Cosmetic Medicine

Case Report

The First Case Report of a Systemic Allergy to OnabotulinumtoxinA (Botox) in a Healthy Patient

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Abstract

To the authors’ knowledge, this is the first report of an allergy to onabotulinumtoxinA. The 43-year-old woman experienced severe itching after injection of Botox and Juvederm. Results of prick and patch testing confirmed a T-cell–mediated allergy to Botox. This case can aid in the evaluation of suspected allergies to Botox.

Level of Evidence: 5

Keywords

Botox Cosmetic, onabotulinumtoxinA, systemic allergy, contact dermatitis, hypersensitivity

OnabotulinumtoxinA, also known as Botox Cosmetic (Allergan, Inc, Irvine, California), is the most commonly injected substance to diminish the appearance of facial wrinkles; it functions cholinergically by relaxing the muscles surrounding the injection site. Botox Cosmetic is a purified version of a toxin produced by the bacterium Clostridium botulinum.

Although Botox Cosmetic is generally considered safe, it may have contributed to 1 death, which resulted from an anaphylactic reaction. However, the patient had been treated with a therapeutic dose of Botox mixed with lidocaine, and therefore Botox could not be proven as the causative agent. Serious local reactions to Botox have been reported and include blurred vision, urinary retention, breathing difficulties, itching, dizziness, dry mouth, and swelling. Serious systemic reactions to Botox are rare but have occurred in patients with certain medical conditions such as cerebral palsy and limb spasticity. Some patients with neuromuscular disorders have experienced dysphagia, dysphonia, muscle weakness, and/or dyspnea after administration of Botox. However, patients with serious systemic reactions had received therapeutic doses of Botox, ranging from 100 to 700 U, rather than the approved cosmetic dose of 20 to 44 U (depending on the area of treatment). Prior to this case, there had been no reports in the international literature of a systemic reaction to any correctly administered, approved dose of Botox Cosmetic. Our report serves as a cautionary alert for similar reactions and a template for assessing such reactions.

CASE PRESENTATION

A healthy 43-year-old woman with a history of allergic rhinitis experienced severe itching after her fourth sequential injection of Botox and second sequential injection of...
hyaluronic acid gel (Juvéderm; Allergan Industries SAS, Mougins Cedex, France). Both injections occurred during a single visit. She received 20 U of Botox in the forehead and 12 U in the glabella. Prior to injection, a standard Botox mixture had been prepared, consisting of 3 mL of preservative-free saline (0.9% sodium chloride) and 100 U of Botox.

The patient’s previous injections of Botox alone (without Juvéderm) had resulted in similar itching, but her previous injections of Juvéderm alone had not elicited this reaction. The patient received Botox treatment a total of 4 times. The first resulted in a swollen eyelid on the morning after treatment. The swelling receded with over-the-counter Benadryl (Pfizer, Inc, New York, New York) as advised by Dr Lorne Rosenfield. Following the second and third treatments, local itchiness continued, and the patient was slightly disoriented. The patient does not recall these symptoms and relied on family and friends for this information. Following the third and fourth treatments, the patient took over-the-counter Benadryl that provided little to no relief. The fourth Botox treatment resulted in the systemic reaction of concern.

Approximately 36 hours after receiving Botox and Juvéderm at the same visit, the patient experienced pruritus in her hands and feet, which gradually became widespread except for the face and scalp. After the itching began, a small flat red dot appeared at the injection site. The patient called the office of Dr Lorne Rosenfield 2 days after the onset of pruritus to report the itching.

The total duration of the allergic reaction was approximately 3 weeks (from initial report to complete resolution of symptoms). Initially, the patient received a course of diphenhydramine (Benadryl; Pfizer, Inc) and topical hydrocortisone cream, which provided no relief. Subsequently, she was referred to allergy specialist Dr Dean Kardassakis and began a 5-day regimen of methylprednisolone (Medrol Dosepak; Pfizer, Inc). Her symptoms resolved upon completion of the treatment. She was evaluated for Gell–Coombs type I (antibody-mediated) and type IV (T-cell-mediated) reactions via prick testing and patch testing, respectively. Serial dilutions of Botox (1:1000, 1:100, 1:10, and undiluted) and a therapeutic intradermal dose were utilized for prick testing (with the Multi-Test II device; Lincoln Diagnostics, Decatur, Illinois) and intradermal testing. Although none of the test product was from the batch of Botox administered to the patient initially, the source and reconstitution were identical.

Results of the prick and intradermal tests were negative, which excluded a Gell–Coombs type I reaction. Patch testing with a Finn Chamber (SmartPractice, Phoenix, Arizona) showed induration of 22 × 29 mm and erythema of 34 × 40 mm when read at 3 days. This positive finding indicated a Gell–Coombs type IV, T-cell-mediated, delayed hypersensitivity reaction. After communication with the manufacturer and a thorough review of the medical literature, we were unable to find any reaction similar to this.

DISCUSSION

To our knowledge, this is the first report of a systemic reaction and confirmed allergy to Botox administered at a cosmetic dose. Since the approval of Botox Cosmetic by the US Food and Drug Administration in April 2002, this combination of adverse events had not been reported. Findings from our case support the diagnosis of a Gell–Coombs type IV reaction to Botox.

Although 1 serious systemic reaction to a Botox-lidocaine combination has been reported, which resulted in death, Botox could not be established as the cause. Moreover, the dose of Botox in that case was much greater than the approved cosmetic dose. One previous anaphylactic fatality due to lidocaine alone has been reported, so the death might not have been related to Botox.

Systemic toxicity has occurred in rats that received high doses of Botox, which is expected. However, no allergy or systemic reaction such as that of our patient was observed in the rat studies. Moreover, not even the possibility of a minor systemic reaction to cosmetic doses of Botox had been reported in the literature.

If a systemic reaction to Botox is suspected, we recommend that the patient be referred to an allergy specialist for proper confirmatory workup and effective treatment of the allergy. Patients can be evaluated in an outpatient, community-based allergy practice. Our patient underwent standard allergy testing with the same type of Botox used clinically for wrinkle reduction. If allergy testing yields a positive finding, appropriate treatment should be initiated and avoidance of Botox should be advised. If the test results are negative, it is possible that Botox could be safely administered in the future. Appropriate precautions should be taken in such cases.

Because we did not test each ingredient of the solution separately, it could be argued that our conclusion may be flawed. However, since each ingredient is present in all solutions of cosmetic Botox, the claim of allergy appears accurate, and physicians should be aware of this possible reaction.

CONCLUSIONS

This case demonstrates that cosmetic Botox has the potential to cause systemic hypersensitivity. The case can serve as a blueprint for evaluating suspected allergies to Botox. Patients with a confirmed allergy to Botox should be discouraged from receiving further treatments with this product.

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**REFERENCES**