CASE REPORT

OnabotulinumtoxinA injections in detrusor facilitate self-catheterisation in a patient with paraplegia and bladder outlet dyssynergia

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SUMMARY

This case report describes the case of improvement of clean intermittent catheterisation procedures after each intradetrusor administration of onabotulinumtoxinA in a 45-year-old man with L1 paraplegia with neurogenic detrusor overactivity and bladder outlet dyssynergia. On three occasions, improvement on clean intermittent catheterisation procedures appeared 10 to 14 days after intradetrusor injections of onabotulinumtoxinA and lasted for 9 months. We hypothesise a possible influence of intravesical injections of onabotulinumtoxinA on the storage reflex. We also discuss the possibility of a dispersion of onabotulinumtoxinA towards contiguous structures such as the urethral sphincter.

BACKGROUND

The normal process of micturition is composed of the association of storage and voiding phases and involves micturition centres localised in the central but also in the peripheral nervous system. During bladder storage, the urinary sphincter contracts while the bladder remains still. On the contrary, when voiding, the urethral sphincter relaxes and the bladder contracts in order to empty its load.

In patients with spinal cord injury (SCI), this complex interaction between lower urinary tract and nervous system is disturbed. According to the level of the SCI, the patient may present neurogenic detrusor overactivity (DOA), defined by involuntary detrusor contractions during the filling phase of urodynamics; and bladder outlet dyssynergia (BOD), defined as detrusor external sphincter dyssynergia (a detrusor contraction concurrent with an involuntary contraction of the urethral and/or periurethral striated muscle¹) and bladder neck dyssynergia (contraction of striated and smooth muscles on bladder neck during bladder contraction).²

Bladder dysfunction of patients with neurological disorders impairs their quality of life and represents a risk of urinary tract infections, bladder stones formation or kidney damage.

Some medications, such as antimuscarinic agents, and specific care procedures, such as clean intermittent catheterisation (CIC), have been widely used to allow a complete and low-pressure bladder emptying, improving urological symptoms and quality of life, and reducing the risk for urinary tract damage.

Recently, the use of onabotulinumtoxinA (BTX) in urology increased. Intradetrusor injection is used as a second-line treatment option for patients with an appropriate antimuscarinic treatment complaining of side effects or failure.

CASE PRESENTATION

The history of a 45-year-old man with an SCI due to an L1 fracture, American Spinal Injury Association Classification C, incomplete motor L4 left and right, sensory L4 right and L3 left, since he was 27 years old (1997) following a fall from a ladder is here described. On initial evaluation, anamnesis revealed urinary retention with preserved bladder sensation. Neuroperineal evaluation pointed out a perineal hemianaesthesia, preserved anal tonus and anal motor control. Urodynamics, performed using International Continence Society guidelines,¹ showed neurogenic DOA and BOD.

In order to avoid elevated storage pressure and its complications (such as urinary tract infections, upper urinary tract damage, bladder stones formation), the patient received anticholinergics and performed CIC in order to allow a complete bladder emptying.

While experiencing no difficulty with self-catheterisation for 14 years, the patient reported in 2011 some recurring difficulties with CIC: procedures were feasible but really more difficult to perform. There was no improvement when changing the self-catheterisation material. Transrectal ultrasonography showed a prostate of 28 g. Endoscopic workup showed a prostatic urethral fausse route. A new urodynamic evaluation showed persisting DOA despite well-conducted anticholinergics therapy.

Bladder neck fausse route was a consequence of catheterisation difficulties related to bladder neck dyssynergia.

As adequate oral therapy could not control bladder overactivity, the patient qualified for injections of 200 UI of BTX in the bladder detrusor. Standard procedure with 20 injection sites was performed.

After 10–14 days, patient expressed an improvement in managing CIC. He could easily reach the bladder without the feeling of resistance that he felt before.

OUTCOME AND FOLLOW-UP

Until now, the patient underwent three endoscopic procedures with BTX.

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Each detrusor BTX injection improved both bladder overactivity and CIC procedures after a 2-week period.

After the first treatment, CIC troubles reoccurred after 9 months and a new sequence of injections was performed.

The second reinjection was performed automatically after 9 months, based on previous period of efficacy.

