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CASE REPORT
Cosmetic

Central Forehead Ischemic Skin Injury following Glabellar Botulinum: A Paradigm Microshift?

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Summary: Vascular occlusion events have surged in incidence due to the increased popularity of cosmetic injectables. Ostensibly, treatments that involve nonparticulate solutions, such as botulinum, have traditionally been thought to carry no risk of vaso-occlusive complications. In this article, we report the first published instance of a suspected ischemic skin injury after botulinum injection to the glabella and surmise on the potential etiological mechanisms that may underlie these rare occurrences. *(Plast Reconstr Surg Glob Open 2023; 11:e4865; doi: 10.1097/GOX.0000000000004865; Published online 10 March 2023.)*

The growing incidence of vascular injuries stemming from cosmetic injectable treatments has prompted a renewed interest into the etiology of iatrogenic arterial occlusions.[1] Despite the currently described mechanisms of injury involving particulate mixtures, such as pharmacologic suspensions and dermal filler gels, occurrences of vascular injuries arising from nonparticulate solutions, such as botulinum, have raised the specter of additional causative agents of arterial obstruction.[2,3] In this report, we describe a case of suspected ischemic insult involving the supratrochlear region of the forehead after glabellar botulinum injection.

CASE REPORT

A previously healthy 35-year-old woman presented with discoloration of the central forehead 72 hours after cosmetic botulinum treatment. Medical records review revealed that the patient had received 30 units of onabotulinumtoxinA (Botox, Allergan, Irvine, Calif.), reconstituted in a standard fashion, injected into the glabella (26 units) and lateral brow only (4 units) via a 30G tuberculin syringe, with no other services rendered. Upon glabellar injection, the patient recalled experiencing sudden, transient discomfort over the left central forehead but no other symptoms. Subsequently, over 72 hrs, she noticed the gradual onset of skin discoloration and tenderness affecting the left central forehead. The patient, herself a physician, initiated oral 325 mg aspirin therapy and sought evaluation by facial plastic surgery. Skin examination performed on post injection day 3 revealed livedoid skin changes over the left distal supratrochlear region (Fig. 1A). The remainder of the examination was normal, without neuroophthalmologic abnormalities. A preliminary diagnosis of ischemic injury from suspected arterial occlusion was issued, and the patient was referred for hyperbaric oxygen therapy. She was started on oral cephalexin/valacyclovir and instructed to apply alternating warm/cold compresses. The patient completed three hyperbaric oxygen therapy treatment sessions with favorable clinical response. Over the following 3 weeks, the skin progressed through livedoid discoloration to include mild superficial desquamation and hyperemia but no vesicular rash, cellulitic changes, or tissue necrosis (Fig. 1B, C). The superficial skin changes gradually cleared without permanent sequelae.

DISCUSSION

The growing incidence of iatrogenic vascular injuries arising from cosmetic injections has sparked a heightened degree of scrutiny into the mechanisms of occlusion stemming from these popular treatments. While the occlusive mechanisms of vascular obstruction have been reasonably established for instances involving dermal fillers, the much-rarer occurrences arising from nonparticulate solutions, such as botulinum, present an etiological enigma that remains unsolved.

Historically, instances of ischemic skin injury arising from accidental intraarterial injections of pharmaceutical mixtures have been assigned the broad diagnosis of *embolia cutis medicamentosa*, known as Nicolau syndrome, originally described a century ago. However, because the properties of injectable medications vary widely (ranging from innocuous IV solutions to potentially-toxic particulate

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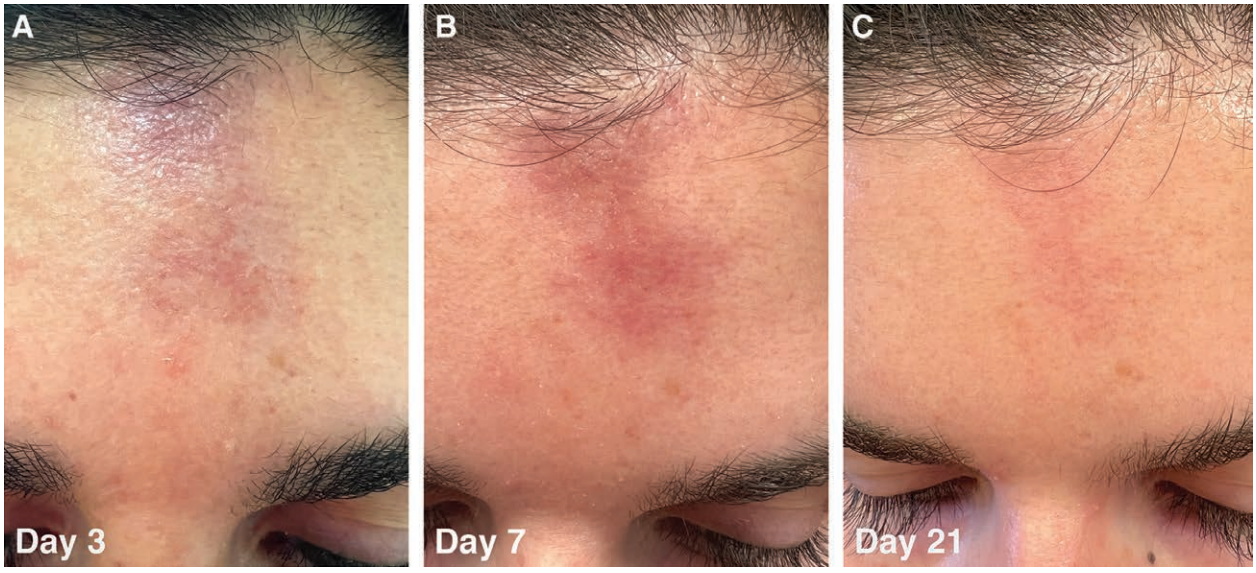

