Case Report

Long-term neurogenic lower urinary tract dysfunction: A case of cardiovascular nightmares

Amanda H.X. Lee ^{1*}, Andrea L. Ramirez ^{1*}, Andrei V. Krassioukov ^{1,2,3},
Matthias Walter ¹

¹International Collaboration on Repair Discoveries (ICORD), Faculty of Medicine, University of British Columbia, Vancouver, British Columbia, Canada, ²Division of Physical Medicine and Rehabilitation, Department of Medicine, Faculty of Medicine, University of British Columbia, Vancouver, British Columbia, Canada, ³G.F. Strong Rehabilitation Centre, Vancouver, British Columbia, Canada

Context: Individuals with spinal cord injury (SCI) suffering from autonomic dysreflexia (AD) due to neurogenic detrusor overactivity (NDO) can effectively be treated with intradetrusor onabotulinumtoxinA. We present a complex case to highlight the treatment's potential limitations to ameliorate AD and improve lower urinary tract (LUT) function in this population.

Findings: A 46-year old man, who was relying on an indwelling urethral catheter for bladder emptying due to severely impaired hand function following a SCI (C5, AIS B) sustained 30 years ago, underwent intradetrusor onabotulinumtoxinA injections for treatment of refractory NDO and associated AD. Although LUT function slightly improved (i.e. cystometric capacity increased while detrusor pressure was reduced), severe bladder-related AD persisted post-treatment.

Conclusions: This case raises awareness of serious considerations when treating NDO-related AD in individuals with longstanding neurogenic LUT dysfunction and compromised dexterity following SCI. Given the limited improvement in LUT function and persisting bladder-related AD following treatment, urinary diversion as advocated in the wider literature should be considered to protect an individual's urinary tract from further deterioration and thus eliminate bladder-related AD consequences long-term. Early treatment and management of NDO and AD is crucial to minimize complications associated with these two major health risks in this population.

Keywords: Autonomic dysreflexia, Neurogenic detrusor overactivity, OnabotulinumtoxinA, Spinal cord injury, Urodynamic investigation

Introduction

In addition to sensorimotor impairment, individuals with spinal cord injury (SCI) may suffer from profound autonomic dysfunctions, such as autonomic dysreflexia (AD) and neurogenic detrusor overactivity (NDO).¹ A frequent cardiovascular consequence following SCI, AD is defined in accordance with the International Standards to document remaining Autonomic Function after SCI as an increase in systolic blood pressure (SBP) of at least 20 mmHg from baseline.² This rapid increase in SBP is caused by an aberrant sympathetic response to either noxious or innocuous stimuli

from below the level of injury that cannot be treated as typical essential hypertension. This condition is highly prevalent in those with SCI at or above T6³ and can occur more than 40 times per day.⁴ As SBP can rise above 300 mmHg during a single episode of AD, consequences can be devastating and lead to stroke, myocardial infarction, or even death.⁵ Considering the increased risk of cerebrovascular⁶ and cardiovascular⁷ disease in individuals with SCI and potentially fatal outcomes of misdiagnosed or mismanaged AD, it is imperative to ascertain and minimize the triggers of AD where possible. Common well-known triggers can be extrinsic (i.e. a tight shoelace or belt) or intrinsic (i.e. bowel or bladder-related). One leading trigger of potentially life-threatening episodes of AD is NDO,⁸

*Contributed equally (i.e. shared first author)

Correspondence to: Andrei V. Krassioukov, ICORD-BSCC, 818 West 10th Avenue, Vancouver, BC, Canada, V5Z 1M9; Ph: + (604) 675-8819. E-mail: krassioukov@icord.org

which is characterized by involuntary detrusor contractions and can occur several times a day. Urodynamic investigation (UDI) is considered the gold standard to evaluate lower urinary tract (LUT) function and detect NDO.⁹ Both AD and NDO place a tremendous burden on individuals with SCI. Therefore, in accordance with the World Health Organization,¹⁰ amelioration of cardiovascular and LUT functions is of primary importance. Recently, we have shown that intradetrusor onabotulinumtoxinA injections, a well-established second-line option to treat NDO, significantly reduced the severity and frequency of AD in this population.¹¹ Herein, we present the case where severe episodes of bladder-related AD persisted despite this appropriate treatment and highlight its limitation in this population.