DISCUSSION

Injection of BTX in the detrusor is a recognised treatment of idiopathic and neurogenic DOA and its use has considerably increased over the last 10 years. For patients with neurogenic DOA, it is recommended to use 200 UI of BTX.³

BTX is injected using a specific needle in 20 sites in the detrusor muscle via cystoscopy, sparing the detrusor. Effects of BTX are mainly attributed to inhibition of acetylcholine release in the presynaptic nerve of the neuromuscular junction at the bladder level.⁴ The overall median period of efficacy of BTX is 9 months.⁵

Besides its use in the bladder, BTX is also used to treat detrusor-sphincter dyssynergia when administered in external urethral sphincter (EUS). However, dosage, injection schedule and period of efficacy vary from article to article. Leippold *et al*⁶ described a longer period of efficacy in repeated injections (9–13 months) in comparison with single injection (2 months).

In the light of this case report, it seems that the use of intravesical BTX for neurogenic DOA could improve symptoms of BOD.

Indeed, the patient experienced easier CIC procedures after injecting BTX in the detrusor muscle.

This work represents reasonable assumptions over possible mechanisms of action which could explain such a clinical picture.

This clinical presentation may suggest that BTX injected in the bladder deletes or reduces the guarding reflex.

Some reflex pathways such as the guarding reflex are organised in central nerve system and coordinate the functioning of bladder and urethra.

Bladder-to-EUS reflex is a mechanism of urinary continence depending on central neural mechanisms and has been widely described in the literature.^{7,8} When the bladder is filled, stimulation of some afferent nerves in the bladder influences EUS activity.

Shafik⁹ also described that during bladder filling, when the vesical pressure increases, the pressure in the internal urethral meatus (urethral smooth muscle) rises.

A change in central mechanisms such as in patients with SCI may increase excitatory reflexes in both EUS and smooth muscles.

Based on literature referenced above, detrusor relaxation by BTX injections in the bladder muscle induces less triggering of the mechanoreceptors in the bladder wall and consequently a decrease in urethral pressure.

A second mechanism of action may be that BTX could have spread to contiguous structures. It means that besides the effect on bladder function, BTX may have an effect on the bladder neck. This idea of dispersion of detrusor-injected BTX towards internal sphincter has been discussed by Caremel *et al*.¹⁰ In this retrospective study of 11 patients with SCI and repeated BTX treatment, Caremel *et al* found a decreased ejaculated volume in 10 patients following BTX treatment in comparison with pretreatment patients, in relation with increased incidence of retrograde ejaculation.

With the same idea of passive distribution, some others described that fewer injection sites of BTX in detrusor were as effective as the established technique with more sites of

injection.¹¹ Despite a very limited location of injection, it implies migration of BTX throughout the whole detrusor meaning a local and systemic diffusion. This has also been described in an animal model.¹²

Of course, it can also result from a combination of the mechanisms described above.

One may wonder to which extent the symptoms of the patient are not related to a benign prostatic hyperplasia (BPH).

Based on the relatively young patient, his prostate volume, the medical history and the chronological order of the complaints, it seems that the difficulties in self-catheterisation are more likely to be related to BOD and guarding reflex than to BPH.

To our knowledge, there are no data concerning the injection of BTX in the bladder in order to treat voiding dysfunction in patients with BPH.

Nevertheless, there are still some studies in which the use of BTX was evaluated in patients with BPH and obstructive lower urinary tract symptoms. McVary *et al*,¹³ in a randomised controlled trial, compared intraprostatic injections of 200 UI BTX versus sham procedure. This study pointed out that BTX and placebo each improved International Prostate Symptom Score from baseline, but no difference was noted between treatment groups due to an exaggerated response to placebo.

Consequently, even if the patient would have had some degree of obstruction due to BPH, it seems difficult to identify BTX as a treatment modality for obstruction especially when the way it has been injected here has never been tested.

Learning points

- ▶ OnabotulinumtoxinA is a recognised treatment of neurogenic and idiopathic detrusor overactivity when injected in detrusor.
- ▶ In this case report, injections of onabotulinumtoxinA in the detrusor muscle facilitated clean intermittent catheterisation procedures in a paraplegic patient with detrusor-sphincter dyssynergia and bladder neck dyssynergia.
- ▶ OnabotulinumtoxinA injected in the detrusor may have a possible influence on the bladder-to-urethra guarding reflex.
- ▶ OnabotulinumtoxinA may spread to contiguous urological structures such as bladder neck and external urethral sphincter when injecting it in the bladder.

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