Prostatic Carcinoma Shrunk After Intraprostatic Injection of Botulinum Toxin

Konstantinos Vezdrevanis

Keywords: prostatic neoplasm, botulinum toxins, injections, adenocarcinoma, disease progression

Urol J. 2011;8:239-41.
www.uj.unrc.ir

University of Ioannina, Greece

Corresponding Author:
Konstantinos Vezdrevanis, MD
23 Kyprou St., GR-46100,
Igoumenitsa, Greece
Tel: +30 266 502 9090
Fax: +30 266 502 9091
E-mail: kvezdrevanis@yahoo.com

Received September 2009
Accepted October 2009

INTRODUCTION

I present a patient with metastatic prostate cancer (PCa), who had an intraprostatic injection of botulinum toxin in order to relieve his prostatic obstruction. One month later, the ultrasonographic appearance of the primary prostatic tumor was improved dramatically.

CASE REPORT

A 68-year-old man presented with metastatic PCa three years earlier with initial serum level of prostate-specific antigen (PSA) 521 ng/mL, Gleason score 4 + 4 = 8, and extensive bone disease. He underwent castration-refractory one year after the primary diagnosis and he was till recently progressing slowly under castration plus dexamethasone and lanreotide.

I performed a transperineal intraprostatic injection of botulinum toxin type A (BT-A) with a dosage of 1000 units of Dysport™/ Ipsen diluted in 0.5% adrenaline solution of water for injection, in a single injection directly between the two apparent hypoechoic areas under transrectal ultrasound (TRUS) guidance, in a total volume of 7 cm^3, in order to relieve his ongoing prostatic obstruction.[1-9]

In the TRUS performed just before the BT-A injection, there were apparent two hypoechoic oval areas at the peripheral zone of the left lateral prostatic lobe, reflecting the digital finding of the left lobe hardness, sized 26 ×14 mm and 16 × 9 mm, respectively. The lesions were obviously infiltrating far outside the prostatic capsule (Figure 1).

Twenty-eight days later, the hardness of the left lobe was much lessened; however, the whole gland was found digitally much smaller. Transrectal ultrasonography revealed only one hypoechoic area located inside the gland measuring 10 × 8 mm (Figure 2). The total prostate volume dropped from

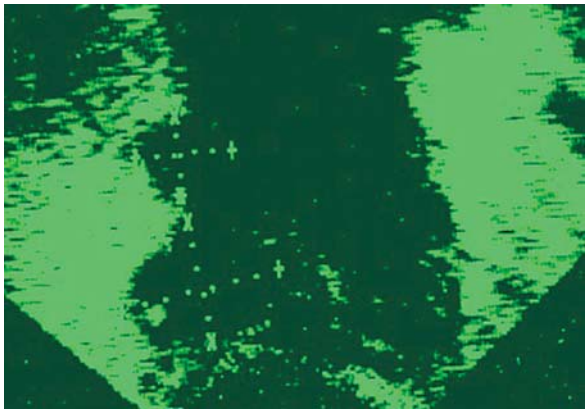

Figure 1. Two hypoechoic oval areas at the peripheral zone of the left lateral prostatic lobe (Just before BT-A injection).

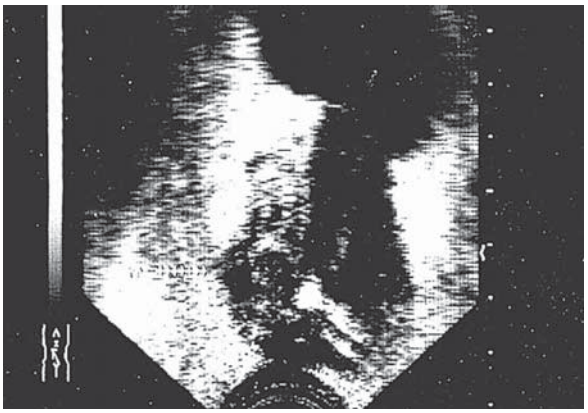

Figure 2. Transrectal ultrasonography shows only one hypoechoic area located inside the gland (one month after BT-A injection).

48.8 to 34.3 cm^3 (30% reduction), ie, much less than the primary tumors' size reduction. The serum level of PSA continued rising from 92 to 131 ng/mL, with an almost stable doubling time of about two months. His serum level of alkaline phosphatase (ALP) rose from 77 to 87 units (normal value < 136 units). The Stamey Mears test was negative for prostatitis or other urinary tract infection. Post-void residual urine volume dropped from 122 to 88 cm^3 while Qmax rose from 5 to 9 mL/min.

Immediately after BT-A injection, alfuzosin with a dosage of 10 mg/day was discontinued, and the patient received a two-week circle of capecitabine with an average dosage of 1.5 gr/day (1 gr/m^2/day). The initial dosage of 2 gr/day had to be reduced twice during the circle due to neurotoxicity and severe fatigue. Finasteride with a dosage of 10 mg/day was added to his treatment.

Two months after the BT-A treatment, the TRUS of the prostate revealed no hypoechoic lesion. The serum level of PSA decreased to 101 ng/mL, and then ALP continued rising, but less quickly, from 87 to 94 ng/mL. In the meantime, the patient received one more circle of capecitabine.