Case presentation

Subject

A 46-year-old man presented with well documented autonomic dysfunction² including AD and NDO as a consequence of his motor complete, sensory incomplete SCI (C5, American Spinal Injury Association Impairment Scale B)¹² which was sustained 30 years ago. He relied on an indwelling urethral catheter for bladder emptying due to severely impaired hand function.

Cardiovascular monitoring

Concurrent to the UDI and intradetrusor onabotulinumtoxinA injections, we episodically recorded SBP, diastolic blood pressure and heart rate (HR) every minute (CARESCAPE V100, GE Healthcare, Milwaukee, WI, USA) in order to detect AD and record its severity throughout the UDI (Fig. 1).

Assessment of lower urinary tract function

Urodynamic investigation (Table 1) along with surface external anal sphincter/pelvic floor electromyography was performed at baseline and post-treatment (Aquarius TT, Laborie Model 94-R03-BT, Montreal, Quebec, Canada) in accordance with the International Continence Society's Good Urodynamic Practices.¹³

Baseline lower urinary tract assessment

Within the first two minutes of bladder filling (Fig. 1A), terminal NDO (maximum detrusor pressure 65 cmH₂O) and AD (increase in SBP 49 mmHg) occurred simultaneously (cystometric capacity 45 mL). Although UDI was stopped immediately as a safety precaution followed by complete bladder drainage, AD (max. SBP 196 mmHg) persisted for an additional five

minutes. During this period, we found no other potential stimuli for AD, such as fecal impaction.

Intradetrusor onabotulinumtoxinA injections

Since the individual was refractory to antimuscarinic medication, he underwent intradetrusor onabotulinumtoxinA (200 UI) injections, a standard second-line treatment option for NDO according to the European Urology Association guidelines on neuro-urology,⁹ to improve the individual's LUT function before considering more invasive treatment options, such as urinary diversion. Considering the iatrogenic risk of cystoscopy to elicit AD,¹⁴ cardiovascular parameters were recorded accordingly. Apparent structural changes (i.e. trabeculations) were observed during cystoscopy. Despite the administration of local anesthesia prior to this intervention, a severe episode of AD occurred (Fig. 1B). Intradetrusor onabotulinumtoxinA injections were completed within eleven minutes. Instrumentation was removed and the bladder was completely emptied; however, the decrease in SBP was gradual and remained above 160 mmHg for ten minutes. Finally, AD ceased after an additional ten minutes.

Post-treatment lower urinary tract assessment

One month post-treatment, a follow-up UDI was conducted to evaluate treatment efficacy (Fig. 1C). Two and a half minutes after commencing bladder filling, the individual reported the onset of goosebumps (a typical symptom of AD). This corresponded to an SBP of 161 mmHg, which exceeded the AD threshold at an infused volume of 80 mL. Thus, UDI was stopped shortly after (cystometric capacity 100 mL; maximum detrusor pressure 22 cmH₂O). After draining the bladder completely, the individual was transferred from a supine into an upright position. However, AD persisted with profound clinical symptoms (headache, sweating and goosebumps). With no other reason evident to explain the persistence of elevated SBP, the individual received nifedipine [5 mg sublingual] in accordance with the 'Consortium for Spinal Cord Medicine' clinical practice guidelines for acute management of AD.¹⁵ Over the next twenty minutes, SBP slowly decreased and returned below the threshold for AD, while his apparent clinical symptoms ceased as well. The individual was discharged shortly after free of complaints. During all three assessments, the individual was not suffering from a symptomatic urinary tract infection (UTI) or pressure sore, both of which may potentially trigger or exacerbate AD.

