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CASE REPORTS

Botulinum Toxin A Relieved Neuropathic Pain in a Case of Post-Herpetic Neuralgia

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ABSTRACT

Botulinum toxin type A (BTX-A®) has been widely used in many clinical disorders including migraine, cervical dystonia, etc. The use of BTX-A in neuropathic pain, however, is uncommon, and the application of the anti-nociceptive effect of botulinum toxin is emerging. Here we report a case of an 80-year-old man who suffered from severe pain of post-herpetic neuralgia which was refractory to the usual therapies. However, this neuropathic pain was dramatically relieved by multiple BTX-A injection and the pain relief lasted 52 days.

Key Words. Allodynia; Botulinum Toxin; Neuropathic Pain

Introduction

Neuropathic pain can occur after injury to the peripheral and/or central nervous system, resulting in spontaneous pain, allodynia, and hyperalgesia. Due to the diversity of neuropathic pain and complicated mechanisms, many treatments including antidepressants, antiepileptic, local anesthetics, opioids, N-methyl-D-aspartate receptor antagonists, etc., have been used with limited effect. Here we present a case of post-herpetic neuralgia with neuropathic pain which was relieved by botulinum toxin type A (BTX-A) (BOTOX®; Allergan Inc., Irvine, CA) injection.

Case Report

An 80-year-old man who had a history of carotid stenosis, gouty arthritis, duodenal ulcer, hypertension, diabetes mellitus, coronary artery disease, renal function impairment, and congestive heart failure was complaining of severe gnawing pain, burning sensation, and tightness over his right chest wall around the dermatome of T2–4 for 1 month. Physical examination showed discolored scarring and allodynia over the right peri-axillary area (Figure 1) and the diagnosis of post-herpetic neuralgia was made for which tricyclic antidepressants, gabapentin, and carbamazepine were prescribed by neurologist with no improvement of his pain. With increasing doses of amitriptyline, gabapentin, dextromethorphan, and oral morphine given in 1 week, the patient's pain was reduced from 10 to 4 by visual analog score (VAS). Unfortunately, severe delirium developed and the treatment was changed to thoracic epidural analgesia. Epidural catheter was inserted through the T5–6 interspace with the tip advanced to T3. After test dose, 1 μg/mL fentanyl in 0.25% bupivacaine was given at the rate of 5 mL/h infusion, but severe pain still persisted, even after the concentration of bupivacaine was increased to 0.375%. Hence, BTX-A injection was used and 100 units of BTX-A were injected subcutaneously in a fanning fashion in divided doses (at four sites, 20 routes in total, 5 units/route) into the area of allodynia with a 23-gauge needle (0.65 × 70 mm, Nipro)

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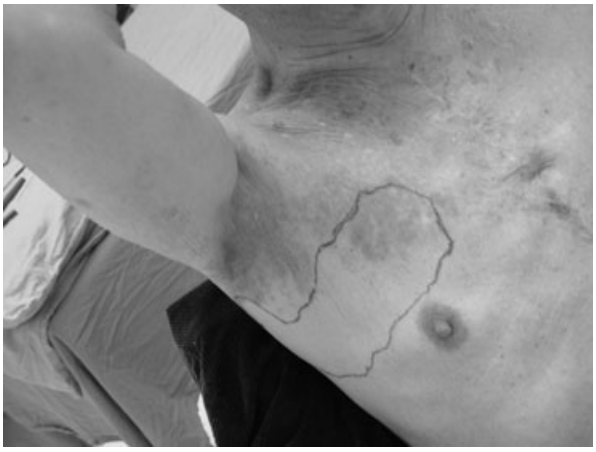

Figure 1 Morphology and distribution of herpes zoster 1 month after diagnosis (allodynia area within the lines).

(Figure 2). The VAS decreased from 10 to 1 gradually after 2 days and lasted 52 days after the injection. Then his pain became severe again for which amitriptyline 25 mg at bedtime and gabapentin 300 mg every 8 hours were given. We evaluated his pain at the next follow-up after 1 week and found that the pain improved and became bearable to him. The VAS was kept between 3 and 4. His pain remained at that level during his periodic follow-ups in the pain clinic continuously for about 9 months up to the time of this report.

