Cryobiology 68 (2014) 79–83

Contents lists available at ScienceDirect

Cryobiology

journal homepage: www.elsevier.com/locate/ycryo

Percutaneous cryotherapy for metastatic bladder cancer: Experience with 23 patients ☆

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ARTICLE INFO

Article history:
Received 8 August 2013
Accepted 16 December 2013
Available online 22 December 2013

Keywords:
Metastatic bladder cancer
Percutaneous cryoablation
Progression-free survival

ABSTRACT

Bladder cancer is the most common malignancy of the urinary tract and in many patients is metastatic at diagnosis. Chemotherapy is the standard treatment for these patients but has serious side effects and in many patients is not tolerated. To avoid the side effects of systemic chemotherapy, patients with late stage bladder cancer have sought cryotherapy in our hospital. We reviewed data for the past 4 years to evaluate the safety and efficiency of percutaneous cryotherapy in 23 patients. Within 3 days after cryosurgery, all complications of bladder cancer (e.g. hematuria, urinary irritation, hypogastralgia, lumbago) had decreased to some degree. No new complications (e.g. bladder perforation) occurred and all complications had disappeared completely after 2 weeks. The progression-free survival (PFS) of these patients was 14 ± 8 months. There was no effect on PFS of tumor location or histopathology; however, differentiation status and tumor size influenced the therapeutic effect of percutaneous cryoablation. In conclusion, percutaneous cryotherapy may be a safe and efficacious therapeutic option in the treatment of metastatic bladder cancer.

Introduction

As of 2013, bladder cancer is estimated to be the fourth most common cancer in new cancer cases and the eighth most common cause of death among all types of cancer in the USA [18]. At the time of diagnosis, approximately 15% of bladder cancers have penetrated the bladder wall and spread, mostly into regional organs (prostate gland, uterus, vagina, or pelvic and abdominal cavity); less often, distant metastasis has occurred. The standard treatment for noninvasive bladder cancer is transurethral resection and intravesical therapy; in patients with metastatic disease, these therapies are obviously useless and systemic chemotherapy is the only treatment that has been shown to improve survival [9,16].

Cryosurgery, which can induce tissue necrosis by ice ball formation, has been used as an alternative therapeutic approach in bladder cancer for half a century. The effects of cryoablation on the bladder were investigated in dogs by McDonald et al. in 1950; typical necrotic lesions were produced [10]. Recently, using modern technology, Permpongkosol et al. investigated the morphologic changes caused by percutaneous full-thickness bladder cryoablation in pigs and achieved controllable transmural necrosis with single and repeated cycles, with no bladder perforation [17]. With the advent of argon–helium cryosurgery and improvements in medical imaging, percutaneous cryosurgery has been used as a novel therapeutic approach to the treatment of benign and malignant tumors, especially unresectable tumors [9]. So, the use of percutaneous cryotherapy in the treatment of metastatic bladder cancer is experimental, and many factors might assist the treatment to success, including the good visibility of the ice ball on computed tomography (CT), close concordance between the area covered by the ice ball and the area of complete necrosis [6,14] and avoidance of damage to the collagenous architecture of the bladder, prostate gland and uterus [7].

In this retrospective study, 4 years of follow-up data for 23 patients obtained from our hospital's database were analyzed to investigate the safety and efficacy of percutaneous cryotherapy in the treatment of metastatic bladder cancer.

☆ *Statement of funding:* This work was supported by Tumor Researching Fund from the Fuda Cancer Hospital, Guangzhou, China.

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http://dx.doi.org/10.1016/j.cryobiol.2013.12.004

Materials and methods

Ethics

The study protocol received ethical approval from the Regional Ethics Committee of Guangzhou Fuda Cancer Hospital. Written informed consent was obtained from each participant in accordance with the Declaration of Helsinki.

Patient selection

Between October 2007 and September 2011, 23 patients with metastatic bladder cancer met our inclusion criteria and were enrolled in the study. These patients had refused to undergo systemic chemotherapy and sought treatment directly in our hospital or after failure of previous chemotherapy. Ideal patients for bladder cryoablation are those with: Karnofsky performance status score $\geqslant 70$; platelet count $\geqslant 80 \times 10^9$/L; white blood cell count $\geqslant 3 \times 10^9$/L; neutrophil count $\geqslant 2 \times 10^9$/L; and no cystitis or urinary tract infection. The diagnosis was confirmed by radiologic imaging and fine needle aspiration biopsy. The common presenting symptoms were gross or microscopic hematuria, urinary irritation (in the form of frequency, urgency or dysuria), hypogastralgia and lumbago. All patients had a single tumor in the bladder and were in the metastatic stage of the disease.