Figure 1 A – Changes in cardiovascular parameters during baseline UDI. (a) Dotted line indicates the start of bladder filling. Prior to that, arterial blood pressure [(BP) in gray, upper border = systolic BP (SBP), lower border = diastolic BP (DBP)] ranged from 135/70–140/80 mmHg with a heart rate [(HR) = thick black line] of 60 beats per minute (bpm) at baseline. No clinical symptoms or signs for autonomic dysreflexia (AD) were present. (b) Three minutes later, bladder filling was stopped (dotted line) due to clinically symptomatic AD with an increase in SBP of 49 mmHg (i.e. 189 mmHg). Furthermore, HR had dropped by 10 bpm (i.e. 50 bpm). Although the bladder was emptied and the catheter was removed, AD persisted for 5 min with a peak increase in SBP of 56 mmHg (i.e. 196 mmHg). B – Changes in cardiovascular parameters during intradetrusor onabotulinumtoxinA injections. (c) Dotted line indicates the start of the flexible cystoscopy. Prior to that, arterial BP (116/70 mmHg) and HR (67 bpm) were unremarkable at baseline. No clinical symptoms or signs for AD were present. (d) Intradetrusor onabotulinumtoxinA injections were completed within eleven minutes. During this period, SBP rose above 200 mmHg. The peak increase in SBP was 125 mmHg (i.e. 241 mmHg). At the same time HR dropped by 31 bpm (i.e. 36 bpm), indicating bradycardia. Following cystoscopy (dotted line), arterial BP and HR recovered to baseline values over the next fifteen minutes. C – Changes in cardiovascular parameters during post-treatment UDI. (e) Start of bladder filling (dotted line). Prior to that, arterial BP (106/61 mmHg) and HR (81 bpm) were unremarkable. No clinical symptoms or signs for AD were present. (f) Bladder filling was stopped after four minutes (dotted line) when clinical symptoms of AD were reported by the individual. By then, SBP had increased by 55 mmHg (i.e. 161 mmHg), while HR had dropped by 38 bpm (i.e. 43 bpm). (g) At the time point of bladder emptying, SBP had increased by 147 mmHg (i.e. 253 mmHg), while HR remained above 40 bpm. (h) Although the bladder was completely empty (without an indwelling catheter *in situ*) and no other evident stimulus for AD present, SBP remained elevated. After oral administration of nifedipine (dotted line), SBP slowly returned below the threshold for AD over the next twenty minutes. AD, autonomic dysreflexia; BP, blood pressure; BPM, beats per minute; DBP, diastolic blood pressure; HR, heart rate; SBP, systolic blood pressure; UDI, urodynamic investigation.

Discussion

Spinal cord injury is one of the most debilitating conditions that immediately alters a person's life; in addition to the significant burden of disability, SCI also results in profound secondary complications, such as autonomic dysfunction, and is considered a financial challenge for affected individuals and society alike.¹⁶ Regaining control of autonomic functions, such as cardiovascular system and LUT, are among the highest priorities for individuals living with SCI.¹⁷ Here, we

present the case of an individual who had been living with a motor complete, sensory incomplete SCI for three decades, and who persistently experienced severe episodes of AD despite having received appropriate NDO treatment. Intradetrusor onabotulinumtoxinA injections are well-established as second-line treatment options for NDO and have been reported to significantly reduce the severity and frequency of AD in individuals with SCI.¹¹ However, structural changes of the urinary bladder, such as trabeculation, as a long-term SCI consequence could potentially limit the efficacy of onabotulinumtoxinA. This case highlights the therapeutic limitations of NDO treatment in individuals with longstanding SCI relying on indwelling catheter for bladder management. Although cystometric capacity increased (+55 mL, +122%), detrusor pressure was markedly reduced (−43 cmH₂O, −66%) and NDO was eliminated, severe bladder-related AD persisted, which can be attributed to the persisting low bladder compliance (5 mL/cmH₂O).

Continuing bladder management with an indwelling catheter (suprapubic or urethral) is not advisable in this individual at this stage, as this option: (1) will further decrease bladder capacity and compliance,¹⁸

Table 1 Comparison between baseline and follow-up urodynamic investigation.

Filling cystometry	Baseline	Follow-up
First sensation of filling [mL]	25	70
First detrusor contraction [mL]	45	n/a [†]
Cystometric capacity [mL]	45	100
Maximum cystometric capacity [mL]	45*	125
Maximum detrusor pressure [cmH ₂ O]	65	22
Compliance [mL/cmH ₂ O]	3	5

*Detrusor overactivity incontinence led to complete bladder emptying. Therefore, maximum cystometric capacity is equal to cystometric capacity at baseline urodynamic investigation.

[†]No detrusor overactivity occurred during one month follow-up urodynamic investigation.

