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High dose botox injection for treatment of high grade vesicoureteral reflux in a complicated pediatric case: A case report

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ABSTRACT

Vesicoureteral reflux (VUR) is a medical condition affecting the bladder and kidneys. Management depends on bladder capacity and compliance. This study found that high-dose BoNT-A is effective in managing high-grade VUR in pediatric patients. In our case, a 3-year-old male with sacral agenesis and neurogenic bladder, experienced a decrease in creatinine levels and improved vesicoureteral reflux after 20 units/kg of BoNT-A were injected into the detrusor and about 100 units were injected into the external sphincter at 3, 9, and 6 o'clock positions.

1. Introduction

Vesicoureteral reflux (VUR) is a medical condition characterized by the retrograde flow of urine from the bladder into the ureters and kidneys and can be classified as either primary or secondary, generally exhibit a malfunctioning lower urinary tract, potentially resulting from obstruction or neuropathology. Secondary VUR occurs as a result of dysfunction within the urinary system, in contrast to the primary type.[1]

In neurogenic bladder patients, secondary VUR is less prone to spontaneous resolution and is less likely to be remedied with antireflux surgery, regardless of the technique or surgical method employed. The prevalent factor that probably distinguishes this patient population from attaining the success rates of the core VUR population is inadequate bladder dynamics. The management of reflux in neurogenic bladder, whether through CIC/anticholinergics, selective and nonselective alpha blockers, ureteral reimplantation, endoscopic surgery, or bladder augmentation, hinges on the optimization or preservation of sufficient bladder capacity and compliance for enhanced outcomes. The risks and advantages of management alternatives must be evaluated with regard to each specific circumstance.[2]

Botulinum Toxin A (BoNT-A) serves as a safe and effective second-line treatment for children with neurogenic bladder who do not respond to standard conservative therapies. Botulinum toxin type A injections have demonstrated efficacy in enhancing continence, augmenting bladder capacity, and decreasing bladder pressure.[3] Botulinum toxin type A injections may be effective in treating vesicoureteral reflux.

Here, we report a case investigating the efficacy and safety of high-dose BoNT-A injections (20 unit/kg) for treating high-grade VUR in a complicated pediatric case.

2. Case presentation

Our case was a three-year-old male with a history of incomplete sacral agenesis and neurogenic bladder who presented with complaints of daytime and nocturnal incontinence, frequent urinary tract infections, and a high serum creatinine level (2.5 mg/dL). In this patient, the left kidney was nonfunctional, and the right kidney had high-grade vesicoureteral reflux (Fig. 1). This patient was refractory to treatment with anticholinergicsm, alpha-blockers and clean intermittent catheterization.

A renal scan with Tc-99m-DPTA showed negligible function of the left kidney, normal perfusion, and function of the right kidney. Differential renal function (DRF) was 96.4 % and 3.6 % for the right and left kidneys, respectively. Several high-amplitude phasic detrusor overactivities, high-pressure low-flow patterns of voiding, and a high post-void residual volume were observed in the urodynamic study.

Finally, 20 units/kg of BoNT-A (MASPORT®500, Masoon Darou, Alborz, Iran) were injected into the detrusor and about 100 units were injected into the external sphincter at 3, 9, and 6 o'clock positions. After injection, the patient's serum creatinine level dropped to 0.8 mg/dl, and he maintained good urinary control. In control VCUG after 6 weeks, significant improvement was seen in the shape of the bladder, and the

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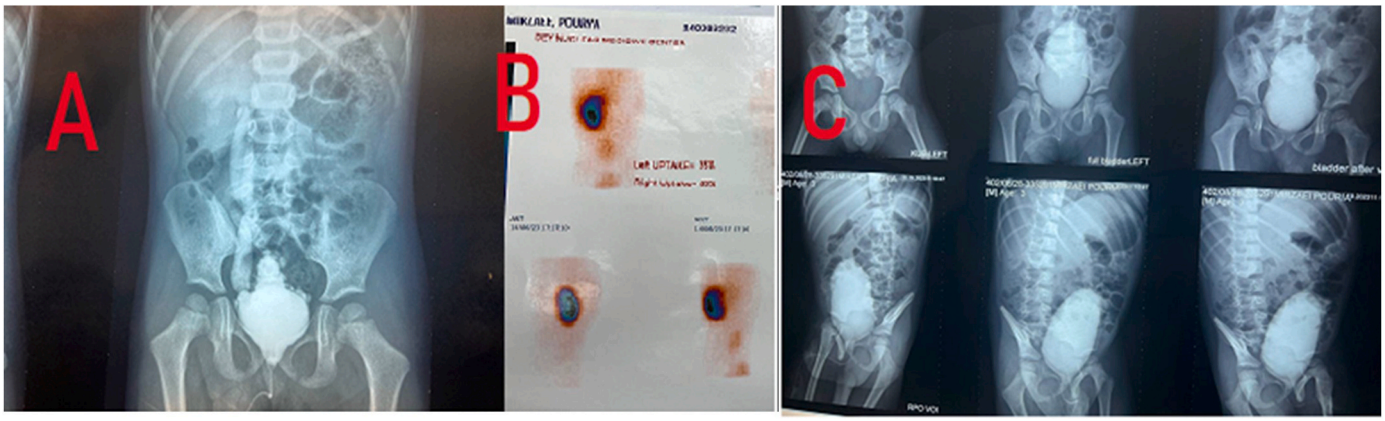

Fig. 1. A: Preoperative VCUG, B: Preoperative DMSA, C: Postoperative VCUG. Significant improvement was seen in the shape of the bladder, and the right vesicoureteral reflux was completely eliminated.

