

Views and Practice

Has subcutaneous botulinum toxin A been prioritised for a painful skin in an elderly patient with post-herpetic neuralgia?

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Introduction

Botulinum toxin A (BTX-A) is known to dermatologists as an effective treatment for hyperhidrosis. Its long-lasting action (maximum: 6 months; median: 3-4 months) makes it suitable also for management of chronic pain such as post-herpetic neuralgia (PHN), that often leads to many visits to the dermatology clinic. Moreover, its dose-dependent side effects, as is well known, are temporary and reversible.¹ Herein, we present a case of an elderly patient with comorbidities and years of chronic pain due to PHN, based on which we recommend that subcutaneous BTX should take priority over the other therapies for intractable PHN.

Case report

A 75-year-old Korean male patient with palm-sized scarring on the left anterior chest wall visited

our clinic. He complained of excruciating pain that had been near-continuous for approximately seven years following a case of herpes zoster. He held hot pack in a pouch sewn into his shirt over this area at all times for pain relief. According to the patient, he had been treated with all of the available options, including nerve blocks. However, nothing had alleviated his pain. On the 0-10 numerical rating scale, his pain ranked 8-9.

The patient's medical history included unstable angina with seven coronary stents, multiple spinal stenosis, and stage 3 chronic kidney disease. He had undergone cholecystectomy and transurethral resection for a bladder tumour 15 years and six months previously, respectively. He was on multiple medications in addition to clopidogrel.

As he was taking anticoagulation therapy (risk of haematoma) and that previous treatments had been ineffective, epidural injection was not attempted. On the patient's first visit to our pain clinic, ultrasound-guided intercostal nerve block using 0.125% bupivacaine with 5 mg triamcinolone was performed, and gabapentin, acetaminophen, and EMLA[®] (lidocaine 2.5% and prilocaine 2.5%) cream were prescribed. At the one-week follow-up, his pain had not been alleviated to any significant extent. The next attempted treatment, entailing local infiltration by injection of 0.125% bupivacaine mixed with 5 mg triamcinolone along with a gabapentin dose

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increase (to 1200 mg/day), was likewise unsuccessful. In response, 1800 mg gabapentin per day was prescribed. At the same time, BTX injection was considered. In order to proceed with BTX treatment, the location of the acute pain in the patient's anterior chest wall was reconfirmed, over which chessboard-like lines were drawn with the patient in the supine position.

A total of 100 units of BTX-A (BOTOX®, Allergan Inc., Irvine, CA, USA) were diluted with 5 ml of 0.9% normal saline (20 units per 1 ml) and injected subcutaneously at the 33 points of intersection using a 26-gauge needle with a 1 ml syringe. Roughly 0.15 ml (3 units) was administered at each site (Figure 1). No side effects were observed, except for injection pain. At the one-week follow-up, the pain had not been relieved. However, by the two-week follow-up, there was some degree of improvement: the patient indicated that it was 60 to 70 percent of that experienced at the time of his first visit, and that his hot pack was no longer needed. The patient was satisfied with the BTX therapy, particularly as none other had been even partially successful; he looked forward to the next injection.



Figure 1. Botulinum toxin A injected subcutaneously in a chessboard-like pattern.

Discussion

BTX-A is composed of a two-chain polypeptide with a protease unit that cleaves the SNAP-25 (synaptosome-associated protein of 25 kd) complex, which is the critical fusion protein related to acetylcholine release in the presynaptic terminal. This prevents formation of the SNARE (soluble N-ethyl maleimide-sensitive factor-attachment protein-receptor) system leading to inhibition of fusion of neurotransmitter vesicles with the presynaptic membrane and the release of neurotransmitters at the synaptic cleft is blocked. Moreover, with decreased release of acetylcholine, CGRP (calcitonin gene-related peptide), substance P, and glutamate, nociceptive fiber discharge likewise is retarded.^{2,3} Although its main pain-relieving mechanism of action is not yet completely clear, several processes by which it can manage neuropathic pain have been demonstrated in laboratory animal experiments.¹ Its main advantage as a choice for chronic pain treatment is its long-duration of action. However, BTX injections used for pain-relief purposes (excepting chronic migraine, the only FDA-approved indication for chronic pain) are off-label.⁴

According to the guidelines of the Therapeutics and Assessment Subcommittee of the American Academy of Neurology (AAN), the levels of BTX-therapeutic efficacy are classified as follows: level A (effective/ineffective), level B (probably effective/ineffective), level C (possibly effective/ineffective), and level U (undetermined). For PHN and trigeminal neuralgia, notably, the efficacy of BTX therapy is level A.¹ Therefore, in cases of intractable PHN, BTX treatment is worth trying.

PHN generally is treated with oral and topical non-steroidal analgesics, anticonvulsants (i.e. gabapentin and pregabalin), antidepressants (i.e. tricyclic agents and norepinephrine-reuptake inhibitors), opioids, and anaesthetic patches (i.e. lidocaine and capsaicin). If pharmacological treatments fail to bring sufficient pain relief, interventional treatments including epidural block,

intrathecal injection, sympathetic nerve block and spinal cord stimulation can be considered.^{1,5} In cases where intense pain persists despite the application of personalised treatment options, BTX, due to its minor and endurable side effects, may be the best alternative approach, especially in elderly patients (as in this case) in polypharmacy for multiple comorbidities may lead to dangerous drug interactions. In earlier BTX treatments of PHN,^{3,6} 100 units of BTX-A were prepared by dilution with normal saline (2 or 4 ml) and injected subcutaneously into the patient's area of acute pain, about 1 cm apart in a grid-like pattern, using a 30-gauge needle. The effect appeared as early as day 3, peaking at week 1 or 4, and was maintained for one or three months. According to another case report,¹ a Visual Analogue Scale pain score of 10 was reduced to 0 at week 2 post-injection. On the basis of this experience and the level A indication of the AAN's treatment-efficacy guidelines, we treated our PHN patient for the smaller area of painful focal neuropathy. In most of the previous successful cases, there was a relatively small affected area.^{1,7} Both intradermal injection of BTX (to prevent effects on muscle tone) and subcutaneous injection have been found to produce direct and effective pain relief in the treatment of PHN.^{3,7}

It is important to avoid combining Botox with other medications eg. Botox-lidocaine mixture as there have been reports of mortality.^{8,9} The side effects can be minimised with a lower dilution and lower injection volume.⁸ As it has been shown that high-dose (>360 accumulative units) administration of BTX-A showed no life-threatening side effects within three months, the maximum dose of BTX-A within a three-month interval is 360 accumulative units.¹⁰ For best BTX-therapy results, we suggest that physicians follow the manufacturer's instructions, which include

gentle, vial-rotation and mixing with preservative-free saline solution, administration within 24 hours, and to store in a refrigerator during this time period.

Although this treatment is used less often than would be expected, BTX-A injection can be the optimum treatment for elderly PHN patients with comorbidities. As long as its specific applications are kept in mind, it can be a good alternative or supplementary treatment for intractable PHN.

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