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Trauma and reconstruction

Conservative management of hostile bladders with intravesical botulinum toxin for successful renal transplantation

Sida Niu*, Paul Black, Priya Padmanabhan

Department of Urology, University of Kansas Medical Center, 3901 Rainbow Boulevard, Kansas City, KS, 66160, USA

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Introduction

Renal transplant is the most desired and cost-effective therapy for patients with end stage renal disease. While a lower urinary tract cause of end-stage renal disease (ESRD) is not an absolute contraindication to renal transplantation, appropriate vesical storage and drainage is imperative for survival and function of the graft.[1] It is crucial to address and resolve any urological causes of renal failure prior to transplantation to prevent subsequent graft failure. Most patients can be managed with conservative measures such as intermittent self-catheterization, but select cases may require more aggressive intervention including bladder augmentation or urinary diversion to address a hostile bladder environment prior to transplantation.[1] To our knowledge, this is the first report of a poorly compliant bladder noted during pre-transplant evaluation that was managed conservatively with intravesical botulinum injections leading to a successful transplantation.

Case presentations

The patient is a 22-year-old female in ESRD with a history of neurogenic bladder of unknown etiology characterized by elevated bladder storage pressures and urinary incontinence. Her history is also significant for recurrent UTIs during her childhood and progressive difficulty with voiding. At the age of 11, the patient started dialysis and began performing clean intermittent catheterization (CIC) four times daily with spontaneous intermittent incontinence. She had previous intravesical botulinum toxin injections as an adolescent to reduce her bladder pressures. At the time of initial evaluation, she was on oxybutynin 15mg XL daily and had not seen a urologist for over two years.

Her pre-transplant urologic evaluation included voiding cystourethrogram (VCUG), cystoscopy, urodynamics (UDS) and MRI of the lumbar and sacral spine. The VCUG revealed no vesicoureteral reflux. Cystoscopic evaluation revealed a small and trabeculated bladder. UDS noted a small capacity bladder with poor compliance and elevated storage pressures (Fig. 1). The patient was unable to void during the study despite receiving permission. MRI of the lumbar and sacral spine did not reveal canal or foraminal stenosis. Given the low bladder capacity, unsafe storage pressures, and the patient's reluctancy to undergo any major operations, recommendation was made for intravesical botulinum toxin injections (300U) and CIC every three hours. The patient reported improvement in urgency between catheterizations after her first intravesical botulinum toxin injection. Following her second injection six months later, a repeat UDS revealed significant improvement of bladder function with increased capacity and normalization of compliance and storage pressures (Fig. 2). The decision was made to continue the scheduled injections instead of pursuing a more aggressive option to manage her elevated storage pressures. She went on to receive a renal transplant after her 6th intravesical botulinum toxin injection and continues to have optimal graft function with scheduled injections every six months and CIC.

Discussion

The success of a renal transplant depends on many factors. From a urologic perspective, the lower urinary tract should be sterile, continent, compliant, with adequate capacity and without bladder outlet obstruction.[2] Optimal bladder compliance and capacity are imperative for graft survival as it is well-established that elevated detrusor leak

* Corresponding author. Resident Physician, Department of Urology, 3901 Rainbow Blvd. MS 3016, Kansas City, KS, 66160, USA.
E-mail address: sniu@kumc.edu (S. Niu).

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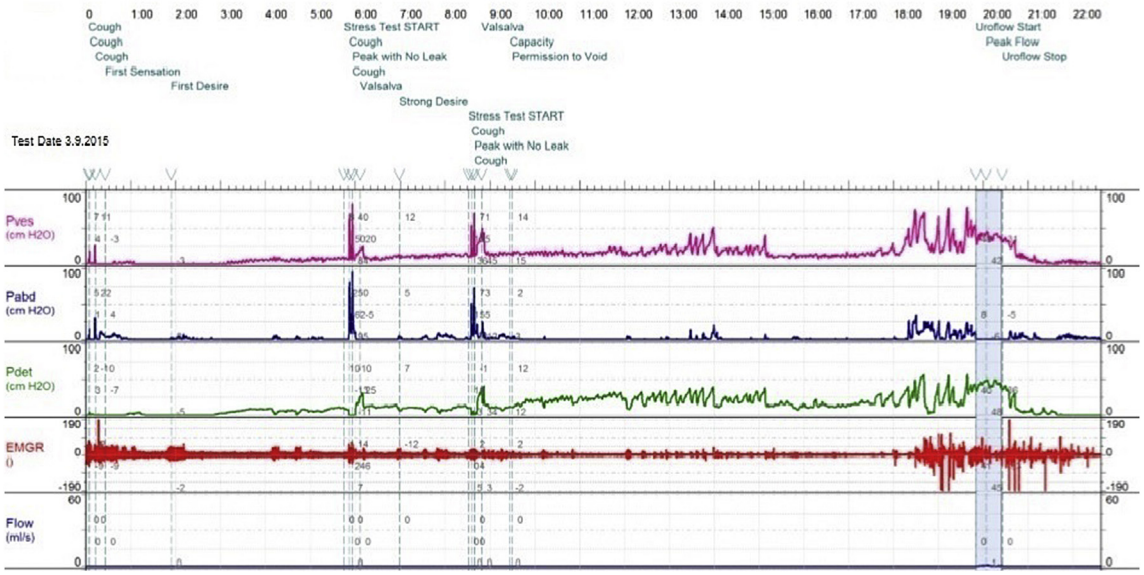

Fig. 1. Urodynamic study performed at initial evaluation prior to initiation of intravesical botulinum toxin injections. The study demonstrated a poorly compliant bladder with a capacity of 201mL and maximum storage pressure of 52cm H_2O. The patient was unable to void during this study.

