

## C A S E R E P O R T

# Facial paresis: A worrying event related to labial herpes simplex and periocular botulinum toxin a injection

Angela Faga<sup>1,2</sup>, Silvia Scevola<sup>1,2</sup>, Elena Dalla Toffola<sup>3</sup>, Giovanni Nicoletti<sup>1,4,5</sup>

<sup>1</sup>Advanced Technologies for Regenerative Medicine and Inductive Surgery Research Center, University of Pavia, Pavia, Italy; <sup>2</sup>“NUOVO” Outpatient Facility, Viale della Libertà, 17, 27100 Pavia, Italy; <sup>3</sup>Physical Medicine and Rehabilitation, Department of Clinical Surgical, Diagnostic and Pediatric Sciences, University of Pavia, Pavia, Italy; <sup>4</sup>Plastic and Reconstructive Surgery, Department of Clinical Surgical, Diagnostic and Pediatric Sciences, University of Pavia, Pavia, Italy; <sup>5</sup>Surgery Unit, Azienda Socio-Sanitaria Territoriale di Pavia, Pavia, Italy

**Abstract.** The Authors report on a case of facial paresis following the recurrency of labial Herpes simplex in a 59 year old woman treated with a sequential periocular BoNTA injection and blepharoplasty. A mild palsy occurred on the whole right hemiface 12 days after upper blepharoplasty, 22 days after the BoNTA injection (40 U) in the periorbital area and in the glabella. The patient was treated with Acyclovir for 5 days and with oral B complex vitamins for 12 weeks. The symptoms slowly disappeared after 4 months. Facial paresis might have been triggered by an invasive treatment-related inflammatory reaction. Nevertheless, the Herpes virus might have promoted the anterograde diffusion of the toxin, previously migrated from the site of injection to the facial nucleus through a retrograde pathway. The Authors suggest Acyclovir prophylaxis in patients affected by recent or recurrent forms of Herpes simplex infections when planning BoNTA injections in the face.

**Key words:** botulinum toxin, *herpes simplex virus*, facial palsy

## Case report

A healthy 59 year old woman, sought to have a more refreshed look in her periocular area.

After a physical examination, a clinical picture of dermatochalasis in the upper eyelids, hen crows and frontal wrinkles were noted (Figure 1).

A total of 40 U of Botulinum Toxin A (BoNTA) was injected in the lateral periorbital area and in the glabella, with the onset of a symmetrical partial weakening of the muscles after 6 days (Figure 2).

Ten days later the patient underwent upper blepharoplasty under local anesthesia. Two days post-operation, a herpetic blister developed on the right lower lip (Figure 3). The patient was immediately treated with Acyclovir 1gr/die per os for 5 days and a topical Acyclovir gel on the blister until it was fully healed which occurred in 10 days' time.

Twenty-two days after the BoNTA injection, a mild facial paresis occurred on the right hemiface, affecting the zygomatic muscles and, to a lesser extent, the orbicularis oculi muscle, causing a significant asymmetrical smile and a mild asymmetry of the eyelids. No parasympathetic nor sensitive symptoms were reported. The palsy signs progressively increased during the following 20 days (Figure 4). The patient was treated with oral B complex vitamins (B1 Thiamine chloride hydrochloride 300 mg/die, B6 Pyridoxine Hydrochloride 450 mg, B12 Cyanocobalamin 1500 mcg/die) for 12 weeks. The patient did not agree to take any other drugs, like steroids or antivirals. During this time, there was a progressive recovery of the muscle function, and after 4 months, there was an almost complete static and dynamic facial symmetry restoration (Figure 5). After 7 months the botulin toxin effects had completely disappeared as hencrows recurred, although a very mild



**Figure 1.** The patient before any treatment, presenting upper eyelids dermatochalasis, hen crows and forehead wrinkles.



**Figure 3.** Two days after blepharoplasty, 12 days after BoNT-A injection: herpetic blister on the lower right lip.



**Figure 2.** Six days after periocular, glabellar and frontal BoNT-A injection (40 U).

asymmetry of the smile could still be noted at this time, as the right nasolabial fold seemed to be slightly shallower than the left one (Figure 6).

