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CLINICAL OPINION

Female Pelvic Medicine & Reconstructive Surgery (FPMRS) challenges on behalf of the collaborative research in pelvic surgery consortium (CoRPS): managing complicated cases series 2: management of urinary incontinence in a neurogenic patient

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Abstract
Discussion and management of incontinence in a patient with spina bifida by four international experts followed by a literature review.

Keywords Botulinum toxin · Neurogenic bladder · Stress urinary incontinence · Urodynamics

Case

A 24-year-old African American nulliparous woman presented with longstanding urinary incontinence. Her history was significant for developing urinary incontinence at the age of 10, and she was found to have a tethered cord and spina bifida. She underwent laminectomy for release of the tethered cord. Immediately following surgery, she was unable to void and began performing clean intermittent catheterization (CIC). After 1 month, she began to urinate spontaneously and discontinued CIC. However, her urinary incontinence never resolved.

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Her symptoms included voiding every 2 h and once at night. With every void she has the sensation of urgency but leaks continuously. She leaks with walking, going up stairs, anxiety, and the sensation of urgency. She changes four soaked incontinence pads per day and one at night. She feels incomplete bladder emptying and strains to urinate. Furthermore, she has constipation with daily hard Bristol I bowel movement. Every 2 months she has a symptomatic culture positive UTIs. She is sexually active and is bothered by incontinence with activity.

Previously she took tolterodine and did not notice improvement.

On examination she has normal anal sphincter tone, but is unable to contract pelvic floor musculature. Straight catheter post-void residual is 75 ml.

Renal bladder ultrasound demonstrated a severely trabeculated bladder and no hydronephrosis. Urine culture was positive for *Escherichia coli*, although the patient was not symptomatic at the time. Video urodynamics was done according to International Continence Society Good Urodynamic Practices. Baseline detrusor pressure (Pdet) was 0 cmH_2O. The patient was filled at a slow rate of 15–30 ml/min, and poor compliance was demonstrated. At 150 ml Pdet had risen to 11 cmH_2O, and the patient began to leak continuously (DLPP 11 cmH_2O). The patient had an involuntary contraction at 180 ml (233 ml fill volume) with Qmax of 3 ml/s and Pdet at Qmax of 14 cmH_2O (3 cmH_2O above baseline). The patient was unable to initiate any voluntary detrusor contractions. EMG demonstrated detrusor sphincter

dyssynergia. Post-void residual volume was 120 ml. Cystoscopy demonstrated severe trabeculation, open lead pipe urethra and bladder neck, positive cough stress test, and a bladder diverticulum at the dome.

How would you proceed?

Expert urogynecologist recommendations

Dr. C. Grimes (Urogynecology, NY, USA)

This patient has a diagnosis of mixed urinary incontinence and neurogenic bladder, constipation, and possibly recurrent UTIs and is refractory to anticholinergic therapy. I would like to evaluate her sacral nerves with a sharp/dull discrimination test, bulbocavernosus and anal wink. I would start initial treatment with a bowel regimen [psyllium fiber, docusate sodium, and polyethylene glycol (PEG)3350] and prophylaxis for recurrent UTIs (either vitamin C 10,000 mg q8h or trimethoprim 100 mg daily).

I would have her restart clean intermittent catheterization and evaluate the impact of these treatments on her symptoms. She could then consider trial of mirabegron. If persistently bothered by urgency incontinence, further treatment could include intradetrusor botulinum toxin injection as the next best step. After this, if she continued to have symptomatic stress incontinence, I would consider biofeedback with electrical stimulation, Poise® impressa®, incontinence pessary, or midurethral sling (after repeat urodynamics). She should be followed on a regular basis at least annually with upper tract imaging.

Dr. T. Asatiani (Urogynecology, Tbilisi, Georgia)

Patients with spina bifida require longitudinal care as they transition from childhood to adolescence and then to adulthood. Despite this need for regular assessment, many adult patient with spina bifida lose coordinated urologic care. In this particular case, I would first treat the neurogenic stress urinary incontinence. Pelvic floor muscle training would be ineffective. The better option would be an autologous fascial sling surgery. I would recommend daily antibiotic prophylaxis for urinary tract infections. To improve bladder storage botulinum toxin type A could be recommended as an antimuscarinics was ineffective. However, this may increase the risk of urinary tract infections, while the antimuscarinics may precipitate and exacerbate constipation. Lifelong routine ultrasound surveillance of the kidneys is recommended with yearly US and tests for renal function as well as urodynamic investigation.

