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Case Report

Image-guided percutaneous cryo-ablation of peri-urethral unresectable recurrent pelvic malignancy: A case report and brief review ☆,☆☆

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ABSTRACT

Recurrent or metastatic peri-urethral pelvic malignancies are a difficult-to-treat entity. Re-resection is recommended when possible but is frequently unfavorable due to scar tissue, fibrosis, and obliteration of tissue planes following previous interventions such as surgical resection and/or radiation therapy. Curative options for patients that have unresectable cancer are limited. Cryo-ablation has been extensively studied in the treatment of unresectable renal, liver and lung malignancies and has the potential to provide definitive treatment for recurrent pelvic malignancy. There is a paucity of reports of salvage cryo-ablation in patients with recurrent pelvic malignancies, as most of these tumors are located close to critical structures that could be irreversibly injured by thermal ablation and are hence treated with some form of radiation therapy. But, for patients who fail surgical and radiation treatments, options are limited. Here, we describe two cases of regional tumor recurrence in the pelvis treated with percutaneous cryoablation using protective techniques to avoid thermal injury to adjacent structures. In each case, cryo-ablation was performed successfully despite extensive previous surgical and radiation interventions. Salvage cryo-ablation resulted in a positive clinical and imaging response with an improvement in quality of life and absence of recurrence on follow-up imaging which continues to persist at the writing of this manuscript about 8 and 12-months following treatment.

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Introduction

Metastatic disease in the urethral and peri-urethral region are infrequent but present unique challenges due to proximity to critical structures. Determining an appropriate management strategy may be challenging, especially following previous surgery or radiation therapy, requiring multi-disciplinary assessment and coordinated care. Cryoablation has been extensively used to treat primary and secondary neoplasms in the lung, liver and kidney; however, there is a paucity of literature on the efficacy and complications of cryoablation in pelvic neoplasms, especially in patients with a complicated history of previous surgery and radiation therapy. In the present report, we describe two cases of metachronous, recurrent metastatic peri-urethral cancer successfully managed with salvage image-guided percutaneous cryo-ablation. Institutional review board approval was received for this study under protocol number 20047777.

Case presentation

Patient 1

A 59-year-old male diagnosed with Gleason 6 (3 + 3) prostatic adenocarcinoma in 2010, initially treated with radical retropubic prostatectomy and radiation therapy. Patient was noted to have a rising PSA in 2019 to 1.1 ng/mL from a nadir of 0.2 ng/mL. Subsequent imaging with a contrast enhanced MRI demonstrated a 1.0 cm x 0.9 cm recurrent, enhancing nodule in the prostate bed, immediately adjacent to the prostatic urethra (Fig. 1A). Mild circumferential enhancement was also seen around the membranous urethra, most likely representing post-surgical changes. An ^{18}F-Fluciclovine (Axumin) positron emission tomography (PET) CT scan was performed to rule out regional and distant metastases. There was avid Axumin uptake in the recurrent nodule but otherwise no evidence of metastasis (Fig. 1B). Due to the complexity of the patient's anatomy secondary to previous surgical and radiotherapeutic interventions, a multidisciplinary approach between Urology and Interventional Radiology using CT guided cryoablation was planned. For the cryo-surgical procedure, the patient was sedated with a combination of intravenous Fentanyl (Sublimaze) and Midazolam (Versed). A pre-operative CT scan was reviewed demonstrating a hypodense lesion in the left posterolateral prostatic bed consistent with the recurrent nodule. A urethral warming catheter was placed to protect the urethra. After infiltration with 1% lidocaine, the Endocare PCS 17-R (Healthcare. Inc, Austin, TX, USA) cryoablation probe was passed directly through the left pelvic nodule in the prostatic bed from a posterior lateral approach under direct CT visualization. The probe was confirmed within the center of the lesion (Fig. 1C). A 10-minute cryoablation ablation cycle was performed, followed by an 8-minute active thaw. CT evaluation of the ice ball consumed the entirety of the lesion and did not involve any surrounding vital structures. Following the thaw cycle, a second cycle was performed followed by probe removal. Immediate postprocedure CT examination demonstrated no hemorrhage or other immediate complications. Following the procedure, the patient had an uneventful postoperative course. He reported one episode of hematuria and mild urgency/frequency which was controlled with Darifenacin (Enablex; Novartis Pharmaceutical, East Hanover, NJ, USA). Twelve-month follow-up contrast enhanced MRI showed no evidence of recurrence (Fig. 1D), and the patient's PSA remained stable at 0.6 ng/mL.

