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Facial Blanching: An Unusual Side Effect after Botulinum Toxin Injection

Abstract

Background: Botulinum toxin (BTX) is widely used in different areas of medicine for treatment of neurological disorders related to muscle hypertonicity and spasticity. However, the results of studies conducted over the past decade suggest that the BTX molecule exerts more complex and diverse effects on the human body, including antinociceptive effect and vascular tone regulation.

Main observations: We report case of a 37-year-old healthy Caucasian woman who complained of pale patches on her forehead 5 days after she had been injected with abobotulinumtoxin A. Previously the patient did not receive any BTX injections. Pale patches corresponded to the BTX injection sites and became visible against hyperemic background following intense physical activity.

Conclusion: The adverse effect of BTX used for aesthetic indications in the form of facial blanshing at the injections sites is a rare manifestation of individual peculiarities of certain patients.

Keywords: Botulinum toxin; Facial blanching; Vascular tone regulation; Hypertonicity; Neurological disorders

Case Report

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Alisa Sharova* and Viktoria Lysikova
Pirogov Russian National Research Medical University, Russia

***Corresponding author:** Alisa Sharova, Pirogov Russian National Research Medical University, Russia, Email: aleca@mail.ru

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Introduction

Botulinum toxin (BTX) is widely used in different areas of medicine. Its major and most obvious effect consists in the block of acetylcholine-mediated nerve-to-muscle signaling transmission determining the unique efficacy of BTX used for treatment of neurological disorders related to muscle hypertonicity and spasticity. BTX-induced transient relaxation of the facial muscles used for elimination of facial wrinkles has made BTX injections the most popular non-surgical aesthetic procedure in the world [1]. The inhibition by BTX of exocrine glands function is based on impairment of the cholinergic innervation. BTX is most commonly used for treatment of hyper hydrosis, but in some cases it is also used to block functioning of the salivary and lacrimal glands.

However, the results of studies conducted over the past decade suggest that the BTX molecule exerts more complex and diverse effects on the human body. The discovery of the antinociceptive effect has given an impulse to studying potential use of BTX for treatment of different pain syndromes. Moreover, there are clinical and experimental data indicating that BTX can regulate the vascular tone. We present a clinical case demonstrating this effect of BTX.

Case Report

We report a case of a 37-year-old healthy Caucasian woman who complained of pale patches on her forehead 5 days after she had been injected with abobotulinumtoxin A. The product was injected into the forehead (total dose 20U) and corrugators (10U per muscle). Previously the patient did not receive any BTX injections. The patient reported that she had experienced facial redness and excessive sweating while being in stressful situations. Pale patches corresponded to the BTX injection sites and became visible against hyperemic background following intense physical activity (jogging) (Figures 1 & 2).

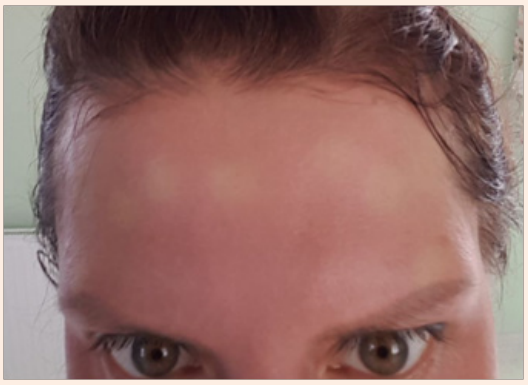

Figure 1: Pale patches on patient's forehead after jogging 5 days after she had been injected with abobotulinumtoxin A.

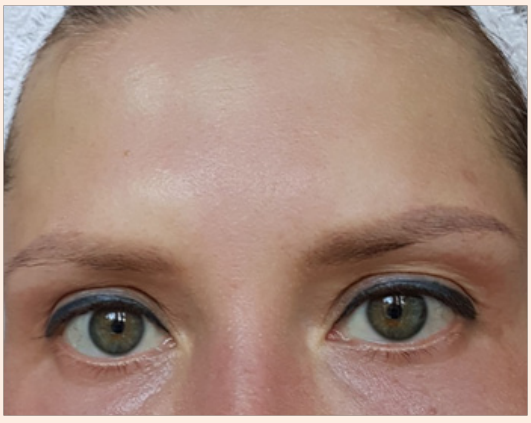

Figure 2: The same patient 1 month after injections.

Discussion

Blanching phenomenon is a rare and unusual adverse outcome of BTX use for aesthetic indications. Only few cases of these reactions have been reported in literature [2- 4].

