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Case Report

The use of Botulinum Toxin in digital reconstruction of patients affected by Raynaud's phenomenon: a case report

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ABSTRACT

Background: Surgical reconstruction in patients affected by Raynaud's phenomenon is a challenging procedure due to the vascular impairment, which prevents flap survival and secondary healing. Botulinum Neurotoxin-A showed vasodilatatory and angiogenic properties in animal studies, increasing blood flow in flap surgery.

Case presentation: We report an off-label application of Botulinum Neurotoxin-A used for digital reconstruction in a patient affected by Reynaud's phenomenon, in order to enhance flap survival and avoid digital amputation. Complete flap survival and symptomatic relief were achieved.

Conclusions: This new approach may be extremely valuable when performing flap reconstruction in patients affected by RP, allowing for increased vascular safety as well as symptomatic improvement.

Background

Raynaud's phenomenon (RP) is a transient digital ischemia that occurs following exposure to cold temperature or emotional distress. The exaggerated vasospastic response induces a triphasic course of paleness, cyanosis and erythema, often associated with pain and paresthesia [1]. Nonhealing ulceration is the most feared complication, further hampering hand function. The compromised local vascularization may not allow for secondary healing, thus often leading to bone exposure. In such cases, flap reconstruction is mandatory to avoid amputation. However, the local vasospasm may severely jeopardize flap survival and, thus, RP is often considered a contraindication to finger reconstruction by local flaps. The use of Botulinum neurotoxin-A (BoNT-A) was primarily conceived to inhibit muscle contraction. Once internalized in the nerve terminal, the toxin cleaves the synaptosomal associated protein-25 (SNAP-25), thus blocking acetylcholine and other vesicles migration and release. Recently, several papers reported the off-label use of BoNT-A in RP, achieving both symptomatic and functional improvements [2]. Moreover, experimental studies described a beneficial effect on flap vascularization and survival, although all limited to animal models [3, 4]. As a consequence, pre-operative BoNT-A injection may be a valuable tool to achieve safer reconstruction when performing digital flaps in patients affected by RP, with the added bonus of symptomatic improvement. The aim of this paper is to describe a previously unreported technique to improve digital flap survival in RP patients by mean of BoNT-A injection.

Case Presentation

A 39-year old patient, affected by scleroderma, was referred to our Department for a non-healing ulceration with bone exposure and partial necrosis at the distal phalanx of the index finger of the left hand (Figure 1a). The patient had previously undergone intravenous administration of iloprost (0.05 mg) and local treatment with polyurethane foam, with no improvement. Amputation of the distal phalanx and coverage with an advancement homo-digital volar skin flap were planned. One week before surgery, BoNT-A injections were performed. Specifically, 100 IU of BoNT-A (Botox®, Allergan, Inc., Irvine, CA) were reconstituted in 2 mL of preservative-free saline solution. Injections were performed in both hands, targeting each neurovascular bundle in the palm at the level of the A1 pulley [5]. Ten IU were injected for each neurovascular bundle. Moreover, 10 IU were injected sub dermally just proximally to the pedicle of the planned flap and gently massaged. (Figure 2). Two days after treatment, the patient reported pain reduction. One week later,

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partial amputation of the distal phalanx and coverage with an advancement flap were performed. The post-operative course was uneventful, with complete flap survival (Figure 1b). The vascular improvement was assessed clinically. Pre-operatively, and two-weeks post-operatively, the patient was asked to rate pain severity, color change (pink as opposed to blue or white fingers) and cold intolerance by mean of 0-to-10 Visual Analogue Scale. Moreover, she was asked to report the number and duration of the vasospastic attacks and to fill the Raynaud's Condition Score [6].

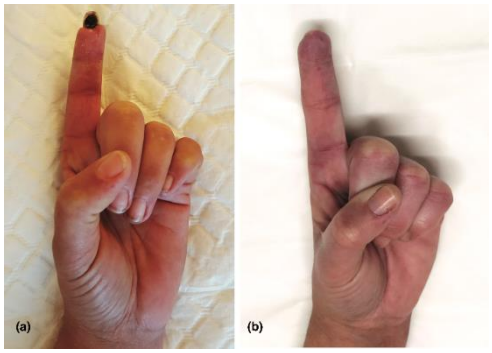

Figure 1: Digital ulceration in patient affected by sclerodermia.

