Morphea-like lesions after botulinum toxin A injections

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INTRODUCTION

There is a marked global increase in the administration of botulinum toxin A (BTXA) for the management of facial rhytids. In proper hands, this procedure is safe, with rare, mild, and self-limiting adverse effects. Because of the extensive worldwide use of BTXA, it is noteworthy when a new possible adverse event is reported. We describe a thus-far unpublished side effect of aesthetic BTXA injections, specifically the development of morphea-like lesions, a phenomenon identified in 3 separate events at unrelated medical centers.

Abbreviation used:
BTXA: botulinum toxin A

CASE SERIES

Case 1

A healthy 35-year-old white woman with an unremarkable medical history and 3-year history of successful treatments with BTXA at another medical facility, was referred to our clinic (Israel) for the diagnosis and management of asymptomatic lesions on her lateral forehead. Notably, 6 weeks before the examination, she had been injected with BTXA for the softening of glabellar and forehead rhytids. By report, 3 weeks after the initial injection, a touch-up treatment was performed to enhance the results on the forehead with the resulting lesions appearing 1 week thereafter.

On examination, 3 round atrophic plaques ranging from 0.5 to 1.0 cm in diameter were noted on the left upper forehead without any associated textural changes (Fig 1, *A*). The injecting physician confirmed that there had been no intentional or unintentional injection of any pharmaceutical agent other than BTXA. The patient was scheduled for skin biopsy to exclude new-onset morphea; however, prior to the performance of the biopsy there was full resolution of the lesions (Fig 1, *B*). The lesions existed overall about 4 weeks.

Case 2

A 36-year-old white woman with a noncontributory medical history and 3 prior uneventful sessions of BTXA injections, presented with a depression on her forehead 1 week after her fourth injection session (In the United States). On examination, noted just above the right eyebrow, there was a marked area of dermal tissue loss (Fig 2, *A*). Concern was for coup de sabre or an alternative presentation of new-onset morphea and a representative biopsy obtained for histopathologic examination.

Pathologic examination found a normal distribution of dermal collagen, adnexal structures, and underlying subcutis. Elastic tissue staining found elastic tissue fibers in normal number and distribution and no evidence of morphea obtained (Fig 2, *B*).

Over the course of the next 3 months, the patient showed gradual resolution of the lesions. Of note, the patient has continued to have BTXA treatments with excellent cosmetic outcomes.

Case 3

A 31-year old white woman with a history notable for atopic dermatitis received BTXA injections for the treatment of glabella, forehead, and periorbital wrinkles (Russia). This was her second injection session with BTXA, the prior one was 2 years earlier. At her 2-week follow-up, satisfactory outcomes were observed. One week subsequently, a

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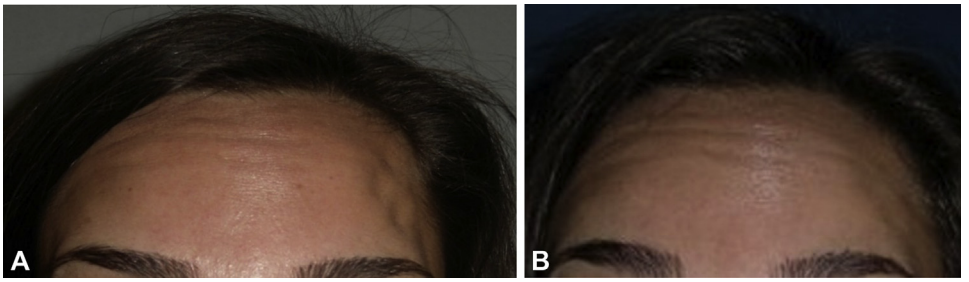

Fig 1. **A**, Initial presentation 6 weeks after BTXA injections to the. glabella and forehead. Three atrophic plaques of the upper forehead. **B**, Follow-up 4 weeks later. Spontaneous resolution of atrophic plaques.

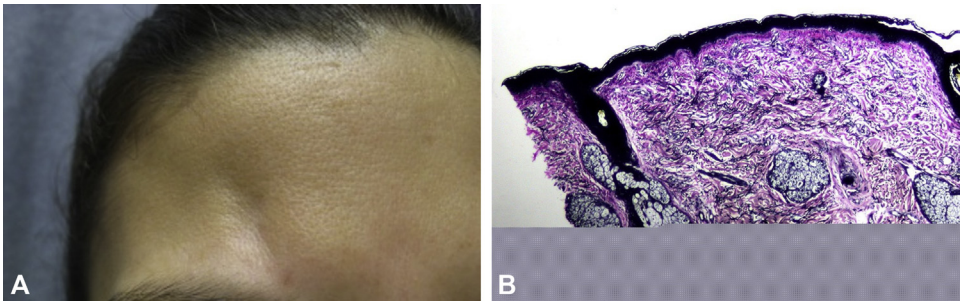

Fig 2. **A**, Initial presentation 1 week after BTXA injection to glabella. and forehead. A dent above the right brow. **B**, Skin biopsy. Normal distribution of dermal collagen, adnexal structures, and elastic tissue.