## Discussion

Herpes simplex virus (HSV1) prophylaxis is suggested in patients with a potential latent infection



**Figure 4.** Thirty days after blepharoplasty, 40 days after BoNT-A injection: partial facial palsy on the right hemiface, affecting the zygomatic muscles and the orbicularis oculi muscle.

undergoing invasive facial aesthetic procedures<sup>1</sup>. Amongst the risks, the post-surgical reactivation of the Herpes simplex might turn to keratoconjunctivitis and the infection might spread to other areas of the eye leading to more severe complications.



**Figure 5.** Four months after the treatment the symmetry of the smile and of the eyelids is almost complete.



**Figure 6.** Seven months after the treatment: recurrence of the hencrows; the right nasolabial fold is slightly shallower than the left.

In this case, the Herpes simplex latent infection was not reported in the patient's medical record, as the last recurrence had happened long before and the patient had forgotten it.

Interestingly, the mild palsy affected only the muscles supplied by the facial nerve, including the ones that had not been previously injected with BonTA. This only occurred on the same side of the herpetic blister.

There was a partial recovery which only lasted 4 months, corresponding to the mean duration of the effects of botulin toxin. However, some slight palsy of the zygomatic muscles was still perceptible after 7 months, likely suggesting an axonal injury related recovery time.

Understanding this paretic complication is not simple.

Facial palsy can onset coincidentally with any traumatic and inflammatory event. In this case there was a surgical technical error: excluding the nerve endings of the right oral corner, having to take into consideration the surgeon's skills and experience. Surgery itself might have acted as a trigger, but the coincidence of paresis with the same site of the herpetic rash casts doubts on this hypothesis. Furthermore, the reactivation of the Herpes simplex infection can be induced by a traumatic event, too.

The correlation between facial nerve disorder and edema of the fallopian canal, induced by HSV1, would be a likely hypothesis; the persistence of mild signs of paresis just at the corner of the mouth in contrast with the complete recovery of the periorbital muscles after 7 months would be consistent with the greater length of branches for the zygomatic muscles and therefore with the longer time needed for the nerve to recover. However in this scenario, HSV1 would have been present in the facial nerve nucleus<sup>2</sup> instead of the semilunar ganglion of the trigeminal nerve, as more commonly reported; in this case, however, it would be difficult to explain the selective damage to the facial motor fibers, sparing the parasympathetic and sensitive fibers. Moreover, HSV1 in the facial nucleus would seem unusual, considering the confinement of the herpetic blisters to the lower lip without spreading to the periorbital area and the eyelids.

While the reactivation of the Herpes zoster virus is not uncommon in patients diagnosed with Bell's palsy<sup>3</sup>, a similar correlation between HSV1 and Bell's palsy has never been assessed and remains controversial<sup>4</sup>.

In this clinical case, the coexisting administration of Botulin toxin further complicates the discussion.

Botulin toxin has been proven to be effective and safe to treat synkinesis resulting from facial palsy<sup>5</sup>.

Nevertheless, according to the literature, the effects of botulinum toxin on HSV1 are conflicting: both the viral reactivation following the periocular injection<sup>6,7</sup> and decreased labial herpes outbreaks in the sites of BoNTA intradermal injection<sup>8</sup> are supported by literary reports.

In this complicated case, a direct effect of botulinum toxin on the central nucleus of the facial nerve might perhaps be hypothesized, too.

According to Caleo<sup>9,10</sup>, BoNTA applied in the periphery can have retrograde effects at the central cholinergic boutons via a retrograde transport and transcytosis, thus actively affecting central circuits, as it does not spread in a passive way from the site of injection to the Central Nervous System.

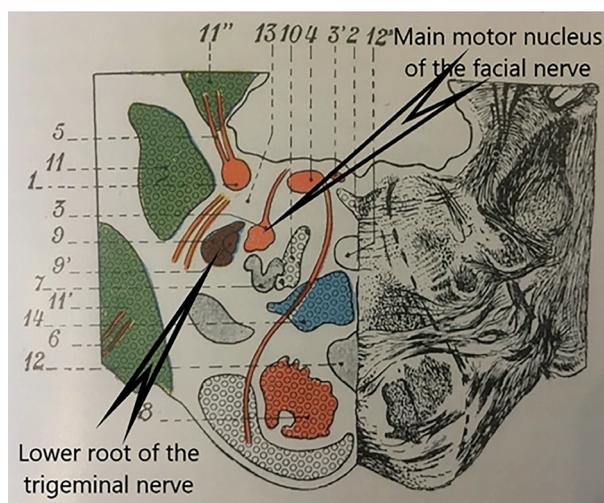
In this case, we might suppose a combined retrograde-antegrade action of BoNT-A, consisting in its migration from the site of injection through the nerve fibers to the central nucleus of the facial nerve and transcytosis from the posterior nuclear cells, which supply the superior facial nerve branches, to the anterior nuclear cells, which supply the inferior facial nerve branches, thus causing the palsy of the peri-oral muscles. The HSV1 virus is likely to have promoted this series of events.