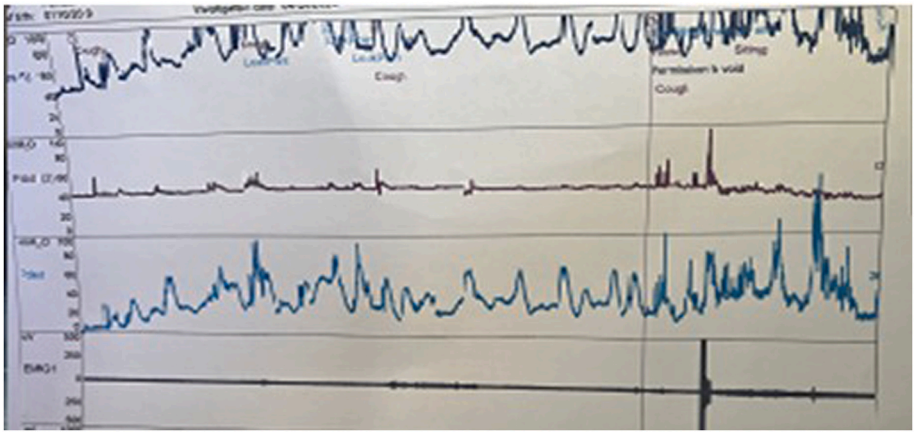

Fig. 2. Urodynamic test (Several high amplitude phasic detrusor overactivities, high-pressure low flow patterns of voiding, and high post-vide residual volume were seen).

right vesicoureteral reflux was completely eliminated (Figs. 1 and 2).

3. Discussion

Botulinum Toxin A (BoNT-A) injections have been effective in treating vesicoureteral reflux (VUR), a disorder characterized by the retrograde flow of urine into the ureters and kidneys.[3] Prior research indicated that a substantial proportion of refluxing ureters either fully resolve or exhibit improvement following BoNT-A therapy. Specifically, it was observed that 40 % of refluxing ureters completely resolved, and 42.5 % improved in a study of children with myelodysplasia who were not responsive to standard conservative therapy.[3] Another study found that reflux disappeared in 53.8 % of ureters and improved in 26.9 % in patients with neurogenic bladders (NB) due to myelomeningocele (MMC).[4]

BoNT-A injections can substantially improve continence. For example, one study found that 71 % of children with urinary leakage between CICs became completely dry after treatment.[3] A meta-analysis indicated a mean enhancement in urine incontinence (UI) scores of 75.87 % within 3–6 months of therapy.[5] A separate trial indicated that 86.7 % of patients experienced effective treatment results.[6] Nevertheless, BoNT-A seems to be less efficacious in treating enuresis (bed-wetting), as one trial indicated a mere 21.1 % success rate.[7]

The typical dose of BoNT-A used is 10 U/kg, up to a maximum of 300–500 U, administered through multiple injections (10–50) directly into the detrusor muscle, while sparing the trigone. These injections are usually done under general anesthesia with a rigid cystoscope.[5]

BoNT-A therapy is typically regarded as safe, with the majority of trials indicating very minor adverse effects, including injection site soreness and urinary tract infections. Urinary retention is a possible adverse effect and may necessitate temporary clean intermittent catheterization (CIC). No significant or systemic adverse effects were documented in the investigations.[7]

Studies indicate that patient age and bladder compliance are significant predictors of treatment success. A meta-regression analysis demonstrated that younger age and higher baseline bladder compliance are associated with better dryness rates.[5] Also, the earlier the treatment was started, the higher the success rate was achieved.

Our case report revealed the substantial efficacy of high dose BoNT-A in managing high-grade VUR in a complicated pediatric case.

There are a lack of long-term prospective studies, a lack of standardized dosing protocols, a lack of standardization in the way of reporting complications, and a need for more placebo controlled studies. Many studies included in the reviews had small sample sizes and there was significant heterogeneity in design, dose, way of administration, outcomes measured and follow-up time.

The outcomes from these cases underline the potential of BoNT-A injections as a viable treatment option for managing high-grade VUR and neurogenic bladder in pediatric patients. BoNT-A exhibits significant advantages in lowering creatinine levels and enhancing urine control, however its efficacy in completely treating VUR is inconsistent. Additional study with more extensive sample sizes is necessary to corroborate these findings and enhance treatment regimens.

4. Conclusions

Our study demonstrates the effectiveness and safety of high-dose Botulinum Toxin A (BoNT-A) injections for managing high-grade vesicoureteral reflux (VUR) and neurogenic bladder in a complex pediatric patient. The medication yielded significant enhancements in urine control, demonstrated by decreased creatinine levels and the alleviation of incontinence in our patients. Although BoNT-A significantly decreased creatinine levels and improved urine control, its efficacy in fully treating VUR differed across individuals.

CRediT authorship contribution statement

Narjes Saberi: Writing – review & editing, Supervision, Project administration, Conceptualization. **Faezeh Sadat Jandaghi:** Writing – original draft, Investigation, Data curation.

Declaration of competing interest

I have nothing to declare.

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