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Research Article

Treatment of Keloid Scars by Botulinum Toxin

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Abstract

Keloid scars are behind an invalidating aesthetic and functional problem for patients as well as pain, and the treatments currently used do not result in total, consistent resolution of this problem. Botulinum toxin type A (BoNT-A) through its anti-inflammatory and antalgic action and its effect on muscular fibres, has an action on these pathological scars. We first treated retro-auricular post otoplasty keloid scarring by injecting type A Botulinum toxin in a 14-year old patient resistant to corticosteroid injections. Both ears were affected. This first patient was injected for 3 years, every 3 months. The treatment on the left ear was only BoNT-A, and on the right was BoNT-A and surgical reduction. After the very encouraging result of this case, we injected 16 other patients. Two were lost to follow-up. For the others, the results on pain and aesthetic appearance are good to very good. Of course, further randomised-controlled studies are required to confirm the present results so that the treatment can become more widespread.

INTRODUCTION

In general, they are found in so-called ''at risk'' areas: particularly in the upper dorsal, pre-sternal, facial or auricular areas [3]. They extend around the edges in a ''claw'' type formation, 3 to 6 months after the traumatism, and do not spontaneously regress after 3 to 6 months, contrary to hypertrophic scars [4].

They cause pain, aesthetic problems, but also in some cases functional issues, such as with retro-auricular post otoplasty keloids, as in our first case study, with a deformation of the ear auricle.

Many therapies have been used to treat keloid and hypertrophic scars, aside from prevention in at risk patients, but these have brought, in most cases, neither entirely satisfactory nor, more importantly, permanent results. Simple surgical treatment often causes even more significant recurrences [5,6]. Cryotherapy with or without surgery is particularly indicated for keloids of less than 12 months [7,8]. The injection of corticosteroids alone is unsatisfactory, and is often painful and thus poorly tolerated. Brachytherapy, particularly after surgery, is an interesting solution, but unfortunately involves carcinogenic risks which limit its use [9,10]. Moreover, pressure therapy, silicosis gels, laser treatment or topical retinoids have also been studied numerous times [11,12].

Botulinum toxin type A (BoNT-A), by its muscular relaxation action, but also thanks to its anti-inflammatory and antalgic role, is, in our study, an effective treatment for resistant, invalidating keloid scars. In fact, these pathological scars, linked to dystrophy in the collagen fibres, are partly due to surrounding muscular tension, but also to excessive cellular proliferation which encourages expansion of the scar. We used BoNT-A, with and without surgical ablation on a cohort of 17 patients [13].

MATERIALS AND METHODS

A standardized protocol of injections in keloid scars of BoNT-A was generated from the collective experience of all authors. Patients were identified from the institutional database after the study was approved by the Institutional Review Board of the University of Montpellier (France).

The first case

The first patient in our study was aged 14 when he was seen in the department at the end of 2010. We began his treatment for bilateral keloid scarring resulting from the consequences of an otoplasty (December 2008), which caused bilateral spliting of the auricle (Figure 1 and 2). He had already received 3 corticosteroid injections in the scar area, with no resulting improvement.

The scar was inflammatory: red, warm and oedematous.

The first injection was given in November 2010: 50 units of Botox were injected into the right ear keloid and 20 in the left

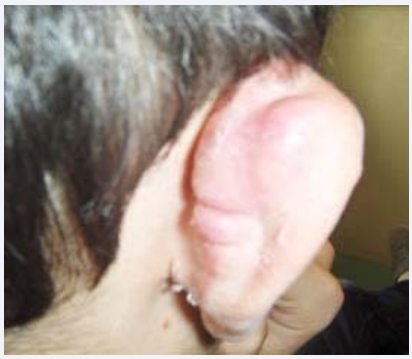

Figure 1 Initial state of the right ear.

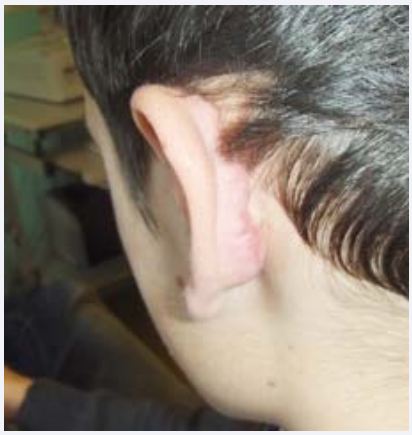

Figure 2 Left ear, 2 years after otoplasty, after 3 corticosteroid injections.

one. The patient was systematically seen every month from the beginning of his treatment. A 2nd injection was carried out in February, increasing the doses: 80 units on the right and still 20 units on the left (Figure 3).

A third injection took place in May, with 100 units of Botox on the right and 30 on the left before carrying out a surgical repair of the scar on the right-hand side in June 2011 : ablation of the scar under general anaesthetic then stitching in two planes with non-resorbable intra dermal continuous suture. Post operatively, the patient wore suitable, made to measure, compressive prostheses.

Then two and five months later, a fourth and fifth injection of botulinum toxin was carried out with the same doses as previously used.

We decreased the rhythm of injections before stopping the treatment in 2013.

We saw this first patient in January 2017 and the ears were exactly in the same state as at the end of the care.

