Case Report

Metastatic retro-crural lymph nodes from transitional cell carcinoma of bladder successfully treated with single session cryoablation✩✩★✩

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ABSTRACT

Bladder cancer (BC) is a relatively common tumor, with a male preponderance. High-grade muscle invasive bladder cancer (MIBC) has a very high incidence of pelvic lymph node metastasis at presentation. Involvement of the retro-crural lymph nodes, although has been described in other pelvic tumors, is very uncommon for BC. Cryoablation in the retro-crural region is extremely challenging due to the proximity to the critical structures like inferior vena cava and aorta and has not been extensively reported. We describe a 56-year-old male patient with MIBC who underwent extensive treatments including radical cystoprostatectomy, chemoradiation and immunotherapy, ultimately with localized disease in the retro-crural region. Single session cryoablation of these lymph nodes was performed with a curative intent yielding a positive response that has persisted for more than 2 years.

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Introduction

Bladder cancer (BC) is the fourth most prevalent malignancy in the United states [1]. Majority of them are transitional cell cancers (TCC) [1]. The likelihood of nodal metastasis increases with the depth of invasion and hence radical cystectomy with pelvic lymph node dissection is the recommended treatment for muscle invasive bladder cancer (MIBC) [2,3]. The obturator and the internal iliac lymph nodes are most commonly involved. Involvement of retro crural lymph nodes, in TCC has not been previously reported. Patients with distant metastatic disease are usually treated with systemic therapy with a palliative intent. In this case report, we describe a case of bladder TCC metastatic to the retro-crural nodes refractory to sys-

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temic therapy, successfully treated with cryoablation yielding a long-term sustained response.

Case report

A workup for asymptomatic hematuria in a 56-year-old male patient with cystoscopy and transurethral resection of bladder tumor (TURBT) revealed high grade muscle invasive TCC. A staging positron emission tomography (PET) scan at the time of initial diagnosis, showed 18-Fluoro deoxy glucose (18FDG) avid retroperitoneal (RP) and pelvic lymph nodes. Based on this his clinical staging was T2N2M0 (stage IV). Following this, he received 6 cycles of neoadjuvant chemotherapy with a combination of methotrexate, vinblastine, doxorubicin, and cisplatin (MVAC) and the follow-up PET scan showed good response with decreased activity and size of the RP and pelvic lymph nodes. Four months after initiating neoadjuvant chemotherapy, the patient was discussed at tumor board and considered a good candidate for radical cystoprostatectomy, bilateral pelvic/RP lymph node dissection and creation of an ileal conduit. Three-months after the surgery the follow up PET, showed 18FDG avid, enlarged RP lymph nodes, suggestive of disease recurrence. Patient was treated with mitomycin + 5 Fluorouracil and concurrent radiation. A dose of 4500 cGy in 25 fractions to the pelvis to include the pelvic and RP lymph nodes was followed by a boost to the PET positive lymph nodes resulting in a final dose of 5400 cGy in 30-33 fractions. The PET scan obtained four months after the final fraction of radiation treatment showed complete response to chemoradiation. Follow-up PET in 4 months, unfortunately showed enlarged 18FDG avid retro-crural lymph nodes. This was considered as first line treatment failure and the patient started on immunotherapy (pembrolizumab).

However, despite immunotherapy, there was stable persistent 18F-FDG activity in the enlarged retro-crural lymph nodes (Fig. 1). The lymph nodes measured 8 & 12 mm in short axis dimensions and demonstrated standardize uptake values of 7.4 and 7.2, respectively (Fig. 1). This was the only site of recurrent/residual disease nine months after initiating immunotherapy. He was discussed at multi-disciplinary tumor board and referred to interventional radiology for cryoablation of this stable metastatic nodal disease.

The procedure was performed in the prone position with conscious sedation. Two PCS-24/RS-24 (Healthcare, Inc, Austin, TX, USA) cryoprobes were used for the ablation. The probes were advanced under Computed tomography (CT) guidance into each of the lymph nodes and positioned appropriately to ensure complete coverage of the lymph nodes (Fig. 2). Two 12-minute freeze separated by a 5-minute thaw cycle were performed. Intraprocedural CT imaging confirmed that both the nodes were included in the resulting ice ball, without involving the adjacent vital structures (Fig. 2). Following the ablation, the probes were withdrawn, and no complications were noted on the post procedure CT. The patient was discharged same day after appropriate recovery from sedation.

