

Single Case

Persistent Facial Blanching after Botulinum Toxin Injection

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Keywords

Facial blanching · Vasodilation · Botulinum toxin

Abstract

We report the case of a 38-year-old male patient who presented with blanching of the face after strenuous exercise or physical exertion. The symptoms regressed in a relaxed state. Three years before presentation, he underwent botulinum toxin injections in the affected areas of the face. Facial blanching is a rare side effect of botulinum toxin injection. The postulated pathophysiology involves different transmitters mainly acetylcholine as well as co-transmitters implicated in vasodilation. Usually, facial blanching resolves shortly after waning of the botulinum toxin. However, in our case, the symptoms persisted for a longer time. Till date, therapy options for post-botulinum facial blanching are lacking, mainly due to the temporary aspect of the disease.

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Introduction

This case report shows a rare side effect of botulinum toxin injection (BTI), the facial blanching (FB).

Case Report

A 38-year-old Caucasian man presented to our outpatient department with a 2-year history of FB on his forehead and cheeks (Fig. 1). Three years ago, the patient underwent BTIs in these affected areas. The lesions appear after stress, physical activity, sweating, or head

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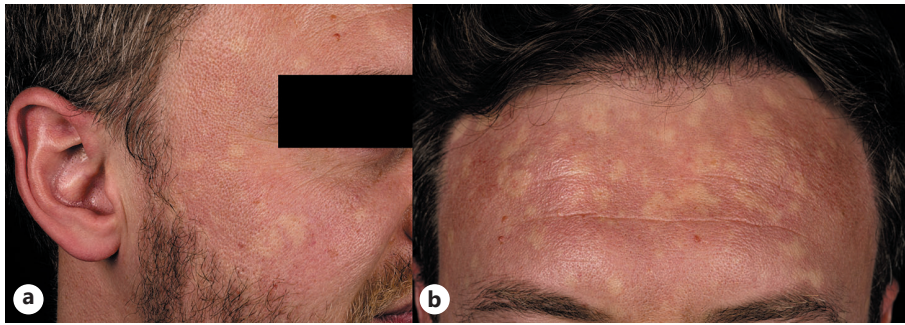


Fig. 1. **a** Lateral view of the right cheek showing whitish macules on a rather hyperemic background. **b** Frontal view showing the patient's forehead after bowing his head several times.

movements and are usually not visible in a normal, relaxed state. The lesions are otherwise asymptomatic and are not associated with pain or sensory problems. Sweating is not affected. There was a temporal delay between the injections and the development of the lesions. Specific details about the injections (name, duration, dose, injection site, etc.) could not be provided. The patient denies having blanching on other locations; he did not have any further injections, cosmetic interventions, infections, or trauma to the face prior to the start of symptoms. The patient has no relevant medical history (especially for vascular anomalies) and does not take any medication.

Discussion

BTI especially botulinum toxin A is a very common cosmetic procedure. Botulinum toxin is a potent neurotoxin produced by the bacteria *Clostridium botulinum* [1, 2]. The neurotoxin binds to receptors on cholinergic nerve terminals and causes a reversible inhibition of acetylcholine release by presynaptic vesicles. The latter leads to flaccid paralysis [1].

Many adverse events have been reported, most of them occurring within a few days after treatment, depending on the injection site and administered volume. These include local reactions such as redness, swelling, hematoma formation, and pain at the injection site. Less commonly, allergic reactions, infections, fever, and other flu-like symptoms can occur. Other neurologic side effects like hypoesthesia, paresthesia, diplopia as well as esotropia have been described [3, 4].

FB is characterized by whitish patches on an erythematous background. The main causes of FB are iatrogenic and include injections of intralesional steroids, local anesthetics, and cosmetic fillers that sometimes lead to intravascular cannulation, as well as the topical application of steroids [5, 6] or sympathomimetic agents such as brimonidine. The differential diagnosis includes facial Raynaud's disease and vascular malformations in the pediatric population.

Interestingly, botulinum toxin can decrease skin flushing and is thus used as a treatment in Frey's syndrome [7], as well as a treatment against facial erythema in rosacea [8]. FB has also been described after BTI, with the first case reported in 2012 by Khan et al. [9].

The exact pathophysiology of BTI-associated FB is still unknown. Cutaneous vasodilation depends on different transmitters, most importantly acetylcholine whose exocytosis from synaptic vesicles is inhibited by BTI [9]. FB is mainly prominent during phases of extended physical activities where the need for vasodilation is increased. Kellogg et al. [10] examined the cutaneous vascular conductance under different conditions including cholinergic nerve

blockade and heat stress. They showed that a selective presynaptic cholinergic nerve blockade with botulinum toxin affects active vasodilator response to hyperthermia [10]. Furthermore, other co-transmitters including prostaglandins, the endothelium-derived hyperpolarizing factor, and nitric oxide have been implicated in vasodilation [9]. Moreover, botulinum toxin inhibits the release of inflammatory mediators such as substance P and calcitonin gene-related peptide which have a vasodilating effect [11].

Most reported cases of BTI-associated FB involve younger adults (<40). Warren et al. [12] hypothesized that this demographic feature is due to the fact that the younger population exercises more thus requiring more acetylcholine leading to a more frequent appearance of FB.

FB usually recedes spontaneously as the effect of the botulinum toxin or local anesthetics (with or without adrenaline) wears off [5, 6]. Even in the case of intra-arterial injections of local anesthetics, blanching seems to be self-limiting. In the case of our patient, the persistence of FB, lasting for several years during physical exertion, is unusual. We hypothesize that the BTI in our patient disrupted vasodilating mechanisms or that the acetylcholine receptors might have been downregulated. There are no causal treatment approaches on record yet.

Conclusion

FB is a rare adverse event following BTI with unknown etiology. It has been hypothesized that a paralytic vascular reaction to botulinum injection takes place. To shed more light on the potential pathophysiology of FB, additional research including more basic science and translational studies are necessary. This neuro-cutaneous phenomenon is usually self-limiting but can, as in our case, last for a longer period of time. In conclusion, dermatologists should be familiar with this rare but significant side effect of BTI to advise patients adequately.

Statement of Ethics

The patient gave us written informed consent to perform all necessary investigations, to take clinical photographs, and to use them for research purposes and publication. Ethical approval is not required for this study in accordance with local or national guidelines.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

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Author Contributions

Fouad Mitri, Katharina Anna Kälber, Alexander Enk, and Ferdinand Toberer contributed to the preparation of the manuscript, had full access to the data, and take responsibility for the integrity of the data and the accuracy of the analysis.

Data Availability Statement

All data underlying the results are available as part of the article, and no additional source data are required. Further inquiries can be directed to the corresponding author Fouad Mitri.

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