Questioning and prying into botulinum toxin after aesthetic treatment

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ABSTRACT

To the author's best knowledge, this is another reported case of an allergy to Botox toxin A. that had arisen shortly after the injection, to be added to the existing literature. A 41-year-old Philippino lady experienced a severe localised reaction, with redness and nodular swelling on her face, after her second Botox injection. The lady did not have any prior medical illness. This case can help in assessment and appraisal of anticipated Botox allergies and raise awareness of the rare infrequent incident.

Key words: botulinum, botulinum toxin A, lump, bump.

Introduction

Botulinum toxin type A (BTA) (also called as Onabotulinumtoxin A, Abobotulinumtoxin A, and Incobtulinumtoxin A) injection is extensively applied in cosmetic dermatology, to give a youthful appearance with minimal downtime (Levy and Emer, 2012, Moon et al, 2017). It works by inducing muscle paralysis at the neuromuscular junction through inhibiting the release of acetylcholine.

It has been noticed that over the last decade, many Botox (BTA) brands have emerged strongly in the aesthetic industry, predominantly from the Republic of Korea (Pickett, 2018). Some are on-label and some are off-label. Notably, all are meant to serve one function; to improve the facial outlook by minimising wrinkles and boosting confidence and stamina. To name some, Nabota/Jeuveau, Meditoxin/Neuronox and Botulax all contain nontoxic accessory proteins and excipients (Park JY, Sunga O, 2020).

The injected brand was Botulax. Botox is a Botulinum A, and Botulax is another Botulinum A; botulinum toxin serotype A (BoNT/A). Botulax is made in Korea, by the manufacturer Hugel. Its active ingredient is Clostridium Botulinum Toxin A type, and it is not FDA approved for use but in some places, it is applied illegitimately. The only FDA approved are Botox, Dysport and Xeomin. However, Botulax is extensively used in Asia, and certain countries including Libya, and is well known and has no problems attached with it.

In the West and America, Onabotulinum toxin A, also recognised as Botox Cosmetic, is one of the commonest injectable constituents to improve and rectify facial wrinkles appearance and is manufactured by the bacterium Clostridium botulinum. BTX is considered safe but it has been reported in rare cases to cause a fulminate anaphylactoid reaction.

My reported case represented a localised allergic reaction to Botulax and shall serve as an admonitory observation for similar reactions should they arise.

Case Report

A healthy 41-year-old Philippino lady sought my medical attention after experiencing severe swelling after 8 hours of receiving her second Botulax injection, with localised bumps and lumps on her face that lasted for more than 48 hours. She was completely healthy and has no other medical conditions. She had one encounter of the same brand injection a year previously and did not elicit any reaction at that time as it was a completely uneventful incident. She did not have any concomitant filler injection. The Botulax preparation and the number of units received were unknown, however, she received the Botulax injection on her glabella, forehead, and the 'crow line'. The total treatments the patient received were two, with a year apart.

On examining her sent photos, there were multiple, tender, firm, well-defined, non-itchy red swellings at all sites of injections, namely cheek, 'crows feet', and the forehead. There were no generalised skin reactions, no headache, no difficulty in breathing, no diplopia or trouble swallowing and no eye, tongue, lips or throat swelling either.

The expected momentarily common self-limiting reactions are pain, itching, erythema and bruising. In this lady, the swelling had receded, without any scars, by itself after 72 hours. She did not take any over-the-counter (OTC) medications. She only received intravenous (IV) drip for whitening her complexion which is a common practice in certain nations.

Skin bumps and lumps are seldomly and unexpectedly seen as consequences of botulinum toxin injection, where no guided consensus is existing to rectify it; but when it happens, it can be notoriously distressing to both the patients and the injecting clinicians.

There was no confusion or disorientation encountered in this lady. There was no facial or scalp complaint. The total duration of the reaction lasted for more than 72 hours and after that the bumps and lumps self-resolve. She was requested to have an assessment for her IgE, C1-esterase inhibitor, prick and patch test; a regular allergy testing, with the same type of Botulax used but the patient opted not to and declined as she had recovered.

Figure 3 and 4 shows complete self-resolution after 3 days.

A communication was initiated with the manufacturer online, but to no avail. Reviewing the existing literature did not yield any similar encounter, which will be disturbing and distressing to both the clinicians and the patients.

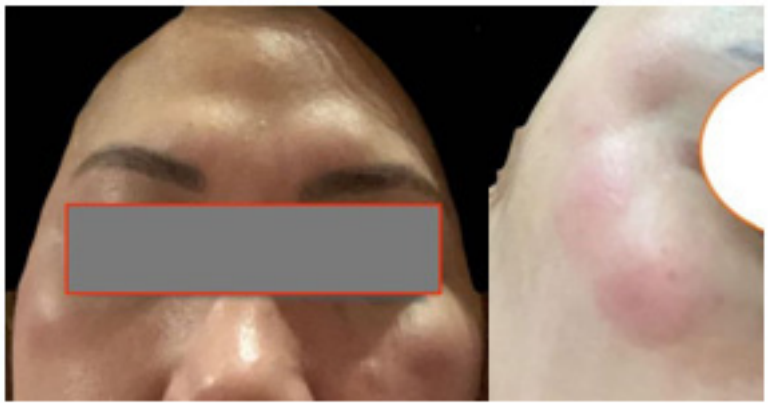

Figure 1

Figure 2

Figure 3

Figure 4

Discussion

With the incremental daily uses of Botox injections, it is projected to see and confront some rare unknown side effects.

