 mg/mL) were applied [6], resulting positive the latter one with a 12x10 mm wheal, 12x12 mm erythema and negative control wheal and erythema of 3x4 mm, confirming immediate hypersensitivity. Histamine (10 mg/ml) and saline solution were used as the positive and the negative control, respectively. Due to the need of a specific antibody for HER-2 treatment, desensitization was adapted from Hong et al [7] with 4 bags and 16 steps, at increasing concentrations of 0.00188, 0.0188, 0.176 and 1.746 mg/mL with a 6.67 hour duration. The patient was premedicated with clorpheniramine (10 mg) and methylprednisolone (40 mg) [8]. Corticosteroids can decrease the intensity of symptoms but do not protect from severe reactions [8]. Ondansetron (8mg) was used to prevent nausea induced by chemotherapy. After tolerating 9 more cycles of the 4-bag 16 step protocol, a 3-bag 12 step protocol with a 5.67 hour duration was
initiated using 0.0176, 0.176 and 1.746 mg/mL (table 1). We administered saline solution at 100 mL/hour throughout the first 11 steps with an increase to 250 mL/hour after step 12. The procedure was well tolerated and up to date after 20 RDD, the patient continues with no hypersensitivity reactions to trastuzumab.

Trastuzumab is known to induce HSRs in 16% of patients, including anaphylaxis in 2% of cases [9]. When a patient presents with HSR to biologics, doctors tend to administer an alternative treatment [4], thus compromising the patient's prognosis by avoiding the optimal first line treatment [4]. In this patient the culprit drug was essential.

Brennan et al. described RDD to trastuzumab in three patients with mild to moderate anaphylaxis, presenting reactions in 29% of the procedures performed [10]. RDD is indeed a high-risk procedure that needs specific resources, trained staff, and must be tailored to the patient's specific needs. Thus, RDD should be only performed by expert allergists who can assess the patient's risk and treat anaphylaxis if needed [10].

We have reported a series of successful and uneventful RDDs to trastuzumab in a high-risk patient (anaphylaxis as initial reaction and positive skin tests). The literature shows how assessment and management by an expert team of allergists is a guarantee for the success of RDD. Thanks to this procedure, the patient could continue with a life-saving treatment that would have otherwise been stopped. Data on RDD to mAb such as trastuzumab is still very limited, so reports such as this on
the successful use of this technique are extremely promising for the future of these patients.

Consent for publication

Written and informed consent for publication was obtained from the patient. The patient was informed that de-identified data would be used in the scientific research and publications.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

Previous Presentations

The abstract “Trastuzumab Desensitization Protocol: A Therapeutic Challenge In A Patient With Metastatic Breast Cancer” was presented as an e-poster presentation in the 2019 ACAAI Annual Meeting held on 11/08/2019 in Houston, Texas.
References


Table 1. 3-bag 12 step desensitization protocol to trastuzumab

<table>
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<th>Step</th>
<th>Solution (Bag)</th>
<th>Infusion (mL/hr)</th>
<th>Time (minutes)</th>
<th>Infused Volume (mL)</th>
<th>Dose administered (mg)</th>
<th>Cumulative dose (mg)</th>
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Adapted from Hong et al [7].