Patient 2

A 60-year-old female diagnosed with T4N0M0 anal squamous cell cancer (SCC) in July 2018. She was initially treated with chemoradiation but subsequently developed a rectovaginal fistula and recurrent SCC requiring a salvage robotic assisted abdominal perineal resection with a Gracilis flap in July 2019. An ^{18}F fluorodeoxyglucose (FDG) PET-CT scan in March 2020 identified a local recurrence of the left pelvic sidewall, 3.0 cm x 4.0 cm with an SUV of 24.2 abutting the urethra and in close proximity to the distal ureter (Fig. 2A). The patient was discussed at multidisciplinary tumor board and it was determined that the tumor was unresectable. It was decided to proceed with a multidisciplinary approach between Urology and Interventional Radiology using cryo-ablation with protective measures and adjuvant systemic chemotherapy. Prior to the procedure, urology placed a left ureteral stent, suprapubic catheter, and warming urethral catheter. A preliminary CT demonstrated a soft tissue density in the left pelvis measuring 5.0 cm in greatest diameter. A total of 3 Endocare V-Probes (Healthcare. Inc, Austin, TX, USA) were passed directly through the left pelvic mass from a posterior lateral approach under direct CT visualization [Fig. 2B]. CT confirmed position of all 3 probes prior to ablation, making sure there would be adequate coverage of the lesion in the ablation zone. Two freeze cycles of 10-minutes separated by an 8-minute passive thaw were performed. CT evaluation of the ice ball seen to consume the entirety of the lesion did not involve any surrounding vital structures. The patient did well post-procedure with no urine retention and no evidence of ureteral or urethral injury. A 3-month FDG PET-CT did not show any evidence of local FDG avidity (Fig. 2C). At 5-month follow-up, the SP catheter and ureteral stent were removed however, she continued to experience persistent perineal pain, mild urinary incontinence and perineal hernia. Subsequent contrast enhanced CT imaging at 8-month shows no local recurrence (Fig. 2D).

Discussion

Recurrent pelvic malignancy can be difficult to treat, especially following primary surgical or radiation treatments. Depending on the location of the recurrence in relation to other vital structures, repeat surgical resection may not be possible or extremely difficult, and may be associated with significant morbidity. Clinically, tumors may be silent or present with pain, obstructive symptoms due to mass effect, hematuria, dyspareunia, fistula, or sexual dysfunction [1]. Reported primary sources include prostatic, bladder, lung,

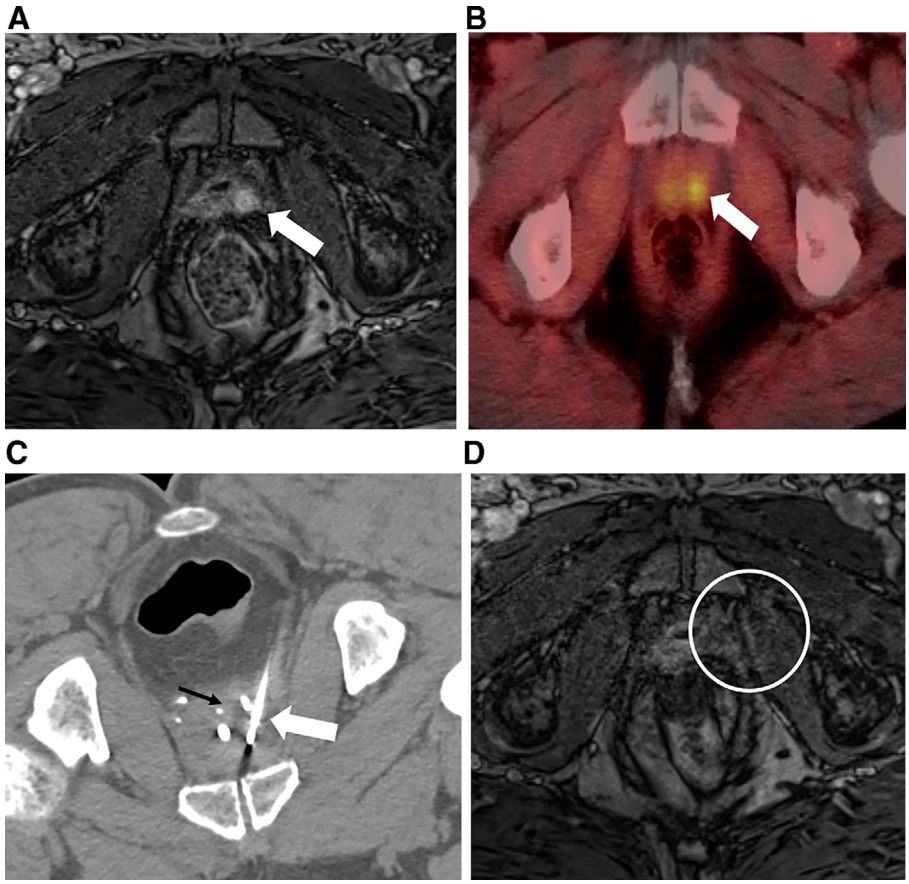

Fig. 1 – A 59-year-old male with recurrent prostatic adenocarcinoma after previous radical prostatectomy and radiation therapy, deemed a non-surgical candidate. (A) Axial contrast enhanced T1-weighted MRI of the pelvis, showing an enhancing nodule in the left periurethral area (white arrow). (B) Axial Axumin PET-CT showing focal uptake in the periurethral area (white arrow) compatible with recurrent tumor. (C) Axial non contrast CT of the pelvis during the procedure showing a cryoablation probe in the area of the periurethral recurrence (white arrow) with ice ball formation (black arrow). (D) Axial contrast enhanced T1 weighted MRI of the pelvis showing no enhancement in the periurethral region (white circle), 12 months postcryoablation.