Four months after the BT-A injection and progressive deterioration of the systemic disease, the patient turned paraplegic, due to pressure to the spinal cord by spinal metastases. He had been irradiated and became better initially, but died thirteen months after the BT-A injection. His death was due to repeated ileus probably due to symphyses caused by the irradiation treatment. No ascites, no bowel or hepatic tumor, and no pulmonary metastasis were seen. He only had a surgical history of cholecystectomy. Due to his general condition, he underwent the evaluation of the prostate under TRUS only once again, five months after the BT-A injection, with absence of hypoechoic lesions and normal digital findings. However, eight months after the BT-A injection and after the progression of the spinal cord involvement, the prostate turned digitally again malignant (PSA = 240 ng/mL, ALP = 101 units).

DISCUSSION

I do not believe that the shrinking of the primary tumors was due to the action of capecitabine or finasteride, but of course, nobody can deny that their combination may be helpful. Possible synergy of castration, dexamethasone, and lanreotide should be taken into account as well.

To the best of our knowledge, this is the first reported BT-A injection in a patient with the PCa. Since long ago, there was evidence of possible action of BT-A against PCa, including the presence of muscarinic, specifically M3, receptors in LNCaP cells[10] and in natural human prostatic carcinomas.[11] Recently, it was reported that BT-A inhibits the growth of LNCaP cells in vitro and in vivo, as xenografts in nude mice.[12]

My findings of the primary prostate tumors being clinically dissolved after local BT-A injection and being effective for at least 5 months (no more than 8 months), with the proviso of a heavy cancerous burden and a very aggressive cancer, supports the former preclinical data and should be investigated further. Unfortunately, ideal candidates to study the clear effect of BT-A injection on the local prostate cancer are only patients with well-documented local disease, suitable for watchful waiting, with prostatic obstruction refractory to medical treatment, and unwilling to undergo transurethral resection of the prostate; and these patients are not so many. Maybe a clinical trial of the patients with the prostate cancer having local irradiation with two types of BT-A and non-BT-A injection could help as well.

CONFLICT OF INTEREST

None declared.

REFERENCES

1. Maria G, Brisinda G, Civello IM, Bentivoglio AR, Sganga G, Albanese A. Relief by botulinum toxin of voiding dysfunction due to benign prostatic hyperplasia: results of a randomized, placebo-controlled study. Urology. 2003;62:259-64; discussion 64-5.
2. Kuo HC. Prostate botulinum A toxin injection--an alternative treatment for benign prostatic obstruction in poor surgical candidates. Urology. 2005;65:670-4.
3. Chuang YC, Tu CH, Huang CC, et al. Intraprostatic injection of botulinum toxin type-A relieves bladder outlet obstruction in human and induces prostate apoptosis in dogs. BMC Urol. 2006;6:12.
4. Chuang YC, Chiang PH, Yoshimura N, De Miguel F, Chancellor MB. Sustained beneficial effects of intraprostatic botulinum toxin type A on lower urinary tract symptoms and quality of life in men with benign prostatic hyperplasia. BJU Int. 2006;98:1033-7; discussion 337.
5. Silva J, Silva C, Saraiva L, et al. Intraprostatic botulinum toxin type a injection in patients unfit for surgery presenting with refractory urinary retention and benign prostatic enlargement. Effect on prostate volume and micturition resumption. Eur Urol. 2008;53:153-9.
6. Brisinda G, Cadeddu F, Vanella S, Mazzeo P, Marniga G, Maria G. Relief by botulinum toxin of lower urinary tract symptoms owing to benign prostatic hyperplasia: early and long-term results. Urology. 2009;73:90-4.
7. Brawer MK, Loeb S, Partin AW, et al. Best of the 2009 AUA Annual Meeting: Highlights from the 2009 Annual Meeting of the American Urological Association, April 25-30, 2009, Chicago, IL. Rev Urol. 2009;11:82-107.
8. Roehrborn CG, Crawford ED, Donnell R, et al. The utility of ultrasound derived prostate parameters in predicting clinical response in men treated with botulinum neurotoxin type A (BONT-A) for benign prostatic hyperplasia (BPH). J Urol. 2009;181:650-.
9. Crawford ED, Donnell R, Hirst K, MIST Study Group. 12 week results of a phase II trial of 100 and 300 units of Botulinum Neurotoxin type A for the management of Benign Prostatic Hyperplasia (BPH). J Urol Suppl. 2009;181:649–50.
10. Rayford W, Noble MJ, Austenfeld MA, Weigel J, Mebust WK, Shah GV. Muscarinic cholinergic receptors promote growth of human prostate cancer cells. Prostate. 1997;30:160-6.
11. Song W, Yuan M, Zhao S. Variation of M3 muscarinic receptor expression in different prostate tissues and its significance. Saudi Med J. 2009;30:1010-6.
12. Karsenty G, Rocha J, Chevalier S, et al. Botulinum toxin type A inhibits the growth of LNCaP human prostate cancer cells in vitro and in vivo. Prostate. 2009;69:1143-50.