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Botulinum Toxin A for the Treatment of Residual Limb Neuropathic Pain Due to Hyperhidrosis: A Case Report

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Background: Postamputation pain is a common condition affecting veterans with amputations. Recognition and treatment of skin conditions play a significant role in treating residual limb pain. Hyperhidrosis or excessive sweating is the most common skin problem reported by amputees and can cause infections, act as triggers for other pain generators such as neuromas, and impede the proper use of a prosthetic.

Case Report: We discuss a case of a 38-year-old man with a left transtibial amputation who presented with refractory neuropathic pain aggravated by persistent hyperhidrosis. Botulinum toxin A was injected both into suspected neuroma sites and areas of hyperhidrosis with a significant decrease in pain and sweating.

Conclusion: Botulinum toxin A can be successfully used in the treatment of neuropathic residual limb pain exacerbated by hyperhidrosis.

Key words: Botulinum toxin A, hyperhidrosis, neuroma, neuropathic pain, postamputation pain, transtibial amputation

BACKGROUND

Postamputation pain has been reported in up to 95% of amputees (1). Etiologies vary from phantom sensations and pain to neuropathic and skin-related conditions. Postamputation pain can prevent successful prosthetic use, which can negatively affect mobility, activities of daily living, and quality of life.

Understanding the skin-socket interface is pivotal to treating postamputation pain. The prosthetic environment exposes skin to excess friction, moisture, and heat, which can cause various skin issues. Among these, hyperhidrosis or excessive sweating is the most common skin problem in lower limb amputees. Up to 66% report interference with daily activities (2). Existing algorithms delineate treatment pathways for axillary hyperhidrosis (3), but options for residual limb hyperhidrosis have seldom been reported.

Here we describe a case of a veteran with a transtibial amputation and chronic neuroma pain aggravated by hyperhidrosis who was treated successfully with botulinum toxin A (BTX-A) injected directly into suspected neuroma sites and into areas of hyperhidrosis. We explore common causes of postamputation pain with an emphasis on skin conditions as well as treatment options for hyperhidrosis.

CASE

The patient is a 38-year-old male veteran with a left transtibial amputation secondary to a remote landmine injury. He is an active K-level 4 prosthetic user who

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enjoys hiking. He wears a total surface-bearing socket with a gel liner, pin-lock, and dynamic shock-absorbing foot. Postoperatively he developed left peroneal nerve neuromas at the amputation site. The neuromas were treated with repeat radiofrequency ablations with initial pain improvement. However, after the third ablation the patient developed an abscess requiring antibiotics and eventual debridement.

The patient presented with intermittent residual limb pain associated with recurrent dermatitis. He reported excessive sweating at the distal end leading to dermatitis flare-ups. Examination revealed a hyperkeratotic patch without open sores or weeping and diffuse moisture greatest at the popliteal fossa. The patient tried clobetasol cream and ammonium lactate with further irritation and an offloading donut craft without relief. He ultimately resorted to using wads of paper towels. His hyperhidrosis, resulting dermatitis, and aggravated neuroma pain limited his ambulation to one mile.

Accordingly, he was deemed an appropriate candidate for BTX-A injections for the treatment of neuroma pain aggravated by hyperhidrosis. Two hundred units of BTX-A were diluted with 2 mL of preservative-free saline. Using a 1.25-inch 30-gauge needle, reported hyperhidrosis sites were injected intradermally with 2.5 to 5 units in one- to 2-cm intervals circumferentially around the limb extending as high as the mid-thigh. Four distal and exquisitely tender suspected neuroma sites were each injected more deeply with 15 to 20 units. Four weeks later the patient returned with markedly reduced symptoms. At 12 and 24 weeks' follow-up, he underwent repeat injections with 400 units and 600 units in a similar fashion, with further reduction of pain and hyperhidrosis. Functionally, he progressed to hiking daily and could use his prosthesis more than he had in the previous 3 years. Additionally, his opioid regimen was significantly tapered.

DISCUSSION

To our knowledge, this is the first reported case describing the successful use of BTX-A in the treatment of neuroma pain aggravated by hyperhidrosis in a veteran with a transtibial amputation. Here we describe common causes of postamputation pain with a focus on skin conditions, hyperhidrosis treatment, and the possible mechanisms through which BTX-A may relieve neuropathic pain aggravated by hyperhidrosis.

Postamputation Pain

Postamputation pain and dysesthesias may occur in up to 95% of amputees (1). Multimodal treatment is often required, ranging from pharmacotherapy and injections to cognitive psychotherapy. Classifying painful and nonpainful sequelae into distinct categories--phantom sensations, phantom limb pain, and residual limb pain--can be useful in guiding intervention.

Phantom sensations are nonpainful perceptions referred to the missing limb. They are present in up to 90% amputees and often appear in the first few days (1). Sensations range from pressure and movement to tingling and vibrations. While prevalent, phantom sensations rarely pose a major clinical problem. In contrast, phantom limb pain is a painful sensation in the distribution of the amputated limb. Sixty percent to 80% of patients report this phenomenon, with symptoms usually presenting early but potentially starting up to years after amputation (4). Pain is usually episodic and localized to the distribution of the missing fingers, palms, toes, and feet, possibly due to the larger cortical representations of the hand and foot. Residual limb pain occurs in up to 74% of amputees (1), although severe pain is only reported in 5% to 10% (4). Pain can localize to a superficial incision, be perceived deep in the limb, or can involve the whole limb. Etiologies are vast and include postsurgical nociceptive, neurogenic, ischemic, referred, and skin-related causes.