and colorectal tumors [2]. Spread is likely either through direct extension, retrograde lymphatic flow, biopsy tract, surgical instrumentation, hematogenous, or paradoxical embolism given the various anastomotic channels between pelvic structures [2–4]. Management for recurrent, metastatic pelvic tumors depends on life expectancy, the presence of distant metastases, and size, number, and distribution of local disease. Primary management of pelvic malignancies such as prostate and colorectal typically involves resection with a curative intent and/or radiotherapy. Despite advances in surgical approaches, local recurrence at 2 years has been reported at 5.3% and 44.6% at 5 years [5,6]. In the cases above, one patient had a previous surgery with subsequent radiotherapy while the other had undergone several previous surgeries in order to achieve negative margins and plastic reconstruction with a Gracilis flap. Previous surgery and/or radiation results in obliteration of anatomical/surgical planes decreasing the benefit-to-risk of re-resection [1]. However, when early re-resection is possible, it may improve disease free survival and provide symptom palliation. Radiation therapy alone as primary treatment causes distinctive changes including atrophy and fibrosis of the target and surrounding tissues [7,8]. Microscopically, the invading tumor may also induce a desmoplastic response in the surrounding tissue further complicating anatomy [9]. Hence, an alternative approach to repeat surgery/radiation is often required.

In recent years, cryo-surgery has emerged as viable option for salvage therapy in patients with locally recurrent pelvic malignancy. Literature related to peri-urethral lesions is primarily from reports of locally recurrent prostate cancer following primary radiotherapy [10–16] with good biochemical disease-free survival [11,14,16–18]. With regards to cryoablation in peri-urethral metastases from recurrent colorectal cancer, there are very few reports [19]. These studies suggest cryo-ablation may be effective for recurrent pelvic malignancies; however, there are no prospective or retrospective studies evaluating the efficacy of cryoablation following complex surgical and radiation treatments. As highlighted in this case report, options are limited in these patients and there is limited data on management to guide clinicians.