The patient's digital ulceration was reconstructed using a local flap following Botulinum Neurotoxin A administration. (a) Pre-operative view. (b) 1 year-follow up post-operative view.

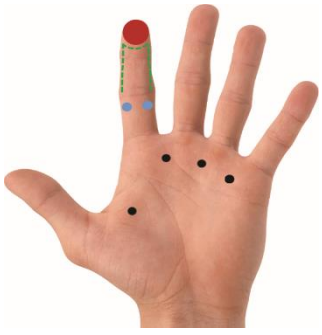

Figure 2: Injection technique model.

The injection technique for distal finger defects (red area): 10 IU are injected at each black dot, targeting the neurovascular bundle in the palm at the level of the A1 pulley; 5 IU at injected subdermally at each blue dot, namely at the base of the planned flap (green lines: skin incisions for flap harvesting).

Results are summarized in (Table 1). The symptomatic improvements in all the digits lasted 6 months. Interestingly, at 2-years follow-up, the patient reported that RP did not occur anymore on the operated finger since surgery.

Raynaud's phenomenon may be "primary" (also referred to as Raynaud's disease), when it is an isolated symptom, or "secondary" (Raynaud's syndrome) if it associates with collagen diseases, medications, physical etiologies, paraneoplastic or endocrine syndromes [2]. The former was found to have a prevalence of 8.1% in men and 9.6% in women; the latter of 18.6% and 19.7% in men and women, respectively [7]. Clinically, it has triphasic course due to vasoconstriction (paleness) followed by blood desaturation (cyanosis) and reactive hyperemia (erythema). In spite of worldwide efforts, to date, there are no clear-cut therapeutic guidelines to address RP and many medications are used off-label with sometimes contrasting results [1]. Moreover, pain and non-healing ulcerations are common complications. Such wounds are often challenging because of the vascular impairment preventing secondary healing. When the bone is affected, or exposed, surgical debridement and reconstruction should be performed. However, such procedures may fail due to post-operative vasospastic attacks, resulting in flap necrosis and the subsequent need for adjunctive, often more difficult, reconstructive techniques or amputation. Although BoNT-A was found to be beneficial for pain reduction and wound healing in both primary and secondary RP[2], the body of evidence about its effects on increasing flap survival is mainly limited to animal studies. Specifically, BoNT-A may increase blood flow by mean of vasodilation. The increased vessels diameter results from chemical sympathectomy, due to the inhibition of norepinephrine release, the abolished cholinergic inhibition of neurogenic relaxation and the prevention of recruitment and activity of α_2 adrenergic receptors [2, 8]. Moreover, in RP patients, the lack of substance P, glutamate and calcitonin gene-related protein releases reduces nociception and, consequently, the sympathetic stimulation induced by pain [9, 10]. Some animal studies also reported an increase in Vascular Endothelial Growth Factor (VEGF), an inducer of angiogenesis, following BoNT-A administration [11]. To the author's knowledge, this is the first report of the use of BoNT-A to improve flap survival in humans. The main limitation of this study is the lack of assessment of blood flow by doppler or angiography.

Table 1: Preoperative and postoperative clinical assessment using VAS score.

	Preoperative assessment	Two weeks follow–up assessment
Pain severity	10	3
Color change	7	2
Cold intolerance	10	6
N. of daily attacks	3	1
Mean duration of attacks	3	2
Raynaud's Condition Score	10	1

Conclusions

The described technique can be also used when other finger flaps are indicated, such as Moberg's, Atasoy's or Kutler's [12-14]. Such an approach may be extremely valuable when performing flap reconstruction in patients affected by RP, allowing for increased vascular safety as well as symptomatic improvement.

Declarations

Conflict of Interest:

The authors declare that they have no conflict of interest

Informed consent:

Informed consent was obtained from all individual participants included in the study.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in

2008 (5). Informed consent was obtained from all patients for being included in the study.

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