Intrapouch injections of botulinum toxin type A for the management of unit contractions of a continent urinary diversion

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Abstract

A 43-year-old woman presented with abdominal pain associated with incontinence from her Indiana pouch continent urinary diversion due to significant unit contractions. The patient's symptoms were refractory to conservative management, including oral and intrapouch antimuscarinic agents. Prior to surgical reconstruction, a trial of intrapouch injections of botulinum toxin type A (BT-A) significantly improved both the abdominal pain and the incontinence. The benefit lasted about 6 months and was subsequently repeated for recurrent symptoms. To our knowledge, this is the first reported case of the management of complications of a continent urinary diversion with BT-A injections.

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Introduction

The experience of botulinum toxin type A (BT-A) in urological practice is increasing dramatically since its first description less than a decade ago. In this case report, we describe a 43-year-old woman who presented with symptoms of pain and urinary leakage from a continent urinary diversion that was managed with intrapouch injections of BT-A. To our knowledge, this is the first report on the use of BT-A in a continent urinary diversion.

Case report

A 43-year-old woman with a significant past urological history presented to our institution with complaints of abdominal pain and urinary incontinence from her Indiana pouch. Her previous history included symptoms of pelvic pain syndrome, including severe lower urinary tract symptoms as well as bowel dysmotility resulting in frequent, painful bowel movements and fecal incontinence. As a result of her refractory bladder symptoms, she underwent an Indiana pouch continent urinary diversion. Three years after surgery she was investigated for urinary incontinence believed to be due to incompetence of the continence mechanism, and she ultimately underwent a revision of the efferent limb. The patient's bladder was left in situ and she continued to have difficulties with pelvic pain and occasional pyocystis. Following her diversion, she continued to have difficulties with frequent bowel movements and dyspareunia. Multiple disciplines were consulted; however, no formal urological, gastroenterological or neurological diagnoses were established.

During her most recent presentation, 10 years after her initial urinary diversion, her management was facilitated by the chronic pain service. Unfortunately, she continued to have difficulties with pelvic pain, fecal incontinence and right-sided abdominal pain associated with urinary incontinence. Video urodynamics demonstrated an Indiana pouch with first sensation at 107 mL with uninhibited, phasic contractions of the pouch at low volumes (170 mL), which coincided with her abdominal pain and stomal leakage. The visible contractions and subsequent leak pressures (measured between 50 and 60 mL H_2O) suggested that the leakage was mostly due to the phasic contractions rather than insufficiency of her continence mechanism. Attempts at conservative management for her unit contractions of the pouch, including oral and intrapouch anti-muscarinics (i.e., tolterodine and oxybutinin) and medical treatments for bowel dysmotility, were unsuccessful. A consultation for neuromodulation was obtained, but, given the patient's constellation of symptoms, it was felt neuromodulation would add little benefit.

Owing to her refractory symptoms, the patient was referred for surgical management, in particular an augmentation of her pouch as well as consideration of either cystectomy or iatrogenic vesicovaginal fistula. Given the growing body of evidence regarding the safety and efficacy of intradetrusor botulinum toxin type A (BT-A) to manage neurogenic and non-neurogenic detrusor overactivity,[1–5] she consented to a trial of BT-A injections into the pouch. Given the discomfort the patient had with any filling of her pouch and bladder, all injections were performed using a general anesthetic. Using a flexible cystoscope and a flexible needle, 200 units of BT-A were injected into multiple sites of the

