Herpes zoster ophthalmicus after onabotulinumtoxin for cosmetic treatment: a case report

Herpes-zóster oftálmico apos injeção de onabotulinotoxina para tratamento cosmético - Relato de caso

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ABSTRACT

Herpes zoster outbreaks following minor procedures have been documented recently in literature. Since the use of botulinum toxin is nowadays spread in several medical areas for different purposes, it is crucial to study its side effects and complications. Literature review revealed 65 cases of zoster reactivation following minor procedures, and three cases related to BTA injections (two for facial lines treatment and one for chronic migraine). In our case, a 43 year old healthy woman had herpes zoster on the face and scalp after receiving BTA injections for cosmetic purpose, with complete recovery after anti-viral treatment.

Keywords: herpes zoster ophthalmicus; herpes zoster; botulinum toxins, type a; dermatologic surgical procedures

RESUMO

Episódios de herpes-zóster após procedimentos têm sido documentados recentemente na literatura. Uma vez que o uso da toxina botulínica atualmente se faz presente em diversas especialidades médicas, é crucial o estudo de seus efeitos colaterais e complicações. Uma revisão da literatura mostrou 65 casos de reativação de zóster após procedimentos, sendo três relacionados a injeções de toxina botulínica tipo A (dois para tratamento de rítides faciais e um para migrânea crônica). Em nosso caso, uma mulher de 43 anos previamente hígida apresentou herpe-zóster na face e couro cabeludo após injeções de toxina botulínica tipo A com fins estéticos, tendo recuperação completa após tratamento antiviral.

Palavras-chave: *Herpes-zóster oftálmico; herpes-zóster; toxinas botulínicas tipo a; procedimentos cirúrgicos dermatológicos*

CASE REPORT

A healthy, 43 year-old woman with absence of history of herpes, received botulinum toxin type A (OnabotulinumtoxinA) for cosmetic treatment. A total of 40 units were injected in the frontal, glabellar and periorbital regions, without any immediate side effects. After three days, the patient complained of pain and paresthesia on her left eyelid and the left frontal area, which then disseminated to the ipsilateral parietal and temporal regions, accompanied by a burning sensation on the left eye and preserved visual acuity. Twelve hours after these first symptoms, the condition progressed with an edema and erythematous papules; she was treated with antibiotics orally, after the diagnostic hypothesis of cellulitis. On the fourth day, the edema and the erythema worsened, with the appearance of some vesicles on her forehead, glabella and the left side of her scalp, followed by superficial

Case report

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erosions and periorbital edema (Figure 1). Five days afterwards, the patient was examined by a dermatologist, who diagnosed her with herpes-zoster on the first branch of the left trigeminal nerve. The patient was treated with 1g of valacyclovir hydrochloride three times a day for seven days, ophthalmologic ointment acyclovir to be applied four times a day for seven days, and 40 mg/day of prednisolone to be taken orally for five days. After ten days, the signs and symptoms had almost completely be resolved, however, the patient was still complaining about pain and edema on her left eyelid, which was treated with an antibiotic typical for blepharitis for seven more days (Figure 2). The ophthalmological exams showed no other changes.

Literature Review

BOTULINUM TOXIN

Botulinum Toxin Type A (BTX-A) blocks acetylcholine by the cleavage of the Synaptosome-Associated Protein 25, which participates in the formation of the exocytic receptor of the Soluble N-ethylmaleimide Sensitive Attachment Protein (SNARE) essential for the fusion of vesicles containing acetylcholine to the presynaptic membrane. The blockage results in the selective chemical denervation of the muscles. The local peripheral injection of Botulinum Toxin Type A also results in the reduction of several substances that sensitize nociceptors, such as the substance P and the calcitonin gene-related peptide, which performs a significant role in neurogenic inflammation.1 The Food and Drug Administration (FDA) has approved the usage of BTX-A for strabismus in 1979, for blepharospasm in 1985, for hemifacial spasm in 1989, and, finally, for glabellar dynamic wrinkles in 2003.2

