Prolonged urinary retention after intravesical botulinum injection for treatment of idiopathic detrusor overactivity

Ashley B. King, MD[1], David E. Rapp, MD[1,2]
[1]Virginia Commonwealth University School of Medicine, Richmond, Virginia, USA
[2]Virginia Urology Center for Incontinence and Pelvic Floor Reconstruction, Richmond, Virginia, USA

KING AB, RAPP DE. Prolonged urinary retention after intravesical botulinum injection for treatment of idiopathic detrusor overactivity. The Canadian Journal of Urology. 2011;(18(2):5657-5659.

Introduction: *Botulinum toxin (BTX) has emerged as a treatment of refractory overactive bladder (OAB) and, while well tolerated, there exists concern regarding postoperative urinary retention.*
Case: *A 75-year-old female underwent intravesical BTX-A injection, which was followed by a prolonged episode of urinary retention, highlighting an unusual duration and degree of UR associated with BTX-A injection in the treatment of idiopathic detrusor overactivity (IDO). This case illustrates clinically significant urinary retention with bladder diaries demonstrating persistent postvoid residual (PVR) measurements exceeding voided volume until 9 month follow up.*
Conclusions: *Notably, this duration and severity of urinary retention remains rare. However, this case underscores the need to appropriately counsel patients regarding the risks associated with intravesical injection of BTX-A.*

Key Words: idiopathic detrusor overactivity, botulinum toxin, urinary retention

Introduction

Overactive bladder (OAB) represents a constellation of symptoms comprising urgency, with or without incontinence, and often accompanied by frequency or nocturia. OAB often has a significant and negative impact on the quality of life of many patients. Anticholinergic medications, biofeedback, and dietary modification represent initial treatments for OAB. However, each is associated with a high failure rate and pharmacotherapy is specifically characterized by a high rate of discontinuation secondary to significant side effects.[1]

Botulinum toxin (BTX) has emerged as a promising therapy for the treatment of refractory OAB. The mechanism of action of BTX-A comprises a paralytic effect owing to the interaction and cleavage of the target protein SNAP-25, and the resultant blockade of acetylcholine release.[1] The frequent finding of involuntary detrusor contractions in patients with OAB suggested a therapeutic use for the toxin in this

Accepted for publication January 2011

Address correspondence to Dr. David E Rapp, 5829 Ascot Glen Drive, Glen Allen, VA 23059 USA

patient population. Numerous investigations have subsequently demonstrated that intravesical BTX-A injection is associated with statistically significant improvements in urodynamic parameters and subjective urinary symptom and quality of life indices.[1] These findings have been confirmed in both idiopathic and neurogenic cohorts.[1]

Reported side effects from intravesical injection of BTX-A most commonly include hematuria and pain. Foremost, urinary retention is a concern given the mechanism of action of botox. Investigation specific to idiopathic cohorts has identified highly variable rates of urinary retention. Larger series report urinary retention rates of 19% to 45%.[2,3] Additional series demonstrate an increased postvoid residual (PVR) after BTX-A injection, but no patients requiring catheterization.[1] Further, multiple reports detailed no incidence of urinary retention requiring catheterization.[4] The duration of associated urinary retention is also variable. Sahai et al report a 28% rate of intermittent catheterization (IC) lasting up to 20 weeks.[5] However, most other series report resolution of urinary retention following short duration IC.

We report a case of prolonged urinary retention following intravesical injection of BTX-A in the treatment of idiopathic detrusor overactivity (IDO).

Case Report

A 75-year-old female was referred for work up and treatment of refractory urge urinary incontinence. Patient history revealed daily urge incontinence episodes requiring two pads daily. She denied urinary hesitancy, straining, and obstructive voiding symptoms. The patient had failed anticholinergic therapy and percutaneous nerve stimulation prior to referral. Urodynamic evaluation revealed detrusor overactivity at 301 cc. Pressure-flow analysis revealed a maximum detrusor pressure and flow of 50 mm Hg and 11 cc/s, respectively. PVR was 0 cc. No leakage with valsalva maneuver was identified. Cystoscopic exam demonstrated no bladder or urethral abnormalities.

Following a discussion of available treatment options, the patient underwent intravesical injection of 200 units of botulinum toxin type A (Botox) (Allergan, Inc., Irvine, California, USA). Injections were performed using an intradetrusor, trigone-sparing protocol. PVR following injection was 0 cc. PVR was repeated at 5 days postoperatively due to symptoms consistent with urinary retention, revealing a volume of 400 cc. The patient was taught clean intermittent catheterization with intermittent catheterization diary completion. Through 6 weeks post-injection, the patient remained in nearly complete urinary retention with voided and postvoid volumes of approximately 50 cc and 400 cc, respectively. Through this follow up, the patient denied any urgency, incontinence, and was extremely satisfied with her clinical status. At 5 month follow up, catheterization diary revealed voided and PVR volumes of approximately 100 cc and 300 cc, respectively. The patient denied any return of irritative voiding symptoms or incontinence. At 7 month follow up, she reported return of urgency symptoms with PVR decreasing to 150 cc. At 9 month follow up, she reported recent return of symptoms to near baseline, including daily urgency incontinence episodes and PVR of 50 cc.