After this result, we injected with BoNT-A all the resistant, invalidating keloid scars.

We have (including the first one) a cohort of 17 patients. 15 patients had keloid scars after otoplasty, one keloid scar was on the cleavage, and one on the forehead.

2 patients (including the woman with the keloid scar on the cleavage) were lost to follow-up.

The other 15 patients had good and very good results. For 12 patients, we added surgery to BoNT-A. And above all, the pain disappeared.

Procedure

The injections were carried out in an aseptic room.

Figure 3 Injection of botulinum toxin: 20 units on the left keloid.

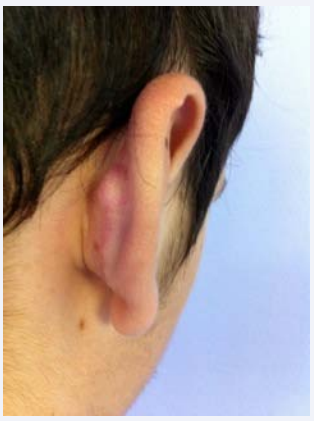

Figure 4a At the end of the treatment on the right side (BoNT-A + surgery).

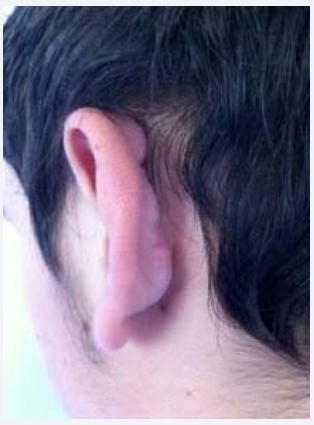

Figure 4b Result on the left side (only BoNT-A).

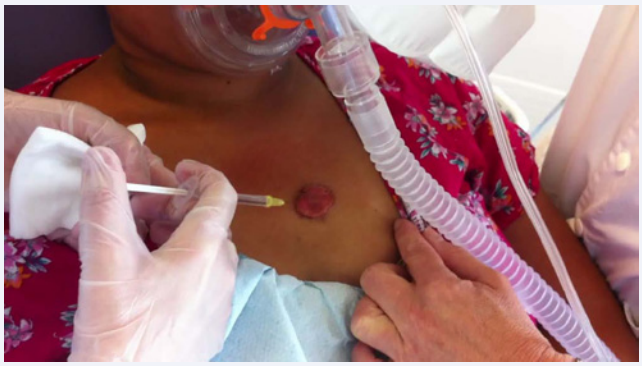

Figure 5 Example of injection.

For some patients, the injections were done with the use of EMONO (equimolar mixture of oxygen and nitrous oxide) because of the increase of the pain during the injecting gesture.

The BoNT-A was diluted in 1 mL of 9% isotonic injectable saline solution in a graduated syringe to make up 100 U/mL. We used Botulinum Toxin type A (Botox®/ Allergan Pharmaceuticals, Westport, Ireland) and all our units are Botox units. The solution was taken-up using a graduated1mL syringe. A 25 G needle of 0,5 mm diameter and 16 mm length was used.

The pain evaluation was defined on the Visuel Analogue Scale (VAS).

DISCUSSION

The injection of BoNT-A in the treatment of resistant, invalidating keloid scars seems to show a very encouraging degree of effectiveness. A sufficient cohort of patients is now necessary to be able to conclude from this its long term effectiveness, as well as its safety, even though its widespread and varied use in numerous other indications has already shown that it means only rare and very low risks of secondary effects.

This effectiveness of BoNT-A in the treatment and the prevention of the recurrence of keloid scarring can be explained by several mechanisms. Firstly, by the anti-inflammatory effect of BoNT-A which has been described by several teams, particularly in rats [14] by inhibition of the salting out of inflammatory mediators such as substance P or glutamate, independently of its effect on muscles. This anti-inflammatory effect allows the process of the formation of keloids to be stopped. In fact this pathological scarring comes from local dystrophy after post-traumatic inflammation [1,2]. The reduction of keloids by injection of toxin, and especially their recurrence after surgical resection can thus partly be explained by BoNT-A's role of inhibiting the mediators of inflammation. A second mechanism has been referred to by Zhibo and Miaobo's team [15,16]: the effect on local tensions and the inhibition of cellular proliferation. In fact, the toxin seems to reduce the muscular tensions which act at the time of the scarring process and which encourage the formation of keloids [16]. It seems to also act on cellular proliferation, particularly that of fibroblasts, thus allowing a reduction in scarring hypertrophy by reducing the fibroblastic dystrophy which causes it [15]. The same team then showed the effectiveness of botulinum toxin on 12 keloid scars using a one-year exploratory study [17]. Xiao and Zhang's team, in the same department as the previous team, published significant results on 19 patients with a follow-up 6 months later [18]. Majid then reported this potential usefulness of botulinum toxin on keloid scars [19]. Finally, several other teams have also reported encouraging results on the effectiveness of botulinum toxin on hypertrophic scars : their appearance and their prevention [20,21].

CONCLUSION

This new treatment of keloid scars could thus be of great help, particularly for resistant or recurrent scarring. A randomized and verified exploratory study must now be carried out in order to show, in a significant way, its long-term effectiveness.

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