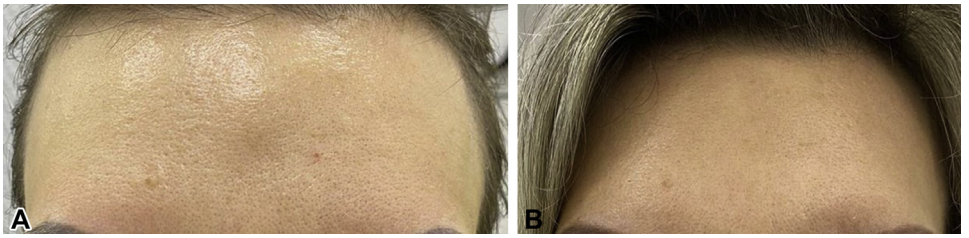

Fig 3. **A**, Initial presentation 3 weeks after BTXA injection to glabella, forehead, and periorbital area. A 1-cm diameter round atrophic lesion is seen in the lower part of the central forehead. **B**, Follow-up 2 weeks later. Spontaneous resolution of the defect.

depression developed in the treatment area of the forehead. On examination, a round atrophic area 1 cm in diameter without any overlying epidermal changes was noted in the lower part of the central forehead (Fig 3, *A*). On the follow-up visit 2 weeks later, the defect had entirely resolved (Fig 3, *B*).

DISCUSSION

We describe 3 discrete cases of atrophic circular depressions on the forehead, appearing subsequent to aesthetic BTXA injections. Patients' histories and previous treatment sessions were uneventful, and histology obtained from one of the patients precluded an unrelated skin disorder.

A single publication describes atrophic lesions in a patient treated by BTXA for tension headaches.[1] In that report, injections were performed (among other sites) to the corrugator musculature. At the follow-up visit, bilateral round indentations were noted at the corrugator injection sites. The indentations described are remarkably similar to the findings in our patients.

Most BTXA-related side effects can be explained by their mechanisms of action.[2] When BTXA is injected into skeletal muscles, such as the masseter or gastrocnemius, transient muscular atrophy is intentionally produced. BTXA is used in this manner to recontour the lower face or refine the shape of the calves.[3,4] Atrophy of another skeletal muscle, the temporalis muscle, was also reported as a result of BTXA injection to treat migraine headaches, causing an hourglass deformity of the upper face.[5]

Clinically visible atrophy of the mimetic muscles after cosmetic BTXA injections has not yet been reported in the dermatologic literature. Yet, when assessed by magnetic resonance imaging, the volume of the mimetic procerus muscle decreases after a single BTXA injection for about 12 months.[6]

We hypothesize that focal atrophy of the muscle can be rarely induced by BTXA injections because of a transient lack of neural stimulation (neurogenic atrophy). This hypothesis is supported by the round shape of the atrophic depressions that follow the action halo of the neuroprotein.[7]

This phenomenon might be completely unrelated to the mechanism of action of the neuroprotein. In a recently published case report of a sclerotic depression on a forehead of a 42-year-old man following BTXA injection, there is a striking clinical resemblance to our cases. In that case, the depression was found to result from BTXA that had been contaminated with a syringe lubricant.[8] There is a widespread lack of awareness to the presence of silicone oil as a syringe lubricant in most of the commercially available syringes. Skin reactions can be caused by silicone when its droplets are dislocated while tapping the syringe to remove bubbles. If not suspected, histologic proof of the presence of silicone oil is near impossible, as tissue sample requires nonstandard preparation before analysis for the oil presence. The biopsy taken in case 2 did not show deeper tissues; therefore, any direct or indirect evidence of silicone-induced reaction could not be definitively established. If a syringe lubricant does play a role, short-term existence of the clinical findings can be possibly explained by a negligible amount of the silicone oil, which can be removed successfully by tissue macrophages. In many instances, skin reactions are misinterpreted to occur from the injectable drug itself rather than a potential contaminant.[9,10]

We report 3 cases of morphea-like changes occurring after aesthetic BTXA injection. These cases represent a previously unreported adverse effect of BTXA. Reported from 3 unrelated medical centers, the cases carry striking clinical resemblance. We propose that the pathologic mechanism is either related to focal neurogenic atrophy of the injected muscle or to dislocation of minuscule amount of syringe lubricant into the injected drug. If the latter is the mechanism, flushing of the syringe, or avoiding of tapping on it, would likely minimize the risk of its occurrence.[8]

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