

CASE REPORT

# Botulinum Toxin Type A as a Tool for Correcting Capsular Contracture after Reconstructive Breast Surgery

Aziz D. Zikiryakhodzhaev, MD\* Galina S. Alekseeva, MD\* Igor V. Reshetov, MD† Marianna V. Starkova, PhD\* Eric K. Saribekyan, MD\* Fedor N. Usov, PhD\* Maria Yu. Vlasova\*† Summary: Capsular contracture is one of the most common complications after breast reconstruction. Surgical treatment is the main option for capsular contracture correction and includes capsulotomy, capsulectomy, and removal/replacement of the affected implant. However, the surgical trauma from reoperation, along with reduced quality of life, in patients with clinically significant capsular contracture has prompted a search for alternative treatment options. The use of the botulinum toxin type A in the treatment of neurological diseases and of keloid scars in aesthetic practice nudged the idea of using the same toxin for the correction of capsular contractures in breast cancer patients. Botulinum toxin type A injection is an easy procedure requiring no anesthesia or inpatient care. The treatment has few side effects. In addition, the injection does not cause sensory loss or dysesthesia. We described a clinical case of the capsular contracture correction using incobotulinumtoxin A. Capsular contracture IV developed 4 months post surgery after long-term lymphorrhea. Radiation therapy was not performed. According to the internal protocol, the patient was advised to undergo incobotulinumtoxin A treatment instead of surgery. Within 1 week after the second injection, all symptoms decreased—specifically, the general shape of the reconstructed breast. Also, the pain syndrome disappeared. (Plast Reconstr Surg Glob Open 2021;9:e3372; doi: 10.1097/GOX.000000000003372; Published online 25 January 2021.)

**B** reast cancer (BC) is one of the most commonly diagnosed cancers among women in the Russian Federation.<sup>1</sup> Surgery has remained a key component of the multimodal strategy and comprehensive care in patients with breast cancer.<sup>2</sup>

According to the American Society of Plastic Surgeons, a total of 101,657 breast reconstruction procedures were performed in 2018; 77.53% of them involved the use of silicone implants.<sup>3</sup> In 2019, breast reconstruction using silicone implants accounted for 54% of all surgeries at P.A.

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Capsular contracture is the commonest complication of breast reconstruction with silicone implants and is typical for this procedure. The incidence of capsular contracture varies from 2.8% to 60%, according to different authors, and depends on several factors (including implant surface, placement technique, patient's inherent response and their propensity to form keloid scars, infection at the incision site, and hematoma).<sup>4-6</sup>

The term "capsular contracture" is understood to mean constriction and hardening of the fibrous capsule, which results in squeezing of the implant, and may lead to the asymmetry and visible deformity of the breast. Capsular contracture is measured by the Baker scale in terms of severity. Grades III and IV are considered clinically significant. Grade IV contracture causes the breast to become painful.<sup>7–9</sup> A number of authors report lower incidence of clinically significant capsular contracture with polyurethane-coated implants.<sup>10–13</sup>

Most grade III/IV capsular contractures develop within the first year after surgery.<sup>14–16</sup> Severe (Baker grades III/IV) grades of capsular contracture are universally deemed as an indication for corrective surgery.<sup>17</sup>

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The idea of using the toxin in the treatment of clinically significant capsular contracture after breast reconstruction in patients with BC is inspired by the improvement of keloid scars with botulinum toxin type A (BoNT-A) in clinical aesthetic practice.<sup>18–20</sup>

BoNT-A reduces mRNA levels of alpha-smooth muscle actin, a protein expressed by myofibroblasts, and also acts through suppression of fibroblast proliferation and differentiation by inhibiting the expression of transforming growth factor (TGF)- $\beta$ 1. Inhibition of TGF- $\beta$ 1 also suppresses fibroblast production of collagen type I, a major component of the extracellular matrix, and induces the differentiation of fibroblasts into myofibroblasts, which in turn causes acceleration of wound contraction.<sup>21</sup> In addition, BoNT-A produces a potent analgesic action linked to the inhibition of peripheral release of glutamate, calcitonin-gene–related peptide and substance P, a mediator of inflammation.<sup>22,23</sup>

The onset of BoNT-A action ranges from 24 to 48 hours after injection, with the peak effect being achieved in about 2 weeks. Duration of the effect ranges from 2 to 6 months.<sup>24</sup>

In this study, we report on successful management of a clinically significant Baker grade III/IV capsular contracture in a patient with BC after an immediate breast reconstruction with a silicone implant.