Indiana pouch through her efferent limb. The BT-A was injected submucosally in a volume of 1 mL and a concentration of 10 units/mL in 4 quadrants starting from deep in the pouch migrating toward the ileo–cecal valve. The injections were performed without incident and the patient reported significant immediate (within 1 wk) improvement in her right abdominal pain as well as a substantial decrease in urinary incontinence, although minor leakage from the stoma still occurred. Owing to this response and a desire to improve her continuous pelvic discomfort, a second procedure was performed 5 months later to inject 300 units of BT-A into the bladder using a previously described template.[2] The patient reported some intital worsening of her pelvic pain for a few days after her bladder injections, consistent with her painful bladder condition. Subsequently, she reported a significant response in her pelvic pain, as well as, surprisingly, her perceived rectal pain and fecal incontinence. These procedures were performed without adverse effects and the response lasted for about 6 months, when the patient requested and received additional injections (300 units of BT-A) into both the pouch and the bladder during a single procedure. On this subsequent bladder injection, the patient did report an episode of pyocystis with increasing bladder pain and purulent discharge from the urethra. This was successfully treated with oral antibiotics and bladder irrigation with a gentamicin solution. The patient's symptoms, including unit contractions of her pouch, bladder and pelvic pain, and fecal incontinence have now been moderately maintained with 3 separate injections of BT-A into both her bladder and her pouch over a 2-year period. This has allowed deferral of surgical management of her symptoms.

Discussion

BT-A is a selective and reversible blocker of acetylcholine release at the neuromuscular junction, resulting in chemical denervation. The use of BT-A in the human detrusor was first described in 2000 by Schurch and colleagues[6] in patients with detrusor hyperreflexia following spinal cord injury. These results have since prompted further studies with other patient populations, including children with neurogenic bladder dysfunction and patients with refractory non-neurogenic detrusor overactivity. This has lead to significant improvement in bladder function with respect to subjective symptoms, quality of life and urodynamic parameters.[2,3]

Despite the increasingly positive reports regarding the efficacy of this novel, minimally invasive therapy, unanswered questions remain regarding its mechanism and ultimate place in our armamentarium for urological diseases. The reported dosages and injection templates vary between studies, with positive results seen with 100–300 U injected into 20–30 sites.[1,2,4,5] It is possible that lower concentrations may result in better overall clinical results[2] owing to a greater area of diffusion.[7] The durability of reported response tends to be longer than predicted by simple denervation of the neuro–muscular junction of efferent nerves and may also be related to the inhibition of afferent bladder pathways, resulting in reduced sensory urgency and urge incontinence.[8,9] It has been proposed that the duration of effect may be due to significant decreases of nerve growth factor resulting in remarkably limited detrusor axonal sprouting.[10,11] It appears that repeated injections do not result in drug tolerance and do not reduce bladder compliance, which may alleviate concerns of inducing iatrogenic bladder fibrosis with repeated injections.[4] Finally, BT-A injections appear to be cost-effective in the management of neurogenic and non-neurogenic detrusor overactivity.[12]

As far as we know, this is the first report of BT-A injection into a continent urinary diversion to aid in the management of complications of unit contractions. BT-A has also demonstrated efficacy in the management of some gastrointestinal disorders. In 88 patients with chronic anal fissures, a combination of topical nifedipine and botulinum injections demonstrated superior healing and recurrence rate versus topical nitroglycerin and pneumatic dilatation.[13] In 31 patients with primary achalasia, botulinum injections were a viable alternative to Witzel dilatation of the lower esophageal sphincter owing to the risk of endoscopic esophageal perforation with dilatation.[14] Further, a prospective study of children receiving botulinum injections of the internal anal sphincter after surgical treatment for Hirschsprung disease demonstrated improvement of chronic constipation in most patients.[15]

Continent urinary diversions have become a mainstay for the management of both benign and

neoplastic bladder diseases. Given the high reported acceptance from patients and the subsequent penetrance of these procedures throughout the urological community, it is possible that we are likely to see more long-term complications of continent diversions, including incontinence secondary to phasic contractions as described in this case. Although incontinence of urinary diversions is multifactorial, low-capacity pouches with unit contractions are well described and notoriously difficult to manage. Prior to surgical revision, a trial of BT-A injections appears to be well tolerated and safe, and may temporarily relieve symptoms.

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