

The impact of COVID-19 infection on botulinum toxin hypersensitivity: Case report and literature review

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Abstract COVID-19 infection showed specific and nonspecific triggering of the immune system with different skin manifestations. Botulinum neurotoxin type A is the most commonly used injectable drug in a cosmetic procedure, and there are few reports regarding the interaction with COVID-19. Herein, an adult woman underwent a local cosmetic botulinum neurotoxin type A injection and unfortunately, at the same time, she was diagnosed with COVID-19 infection. After 4 hours following injection, the patient developed local pain and pruritus with periorbital swelling and red plaques involving the medial canthus and lower eyelids, with erythema that spread to both cheeks. Previously, she had a history of uncomplicated twice cosmetic botulinum neurotoxin type A procedures for face wrinkles. An outpouring of several cases of hyper-reactivity to cosmetic botulinum neurotoxin type A might happened during COVID-19 pandemic. During cosmetic procedures, dermatologists and plastic surgeons should be aware of the possibility of life-threatening anaphylaxis that might happen during COVID-19 infection or its vaccination.

Key words

COVID-19; Botulinum toxin hypersensitivity; Periorbital swelling; Face wrinkles.

Introduction

A great revolution occurred in every field of medicine during the coronavirus pandemic, this leads to limitations in all medical specialties. The increased awareness and interest of the world population in cosmetic and esthetic medicine requires certain safeguards for harmless practice during the COVID-19 pandemic.¹ Furthermore, this cosmetic intervention is some kind of relatively grandeur lifestyle than a necessity, since the number of esthetic interventions has a significant waning.²

Botulinum purified neurotoxin type A (BTA) produced by *Clostridium botulinum*, induces flaccid muscle immobility by reversibly preventing neurotransmitter release. The cosmetic Botox has the potential to cause a local and systemic reaction. Individuals with a confirmed allergy to BTA should avoid further treatments with this drug.^{3,4}

Currently, BTA is the most extensively used injectable drug both for therapeutic and cosmetic goals. Its use is continuously expanding due to its advantage and rare reports of serious adverse effects.⁵ Meanwhile, a growing number of drawbacks was also reported rendering to the FDA adverse event reporting system.⁶

In the review of the PubMed database, only six individuals reported different types of hypersensitivity responses to cosmetic BTA

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Figure 1 A 41 year old patient showing periorbital swelling and red plaques involving the medial canthus and lower eyelids following 4 hours after BTA.

injection (**Table 1**). Hence, this case description serves as a cautionary alert and varies from the earlier cited reported patients in that the typical local sensitivity to Botox injection occurred during the COVID-19 infection.

Case report

A 41-year-old female complained of a 1-day duration of local pain and pruritus with periorbital swelling and red plaque involving the medial canthus and lower eyelids (**Figure 1**). The condition started after 4 hours following local BTA injection. The erythema spread to involve both cheeks only, but there were no ecchymoses at the injection sites. Previously, she had achieved twice cosmetic BTA procedures for face wrinkles by the same dermatologist, and she had very well responses without any reported side effects.

A thorough history revealed that she and 2 of her family had complained of flu-like symptoms of 1 week earlier, characterized by headache, nasal discharge, myalgia, and malaise. During this period, she received a paracetamol tablet. At the time of the presentation of the skin reaction, full laboratory tests were done, and unpredictably RT-PCR for COVID-19 was positive. The management of the patient started with a single daily oral non-sedating antihistamine and twice

application of betamethasone cream and responded rapidly with complete recovery within 5 days. An agreement for the publication of the patient's medical condition and here picture has been obtained.

Discussion

Corona viral infection might trigger or present with different dermatological manifestations.¹ During COVID-19 disease, the neutrophils express an excessive response, and the immunity and complement become hyperactive.¹¹ These nonstandard immune reactions have a role in the pathogenesis of many skin problems.¹²

Many cosmetic procedures are considered a form of luxury and not a necessity. This should be perceived by humans, especially when the susceptibility to the corona virus is high. Herein, an adult female reported local sensitivity to Botox injection occurs during the COVID-19 infection. Following extensive a literature review only 6 other similar cases were reported and also in women with a different medical history and COVID-19 related infection or vaccination (**Table 1**).^{6,13} BTA is a protein and neurotoxin formed by the bacterium *Clostridium botulinum*, and it was approved by FDA in 2002 to temporarily improve the appearance of facial wrinkles, and the frequently reported side effect is eyelid oedema which is unrelated to infection.⁷ Allergic responses are possible, but are extremely rare, and range from non-serious to grave skin eruptions and granuloma development and this could be localized or general anaphylactic responses.^{4,14} The popularity of BTA injection plus the growing number of described adverse effects specifies the importance of gaining suitable information about its safety and complications.¹⁵

Two actual concerns of this case report were previous COVID-19 infection, and the sub-acute

Table 1 Reported cases of local hypersensitive response to cosmetic BTA injection in PubMed.

