MÆDICA - a Journal of Clinical Medicine

CASE REPORT

MAEDICA – a Journal of Clinical Medicine
2024; 19(1): 182-185
https://doi.org/10.26574/maedica.2024.19.1.182

# Case Report on Botulinum Toxin Treatment for Complex Regional Pain Syndrome in a Digit Reconstruction

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*ABSTRACT*

***Objective:*** *To evaluate subcutaneous Botulinum toxin type A (BTX-A) efficacy in alleviating severe allodynia in complex regional pain syndrome (CRPS) type II post-digit reconstruction.*

***Methods and methods:*** *After surgical debridement and flap reconstruction for post-traumatic necrosis, a CRPS type II patient received subcutaneous BTX-A. Assessments tracked symptom changes and daily life improvements.*

***Discussion:*** *There are various CRPS management modalities, including rehabilitation and pharmacology. The limited efficacy of conventional non-steroidal antiinflammatory drugs contrasts with promising subcutaneous BTX-A, offering rapid pain relief.*

***Conclusion:*** *Our case underscores the efficacy of subcutaneous BTX-A in CRPS type II, prompting further research and safe outpatient protocol development.*

**Keywords**: complex regional pain syndrome, digit reconstruction, Botulinum toxin type A.

## INTRODUCTION

Complex regional pain syndrome (CRPS) is a debilitating pain disorder characterised by alterations in sensory, vasomotor and motor systems, often accompanied by oedema (1). While a part of known CRPS cases resolve within a year following onset, the majority of patients endure allodynia and significant disability (2). Despite diverse approaches to pain management, CRPS remains an elusive condition to cure, with prognosis often being less than optimistic.

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*Article received on the 6th of December 2023 and accepted for publication on the 1st of March 2024*

Botulinum toxin type A (BTX-A) treatment has been explored as a potential intervention for pain relief in CRPS (3). Notably, BTX-A emerges as a suggested third-line therapeutic option for managing neuropathic pain, which constitutes a central feature of CRPS (5).

The pathophysiology of CRPS involves peripheral sensitisation driven by neurogenic inflammation as well as central sensitisation (6). Botulinum toxin type A holds promise in mitigating neurogenic inflammation by suppressing nociceptive neuropeptides and may also possess the capacity to inhibit central sensitisation (7). Furthermore, BTX-A injections have been employed for pain alleviation in various central and peripheral neuropathic pain conditions (8, 9).

The effectiveness of BTX-A in alleviating CRPS-associated pain has yielded variable findings. There are reports of substantial pain relief, while others have contended that the procedure was excessively painful to tolerate or had no discernible effect (10, 11).

We report a case of successful treatment of CRPS with BTX-A subcutaneous injections into the base of a proximal phalanx after a crush injury requiring flap reconstruction. ❑

## CASE REPORT

A 47-year-old male patient came to our plastic surgery department with a crush injury to the distal phalanx of his right third digit with medial nail and pulp involvement (Figure 1). He had sustained this injury three months prior to presentation whilst working with cement blocks at work. He was a smoker with no significant comorbidities and did not take any medication. One month after his injury, the pain had not resolved with necrotic skin ensuing and therefore, the patient sought treatment at his local hospital, where he underwent a surgical fingertip debridement with primary closure. Ten days after surgery, he noticed pus and allodynia for which his nail was partially removed to relief pressure, with no antibiotic therapy upon discharge. Shortly after this procedure, he presented for the first time to our department with worsening of postoperative infection of his affected digit.

Upon admission, he underwent surgical finger tip debridement with removal of the remaining nail to treat the underlying soft tissue infection. There were no immediate postoperative complications. After 48 hours of IV antibiotics postoperatively, his wound remained clean and therefore we closed his defect with a V to Y flap. He was safely discharged with instructions to complete his oral course of antibiotics consisting of Augmentin 650 mg three times *per* day. A clinical review four weeks after surgery showed a completely healed reconstruction site with no signs of infection.

**FIGURE 1.** Clinical picture of the third digit at the time of presentation

Forty five days postoperatively, he presented with severe allodynia and paresthesia. Blood tests and vital signs excluded underlying infection with an intact and healed reconstruction wound site. A magnetic resonance imaging (MRI) excluded the possibility of underlying osteomyelitis. There was an inability to mobilise his entire digit with accompanying weakness which resulted in no longer being able to perform daily tasks. Therefore, the patient was diagnosed with type II CRPS according to Budapest criteria (Table 1).

