

Treatment of male genital dysesthesia with botulinum toxin



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INTRODUCTION

Scrotal dysesthesia is a common condition characterized by hyperalgesia and burning that can cause significant disruption to social and sexual life. While no standard treatment exists, treatment options typically include topical neuromodulators, corticosteroids, and serotonin-noradrenaline reuptake inhibitors.¹ Treatment is challenging, and symptoms may persist for months or years. Botulinum toxin is frequently used for management of diseases characterized by chronic pain, including neuropathic pain, headaches, and arthritis. We present the case of a patient suffering from scrotal and inguinal dysesthesia, who proved refractory to multiple conventional therapies but responded well to treatment with botulinum toxin.

CASE DESCRIPTION

A 63-year-old male presented to our clinic with a 2-year history of progressive worsening pain and burning sensation localized to his scrotum, inguinal creases, medial aspects of the thighs, and perineum. His symptoms, which were more severe on the left side, were constant and disruptive to his normal daily life. The patient reported worsened pain with sweating, sitting, and following light friction.

His medical history was significant for atrial fibrillation, osteoarthritis, and L5 radiculopathy. The patient also had a history of genital herpes simplex virus for 40 years, for which he took valacyclovir during outbreaks, which occurred approximately twice per year. The patient had consulted several specialists and had been managed with different treatments including topical antifungals, mid-potency corticosteroids, duloxetine,

pregabalin, baclofen, and gabapentin, all without any substantial relief. Oxycodone partially alleviated some of his symptoms.

On physical exam, the patient had Fitzpatrick skin type 2, and examination of the genital, inguinal, and gluteal skin revealed no erythema, lichenification, blisters, or erosions. A trial of topical aluminum chloride hexahydrate was initiated but failed to control his discomfort.

Given the patient's radiographic evidence of L5 radiculopathy, his symptoms were deemed to be most consistent with scrotal dysesthesia in the setting of neuropathic disease. After reviewing the risks and benefits of therapy and obtaining his verbal consent, treatment with botulinum toxin was initiated to target the patient's discomfort and reduce the scrotal sweating, which exacerbated his baseline discomfort. A total of 80 units of botulinum toxin was delivered intradermally across the affected areas (20 units across the scrotum, 50 units distributed across the inguinal creases, medial aspects of the thighs, and inferior mons, and 10 units across the buttocks and perineum). At his two-month follow-up visit, the patient reported that his pain and burning sensations had improved. Breakthrough of symptoms occurred when the patient underwent steroid injection into the left hip for osteoarthritis and again after surgical repair of an inguinal hernia. Repeat treatment with botulinum toxin treatment reduced his symptoms once again. The patient did not experience any side effects with the botulinum toxin.

DISCUSSION

Scrotal dysesthesia refers to cutaneous burning, irritation, and discomfort localized to the scrotum.¹ It

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Table 1. Overview of previously reported treatments for idiopathic scrotal dysesthesia

Treatment	Proposed mechanism	Previously reported dosing regimen	Response	Level of evidence*	Citation
Doxycycline	Anti-inflammatory	100 mg BID for 1 month then QD until resolution	Improvement within 2-4 weeks, and complete resolution within 1-4 months	IV	Abbas et al, 2008 ⁴
Doxycycline + Amitriptyline	Anti-inflammatory and neural modulation	Doxycycline (100 mg BID) and Amitriptyline (50-75 mg per day)	Near-complete resolution by 1.5-3 months	IV	Narang et al, 2013 ⁵
Doxycycline + Tacrolimus	Anti-inflammatory	Doxycycline QD and tacrolimus 0.1% ointment BID	Complete remission within 4 weeks	IV	Wollina, 2011 ⁶
Doxycycline + Pregabalin	Anti-inflammatory and neural modulation	Doxycycline (100 mg BID) and pregabalin	Near-complete resolution by 1.5-3 months	IV	Narang et al, 2013 ⁵
Gabapentin	Neural modulation	NA	Mild improvement after 2 weeks	IV	Wollina, 2011 ⁶
Pregabalin	Neural modulation	50 mg TID	Complete remission	IV	Miller et al, 2016 ⁷
		150 mg QID for 3 months	Complete remission	IV	Cardenas-de La Garza, 2019 ⁸
Ivermectin	Anti-inflammatory	12 mg (oral) QW for 4 weeks then 10 mg/g topical cream QD until resolution	Improvement within 4 weeks	IV	Martinez et al, 2020 ⁹
Carvedilol	Vasoconstriction of the cutaneous arteries	6.25 mg QD	Improvement after 2 weeks and complete remission after 4 weeks	IV	Merhi et al, 2017 ¹⁰
Timolol	Vasoconstriction of the cutaneous arteries	Topical 0.5% gel	Improvement within 2 weeks	IV	Pyle et al, 2019 ¹¹