Discussion

Generally well tolerated, one common adverse event observed following BTX-A injection is urinary retention. Given inhibitory action of BTX-A on muscle contraction, varying degrees of detrusor hypocontractility and urinary retention are frequently observed. Importantly, higher rates of urinary retention are generally seen in neurogenic patients.[1] In this specific patient population, bladder atony is often a beneficial effect as many neurogenic patients require catheterization prior to toxin injection. In contrast, prolonged urinary retention may represent a significant complication in idiopathic patients.

As described, the majority of reported series specific to idiopathic patients detail a short duration of urinary retention when observed. However, recent investigation has reported more prolonged durations of urinary retention. Jeffery et al reported one patient requiring IC at 9 month follow up.[6] Of note, Dysport (500 U) was used in this investigation, a preparation that may be associated with a higher incidence of adverse events due to a higher degree of diffusion.[7] Further, these authors fail to describe the criteria for instituting catheterization or that used to define urinary retention. Certainly, the analysis of urinary retention rates is complicated by the lack of consensus regarding a definition for urinary retention or for recommending IC.

Based on these data, associated research has attempted to identify the optimal total BTX-A dose, allowing for both maximal efficacy and minimal side effects. Accordingly, Schurch et al demonstrated a lower incidence of adverse events with lower dosing in a randomized comparison of 200 versus 300 units.[1] Similar success rates were seen in this dose response comparison. Ksibi et al identified a risk of

urinary retention as low as 4% to be associated with 100 U.[8] We utilized a 200 U dose, which has generally been reported to be well tolerated in the idiopathic population.

Interestingly, the effect of repeat BTX-A on bladder function and related outcomes is unknown. While some investigation has demonstrated that the duration and extent of clinical benefit appears to remain constant through repeat injections, other study suggests that subsequent injections may last longer than initial injections.[1] Accordingly, in patients experiencing transient urinary retention following injection, it may be possible that the duration or extent of this adverse event may be greater if repeat injection is performed. This question is important particularly in cases such as this, where the patient remained pleased with her clinical outcome despite the development of urinary retention and has requested counseling regarding repeat injection.

Sahai et al investigated pretreatment urodynamic variables in an attempt to identify parameters that may predict for urinary retention after intravesical BTX-A injection.[5] These authors found that patients who required IC postoperatively had lower pretreatment maximum flow rates, projected isovolumetric pressures (PIP1), and bladder contractile indices (BCI). PIP1 and BCI are urodynamic derivatives used as by these authors as markers of detrusor contractility. There has been limited additional work to assess pretreatment indicators associated with increasedrisk of urinary retention after BTX-A injection.

We report a case of prolonged urinary retention following intravesical injection of 200 U BTX-A in the treatment of IDO. We could find no other cases describing a similar duration and degree of urinary retention in the treatment of IDO using the Botox preparation. Indeed, this case illustrates clinically significant urinary retention with bladder diaries demonstrating persistent PVR measurements exceeding voided volume until 9 month follow up. Notably, this duration and severity of urinary retention remains rare. However, this case underscores the need to appropriately counsel patients that, although most cases of urinary retention will resolve in the short term period, there exists a risk for prolonged urinary retention following intravesical injection of BTX-A. □

References

1. Rapp D, Bales G. Application of Botulinum Toxin Injection in the Treatment of Urologic Disorders. Current Applications in Botulinum Toxin. Cooper G (Ed). New Jersey: *Humana Press Inc.*, 2007.
2. Kessler TM, Danuser H, Schumacher M, Studer UE, Burkhard FC. Botulinum A toxin injections into the detrusor: an effective treatment in idiopathic and neurogenic detrusor overactivity? *Neurourol Urodynam* 2005;24(3):231-236.
3. Petrou SP, Parker AS, Crook JE, Rogers A, Metz-Kudashick D, Thiel DD. Botulinum-A toxin/dimethyl sulfoxide bladder instillations for women with refractory idiopathic detrusor overactivity: a phase 1/2 study. *Mayo Clin Proc* 2009;84(8):702-706.
4. White WM, Pickens RB, Doggweiler R, Klein FA. Short term efficacy of botulinum toxin-A for refractory overactive bladder in the elderly population. *Urology* 2008;180(6):2522-2526.
5. Sahai A, Sangster P, Kalsi V, Khan MS, Fowler CJ, Dasgupta P. Assessment of urodynamics and detrusor contractility variables in patients with overactive bladder syndrome treated with botulinum toxin-A: is incomplete emptying predictable? *BJU Int* 2009;103(5):630-634.
6. Jeffery S, Fynes M, Lee F, Wang K, Williams L, Morley R. Efficacy and complications of intradetrusor injection with botulinum toxin A in patients with refractory idiopathic detrusor overactivity. *BJU Int* 2007;100(6):1302-1306.
7. Roger AK. Botulinum neurotoxin serotypes A and B preparations have different safety margins in preclinical models of muscle weakening efficacy and systemic safety. *Toxicon* 2002:40(7):923-928.
8. Ksibi I, Godard AL, Azouvi P, Denys P, Dziri C. Botulinum toxin and refractory non-neurogenic overactive detrusor. *Ann Phys Rehabil Med* 2009;52(9):668-683.