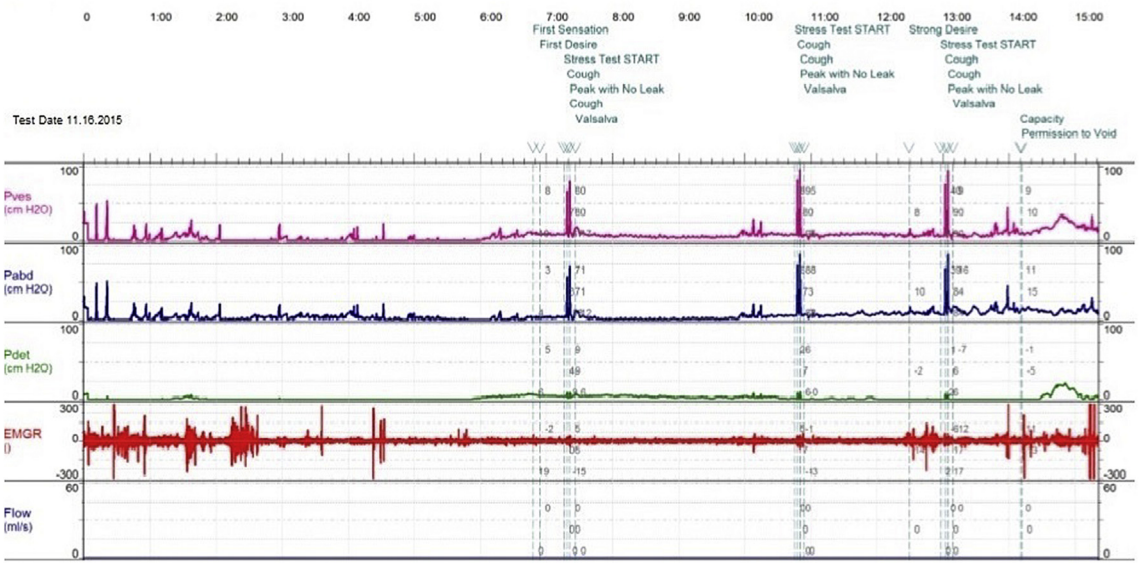

Fig. 2. Urodynamic study performed after the second intravesical botulinum injection, which revealed improved capacity to 331mL, and normalization of compliance and storage pressures. Like the first study, the patient was unable to void despite permission to do so.

point pressures in neurogenic bladders is associated with upper tract deterioration.[3] When a poorly compliant bladder is encountered in the pre-transplant setting, steps must be taken to create a low pressure reservoir that can be emptied in a safe and repeatable method before proceeding with renal transplantation.

Traditionally, poorly compliant bladders have been managed with anticholinergics and CIC, bladder augmentation or urinary diversion. Bladder augmentation has historically been the gold standard for management of anti-cholinergic refractory, poorly compliant bladders because it reliably increases bladder capacity and improves compliance to maintain safe storage pressures. Alternatively, urinary diversion bypasses the dysfunctional or non-compliant reservoir. However, these major surgical operations carry significant short-term and long-term complications including mucus production, bladder stones, electrolyte abnormalities and bladder perforation.[4] The advent of intravesical botulinum has provided an alternative non-surgical management option to improve bladder compliance when more conservative methods have failed.

Intravesical botulinum injections can significantly increase bladder capacity, improve compliance and decrease detrusor overactivity and urge incontinence in patients with neurogenic bladders.[5] As a minimally invasive treatment alternative, it spares or potentially delays patients from morbidities and mortalities associated with more invasive surgical options. While these advantages make intravesical botulinum an attractive alternative to bladder augmentation and urinary diversion, we must be cognizant of the need for repeated botulinum injections since the effect of the toxin eventually wears off. This is undeniably one of the biggest disadvantages of the therapy as it subjects patients to repeated risks associated with the procedure and anesthesia. Patients may overlook the risks and inconvenience of receiving repeated injections indefinitely due to the desire to preserve their native bladder, which was the preference of our patient. These patients must be carefully counseled on the importance of routine follow-up and have a clear understanding that their bladder dynamics may change over

time even with scheduled injections, and that if their bladder parameters no longer respond to intravesical botulinum toxin injections then a more aggressive surgical management options may need to be pursued. The described case of a hostile bladder optimized in the pre-transplant setting with intravesical botulinum injections, ultimately leading to successful renal transplantation without surgical intervention of the lower urinary tract demonstrates utility of botulinum toxin in this patient population. While the long-term benefits of botulinum toxin in this setting is yet to be determined, we believe that this management strategy warrants further evaluation.

Conclusion

We found through our experience that intravesical botulinum injections offers a conservative approach to increase bladder compliance and lower storage pressures thereby permitting safe renal transplantation. This management strategy can be employed in carefully selected patients who have failed oral anticholinergics and CIC, and wish to avoid bladder augmentation and urinary diversion. Careful follow-up is necessary to detect changes in urinary symptoms and bladder parameters, which may be a sign of possible botulinum failure necessitating the need to revisit more aggressive management options.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.eucr.2018.10.017.

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