Fig. 1. Appearance of the patient's forehead at different time points after injury: 72 hours (A), 1 week (B), and 3 weeks (C).

suspensions or gels not approved for intravascular therapy), this etiology itself demands further inquiry into the specific inciting agent. Correspondingly, several studies have since shown that Nicolau syndrome is likely to arise with pharmaceutical suspensions (capable of generating embolic/thromboembolic showers when accidentally injected intraarterially) or with solutions of an arterionoxic agent, such as thiopentone, capable of inducing intense arteriospasm and/or intravascular coagulation.[4,5]

Type A botulinum toxin preparations, which have been available for intramuscular/dermal injection in the United States for more than 30 years, consist of lyophilized, albumin-stabilized powders that produce clear homogeneous solutions upon saline reconstitution. Numerous toxicity studies in primates have failed to reveal any potential for intravascular thromboembolic reactions, and its routine intramuscular use in humans regularly places it within well-vascularized tissues with an incredible record of safety.[6] Therefore, the traditional mechanisms of arterial occlusion invoked for instances of Nicolau syndrome cannot be used to fully explain the case herein described or the additional rare cases reported in the literature.[2,3] As such, we advance the possibility of an embolic event involving an external contaminant—in particular, one from an especially common source: needle micro-coring.

Needle coring has been recognized as a potential source of contaminating debris in parenteral solutions since the 1950s.[7] Needle cores are cylindrical fragments of dermal tissue or rubber that are accidentally punched and captured by the sharp bevel of a needle and remain trapped within its lumen. Studies evaluating the frequency of needle coring have pointed to an incidence ranging between 60% and 80% with conventional 18G–25G needles.[8] With the advent of modern, ultra-fine needles, the concept of micro-coring (ie, submillimeter, 1–1000 μm) has been added to the lexicon. A recent study by Soares et al showed that 31G tuberculin needles (routinely used in botulinum injections) can capture dermal micro-cores measuring 100–300 μm in size (Fig. 2), with an overall coring incidence of 0.7%.[9] The size of cored fragments produced by 31G needles is determined by the shape and angulation of the bevel and, at 300 μm, is capable of occluding many cutaneous arterial conduits, including the distal supratrochlear artery, which measures ~300 μm at the level of the midforehead.[10] In addition, dermal micro-cores may further incite an intravascular thrombotic response capable of exacerbating the extent of injury. Given the infrequency of micro-coring, and the low likelihood of capture with simultaneous intraarterial injection of a micro-core, this etiology presents a plausible explanation for these extremely rare injuries, though further research remains necessary for confirmation.

In this instance, the absence of histological findings precludes the conclusive determination of the cause of injury. Nonetheless, the limited cutaneous territory affected suggests a distal blockade characteristic of an

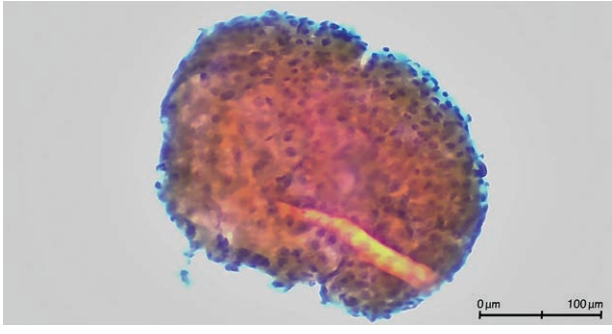

Fig. 2. High-power microscopic images of ThinPrep coring samples, revealing the presence of epithelial core measuring up to 300 μm in the longest dimension.

embolic phenomenon. Furthermore, the timing, presentation, and absence of other skin changes (such as the vesicular eruption characteristic of *zoster*, or cellulitic features of bacterial infection) exclude an infectious etiology. This report may thus describe the first suspected ischemic skin injury arising from botulinum injection. Aesthetic practitioners must be mindful of this rare etiology to minimize delays in diagnosis and therapeutic interventions.

CONCLUSIONS

Despite the rarity of ischemic events arising from nonparticulate injectable treatments, these potentially damaging occurrences still present a risk to patients. We describe an instance of suspected ischemic injury after botulinum injection into the glabella and surmise on the potential etiologies underlying these acute vascular events. Practitioners should keep this rare etiology in mind to help minimize delays in the identification and management of this infrequent complication.

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PATIENT CONSENT

The patient provided written consent for the use of her image.

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