Follow up PET scan 6 months after the cryoablation, revealed resolution of the 18FDG avidity and significant decrease in size of both the lymph nodes, (Fig. 3) suggesting a complete response to treatment. The positive response to cryoablation has lasted for more than 2 years, at the time of writing this manuscript, as confirmed by follow up PET scans obtained at 6-month intervals from the time of the procedure. No additional sites of recurrence have been noted either.

Discussion

BC is the 9th most common cancer worldwide, 4th most common cancer in the United States and the 7th most common cancer in men [1,4] Majority of the patients are men with a mean age 73 years at diagnosis [4]. Risk factors for BC include, male sex, older age, cigarette smoking, white race, exposure to certain chemicals, pelvic radiation, chronic bladder infection/irritation [5]. TCC is the most common type of BC, accounting for approximately 90% of cases [6]. Painless hematuria is the most common presenting symptom of BC [7]. Patients with advanced disease may present with symptoms related to metastatic involvement. The most common sites for metastasis are lymph nodes, bone, lung, liver, and peritoneum [8,9]. Adrenal gland metastasis is rarely seen [10]. Cystoscopy combined with CT urography is commonly employed in the diagnosis and work up of patients with BC [1,7]. PET/CT is
used for overall staging of the disease given its high specificity to identify lymph node metastasis [11–13]. Patients with abnormal findings on cystoscopy usually undergo TURBT, which removes the visible tumor, provides information needed for definitive diagnosis, grading, and assess the depth of invasion [14,15]. Treatment of BC depends on the pathologic extent of disease at the time of TURBT and on subsequent staging according to the tumor-node-metastasis classification system. Most tumors are nonmuscle-invasive bladder cancers. The primary treatment for nonmuscle-invasive bladder cancers is TURBT, followed by instillation of Bacillus Calmette–Guérin or intravesical chemotherapy [1,16]. However for MIBC, more aggressive treatments in the form of cisplatin-based neoadjuvant chemotherapy followed by radical cystectomy with bilateral pelvic lymphadenectomy are strongly recommended [17–20]. Extensive lymph node dissection has been shown to improve progression-free and overall survival [21,22]. However, in patients with metastatic disease at presentation chemotherapy is the preferred treatment option [23,24]. Immunotherapy is approved as a second-line treatment for metastatic BC in patients who fail or cannot tolerate chemotherapy [25,26]. Chemoradiotherapy is recommended for recurrent or persistent disease in MIBC [1].

Lymph node metastasis has been described for other malignancies like ovarian cancer, to our knowledge we did not find reports of BC metastasis to this lymph node network [33–35].

Cryoablation has been safely and effectively used in the definitive treatment of primary lung, liver, prostate, and renal cancers [36–40]. The biggest advantage of cryoablation over surgery is that it is minimally invasive, making it an attractive option for patients with several co-morbidities which would render them inoperable. Cryoablation achieves cellular damage in two phases: a directly cytotoxic freezing phase followed by a thawing phase. The freezing cycle induces cellular dehydration and ice formation which disorganizes cellular structures and function, which are then completely disrupted by the intracellular water flux that occurs during the thawing phase [41–43].

Percutaneous ablation in general is an underutilized tool in management of recurrent/ metastatic disease. As with surgery, cryoablation when properly performed can destroy tumor cells, thereby eliminate localized disease, and improve overall survival as in our patient who is disease free 2 years into his cryoaolation procedure. The retro-crural area is close to critical structures like inferior vena cava and aorta, which makes cryoablation of lesions in this area more challenging than elsewhere, and perhaps the reason why there are not many reports of ablations performed in this zone. This along with the long-lasting positive response to cryoablation.
of lymph nodes in an area which is unusual for spread of BC, make this case worthy of report.

**Contributorship statement**

Study conception (AB, JM, JH, RD), Data collection (JM, AB), Manuscript writing (JM, AB, JH, RD), Critical revision (AB, JM), Final approval (AA, JH, RD, JM, AB).

**Data sharing**

Data used in this study are not shared publicly.

**Supplementary material**

Supplementary material associated with this article can be found, in the online version, at 10.1016/j.radcr.2020.05.022.

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