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CASE REPORT

Management of Spasticity Caused by Thrombotic Brain Injury with Incobotulinumtoxina in a Young Patient: A New Paradigm

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ABSTRACT:

Case: Acquired brain damage is one of the most complex pathologies that affect the central nervous system, there is great variability in its pathophysiology, from traumatic focal injuries to diffuse axonal injuries, including spasticity. It supposes a great comorbidity and functional repercussion in patients, hindering their subsequent recovery. We report a case of a young patient with a history of quadriplegia due to acquired brain damage secondary to thrombosis of the dural sinus. The patient presented sensorimotor deficit, restricted function, and a great situation of dependency. He required three cycles of high doses of incobotulinumtoxinA (IncoBoNT) according to his specific need, the first infiltration was 800 U, the second 800 U, and the last 500 U over a period of 14 weeks. Thanks to the previous objectives agreement with the patient the results were satisfactory and relevant for him, presenting a great functional improvement of spasticity and associated pain, as assessed by the visual analog scale score.

Conclusion: IncoBoNT at high doses and short intervals has been shown to be an effective and valuable tool for personalized treatment adapted to the needs of severely affected neurological patients.

Keywords: High doses, short interval, incobotulinumtoxin A.

Introduction:

Acquired brain damage is one of the most complex pathologies that affect the central nervous system. It involves a loss of cerebrovascular autoregulation and neuronal functional changes that impact subsequent neurological function and patient recovery. There is great variability in its pathophysiology, from traumatic focal injuries to diffuse axonal injuries, including spasticity, causing great diversity in its repercussions[1]. Spasticity is defined as a clinical sign of damage to the upper motor neuron in which a lesion of the dorsal spinal [2]It supposes a great comorbidity and functional repercussion in patients, hindering their subsequent recovery. Botulinum toxin type A is a protein produced by the gram-negative bacillus *Clostridium botulinum* which ~~it~~ inhibits the release of acetylcholine in the presynaptic endings, preventing muscle contraction[3] . It has been claimed as the first treatment step in the management of focal spasticity, it is safe, effective and with few adverse reactions described [4] . IncobotulinumtoxinA (IncoBoNT) is one of the type A botulinum toxins available on the market. It is characterized by being free of complex proteins, thus reducing its antigenicity and containing a higher specific concentration of neurotoxin[5-6] . On many occasions, the units of botulinum toxin used are insufficient for the approach and subsequent neurorehabilitation of patients affected by severe spasticity. The concept of appropriate treatment according to the clinical needs of patients has recently been introduced, where high doses of botulinum toxin type A (from 100 to 1000 IU) can modulate the clinical needs of each patient in a more effective and personalized way[7] . This reaffirms the fact that high doses of botulinum toxin type A, greater than ≥400 IU are safe without toxic or adverse effects at the systemic level[8] . Besides, in the long term, high doses together with short intervals have been shown to be effective, determining an improvement in the quality of life of neurological patients[9–11] . The available literature shows that ultrasound guidance for botulinum toxin type A injections is more precisely and could improve clinical outcomes better than anatomical localization without ultrasound in post-stroke patients with spasticity[11].

Clinical case:

We present the clinical case of a 16-year-old Caucasian male patient with a history of quadriplegia due to acquired brain damage secondary to thrombosis of the dural sinus in the context of multiple bilateral arteriovenous fistulas at the level of the transverse sinus. The patient presented sensorimotor deficit, restricted function, and an important situation of dependency. He was diagnosed with tetraparesis, presenting a pattern of internal rotation/adducted shoulder of the right upper limb, flexed elbows, flexed wrists, pronated forearms, thumbs in palm and tendency to clenched fist, external rotation of both hips, flexed knees, and bilateral equine varus. A comprehensive IncoBoNT treatment approach based on three cycles of ultrasound-guided injections was performed. The degree of spasticity and spasticity-related pain were determined using the Modified Ashworth Scale (MAS) and the visual analog scale (VAS), respectively, at baseline and four weeks after each injection cycle. The number of injection sites per muscle, the injected doses and the treatment intervals were individualized according to the specific needs of the patient to provide maximum benefit (figure 1).

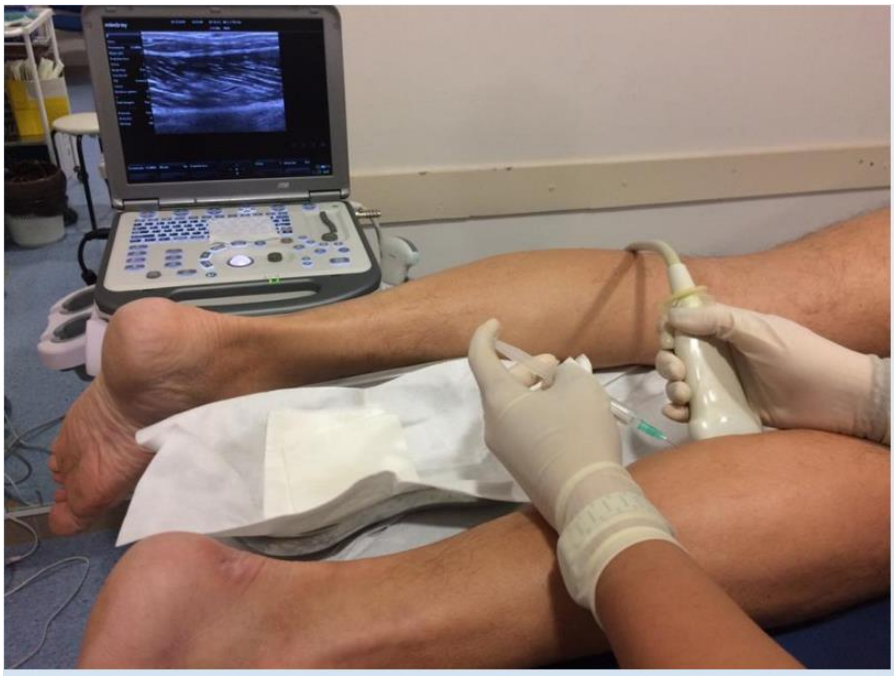

Figure1. IncoBoNT injection in gastrocnemius, ultrasound guided technique.

