

## BRIEF ARTICLE

## Turning Down the Fire: The Role of Botulinum Toxin Microdroplets in Refractory Rosacea Erythema

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### ABSTRACT

**Introduction:** Dermal “micro-injections” of botulinum toxin A (BTX-A) treatment can improve facial flushing and erythema in patients with refractory rosacea. We present a case of a patient with longstanding papulo-pustular rosacea with flushing, refractory to laser, topical and systemic therapies, where intradermal microdroplet BTX-A injections successfully controlled erythema and flushing.

**Case Description:** A 49-year-old White female with a 4-year history of refractory papulo-pustular rosacea presented with bright, central facial erythema and telangiectasias after failing multiple 595 nm pulsed dye laser, topical (azelaic acid 15% gel, 0.025% tretinoin cream, and metronidazole cream 0.75%) and systemic (isotretinoin 20 mg daily, spironolactone 25 mg daily and doxycycline 100 mg twice daily for 14 days) treatments. At treatment 1, 20 U of BTX-A was injected intradermally (0.05 mL of 1.25 IU/0.1 mL per microdroplet) to the erythematous lesions. Treatment 2 was performed at her 4-week follow-up where we administered 15 U of BTX-A intradermally (0.05 mL of 1.25 IU/0.1 mL per microdroplet). The patient was seen 4, 8, and 16 weeks after her second treatment where no BTX-A was administered due to a significant reduction in erythema and lasting results.

**Discussion:** Significant clinical improvement and patient satisfaction were achieved. No adverse events were reported after treatment aside from mild, localized injection site pain during the procedure. BTX-A administered as intradermal microdroplet injects can be a safe and efficacious option in the treatment of refractory rosacea erythema. Microbotox may be an effective adjunct, especially when topical and systemic therapies have failed.

### INTRODUCTION

Growing interest and use of botulinum neuromodulators in the battle against skin aging has led to the discovery of several novel, off-label uses. After years of proven efficacy and safety, anecdotal reports of improved facial flushing, erythema and inflammation are emerging following botulinum toxin A (BTX-A) treatment for cosmetic rejuvenation. Dilute, intradermal BTX-A (microdroplet BTX-A) can improve

facial erythema and skin quality, as denoted by reduced sebum production and facial pores. Several studies and case reports have reported clinical improvement in flushing, erythema, and facial rejuvenation after treatment with BTX-A.<sup>1</sup> We present a case of refractory papulo-pustular rosacea in which intradermal microdroplet BTX-A injections were successfully used to control erythema.