## **CASE REPORT**

In February 2019, patient G, a 45-year-old woman, discovered a mass in her left breast.

Breast ultrasound performed in February 2019 showed an avascular, mildly hypoechoic mass (size:  $10 \times 8 \times 16$  mm), with smooth contours and distinct margins. Mammography performed in February 2019 showed a nodular formation occupying part of both upper quadrants ( $12 \times 10$  mm), with an indistinct border and an irregular edge (Fig. 1). Core biopsy of the suspicious mass was performed. The morphological study revealed a low-grade tubular cancer. Immunohistochemical test results were as follows: ER Allred score: 8; PR Allred score: 8; Her2/neu: negative; Ki67: 15%; luminal A subtype.

The patient underwent further extensive testing that included abdominal and retroperitoneal sonography, pelvic ultrasound, chest CT scan, and bone scintigraphy. No signs of regional or distant metastases were detected.

Based on the test results, we established the following diagnosis: I stage left-side breast cancer,  $T_1N_0M_0G_1$ , luminal A subtype. Surgery was recommended as the first step of treatment.

In April of 2019, the patient underwent subcutaneous mastectomy with immediate prepectoral breast reconstruction using a polyurethane implant 420 cm<sup>3</sup>, and sentinel lymph node biopsy was performed in the P.A. Hertsen Moscow Oncology Research Center. Further anti-estrogen therapy with tamoxifen (20 mg/day) was recommended.

A seroma persisted during the postoperative period, from May to September 2019. Then, starting in July 2019, the patient began to notice mild firmness of the reconstructed left breast.

In August 2019, she presented with a marked contour deformity of the reconstructed breast, and shape



Fig. 1. Mammography, oblique projection in February 2019.

asymmetry. The reconstructed breast was painful to palpation. The clinical picture thus corresponded to Baker grade IV capsular contracture. Starting in September 2019, the pain began to intensify (the patient rated her pain as 8, on the visual analog scale pain rating scale).

According to the internal protocol, the patient was advised treatment with incobotulinumtoxin A in an effort to manage the contracture conservatively. In November 2019, subcutaneous injections of incobotulinumtoxin A were administered at the pre-marked



Fig. 2. Injection of BoNT-A.



**Fig. 3.** View of the patient before and after botulinum toxin therapy. A, The patient presenting with Baker grade IV capsular contracture in November 2019, before botulinum toxin therapy. B, The patient presenting at 1 week after the second series of incobotulinum toxin A injections. A marked improvement in the shape of the reconstructed breast is noted, and complete pain relief is achieved.

injection points as follows: 25 U into the area of the surgical scar, 20 U into the anterior leaf of the capsule, along the upper pole, and 25 U into the pectoralis major insertion. The total dose given was 70 U. The patient reported improvement in pain intensity on the third post-injection day, rating her pain 2 on the visual analog scale. Complete pain relief was achieved within a week after the first injection.

At the follow-up visit 11 days later, improvement of the contracture was noted: the appearance of the scar reduced, and the capsule softened. The patient received another series of incobotulinumtoxin A injections as follows: 30 U into the area of the surgical scar and 90 U into the area of the upper slope. The total dose given was 120 U (Fig. 2).

At 1 week after second injection, the patient had pronounced improvement in symptoms, specifically, the general shape of the reconstructed breast (Fig. 3). Furthermore, she reported complete pain relief (score 0 on the visual analog scale pain rating scale). Since she began botulinum toxin therapy, the patient has not experienced any recurrent episodes of pain.

### DISCUSSION

Our case report demonstrates the use of incobotulinumtoxin A injections as an alternative method of correcting a capsular contracture after breast reconstruction. Given in adequate doses and with regular treatment cycles, BoNT-A has yielded a distinct improvement in terms of capsule hardening and pain.

In summary, botulinum toxin type A injections can be a socially relevant treatment for capsular contracture after immediate breast reconstruction. BoNT-A allows oncology patients to return to a normal lifestyle, thus improving their quality of life.