Cryoablation procedure

With the patient supine, the tumor was located by CT and the middle abdomen or groin was used for puncture points according to the tumor's position. Percutaneous cryotherapy was performed on all patients, with the complete cryoablation of all obvious intra- and extracystic masses. Cryosurgery was performed using an argon gas based cryosurgical unit (Endocare, Irvine, CA, USA) and cryoprobes of 1.7 mm diameter (Endocare); one to four cryoprobes were inserted into the mass from the abdominal skin and two freeze/thaw cycles were performed, each reaching a temperature of −120 °C at the tip of the probe. The duration of freezing was dependent on the achievement of an ice ball, visible as a low density area under CT guidance (Fig. 1). Generally, the tumor was frozen for a maximal time of 15 min and thawed for 5 min; this procedure was then repeated. A margin of at least 0.5 cm of normal tissue was frozen circumferentially around the tumor. During the freezing process, attention was paid to avoiding injury to the ureter, urethra, prostate, vagina, uterus and bowel. For masses of 1–1.9 cm in longest diameter, one cryoprobe was used to ensure freezing of the entire tumor; two cryoprobes were necessary for masses of 2–3.9 cm and three or four cryoprobes for tumors of 4–5.9 cm or 6–8 cm, respectively. Compression bandaging was applied to the puncture points after procedure. If the patient can urinate normally and no obvious postoperative hematuria, showing that no cancer plug or severe bleeding, bladder irrigation was usually begun the night after cryosurgery (physiologic saline, daily use 100 ml), otherwise bladder irrigation will be performed at once and continued for 3–5 days until hematuria had disappeared completely.

Tumors in organs other than the bladder (e.g. liver and abdomen) were usually percutaneously ablated during the same procedure as the bladder tumor (so-called "comprehensive cryosurgery" [2,3,11,15]), small satellite lesions will be irrelevant to the outcome.

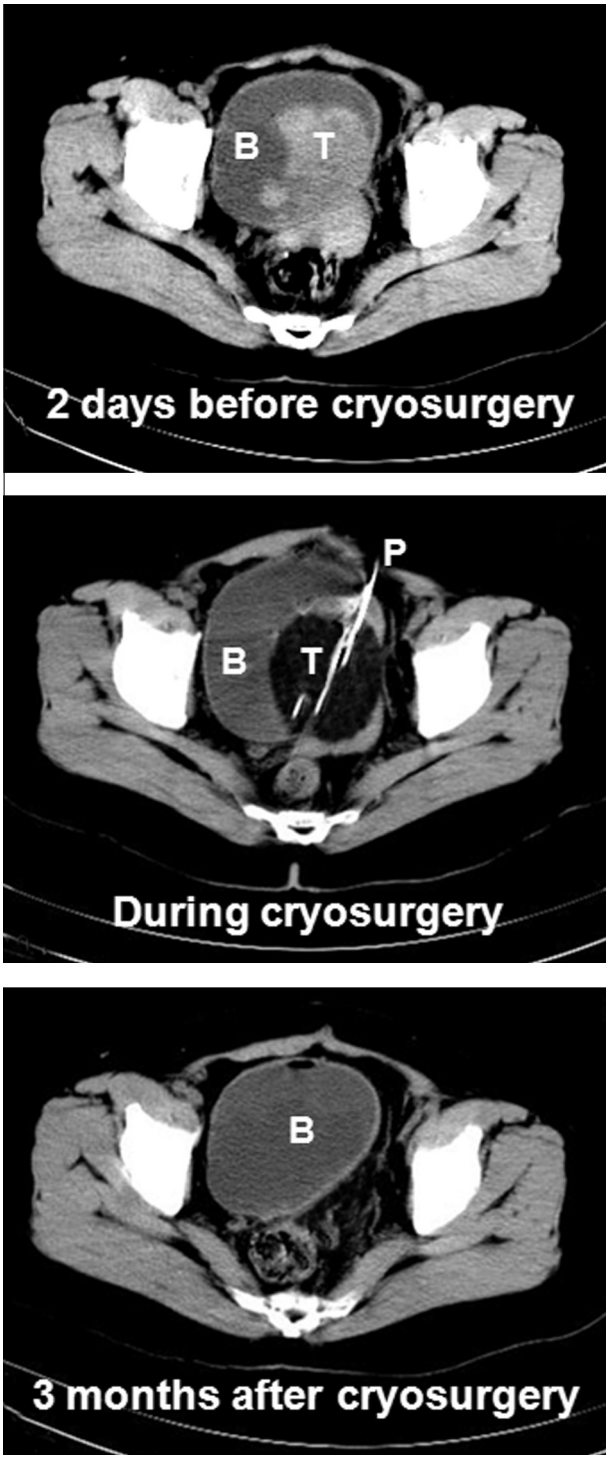

Fig. 1. CT images of a patient with cancer in the right wall of the bladder. Two days before cryosurgery, the tumor (T) occupied more than half of the bladder (B). During cryosurgery with three probes (P), the ice ball grew gradually, surrounded the tumor and formed a low density area. Three months after cryosurgery, the structure of the bladder wall remained intact and tumor inside and outside the bladder had disappeared.

Evaluation and statistical analysis

Complications were recorded and classified in accordance with the Common Terminology Criteria of Adverse Events v4.0. Radiographic local tumor control was assessed using image-guided tumor ablation criteria [5]. A Wilcoxon matched pairs signed rank