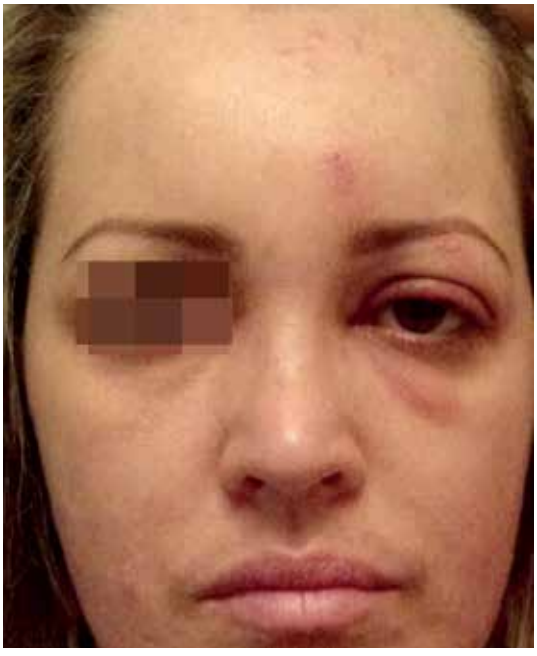

Figure 1: Edema, erythema, vesicles and erosions on the region innervated by the ophthalmic branch of the trigeminal nerve

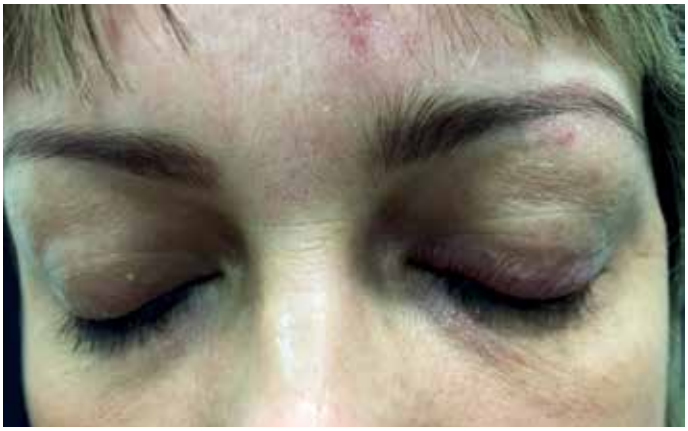

Figure 2: After ten days, remaining left eyelid pain and edema were treated as blepharitis for 7 more days, with full resolution

In reviewing the literature, 65 cases of herpes zoster reactivation were found following procedures, most of them in young patients without any specific risk factors, which suggests that the presence of herpes zoster related to trauma is not uncommon. There are only three reported cases of herpes zoster following the application of BTX-A. In a controlled study, Thomsd et al. have shown the presence of increased risk of an outbreak of herpes zoster in the site related to the trauma during the month subsequent to the procedure.[3] Juel-Jensen reported 38 herpes zoster outbreaks related to the trauma in a series of cases involving 100 patients who were herpes zoster carriers.[4] In a wide review of the literature, Gadient et al.[5] have indicated several causes associated to the reactivation of herpes zoster, such as: radiotherapy for breast cancer (41 patients), dental treatment and orofacial surgery (six patients); placement of central venous catheter (two patients); liposuction of the back and flank; surgical repair of orbital fracture; intra-articular injection of corticosteroids; laser surgery for myopia; cryosurgery for actinic keratoses; hepatic biopsy for hepatitis C; skin graft following burns; thoracic sympathectomy; axillary nerve block; breast reconstruction under intercostal nerve block; and endotracheal intubation for esophagogastrostomy.[5]

HERPES ZOSTER

Subsequent to the primary infection (varicella), the varicella zoster virus (VZV) remains dormant in the dorsal root ganglion; its reactivations causes herpes zoster, clinically characterized by the sudden onset of vesicles in a specific dermatome, unilaterally, more commonly appearing on the thoracic and cranial distributions, generally being followed by prodromal symptoms such as pain, dysesthesia, malaise and pruritus.[6]