Botox has immunogenic potential which is attributed to some factors, namely, the assembly of its biochemical material, which involves denaturation by oxidation, the storage and packing, impurities, dose and frequency with sites of injections, and the genetic makeup of each individual (Brüggemann et al, 2009, Namazi, et al, 2016). Both BOTOX® and DYSPORT® encompass a crystalline composite of purified toxin and a binding protein, known as haemagglutinin. However, DYSPORT® unify human serum albumin and lactose, which is capable of triggering an allergic reaction, but the lactose role remains conjectural (Namazi, et al, 2016).

According to Anabtawi et al's 2020 review, five cases were reported with nodular outbursts after various brands of Botox administration respectively (Dysport ®, Germany, Botox ®, Allergan, and Neuronox ®, South Korea, and Botulax ®, Korea), all of which were females between 42 and 57 years old, of whom, two had sarcoidosis, one was hypertensive and two were completely fit and well. Presentation varied between a few weeks to six years and biopsies results varied between granuloma formation, to foreign body formation.

One postulation could be the protein (human serum albumin or gelatin) component of Botox-A product which could cause a foreign body reaction and initiate immune reactions. Also, the skin reactions after Botox injection can be attributed merely to sensitized, pseudosensitized and intolerance responses.

The concern about BoNT/A-induced immunogenicity is significantly disputed, as they are loaded with higher amounts of inactive total neurotoxin that renders patients to potential immunogenic reactions. Additionally, multiple reports of treatment failures necessitate repeated injections, due to BoNT/A-induced neutralizing antibodies, and thus cumulative exposure to potential immunogens (Park JY, Sunga O, 2020).

Hypersensitivity and allergic body reactions are classified under the main four well-known groups. The first, type I, is the immediate body reaction after exposure to an antigen, which can be anaphylaxis or anaphylactoid, where the mast cell will determine the reaction type by either IgE or non-IgE-mediated factors.

While in type II reaction, it comprises a dependent antibody reaction by stimulating the complement system (natural killer cells or macrophage) within the initial 12 hours. In type III hypersensitivity, it involves the formation of the immune complex (IC) within hours after repeated triggering to the complement system. The delayed reaction, IV, is characterised by sensitisation of the cytotoxic T-cells, where symptoms prevail between 2-3 days. However, in pseudosenstisation, the symptoms develop due to histamine release directly and are dose related, whereas, intolerance reaction occurs due to imbalance in both the histamine release and degrading systems (Brüggemann et al, 2009).

Careta et al, 2015, reported a case with known allergy, developed post Botox immediate urticarial plaques reaction, minutes after, and it has been documented after a Chinese Botulinum toxin (CBTX-A) injection to correct dynamic wrinkles. Whereas, Namazi et al, 2016, documented a case of vasculitis with panniculitis post Chinese Botulinum toxin injection.

In this case, the time course had been in keeping with either type II, type IV hypersensitivity pathway or an intolerance response. It is not clear as biopsy was not examined. The explanations for these reported case skin reactions currently remain unidentified but speculative. As there are scarcely any reported cases in the existing literature, it is quite challenging to establish the tangible cause. Grounded on the existing information, no firm conclusion can be arrived at regarding the risk of skin reactions between different preparations of Botox. However, it would be wise to be wary, when applying Botox for the possibility of any peculiar skin allergic reactions, or bumps and lumps post Botox injections.

To my knowledge this is another case reported to be added to the existing literature.

With current COVID times in mind, it would be presumed that the providing clinic in the Philippines had followed the utmost standard etiquette in Botulax® formulation and reconstitution, as per the standard technique advised by the Korean producer; Hugel. The freeze-dried botulax100 U, prior to injection, is reconstituted with 0.9% preservative-free, sterile saline to make 100 U/2.5 mL (4 U/0.1 mL), which should be administrated within four hours after dilution technique, as per their web page instruction. This was discussed with the patient who affirmed that protocol was exercised.

For the regular allergy testing, if it was a positive verdict, then advice should be given to avoid the used brand in future, however, if the test results were negative, then it would be possible that the used brand can be safely given in the future (Rosenfield et al, 2014). After all, appropriate precautions should be exercised and taken seriously with strict cautions in such cases, to avoid any misfortune.

As the ingredient was not tested, then the argument would not be complete and valid. There are many possible explanations for this allergic reaction encountered as explained. The strong claim is that botulax allergy seems to have happened in this case and thus injecting physicians should be conscious of the possibility of this brand reaction.

Conclusion

Botox generally speaking, is well-known to be a safe, well-tolerated and an effectual treatment for cosmetic wrinkles improvement without down time, or serious drawbacks.

I report a lady patient who developed extraordinary, localised skin bumps and lumps 8 hours post Botulax injection (BoNT/A), which can be added to the existing literature to learn and share knowledge.

This case showed that Botulax can cause a severe localised skin reaction on the face and this report can serve as a blueprint and a proposal to assess and evaluate cases of Botulax allergies. Thus, patients with a confirmed allergy to Botulax should refrain from receiving further treatment with this product. The patient agreed to keep me updated once having her next Botulax injection.

Additional appraisal and research assessment are needed to reach a consensus on management. However, due to the scarcity of reported cases, this can be hard to achieve.

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