Discussion

Cervero and Laird [1] had shown that hyperactivity of A-β afferents following nerve injury could result in touch-evoked pain and spontaneous pain via a presynaptic activation of C afferent terminals. Significant anti-allodynic effects of various N-methyl-D-aspartate glutamatergic receptor antagonists had been shown in neuropathic animal [2] and human subjects [3–6]. However, the precise mechanism of allodynia remains unclear. In our patient we found that BTX-A injections were able to relieve the intractable neuropathic pain with allodynia after post-herpetic neuralgia. Subcutaneous application of BTX-A had been used in relieving central burning pain and allodynia with spinal cord pathology [7]. The pharmacologic effect of botulinum toxin stems from inhibition of the release of the neurotransmitter, acetylcholine, from the axon terminals of motor neurons, preganglionic sympathetic, parasympathetic neurons, and postganglionic parasympathetic nerves by a multistep mechanism [8]. BTX-A blocks acetylcholine by cleaving synaptosome-associated protein-25 [9], which participates in the formation of the exocytotic SNARE complex (soluble N-ethyl-maleimide-sensitive factor attachment protein receptor complex) which is essential for the fusion of acetylcholine-containing vesicles with the presynaptic membrane [10].

The injection of botulinum toxin may reduce various substances that sensitize nociceptors [11]. Cui et al. [12] demonstrated that the anti-nociceptive effect of local peripheral BTX-A injection is associated with the inhibition of formalin-induced glutamate release, and they also imply that BTX-A may reduce the peripheral nociceptive input by inhibiting the release of substance P and calcitonin-gene-related peptide, both of which would play a very important role in neurogenic inflammation. The effectiveness of BTX-A in treating neuropathic pain in post-herpetic neuralgia implies a direct action on sensory neurons and possibly with an indirect central action. Direct effects on muscle nociceptors and alteration of afferent derived from muscle spindle might play a role according to Arezzo [13], especially in reducing the myofascial pain by inhibiting muscle spasms, which might be a component of this patient's pain. Glutamate exerts its postsynaptic effect via N-methyl-D-aspartate receptors, which are important for the induction and maintenance of central sensitization of pain [14]. We postulate that inhibition of glutamate release after BTX-A injection would be associated with reducing peripheral nociception and/or central sensitization and possibly "reorganization" in the central ner-

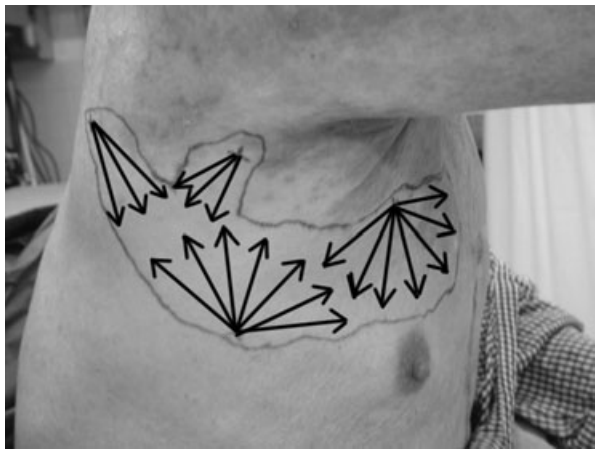

Figure 2 Routes of Botulinum toxin type A (BTX-A) injection (arrows). The needle was withdrawn and redirected repeatedly in a fanning fashion and BTX-A was injected only during needle withdrawal.

vous system. That would explain the effectiveness of BTX-A in this patient. Of course, there is always the question whether we are observing a placebo effect from the BTX-A injection. As this patient had multiple injection therapies before without effect and the pain relief was so dramatic and long lasting after BTX-A treatment, a placebo effect probably is not likely. Further study with series cases treated with BTX-A injection will be most definitely needed.

We conclude that BTX-A injection may be an alternative treatment in relieving neuropathic pain of post-herpetic neuralgia.

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