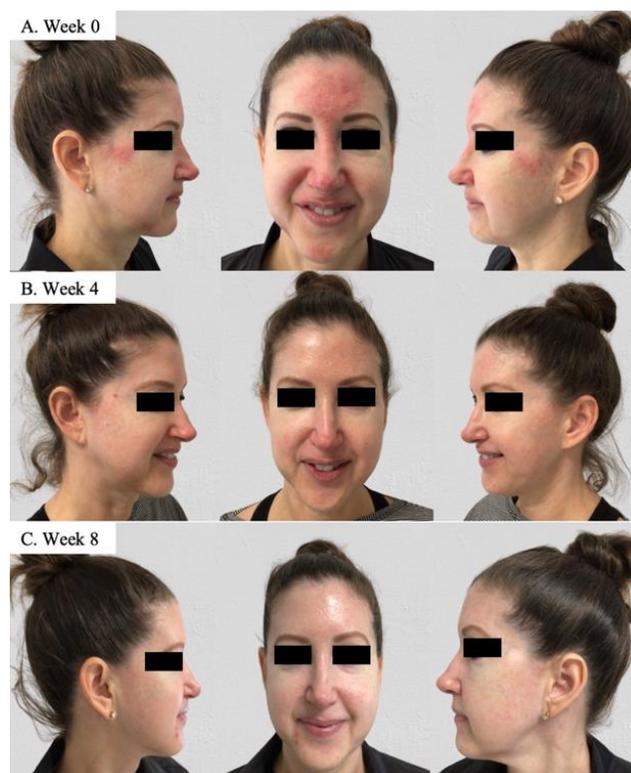
### CASE DESCRIPTION

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A 49-year-old White, Non-Hispanic female with a 4-year history of refractory papulopustular rosacea presented to our tertiary care dermatology clinic with bright, central facial erythema and telangiectasias after failing multiple laser treatments, topical therapies, and systemic medications. Episodes of facial erythema and flushing were provoked by heat, exercise, sun exposure, and spicy foods. Her past medical history included complex regional pain syndrome, breast cancer (taking tamoxifen), hormonal acne, and a positive antinuclear antibody test. She had previously failed extensive treatment, including nine treatments of pulsed dye laser (595 nm) over the past three years. Energy densities ranging from 6 to 6.5 J/cm<sup>2</sup>, pulse durations from 3-6 ms using the 7- or 10-mm hand piece, and total pulses ranging from 53-153 were tried. Additionally, several topicals (azelaic acid 15% gel, 0.025% tretinoin cream, and metronidazole cream 0.75%) and systemic therapies (isotretinoin 20 mg daily, spironolactone 25 mg daily, and doxycycline 100 mg twice daily) were trialed with minimal, inconsistent improvement.

The patient received a total of 35 U of intradermal microdroplet BTX-A over two treatments. Botulinum toxin A (Allergan, Campbell, Calif., USA) was reconstituted with sterile saline to achieve the desired concentration. The microdroplet BTX-A dilution used was chosen in reference to a previous study.<sup>2</sup> At treatment 1, 20 U of BTX-A was injected intradermally at 5 mm intervals (0.05 mL of 1.25 IU/0.1 mL per microdroplet) to erythematous lesions at the glabella, cheek, nose and chin using a 30-gauge syringe (Fig 1). Isotretinoin 20 mg daily was concomitantly started at treatment 1. After 4 weeks, her condition improved significantly with some persistent flushing and no change in facial movements or animations. Treatment 2 was performed at

her 4-week follow-up when we administered 15 U of BTX-A at the same dilutions, and intervals, and sites. The patient was seen in follow up 4, 8, and 16 weeks after her second treatment. No BTX-A was administered due to a significant reduction in erythema and lasting results. No adverse events were reported after treatment aside from mild, localized pain at the injection site during the procedure.



**Figure 1.** 49-year-old female with refractory papulopustular rosacea erythema (a) before receiving intradermal microdroplet BTX-A injections for facial erythema and flushing (b) 4 weeks after treatment 1 with 20 U of BTX-A (0.05 mL of 1.25 IU/0.1 mL per microdroplet) injected at 5 mm intervals to erythematous lesions on the glabella, cheek, nose, and chin (c) 4 weeks after treatment 2 receiving 15 U BTX-A at the same dilutions, intervals, and sites.

## DISCUSSION

Rosacea, a common, chronic inflammatory skin condition, can present with varying clinical symptoms depending on disease classification and stage. Patients may suffer from intermittent or persistent erythema, inflammatory papules and pustules, phymatous change, or ocular ailments.<sup>3</sup> Rosacea erythema and flushing are frequently observed in erythematotelangiectatic or papulopustular subtypes. Anecdotal reports have linked rosacea facial erythema to diminished quality of life and self-confidence. To date, effective treatment modalities remain scarce with limited efficacy, particularly for patients with telangiectasias or flushing.

While the pathogenesis of facial erythema in rosacea and the role of BTX-A remains unclear, neurogenic and immunologic etiologies have been thought to play a role. BTX-A has been shown to diminish neurogenic inflammation by way of inhibiting vasodilating neuropeptides (acetylcholine and vasoactive intestinal peptide) and neurotransmitters (substance P and calcitonin gene-related peptide) which may play a role in rosacea's complex mechanism.<sup>3</sup> Additionally, BTX-A has been shown to significantly reduce mast cell counts and their subsequent pro-inflammatory and vasoactive secretions, which are regularly elevated in rosacea erythema.<sup>4</sup> Studies also suggest that upregulation of matrix metalloproteinases (MMPs) may play a potential role in telangiectasia formation by influencing collagen formation.<sup>5</sup> In one study by Oh et al., BTX-A has been reported to enhance type I collagen formation while also diminishing the influence of MMPs on human dermal fibroblasts.<sup>6</sup>

Significant clinical improvement and patient satisfaction were achieved with no major adverse effects. Although the patient was

concomitantly treated with both BTX-A and isotretinoin, we attribute the reduction in erythema and flushing to her microdroplet BTX-A treatments since her most significant improvement was observed in the injected areas. This study is limited by the potential confounder of isotretinoin treatment, lack of control group, and no scoring or grading system used to assess outcomes. BTX-A administered as intradermal microdroplet injections can be a safe and efficacious option in the treatment of refractory rosacea, especially when lasers, topical, and systemic therapies have failed.

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