In our patient, if the virus had been homed in the facial nucleus, it would have directly promoted the antegrade diffusion of the migrated toxin.

Nevertheless, considering the close anatomical proximity between the facial nucleus and the bulbar root of the trigeminal nerve (Figure 7), the migration of the toxin between the two cranial nerves through transcytosis could also be hypothesized.

## Conclusions

To affirm what has been covered, in our opinion understanding this case remains an ongoing dilemma. However, although there is not proof of a direct correlation between facial palsy and the administration of BoNTA, in order to be extra cautious with patients suffering from recent or recurrent forms of a Herpes simplex infection, prophylaxis might be recommended when planning a BoNTA injection in the face.



**Figure 7.** Section through the lower portion of the pons: the main motor nucleus of the facial nerve is very close to the lower root of the trigeminal nerve. (reprinted from: Testut L, Latarjet A: «Trattato di Anatomia Umana», UTET» publ., Torino, Italy, 1966).

**Conflict of Interest:** The Authors declare that they have no conflict of interest.

## References

1. Bisaccia E, Scarborough D. Herpes simplex virus prophylaxis with famciclovir in patients undergoing aesthetic facial CO2 laser resurfacing. *Cutis*. 2003; 72(4):327-8.
2. Theil D, Horn A, Derfuss T, Strupp M, Arbusow V, Brandt T. Prevalence and distribution of HSV-1, VZV, and HHV-6 in human cranial nerve nuclei III, IV, VI, VII, and XII. *J Med Virol*. 2004; 74(1):102-6.
3. Freire de Castro R, Crema D, Neiva FC, Pinto RASR, Suzuki FA. Prevalence of herpes zoster virus reactivation in patients diagnosed with Bell's palsy. *J Laryngol Otol*. 2022; 136(10):975-978.
4. Kennedy PG. Herpes simplex virus type 1 and Bell's palsy—a current assessment of the controversy. *J Neurovirol*. 2010; 16(1):1-5.
5. Mandrini S, Comelli M, Dall'Angelo A, et al. Long-term facial improvement after repeated BoNT-A injections and mirror biofeedback exercises for chronic facial synkinesis: a case-series study. *Eur J Phys Rehabil Med*. 2016; 52(6):810-818.
6. Ramappa M, Jiya PY, Chaurasia S, Naik M, Sharma S. Reactivation of herpes simplex viral keratitis following the botulinum toxin injection. *Indian J Ophthalmol*. 2018; 66(2):306-8.

7. Das N, Das J, Basak S. A Case of Reactivation of Herpes Simplex Virus Corneal Endotheliitis Following Periocular Botulinum Toxin A Injection. *Ophthalmic Plast Reconstr Surg.* 2020; 36(3):e73-e75.
8. Gilbert E, Zhu J, Peng T, Ward NL. Decreased labial herpes simplex virus outbreaks following Botulinum neurotoxin type A Injection: A Case Report. *J Drugs Dermatol.* 2018; 17(10):1127-1129.
9. Caleo M, Spinelli M, Colosimo F, et al. Transynaptic Action of Botulinum Neurotoxin Type A at Central Cholinergic Boutons. *J Neurosci.* 2018; 38(48):10329-10337.
10. Antonucci F, Rossi C, Gianfranceschi L, Rossetto O, Caleo M. Long-Distance Retrograde Effects of Botulinum Neurotoxin A. *J Neurosci.* 2008; 28(14):3689-96

---

**Corresponding author:**

Received: 30 October 2022

Accepted: 6 September 2023

Prof. Angela Faga

Advanced Technologies for Regenerative Medicine  
and Inductive Surgery Research Center

University of Pavia, Italy

Phone: +39 335 6465799

E-mail: [angela.faga@unipv.it](mailto:angela.faga@unipv.it)