While phantom and residual limb pain often occur together, distinguishing between the 2 can help identify targets of intervention. In this case, the patient developed recurrent neuroma pain in the setting of hyperhidrosis. One study found that swollen neuromas were equally present in amputees with pain compared to amputees without pain (5), suggesting that some neuroma pain is driven by other triggers such as skin inflammation or edema. Recognition and treatment of common skin conditions can be pivotal in treating residual limb pain.

Postamputation Skin Conditions

A review by Ghoseiri et al (6) suggests that 32% to 74% of amputees experience at least one skin problem. Residual limbs are exposed to environments with increased heat, moisture, and friction. These elements lead to various physical dermatoses that can affect prosthetic use. Stress and shear forces can cause keratin plugging, resulting in epidermoid cysts that can lead to skin breakdown, ulceration, and sinus tract discharge. Moreover, amputees may have a higher risk of develop-

ing folliculitis and furuncles as residual limb skin has been shown to harbor more abundant bacterial flora than the contralateral limb (7). Poor fit and persistent limb edema can result in verrucous hyperplasia or wart-like lesions of the residual limb. These lesions are treatment-resistant, prone to infection, and can contribute to an increased risk of developing squamous cell carcinoma (7).

Additionally, topical treatments for dermatoses and infections, interventional procedures, and prosthetic materials including varnishes, lacquers, and resins may cause dermatitis (7). Findings can range from mild lichenification or swelling to weeping eczema. When allergic dermatitis is suspected, patch testing may be helpful in identifying responsible irritants.

Among lower limb amputees, hyperhidrosis is the single most reported skin problem (2). Hyperhidrosis or dysfunctional sweating exceeding the amount necessary for thermoregulation is usually idiopathic from neurogenic overactivity of the sweat glands. Warmth and moisture from perspiration can not only cause folliculitis and cellulitis, but also may exacerbate existing pain generators such as neuromas.

Treatment of Hyperhidrosis

Topical antiperspirants are considered first-line treatments (3). They contain metal salts, most commonly aluminum chloride, which work by blocking sweat ducts or promoting vacuolization and atrophy of glandular secretory cells (8). In severe cases, excess sweat can react with aluminum chloride to form hydrochloric acid which may further irritate skin. While considered first-line for axillary hyperhidrosis, there is scant data for residual limb hyperhidrosis with one study finding antiperspirants completely effective only 10% to 13% of the time (2).

Tap water iontophoresis may ameliorate hyperhidrosis by using current to perturb endogenous electrical gradients, alter sweat flow, and inactivate sweat glands (9). While success has been demonstrated with palmar hyperhidrosis (9), its effectiveness in transtibial amputations is poorly characterized. Additionally, use is limited by difficult administration and skin irritation, burns, and pain resulting from direct current. Oral anticholinergics such as atropine are seldom used as the doses needed to alleviate hyperhidrosis can result in dry mouth and eyes, blurred vision, and urinary retention.

Modification of prostheses, liners, and socks and prosthetic cooling systems have been proposed as treatments. The efficacy of breathable nanomaterials with high thermal conductivity is not well studied and there is not convincing data that certain liner types are superior. While prosthetic cooling symptoms are in development, their use is limited by availability and cost.

BTX-A has been recommended as a first-line treatment for severe hyperhidrosis (8). While guidelines for axillary hyperhidrosis exist (7), several studies have reported success in lower limb amputations too (10,11). BTX-A may target hyperhidrosis through multiple mechanisms including blocking exocytotic release of acetylcholine and inducing functional denervation of sweat glands (8). Optimal dosing and frequency are unknown but efficacy has been noted for up to 6 months (12).

In this report, we suggest that BTX-A can be successful for both treatment of neuroma pain and prevention of hyperhidrosis-induced dermatitis, which can serve as a trigger. Decreasing acetylcholine release at the neuromuscular junction not only reduces sweating, but also alleviates painful spasms and abnormal tone. Beyond its junctional activity, BTX-A is thought to have antinociceptive effects by suppressing the release of neuronal signaling markers including glutamate and substance P, thereby inhibiting peripheral sensitization and subsequent central sensitization (13). This mechanism may explain BTX-A's demonstrated success in several neuropathic conditions (14); however, its effectiveness in postamputation pain is less frequently described. Here we highlight a successful case of BTX-A used in the treatment of both neuroma pain and hyperhidrosis.

CONCLUSION

Postamputation pain is a frequently reported complication by veterans with transtibial amputations. Recognition and treatment of common skin conditions is crucial in treating residual limb pain and maintaining function and quality of life for veterans. BTX-A can be successfully used in treatment of neuropathic residual limb pain exacerbated by hyperhidrosis.

Ethical Disclosure

The patient provided consent to publish this report in accordance with HIPAA privacy regulations. To protect the patient's confidentiality, all personal identifiers were removed from the case report and special care was taken in the data contained in description of the case so that the individual cannot be identified. The research was supported by NYU and/or a NYU-affiliated entity. The views expressed in this replication represent those of the author(s) and do not necessarily represent the official views of NYU or any of its affiliated entities.

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