This patient was once again admitted for optimisation of treatment. He was given oral ibuprofen 400 mg every six hours with no benefit, and with a subsequent peripheral nerve block at the base of the affected digit, which provided only temporary pain relief for approximately four hours and was therefore deemed unsustainable. The patient could not tolerate Gabapentin.

| Budapest diagnostic criteria |
|---|
| 1. Continuing pain, disproportionate to any inciting event |
| 2. Must report at least one symptom of the three following categories: |
| - Sensory: reports of hyperesthesia and/or allodynia |
| - Vasomotor: reports of temperature asymmetry and/or skin colour asymmetry |
| - Motor/trophic: reports of decreased range of motion, and/or motor dysfunction (weakness tremor, dystonia) and or trophic changes (hair, nail, skin) |
| 3. Must display at least one sign at the time of evaluation in two or more of the following categories: |
| - Vasomotor: evidence of temperature asymmetry and/or skin colour asymmetry |
| - Edema: evidence of edema, sweating changes |
| - Motor/trophic: evidence of decreased range of motion, and/or motor dysfunction (weakness tremor, dystonia) and or trophic changes (hair, nail, skin) |
| -Motor trophic: evidence of decreased range of motion and/or motor dysfunction |
| 4. There is no other diagnosis that better explains the signs and symptoms |

**TABLE 1.** Budapest diagnostic criteria

The interventions offered to the patient were ineffective whilst his allodynia remained intolerable, which affected all daily activities using his right hand. Subcutaneous injections of BTX-A into the base of the right middle digit was trialled. Botulinum toxin type A injections were performed (Botox®, Allergan hellas, Greece). A total dose of 10 IU across five sites was administered. The allodynia significantly improved within two days. The patient regained function of his hand and his daily activities were slowly re-initiated. A follow-up six months after treatment showed complete resolution of CRPS symptoms. ❑

## DISCUSSION

A spectrum of therapeutic modalities is available for the management of CRPS, encompassing physical rehabilitation, pharmacological interventions and interventional procedures. Within the realm of pharmacotherapy, conventional approaches involving non-steroidal anti-inflammatory drugs (NSAIDs) have demonstrated limited efficacy in producing improvements. Conversely, certain pharmacological agents have showed varying degrees of promise in clinical investigations, including short-course steroids, bisphosphonates, gabapentin and ketamine. Furthermore, the exploration of antioxidant therapy has yielded encouraging findings, most notably high dose of vitamin C. Additional pharmacotherapeutic options involve the utilisation of low-dose naltrexone and BTX-A in the pursuit of ameliorating symptoms (11).

Emerging avenues of investigation encompass the application of BTX-A (12, 13). Previous empirical evidence was primarily confined to isolated case studies employing proximal BTX-A injections for individuals afflicted with CRPS linked to myofascial pain syndrome (MFPS) (13, 14). However, a recent comprehensive study involving 20 patients experiencing refractory CRPS, who underwent BTX-A injections, exhibited a noteworthy reduction in pain scores (7). Furthermore, a recent meta-analysis of 25 randomised controlled trials (RCTs) concluded that BTX-A exhibited efficacy in alleviating pain across a spectrum of conditions, encompassing both muscle-related conditions such as spasticity and dystonia as well as non-muscle-based pain disorders, including CRPS and diabetic neuropathy. This body of evidence provides substantial support for the utilisation of BTX-A as a novel and viable therapeutic approach (15).

Botulinum toxins represent an emerging option against the nociceptive and neuropathic pain condition, possibly by modulating inflammatory mediators such as substance P and calcitonin gene related peptide (10). Attal *et al* reported significant pain relief to peripheral neuropathic pain at six months after administration of BTX-A to human subjects (16).

However, it is worth nothing that there are no reports concerning the treatment of subcutaneous botox injections in a single digit with CRPS. Kwak *et al* reported good benefit from subcutaneous BTX-A injection into the palm of a patient's hand after sustaining a crush injury. However, there was use of peripheral nerve blocks prior to administration of BTX-A which may have aided in the resolution of allodynia. In our patient, we offered an isolated single peripheral block with no benefit, after which we opted to trial BTX-A.