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#### REFERENCES

- 1. Kaprin AD, Starinsky VV, Petrova GV. Malignant tumors in Russia 2018. *Morb Mortal*. 2019;249.
- Jones C, Lancaster R. Evolution of operative technique for mastectomy. Surg Clin North Am. 2018;98:835–844.
- American Society of Plastic Surgeons. Plastic Surgery Statistics Report. Available at https://www.plasticsurgery.org/documents/ News/Statistics/2019/plastic-surgery-statistics-full-report-2019. pdf. Published 2019. Accessed July 8, 2020
- Kostenko EV, Petrova LV, Lebedeva AV, Boiko AN. Comprehensive rehabilitation of patients with post-stroke spasticity of the arm in out-patient settings. *J Dis Nerv Syst.* 2013;3:30–38.
- Kurenkov AL, Nikitin SS, Artemenko AR, Al E. Botulinum toxin type A chemodenervation treatment in spastic forms of cerebral palsy. *Neuromuscul Dis.* 2013;3:40–47.
- Carvajal J, Carvajal M, Hernández G. Back to basics: could the preoperative skin antiseptic agent help prevent biofilm-related capsular contracture? *Aesthet Surg J.* 2019;39:848–859.
- Karapetyan GE, Pakhomova RA, Vinnik YS, Al E. Capsular contracture around breast implants. J Mod Probl Sci Educ. 2015;5: 308–308.
- Semiglazov VF, Krivorot'ko PV, Semiglazov VV, Dashyan GA, Paltuev RM. Clinical guidelines for the management of patients with breast cancer. *Appl to J Med advice*. 2017;14:5–238.
- Spear SL, Baker JL Jr. Classification of capsular contracture after prosthetic breast reconstruction. *Plast Reconstr Surg.* 1995;96: 1119–1123.
- Duxbury PJ, Harvey JR. Systematic review of the effectiveness of polyurethane-coated compared with textured silicone implants in breast surgery. J Plast Reconstr Aesthet Surg. 2016;69:452–460.
- Vázquez G, Pellón A. Polyurethane-coated silicone gel breast implants used for 18 years. *Aesthetic Plast Surg.* 2007;31:330–336.
- Zikiryakhodzhaev AD, Shirokih IM, Ablitsova NV, Al E. Immediate breast reconstruction and postoperative radiation therapy: capsular contracture formation. *J Probl Oncol.* 2019;65:374–385.
- Batiukov D, Podgaiski V, Ladutko D. Removal of polyurethane implants. Aesthetic Plast Surg. 2019;43:70–75.
- Henriksen TF, Hölmich LR, Fryzek JP, et al. Incidence and severity of short-term complications after breast augmentation: results from a nationwide breast implant registry. *Ann Plast Surg.* 2003;51:531–539.
- Handel N, Cordray T, Gutierrez J, et al. A long-term study of outcomes, complications, and patient satisfaction with breast implants. *Plast Reconstr Surg.* 2006;117:757–767.
- Araco A, Gravante G, Araco F, et al. A retrospective analysis of 3,000 primary aesthetic breast augmentations: postoperative complications and associated factors. *Aesthetic Plast Surg*. 2007;31:532–539.

- Prantl L, Schreml S, Fichtner-Feigl S, et al. Clinical and morphological conditions in capsular contracture formed around silicone breast implants. *Plast Reconstr Surg.* 2007;120:275–284.
- Robinson AJ, Khadim MF, Khan K. Keloid scars and treatment with botulinum toxin type A: the belfast experience. *J Plast Reconstr Aesthet Surg*, 2013;66:439–440.
- Fanous A, Bezdjian A, Caglar D, et al. Treatment of keloid scars with botulinum toxin type A versus triamcinolone in an athymic nude mouse model. *Plast Reconstr Surg.* 2019;143:760–767.
- Leventhal D, Furr M, Reiter D. Treatment of keloids and hypertrophic scars: a meta-analysis and review of the literature. *Arch Facial Plast Surg.* 2006;8:362–368.
- 21. Jeong HS, Lee BH, Sung HM, et al. Effect of botulinum toxin type a on differentiation of fibroblasts derived from scar tissue. *Plast Reconstr Surg.* 2015;136:171e–178e.
- 22. Kim S, Ahn M, Piao Y, et al. Effect of botulinum toxin type A on TGF-β/Smad pathway signaling: implications for siliconeinduced capsule formation. *Plast Reconstr Surg.* 2016;138:821e– 829e.
- Timerbaeva SL. Botulinum toxins in clinical practice. Atmos J Nerv Dis Clin Pharmacol Sect. 2004;2:34–38.
- Dutta SR, Passi D, Singh M, et al. Botulinum toxin the poison that heals: a brief review. Natl J Maxillofac Surg. 2016;7: 10–16.