BOTULINUM TOXIN AND HERPES ZOSTER

The mechanism of reactivation of VZV is not clear. The primary risk factors for herpes zoster reactivation are immunosuppression, advanced age, systemic diseases, and certain malignancies. VZV is not uncommon after major surgeries due to im-

mune stress. After small procedures, reactivation of the varicella is likely related to localized trauma or inflammation.[3, 6, 7] *In vivo* studies show that specific cytokines, such as IL-6 and alpha-TNF, as well as the VP16 viral protein, are related to the reactivation of the Herpes Virus Simplex Type 1, while VZV can be triggered in similar ways.[5,8] Gadient et al.[5] suggested that stress-generating agents (radiation, laser, chemical, thermal and mechanical agents) exert local epigenetic influence on viral transcription, allowing their reactivation.

As reported by Gadient and Graber,[5, 6] it is suspected that repeated administration of BTX-A causes reactivation of VZV. On the other hand, no cases of herpes zoster were reported in another study with 513 subjects who were treated with BTX-A for chronic migraine (patients were followed up for 56 weeks).[9]

DISCUSSION

According to the literature, the present report describes the fourth case of a herpes zoster outbreak after a BTX-A injection. Until then, only three cases had been attributed to this procedure (two following cosmetic treatment with BTX-A on the forehead, glabella and periorbital areas;[6] and one after BTX-A was used to treat chronic migraine).[5] In the cosmetic case, herpes zoster was diagnosed after one week[6] and in the migraine case, 48 hours after treatment.[5]

In one case, a 55-year-old female with no previous history of herpes zoster or any risk factors received 50 units of onabotulinum toxin type A for the treatment of facial expression lines in the glabellar, frontal and periorbital areas.[6] The patient had undergone eight previous treatments with BTX-A. Differently from our case, in which the patient had undergone the treatment for the first time; seven days after the injections, the patient complained of swelling, itching and pain in the left frontal region and glabella, presenting poorly demarcated erythema and edema, with superficial erosions in the region, not exactly in the same place of the injections. In the present case report, the lesions occurred three days afterwards in the left frontal region and glabella, as in the aforementioned patient. After the diagnosis of herpes zoster ophthalmicus, the patient received 1g of valacyclovir hydrochloride three times a day for ten days, which resulted in complete resolution of symptoms after one week. Six months later, the BTX-A treatment was repeated for the same purpose (cosmetic), and the patient received oral antivirals, with no recurrence of herpes zoster.[6]

The same study also reports the case of a 48-year-old woman with no history of herpes zoster nor any risk factor, nor previous use of botulinum toxin of any kind, as in the present case report. The patient was treated with BTX-A in the glabellar, frontal and periorbital areas.[6] Six days after the treatment, she presented with paresthesia in the right outer ear, constant headache on the right side and, on the seventh day, vesicles developed on the glabella and on the right side of the frontal region. The clinical signs and symptoms were similar to those of the present case report, except for the fact that the contralateral area was affected. Orally-administered treatment with valacyclovir was successful.

The third case, reported by Gadient et al.,[5] was that of a 72-year-old woman who received BTX-A injections every three months for three years to treat chronic migraine, absent of incidents. It was the first published report on herpes zoster after the use of BTX-A to treat chronic migraines. Two days after the procedure, the patient developed a periorbital edema and a possible cellulitis, was treated with oral antibiotics, just as in the present case report. Herpes zoster was diagnosed only one week later and, therefore, the patient was not treated with antivirals.

CONCLUSION

Although the exact mechanisms for VZV reactivation remain unknown, this condition has been reported following minor procedures and related to localized trauma or inflammation. Herpes zoster outbreaks following BTX-A have recently been documented in the literature, not only for cosmetic purposes but also for the treatment of chronic migraine. Since the application of BTX-A is a very common procedure, it is important that dermatologists are attentive, thus avoiding diagnostic errors.[1]

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