The efficacy of BTX-A in our patient was evident within 48 hours with a singular session of subcutaneous injections, administered in a single session. ❑

## CONCLUSIONS

In summary, our case report shows efficacy of single subcutaneous administrations of BTX-A in a CRPS type II patient, warranting further research to investigate the mechanisms of action and to develop safe protocols which can be implemented in outpatient settings. ❑

*Conflicts of interest: none declared.*

*Financial support: none declared.*

*Informed consent: We undersign, certificate that we have the written consent of the identifiable person in order to describe the cases in this scientific paper.*

# References


1. **Harden RN, Bruehl S, Perez RS, et al.** Validation of proposed diagnostic criteria (the "Budapest Criteria") for complex regional pain syndrome. *Pain* 2010;150:268-274. doi: 10.1016/j.pain.2010.04.030.
2. **Bean DJ, Johnson MH, Heiss-Dunlop W, Kydd RR.** Extent of recovery in the first 12 months of complex regional pain syndrome type-1: A prospective study. *Eur J Pain* 2016;20:884-894. doi: 10.1002/ejp.813.
3. **Kharkar S, Ambady P, Venkatesh Y, Schwartzman RJ.** Intramuscular botulinum toxin in complex regional pain syndrome: case series and literature review. *Pain Physician* 2011;14:419-424.
4. **Finnerup NB, Attal N, Haroutounian S, et al.** Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis. *Lancet Neurol* 2015;14:162-173. doi: 10.1016/S1474-4422(14)70251-0.
5. **Goh EL, Chidambaram S, Ma D.** Complex regional pain syndrome: a recent update. *Burns Trauma* 2017;5:2. doi: 10.1186/s41038-016-0066-4.
6. **Aoki KR, Francis J.** Updates on the antinociceptive mechanism hypothesis of botulinum toxin A. *Parkinsonism Relat Disord* 2011;17:S28-S33. doi: 10.1016/j.parkreldis.2011.06.013.
7. **Safarpour Y, Jabbari B.** Botulinum toxin treatment of pain syndromes–an evidence based review. *Toxicon* 2018;147:120-128. doi: 10.1016/j.toxicon.2018.01.017.
8. **Park J, Chung M.** Botulinum toxin for central neuropathic pain. *Toxins* (Basel). 2018;10:224.
9. **Birthi P, Sloan P, Salles S.** Subcutaneous botulinum toxin A for the treatment of refractory complex regional pain syndrome. *PM R* 2012;4:446-449. doi: 10.3390/toxins10060224.
10. **Safarpour D, Salardini A, Richardson D, Jabbari B.** Botulinum toxin A for treatment of allodynia of complex regional pain syndrome: a pilot study. *Pain Med* 2010;11:1411-1414. doi: 10.1111/j.1526-4637.2010.00897.x.
11. **Taylor SS, Noor N, Urits I, et al.** Complex Regional Pain Syndrome: A Comprehensive Review. *Pain Ther* 2021;10:875-892. doi: 10.1007/s40122-021-00279-4. Erratum in: *Pain Ther* 2021 Jul 26.
12. **Argoff CE.** A focused review on the use of botulinum toxins for neuropathic pain. *Clin J Pain* 2002;18(6 Suppl):S177-S181. doi: 10.1097/00002508-200211001-00010.
13. **Siongco PRL, Rosales RL, Moore AP, et al.** Botulinum neurotoxin injections for muscle-based (dystonia and spasticity) and non-muscle-based (neuropathic pain) pain disorders: a meta-analytic study. *J Neural Transm* 2020;127:935-9951. doi: 10.1007/s00702-020-02163-5.
14. **Birthi P, Sloan P, Salles S.** Subcutaneous botulinum toxin A for the t treatment of refractory complex regional pain syndrome. *PM R* 2012;4:446-449. doi: 10.1016/j.pmrj.2011.12.010.
15. **Lessard L, Bartow MJ, Lee J, et al.** Botulinum toxin A. *Plast Reconstr Surg Glob Open* 2018;6:e1847. doi: 10.1097/GOX.0000000000001847.
16. **Attal N, de Andrade DC, Adam F, et al.** Safety and efficacy of repeated injections of botulinum toxin A in peripheral neuropathic pain (BOTNEP): a randomised, double-blind, placebo-controlled trial. *Lancet Neurol* 2016;15:555-565. doi: 10.1016/S1474-4422(16)00017-X.