A mean baseline MAS score of 1+/2 was observed in the left and right upper limbs as well as in the left and right lower limbs spasticity patterns. The baseline VAS score assessed by the patient for shoulder pain was 8 out of 10. The first cycle involved a total body dose of 800U of IncoBoNT injected into 14 upper and lower extremity muscles (table 1), one injection site per muscle: right and left pectoralis (50 U), right teres mayor (25 U), right subscapularis (25 U), right flexor digitorum profundus (25 U) and right flexor digitorum superficialis (25 U), right and left sartorius (100 U), bilateral gastrocnemious (200 U) , soleus (200 U) and hamstring (200 U). The patient showed a significant improvement in spasticity with gain in joint range (mean MAS score of 1), increase ability to initiate manual handling activities and spontaneous lower extremity mobilization at 4 weeks post-injection. The VAS score for the shoulders improved to 0. Seven weeks after the first IncoBoNT injection, a second injection course with 800 U was considered medically necessary for the patient with a special focus this time in obtaining a stable standing position and improve gait (figure 2), one injection in the right and left biceps femoral (200 U), semimembranous (200 U), soleus (200 U) and gastrocnemious (200 U). A dose of 500 U was injected again after 7 weeks to maintain stable standing and walking. The patient required 4 injections throughout the year, the duration of the effect was verified at the follow-up 24 months after the first injection, the patient was stable and subsequently received only periodic injections in the gastrocnemius and hamstrings. No side effects or complications were found after repeated injections of incoBoNT.

Upper Limb			Lower Limb		
Muscles	**Right (U)**	**Left (U)**	**Muscles**	**Right (U)**	**Left (U)**
Pectoralis	25 U*	25 U	Sartorius	50 U	50 U
Teres Mayor	25 U	-	Gastrocnemious	100 U	100 U
Subscapularis	25 U	-	Soleus	75 U	75 U
Flexor digitorum profundus	25 U	-	Hamstring	100 U	100 U
Flexor digitorum supercialis	25 U	-	-	-	-

Table 1. First injection session of IncoBoNT. Dose: 800 U distributed bilaterally in upper and lower limbs. U* units of IncoBoNT

Lower Limb	Right	Left
Biceps Femoris	**100 U***	**100 U**
Semimembranous	**100 U**	**100 U**
Soleus	**100 U**	**100 U**
Gastrocnemious	**100 U**	**100 U**

Table 2. Second injection session of IncoBoNT. Dose: 800 U distributed bilaterally in lower limbs. U* units of IncoBoNT

Discussion:

Spasticity is defined as a neurological disorder suffered by patients with acquired brain damage as a result of a lesion in the central nervous system[10] . The muscle retraction characteristic of spasticity leads to abnormal gait patterns and pain that require a comprehensive approach to the patient[11] .

The use of botulinum toxin A has been shown to be the mainstay of treatment for patients affected by spasticity[12] .The available literature shows that spasticity occurs in 40% of patients with stroke, and that 4%-20% will present great disability post stroke[13] . Botulinum toxin type A acts by improving muscle tone by blocking the release of acetylcholine from presynaptic nerve terminals at peripheral neuromuscular junctions and reducing pain transmission by inhibiting the release of pro-inflammatory substances such as glutamate or substance P, which determine the perpetuation of pain and a loss of quality of life in these patients[14] . High doses of IncoBoNT toxin have been shown to be safe and effective in severe spasticity, improving functional recovery and providing better patient satisfaction[11] . It is-less invasive than other types of treatment and is better tolerated by patients, providing an improvement in muscular tone and joint balance, providing them with an increase in their functional capacity. The current literature shows that this dose regimen of IncoBoNT does not increase the number of adverse effects. Also, an increase in toxin-neutralizing antibodies was not observed[15] .

These studies highlight the fact that current approved doses of botulinum toxin are not sufficient to achieve substantial improvements in patients with severe spasticity and higher doses of BTX than those recommended in clinical practice guidelines are often used based on functional goals in selected patients [10,16] . IncoBoNT at high doses and short intervals has been shown to be an effective and valuable tool for personalized treatment adapted to the needs of severely affected neurological patients [11] .

Conclusion:

Several reports and published studies have shown that in patients with severe and disabling spasticity, individualized doses, and short interval injections can better modulate spasticity with a good safety profile. In this patient with severe upper and lower extremity spasticity after ABI, an individualized treatment schedule with IncoBoNT doses and dosing intervals tailored to the patient's condition (multi-pattern approach) and medical needs resulted in better clinical outcomes and patient comfort with good tolerability. IncoBoNT has been provided an effective, safe, and valid tool for the treatment and improvement of quality of life of these patients. These findings represent a positive and encouraging future regarding to treatment and recovery for neurological patients.

Conflict of Interest Statement: The authors declare that they have no competing interests.

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