(2) is associated with higher odds of UTI compared to other methods of bladder emptying;¹⁹ (3) is a known risk factor for bladder cancer;²⁰ and (4) is prone to encrustation (i.e. risk of catheter blockage) and bladder stone formation,²¹ thus presenting as a potent trigger for bladder-related AD. In addition, an indwelling urethral (Foley) catheter requires stabilization (i.e. taping to the thigh/abdomen) to prevent drag/traction, which otherwise could result in urethral damage. Furthermore, individuals need sufficient manual dexterity to operate an attached leg bag. Considering the aforementioned concerns, urinary diversion should be considered, especially given the extent of this individual's NDO (with a high risk of long-term upper urinary tract deterioration).²² Both continent²³ and non-continent²⁴ diversion techniques have been shown to improve urinary tract function long-term^{25,26} and have a beneficial effect on ameliorating AD²⁷ in this population. For example, bladder augmentation (continent diversion) improves LUT function by decreasing detrusor pressure and increasing bladder volume without the need to entirely remove the bladder. On the other hand, a non-continent diversion, such as an ileal conduit (i.e. replacement of the bladder as a urine reservoir), has also been shown to be a safe, well-tolerated intervention with a relatively low incidence of post-operative (36%) and long-term (<20%) complications in patients with SCI.²⁴ In light of this individual's limited hand function, which deters intermittent self-catheterization (e.g. necessary after bladder augmentation), an ileal conduit may be the most suitable option for bladder management in this case.^{28,29} Taken all into consideration, the decision for one specific type of urinary diversion should reflect the individual's situation including one's capability to self-catheterize (e.g. manual dexterity)²⁹ and social aspects (i.e. availability of caregiver, help from partner or family). Thus, commencing appropriate treatment early may prevent or at least limit long-term deterioration of LUT and cardiovascular function in this population.

Acknowledgement

We thank the individual, who provided written informed consent, for participation and publication of this case. We would like to thank Dr. Mark Nigro (Department of Urologic Sciences, UBC, Vancouver, Canada) for the application of onabotulinumtoxinA. Furthermore, we would like to thank Ivy Allard and Tammy Wilder (Vancouver Coastal Health, Vancouver, Canada) for their assistance with the urodynamic assessments.

Disclaimer statements/funding

Contributors None.

Funding M. Walter is a recipient of the Michael Smith Foundation for Health Research Trainee Award in partnership with the Rick Hansen Foundation.

Conflicts of interest Authors have no conflict of interests to declare.

ORCID

Amanda H.X. Lee <http://orcid.org/0000-0002-5941-270X>

Andrea L. Ramirez <http://orcid.org/0000-0002-3514-7841>

Andrei V. Krassioukov <http://orcid.org/0000-0002-0022-7972>

Matthias Walter <http://orcid.org/0000-0001-5347-1584>

References

- Walter M, Krassioukov AV. Autonomic nervous system in paraplegic athletes with spinal cord injury. *Phys Med Rehabil Clin N Am.* 2018;29(2):245–66.
- Krassioukov A, Biering-Sorensen F, Donovan W, Kennelly M, Kirshblum S, Krogh K, *et al.* International standards to document remaining autonomic function after spinal cord injury. *J Spinal Cord Med.* 2012;35(4):201–10.
- Curt A, Nitsche B, Rodic B, Schurch B, Dietz V. Assessment of autonomic dysreflexia in patients with spinal cord injury. *J Neurol Neurosurg Psychiatry.* 1997;62(5):473–7.
- Hubli M, Gee CM, Krassioukov AV. Refined assessment of blood pressure instability after spinal cord injury. *Am J Hypertens.* 2015;28(2):173–81.
- Wan D, Krassioukov AV. Life-threatening outcomes associated with autonomic dysreflexia: a clinical review. *J Spinal Cord Med.* 2014;37(1):2–10.
- Wu JC, Chen YC, Liu L, Chen TJ, Huang WC, Cheng H, *et al.* Increased risk of stroke after spinal cord injury: a nationwide 4-year follow-up cohort study. *Neurology.* 2012;78(14):1051–7.
- Cragg JJ, Noonan VK, Krassioukov A, Borisoff J. Cardiovascular disease and spinal cord injury: results from a national population health survey. *Neurology.* 2013;81(8):723–8.
- Walter M, Knupfer SC, Cragg JJ, Leitner L, Schneider MP, Mehnert U, *et al.* Prediction of autonomic dysreflexia during urodynamics: a prospective cohort study. *BMC Med.* 2018;16(1):53.
- Groen J, Pannek J, Castro Diaz D, Del Popolo G, Gross T, Hamid R, *et al.* Summary of European Association of Urology (EAU) guidelines on neuro-urology. *Eur Urol.* 2016;69(2):324–33.
- Organization WH. Spinal Cord Injury. 2013 [2019/04/14]. Available from: <https://www.who.int/news-room/fact-sheets/detail/spinal-cord-injury>.
- Fougere RJ, Currie KD, Nigro MK, Stothers L, Rapoport D, Krassioukov AV. Reduction in bladder-related autonomic dysreflexia after onabotulinumtoxinA treatment in spinal cord injury. *J Neurotrauma.* 2016;33(18):1651–7.
- Kirshblum SC, Burns SP, Biering-Sorensen F, Biering-Sorensen F, Donovan W, Graves DE, *et al.* International standards for neurological classification of spinal cord injury (revised 2011). *J Spinal Cord Med.* 2011;34(6):535–46.
- Schafer W, Abrams P, Liao L, Mattiasson A, Pesce F, Spangberg A, *et al.* Good urodynamic practices: uroflowmetry, filling cystometry, and pressure-flow studies. *Neurourol Urodyn.* 2002;21(3):261–74.
- Liu N, Zhou M, Biering-Sorensen F, Krassioukov AV. Iatrogenic urological triggers of autonomic dysreflexia: a systematic review. *Spinal Cord.* 2015;53(7):500–9.