BID, Twice daily; QD, once daily; QW, once weekly; TID, thrice daily.

*Based on the Oxford Center Evidence-based Medicine, Levels of Evidence Pyramid.

is a non-specific finding and usually a symptom of an underlying disorder. In most patients, the cause of scrotal dysesthesia is an inflammatory dermatosis or infectious disease. When no recognizable primary skin disease is found, scrotal dysesthesia may be related to a neuropathic etiology and analogous to vulvodinia in women.^{1,2} The condition can be accompanied with persistent scrotal erythema, which is described as red scrotum syndrome.³ In patients with isolated scrotal dysesthesia, lumbosacral radiculopathy may be an attributable cause.² Scrotal dysesthesia can substantially affect the quality of life of patients by interfering with sleep, sexual functions, and many daily activities.

Our patient exhibited no visible scrotal abnormalities or persistent erythema, which ruled out red scrotal syndrome. Common dermatoses, such as atopic dermatitis, contact dermatitis, psoriasis, and fungal or bacterial infections were also excluded due to lack of clinical features suggestive of these

diagnoses and by lack of response to topical treatments. In light of this patient's history of lumbosacral radiculopathy, a diagnosis of neuropathic scrotal dysesthesia due to nerve or nerve root compression was favored. Diagnosis is clinical, as there are no specific histological findings.²

The management of scrotal dysesthesia can be challenging as no treatment has been found to be universally effective in scrotal pain management.¹ The specific management of red scrotum syndrome relies on cessation of topical steroids, as dysesthesia has been attributed to prolonged use of corticosteroids.³ Other treatment modalities described in the literature for scrotal dysesthesia include doxycycline, tricyclic antidepressants, gabapentin, pregabalin, β -blockers, and topical calcineurin inhibitors.^{1,3} A list of previously published treatment options for scrotal dysesthesia is provided in Table 1. Our patient had previously failed treatment with duloxetine, pregabalin, and gabapentin.

The use of botulinum toxin to manage pain has become more frequent in recent years, particularly in efforts to reduce neuropathic pain conditions. The exact mechanism by which botulinum toxin reduces pain is not completely understood but is likely multifaceted. Historically, inhibition of acetylcholine release from motor neurons and subsequent muscle relaxation has been cited as the source of the toxin's analgesic effects. Studies in tissue culture and in animal models of various types of pain, however, demonstrate that botulinum toxin reduces neurotransmitter and neuropeptide release by sensory nerve fibers.¹² Botulinum toxin has also been reported to inhibit sodium channel function, required for neurotransmission by both central and peripheral nerves, and to downregulate the peripheral nerve-expression of the TRPV1 channel,¹³ a receptor ion channel known to play a role in modulating pain sensation.¹⁴ Some evidence suggests that botulinum toxin may reduce local edema and tissue inflammation,¹⁵ although this remains controversial due to several conflicting reports in other animal and human pain models.¹⁶

Recent studies have reported the successful use of botulinum toxin in the treatment of genital pain conditions, including anal fissures, vulvodynia, and vaginismus.^{17,18} In these studies, pain generally improved on the orders of days after injections and lasted for a duration of 12-24 weeks. In the current case, the patient's pain and burning sensation dramatically improved and he remained virtually asymptomatic for ~12 weeks. The benefits of botulinum toxin include its relative safety and rapid and sustained effects after a single administration. Reported side effects of botulinum toxin in genital pain have been minimal.

We were unable to find any previous publications suggesting that botulinum toxin is a successful therapeutic option in managing scrotal dysesthesia. Larger randomized trials are needed to confirm our findings.

Conflicts of interest

None disclosed.

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