<i>Authors</i>	<i>Gender/ Age</i>	<i>Year</i>	<i>Country</i>	<i>Previous times of BTA injection</i>	<i>Dose of BTA, site</i>	<i>Drug history</i>	<i>medical history and Covid-19 related history</i>	<i>Symptoms</i>	<i>Onset/duration</i>	<i>Treatment</i>
Rosenfield et al [4]	Female/ 43 yrs.	2014	USA	3	32 U, forehead, glabella	hyaluronic acid gel injection	Local swelling and pruritus during previous Botox injections	Generalized itchiness; small flat red dot at the injection site of the face	36 hrs/3 wks.	Methylprednisolone
Careta et al [7]	Female/ 44 yrs.	2015	Brazil	No	32U, glabella, orbicularis, frontalis	No	Nil	Red plaques (urticaria like)	20 mins/72 hs.	Oral corticosteroids &antihistamine
Moon et al [8]	Female/ 35 yrs.	2017	Korea	1	50U, the masseter muscle	anesthetic cream	Allergic rhinitis, allergic reaction to latex.	Swollen eyes, severe rhinorrhea, wheals on extremities, mild dyspnea, chest tightness	5 mins/4 hrs.	Epinephrine, oral corticosteroids &antihistamine
Akdogan et al [9]	Female/ 55 yrs.	2021	Turkey	14	NA, Glabellar frown, the sides of the eyes (crow's feet), and forehead creases	levothyroxine	COVID-19 infection. hypothyroidism for 20 years.	Severe not tolerated local pain	sudden	Injection stopped, applied cold packs
Guo X et al, 1 st case [10]	Female/ 35 yrs.	2021	China	4	60-100 U, the glabella and crow's feet	No	SARS-Cov-2 Vaccine before 2 weeks	facial swelling, flu-like symptoms, and headache	3 hs, 7 days	Dexamethasone, and Loratadine
Guo X et al, 2 nd case [10]	Female/ 34 yrs.	2021	China	2	100U, the glabella	No	SARS-Cov-2 Vaccine before 2 weeks	facial swelling and flu-like symptoms	2hs, 14 days	dexamethasone and antihistamine
Presenting case, 2023	Female/ 41 yrs.	2022	Iraq	2	30U, the lower parts and inner sides of the eyes	Paracetamol	COVID-19 infection	Periorbital swelling and red Plaque at the injection sites, associated with local pain and pruritus	4hs, 7 days	Topical steroid and antihistamine

BTA = botulinum toxin type A, NA = not applicable.

oversensitive responses to BTA of the eyelids, which might progress into a life-threatening condition.⁴

Previously a total of 6 cases have been reported with an allergic reaction to cosmetic BTA among them, one patient after COVID-19 infection, and 2 cases following SARS-Cov-2 Vaccine before 2 weeks of the procedure. While other reports earlier than COVID-19 pandemic and only two of preceding reported subjects had local skin reactions with simple management, while others presented with systemic manifestations that urged an oral or parental steroid and antihistamine.^{6,13} Although the presenting case was a local reaction, still systemic anaphylaxis could be anticipated and cautions should be taken but fortunately, the local symptoms were recovered promptly within 5 days after topical corticosteroid and an oral antihistamine. According to an earlier report, about 70% of the cases of anaphylaxis are usually rapid onset and starts within 20 minutes following injections.¹⁶ Regarding the present case study, the patient experienced progressively periorbital swelling and red plaques at the injection sites, associated with local pain and pruritus and the onset of symptoms was 4 hours after the procedure of cosmetic BTA, which exceeded the essential follow-up of patient in the clinic.

These cases of BTA allergy were extremely rare but the record of these cases was increasing during the epidemic of COVID-19. Accordingly, one should be very cautious regarding BTA injection especially in patient with fever or suspicion of corona virus infection.

Conclusion

The present case of allergic reaction to BTA during corona viral infection should make dermatologist or cosmetologist be aware of this

possibility of hypersensitive reaction. This reaction could be localized or generalized which was controlled by oral antihistamine and twice application of betamethasone cream. Following the COVID-19 pandemic, upsurge of several cases of hyper-reactivity to cosmetic BTA were reported. A cautionary note for doctors is that life-threatening anaphylaxis might happen during COVID-19 infection or its vaccination. This probable association deserves great care and efforts to understand the actual pathogenesis of over-reactivity. Learning about the immune response toward botulinum toxin is a widely challenging mission. Also, a caution should be considered in any patient receiving BTA injection while has any viral infection or its vaccine.

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