Dr. E. Brennand (Urogynecology, Alberta, Canada)

A stepwise approach is recommended as well as setting realistic treatment expectations. A full treatment plan may take many months to develop.

I would not order any additional testing above what has already been performed. I would focus on her urgency and frequency symptoms first because of concerns of possibly flaring overactive symptoms through intervention for stress incontinence. Given the association between constipation and overactive bladder, I would provide education regarding a healthy bowel routine through dietary choices and supplementary fiber and offer pharmacologic options such as osmotics (PEG 3350, magnesium) or a guanylate cyclase-C agonist (linaclotide). I would have the patient complete a baseline 3-day bladder diary and subsequent diaries after initiating therapy as I find the quantitative nature of this information of most use when determining "success" or "failure." Given that one anti-cholinergic has been trialed and deemed ineffective, I would move on to a beta 3 agonist. Should oral pharmacologics fail to improve the patient's overactive symptoms, I would feel comfortable offering a trial of intravesical bladder botulinum toxin. Should that option fail, trial of percutaneous tibial nerve stimulation or a peripheral nerve evaluation for sacral neuromodulation could be considered as success of both modalities has been reported in patients with spinda bifida.

Once improvement in OAB has been achieved, I would focus on the stress urinary incontinence. I would involve pelvic floor physiotherapists to see if improvement of the pelvic floor function can be achieved. Additionally, I would offer the patient a pessary fitting. If the patient desires a procedural intervention, my recommendation would be urethral bulking because of her age, possible future childbearing, and anatomic abnormality of an open bladder neck. At our center, we use polyacrylamide gel. I recommend delaying consideration of a synthetic mesh or fascial sling until the patient has completed or decided against childbearing. While no strong evidence exists regarding the optimal age of sling surgery, I generally counsel that women wait until age 35 or later because of risk of failure over time.

Dr. A. Wang (Urology, Sydney, Australia)

This patient is best managed under a multidisciplinary team with a rehabilitation physician, continence nurse, pelvic floor physiotherapist, psychologist, neurosurgeon, colorectal surgeon, and urologist. In terms of further evaluation, an up-to-date MRI and neurosurgical review are important to ensure stable neurology. I will assess her mobility and hand-eye coordination for CIC.

For her treatment plan, I would explain UDS findings to the patient and her family and highlight the need to manage her detrusor overactivity and compliance issue first before

embarking on surgical treatment for stress urinary incontinence. I would re-institute CIC and trial her on medical therapy with an alternate antimuscarinic, e.g., solifenacin or darifenacin, a beta 3-adrenergic agonist with mirabegron, or a combination of both. I would advise her to avoid straining to void and highlight the need to manage her constipation. Review by a pelvic floor physiotherapist for pelvic floor muscle training and a continence nurse to review her CIC technique at this stage will be beneficial. Regarding UTI prevention, I would advise her to drink 1.5-2 l of water daily and consider prophylaxis with a low-dose postcoital antibiotic if relevant or alternatively with D-mannose or Hiprex and vitamin C. Follow-up will be arranged in 6 weeks with a midstream urine (MUS), a bladder diary documenting her fluid intake, voided volumes, and residual via CIC, and a 24-h pad weight. If she has refractory OAB symptoms, intravesical botulinum toxin injection can be considered. I will start with 200 units of onabotulinum toxin and repeat her urodynamic study in 2–3 months. Dose escalation to 300 units may be necessary. Regarding her stress urinary incontinence, my preference is to perform an autologous pubovaginal fascial sling although an artificial urinary sphincter is also an option. I would avoid a mesh midurethral sling in this setting and a urethral bulking agent is unlikely to make her dry in view of her very low leak point pressure. If she has refractory detrusor overactivity or decreased compliance after treatment with onabotulinum toxin, concomitant augmentation cystoplasty at the time of her sling surgery can be performed. It is important that she understand the need for ongoing CIC, and if there is any technical issue with regard to access or positioning, formation of a catheterizable stoma needs to be considered also.

Ongoing follow-up is required with an annual renal tract US, bladder diary, and MSU. I will repeat her urodynamic study after sling surgery especially if she is maintained on medical therapy or intravesical onabotulinum toxin injection to ensure adequate treatment of her detrusor overactivity and probable decreased compliance.