However, BTX has been used for treatment of conditions related to vasodilation and flushing for quite a long time. Numerous articles have been published confirming its efficacy for treatment of the Frey's syndrome [5], rosacea [6], menopausal [7] and heat stress [8-10] flushings and Harlequin syndrome [11].

The mechanism of BTX action on the vascular tone has not been fully understood. Low DA et al. [12] was demonstrated the significant increase of the skin sympathetic nerve activity in the peroneal nerve during hot flashes and return to pre-hot flash levels after the flashes.

BTX injections into the forearm and the glabellar skin results in decreased blood circulation in BTX-treated sites relative to the adjacent untreated sites. Thus, regulation of the vascular tone (at least in part) is mediated by BTX-sensitive nerves, presumably sympathetic cholinergic ones.

These data agree with the results of the studies conducted earlier by Kellogg DL et al. [13], which demonstrated that cutaneous active vasodilation was not affected through muscarinic receptors and that cholinergic nerve activation mediated cutaneous active vasodilation through release of an unknown co-transmitter, not through ACh [13]. BTX injections may impair vasodilator responses to heat stress blocking the release of these neurotransmitters. Possible candidates for the role of these vasodilation activators include prostaglandins, and the endothelium-derived hyperpolarizing factor (EDHF) [4]. There are controversial data regarding NO. This molecule is one of the most potent vasodilators; however, its release apparently does not depend on the action of BTX [14].

The impact of BTX on the vascular tone is the most obvious during treatment of the Frey's syndrome since it reduces the manifestations of skin flushing. Despite the fact that so far the level of evidence for this therapeutic indication of BTX is only 4 [15], the majority of publications suggest its reliable efficacy in respect of elimination of the major symptoms of this disease including the flushing.

The relevance of BTX use for treatment of menopausal disorders is less obvious. On the one hand, the experiments carried out as a part of an interesting study by Crandall team [12] demonstrated that increase in blood circulation during postmenopausal hot flashes was mediated primarily through BTX-sensitive nerves. On the other hand, other authors believe that NO plays the most important role in vasodilation during menopausal flushes [16], while its release is weakly dependent on the BTX-induced block of sympathetic transmission [14]. In addition, the symptoms of menopausal hot flushes are systemic, while BTX can only be used locally, thus providing no radical solution of the problem [17].

The mechanisms of vascular tone regulation are extremely complicated and include multiple pathways. In different disorders, some elements of this system may be strongly affected, while the others are weakly affected. In the presented clinical case report we can observe a paralytic vascular reaction at BTX injections sites in a healthy and relatively young female patient with stress- and hot-flushing history. According to published data and our own clinical experience, we can conclude that this reaction is quite uncommon. In some people, it is probably related to certain individual peculiarities of the vascular tone regulation, e.g. more important role of acetylcholine as a primary mediator of cutaneous vasodilation. That is why it is of particular interest to evaluate the experience of using BTX in healthy volunteers or healthy people experiencing facial flushing.

In 2004, Yuraitis M & Jacob CI [8] described a case of successful use of BTX in a patient suffering from persistent facial flushing, in whom multiple pulsed dye laser treatments had been proven ineffective. More recent prospective study, which enrolled 18 female and 4 male subjects, aged 18 to 48 years with severe idiopathic neck and anterior chest wall flushing confirmed that intradermal injections of BTX were effective and safe therapy for facial flushing [10]. This conclusion was made based on comparison of the DLQI (Dermatology Quality of life Index questionnaire) parameters assessed before and after treatment. Other similar in design study that enrolled 24 female subjects aged 18 to 60 years with facial flushing also confirmed the efficacy of BTX use in elimination of flushing symptoms [9].

However, there are negative opinions on the efficacy of therapy for facial flushing with BTX. In 2011, a group of Korean investigators published the results of a randomized, split-face trial for evaluation of efficacy of BTX-B treatment of facial flushing [18], which enrolled fifteen Korean subjects who complained of facial flushing. Changes in skin tone during flushing episodes were evaluated using an overall self-assessment and an objective mexameter. The results of this study suggest that BTX-B is ineffective in treatment of facial flushing. However, it should be taken into account that in this case BTX-B was used, whose mechanism of action is similar to BTX-A, but not identical.

Conclusion

The adverse effect (pale patches against hyperemic background at the injections sites) of BTX used for aesthetic indications is a manifestation of individual peculiarities of certain patients. The mechanisms underlying the process of vasodilation imply the involvement of different neurotransmitters. Further studies are required to determine the exact role of each of them. BTX may exert a significant effect on the vascular tone regulation causing blockade of synaptic transmission of acetylcholine and associated co-transmitters without affecting the activity of the others.

Acknowledgement

None.

Conflict of Interest

The authors declared that there no conflicts of interest.

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