- 15 Consortium for Spinal Cord Medicine. Acute management of autonomic dysreflexia: individuals with spinal cord injury presenting to health-care facilities. *J Spinal Cord Med.* 2002 Spring;25 (Suppl 1):S67–S88.
- 16 Krueger H, Noonan VK, Trenaman LM, Joshi P, Rivers CS. The economic burden of traumatic spinal cord injury in Canada. *Chronic Dis Inj Can.* 2013 Jun;33(3):113–22.
- 17 Anderson KD. Targeting recovery: priorities of the spinal cord-injured population. *J Neurotrauma.* 2004;21(10):1371–83.
- 18 Consortium for Spinal Cord Medicine. Bladder management for adults with spinal cord injury: a clinical practice guideline for health-care providers. *J Spinal Cord Med.* 2006;29(5):527–73.
- 19 Roth JD, Pariser JJ, Stoffel JT, Lenherr SM, Myers JB, Welk B, Elliott SP. Patient subjective assessment of urinary tract infection frequency and severity is associated with bladder management method in spinal cord injury. *Spinal Cord.* 2019. doi:10.1038/s41393-019-0268-2
- 20 Welk B, McIntyre A, Teasell R, Potter P, Loh E. Bladder cancer in individuals with spinal cord injuries. *Spinal Cord.* 2013;51(7):516–21.
- 21 Park YI, Linsenmeyer TA. A method to minimize indwelling catheter calcification and bladder stones in individuals with spinal cord injury. *J Spinal Cord Med.* 2001;24(2):105–8.
- 22 Elmelund M, Oturai PS, Toson B, Biering-Sorensen F. Forty-five-year follow-up on the renal function after spinal cord injury. *Spinal Cord.* 2016;54(6):445–51.
- 23 Phe V, Boissier R, Blok BFM, Del Popolo G, Musco S, Castro-Diaz D, et al. Continent catheterizable tubes/stomas in adult neuro-urological patients: a systematic review. *Neurourol Urodyn.* 2017;36(7):1711–22.
- 24 Chartier-Kastler EJ, Mozer P, Denys P, Bitker MO, Haertig A, Richard F. Neurogenic bladder management and cutaneous non-continent ileal conduit. *Spinal Cord.* 2002;40(9):443–8.
- 25 Chartier-Kastler EJ, Mongiat-Artus P, Bitker MO, Chancellor MB, Richard F, Denys P. Long-term results of augmentation cystoplasty in spinal cord injury patients. *Spinal Cord.* 2000;38(8):490–4.
- 26 Gurung PM, Attar KH, Abdul-Rahman A, Morris T, Hamid R, Shah PJ. Long-term outcomes of augmentation ileocystoplasty in patients with spinal cord injury: a minimum of 10 years of follow-up. *BJU Int.* 2012;109(8):1236–42.
- 27 Sidi AA, Becher EF, Reddy PK, Dykstra DD. Augmentation enterocystoplasty for the management of voiding dysfunction in spinal cord injury patients. *J Urol.* 1990;143(1):83–5.
- 28 Peterson AC, Curtis LH, Shea AM, Borawski KM, Schulman KA, Scales CD, Jr. Urinary diversion in patients with spinal cord injury in the United States. *Urology.* 2012;80(6):1247–51.
- 29 Sorokin I, De E. Options for independent bladder management in patients with spinal cord injury and hand function prohibiting intermittent catheterization. *Neurourol Urodyn.* 2015;34(2):167–76.