How the CASE was managed

The patient was placed on a bowel regimen of PEG 3350, docusate sodium, and senna. With this regimen she was able to have a soft bowel movement daily. She was retaught CIC and tried catheterizing every 3–4 h but was still leaking three large pads during the day and one at night. She was offered trial of mirabegron but did not want to take any oral medications. Next, she received intradetrusor onabotulinumtoxin A (200 U). Afterwards she was completely dry, catheterizing every 6 h for 500 ml at a time, and reported no symptomatic UTIs. One year later she began leaking again and underwent repeat onabotulinumtoxin A injection. Renal ultrasound demonstrated no hydronephrosis and serum creatinine remained normal and stable 1 year later.

Literature review

Spina bifida is the most common cause of congenital neurogenic bladder with an incidence of 30 per 100,000 live births [1, 2]. Neurologic lesions in spina bifida vary, depending on the severity of fusion abnormality, and can affect the somatic, parasympathetic, and sympathetic innervation of the bladder. This translates to difficulty with bladder storage and emptying as well as the potential for chronic kidney disease due to poor bladder dynamics. Up to 90% of patients with this condition suffer from lower urinary tract symptoms [3]. Previously urinary tract complications were the leading cause of death in these patients [4].

In this case, the patient had an open bladder outlet as well as small capacity bladder with poor compliance and detrusor overactivity. She also lacked the ability to void with volition. It is common with neurogenic bladder to have problems with both the bladder outlet and bladder function. Among our experts, three of the four felt it important to first address the bladder function and detrusor overactivity with poor compliance. All agreed it was reasonable to first trial an oral agent, either another antimuscarinic or beta agonist, and if the patient remained refractory to quickly move to onabotulinumtoxin A. Similarly, in our case, given her refractory nature to a prior antimuscarinic and desire to avoid oral medications, we chose to treat with onabotulinumtoxin A. Two of the four experts emphasized the importance of continued CIC to prevent upper tract damage, given the poor compliance and elevated residual of 120 ml, and treatment of constipation.

Interestingly, recommended options for the treatment of her stress urinary incontinence varied. One expert offered a pessary, biofeedback, pelvic floor physical therapy, and a midurethral sling. Another recommended a bulking agent given her young age and potential for childbearing. Two experts recommended an autologous sling. Two experts felt strongly about avoiding a mesh sling in this patient because of young age and low leak point pressures. When deciding on treatment for stress urinary incontinence (or the bladder outlet), it is also important to consider the fact that the patient will be continuing to perform CIC.

This case highlights the controversy as to whether or not the bladder outlet should be addressed at the same time as the bladder function. Goals of treatment of neurogenic bladder are to achieve continence, prevent upper tract damage, prevent infection, and improve quality of life. In this case, we chose to treat first the bladder function given the detrusor overactivity and the fact that she had poor compliance. Treating the outlet first has the potential in this patient to lead to upper tract damage. Afterwards, she was not symptomatic from her bladder outlet. To address her inability to initiate voiding and her incomplete bladder emptying, we started her on CIC. The

experts are in agreement regarding treatment of her bladder function and if failure to medication, onabotulinumtoxin A would be the next recommended step.

Previously, the most commonly performed procedure for bladder dysfunction in spina bifida patients was augmentation cystoplasty [1]. Intradetrusor injection of onabotulinumtoxin A (BTX-A) was first described by Schurch et al. in 2000 [5]. The DIGNITY randomized controlled trials demonstrated that intradetrusor injection of onabotulinumtoxin A was safe and effective for neurogenic detrusor overactivity. However, these trials were limited to patients with spinal cord injury (SCI) or multiple sclerosis (MS) [7, 8]. In 2009, Game et al. published the results of a systematic literature review that included six articles evaluating the safety and efficacy of (BTX-A) in children with neurogenic detrusor overactivity and incontinence; 93% of these patients had a diagnosis of myelomeningocele. The authors found that when 10–12 U/kg with maximal dose of 300 U was injected under cystoscopic guidance, 65–87% of patients became completely dry. Recently, Peyronnet et al. reported on outcomes of BTX-A injection in 125 adult patients with spina bifida. Global success rate of first injection was 62.3%, and 73.5% of patients reported being dry [6].

There is literature supporting the use onabotulinumtoxin A for spina bifida patients, and most experts agree this is an appropriate treatment for patients refractory to medication. Interestingly, the approach to treatment of her bladder outlet once bladder function improved and if the patient had refractory stress urinary incontinence varied among the experts. There are few data to guide treatment of the bladder outlet in these patients.

Compliance with ethical standards

Conflict of interest Dr. Erin Brennand is the principle investigator for a prospective cohort funded by Contura International and RCT by Boston Scientific: ClinicalTrials.gov Identifier: NCT02480231. No other authors have any disclosures or conflicts of interest.

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