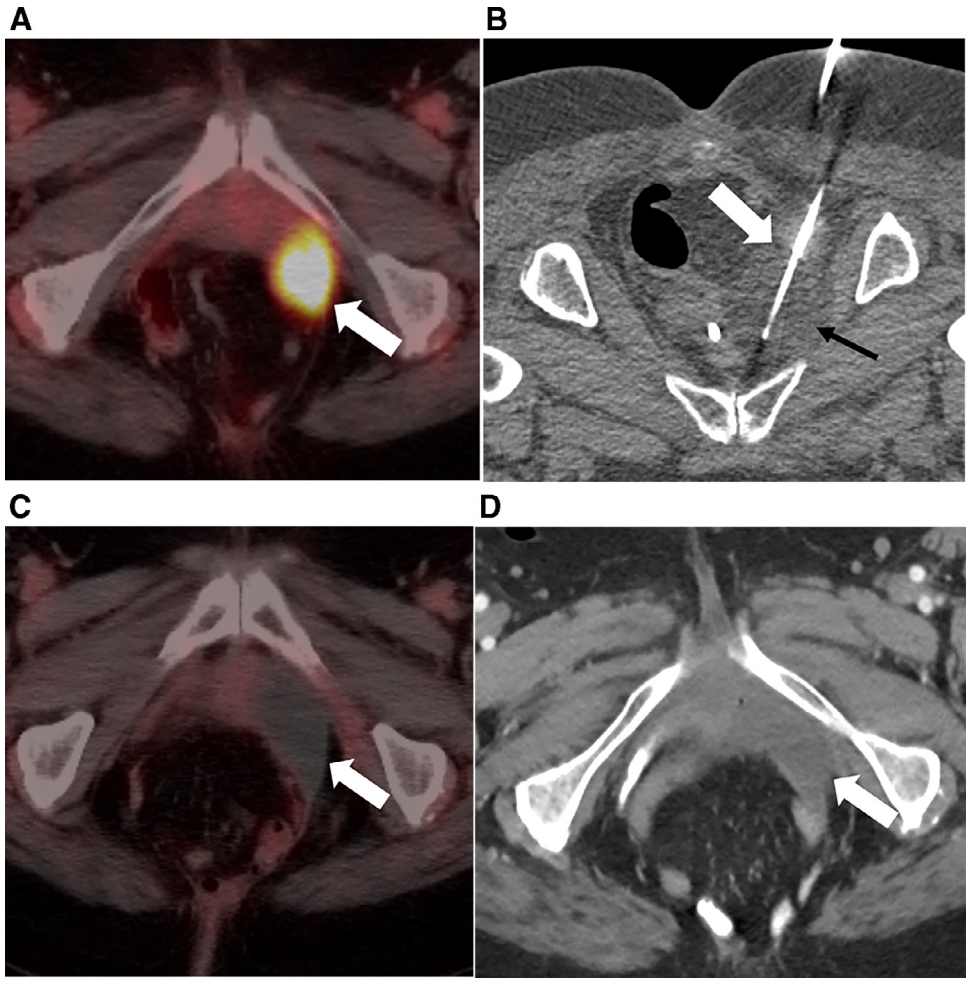

Fig. 2 – A 60-year-old female with recurrent anal squamous cell cancer in the pelvis initially managed with chemoradiation and abdominal perineal resection, deemed inoperable. (A) Axial FDG PET-CT of the pelvis showing an FDG avid nodule in the left periurethral area, compatible with recurrent anal cancer metastasis. (B) Axial procedural CT of the pelvis in the prone position, showing the cryoablation probe in the recurrent nodule (white arrows) with a well-formed ice ball encompassing the lesion (black arrows). (C) Axial FDG PET-CT of the pelvis showing no uptake in the nodule (white arrows) 5 months post cryoablation. (D) Axial contrast enhanced CT of the pelvis showing no recurrence in the left periurethral region (white arrow) 8 months post cryoablation.

There are important anatomical considerations with periurethral salvage cryo-ablation [7]. MRI is extremely valuable not only to identify recurrent disease but also delineate the anatomy in the region. It should be noted that inflammation or granulomatous reaction may mimic recurrence. In these instances, various nuclear medicine agents may aid in the diagnosis of recurrent pelvic cancer. For colorectal and prostate metastasis, FDG-PET remains a valuable, especially considering lymph node metastases are frequently <1 cm [7,20]. Local recurrence typically has a high FDG avidity in comparison to granulomatous reactions. Several additional agents including ^{11}C-Choline, ^{18}F-Fluciclovine (Axumin) and ^{68}Ga-prostate specific membrane antigen may provide increased sensitivity for detecting recurrent prostate cancer [7].

Among the modalities for thermal ablation, cryoablation has the inherent advantages of being less lethal to critical structures, associated with improved pain control, and visualization of the ice ball with CT guidance [21]. In areas with critical or complex anatomy, cryotherapy has been the ablative modality of choice [22]. The pelvic region may present a technical challenge when considering salvage cryo-ablation. The close proximity of muscles, fascia, organs and their associated neurovascular bundles requires, expert understanding of the pelvic anatomy, extensive pre-procedural planning and collaboration to achieve precise ablation and minimize collateral damage. This may be one of the reasons that radiation therapy has been historically preferred for recurrent tumors over thermal ablation. Following salvage cryoablation patients experience more urinary and erectile dysfunctions than after primary cryoablation, mostly due to unintended damage superimposed by the ablation on the periurethral nerve plexus and muscle complexes which have been traumatized by prior therapies [13]. With any form of ablation key to success is achieving an adequate balance between

ablation size and minimizing collateral damage. These cases also demonstrate that cryo-ablation can be highly efficacious as a salvage option in patients who are no longer candidates for surgery or radiation and have a limited tumor burden. In addition to careful planning and diligent technique in both the cases, we used a warming catheter to protect the urethral mucosa and minimize collateral damage from cryoablation in this region. As the urethral mucosa and submucosa are only several millimeters thick, there is only a small margin for error with urethral damage associated with pain and potential urethral stricture/urinary retention [23]. Therefore, the cryo-surgeon, in collaboration with a multi-disciplinary team, should determine beforehand the intent and aggressiveness of treatment in line with benefits/risks and patient goals.

Conclusion

In conclusion, percutaneous image guided cryo-ablation may be an appropriate salvage therapy and may provide sustained local tumor control, in patient who have had prior treatments in the pelvic area. However, further large scale single or multi-center studies are required. Multi-disciplinary management is critical for treatment of recurrent peri-urethral pelvic tumors. Clinicians should consider interventional radiology consultation in such cases as cryo-ablation may be the best salvage approach in certain patients and can be performed safely despite significant previous damage to the tissue.

Author contributions

MN wrote the paper and participated in the editing process. AB participated in the editing process. MW and RD planned and performed the surgery and/or cryo-ablation procedures, wrote the paper and participated in the editing process.

Informed consent

Informed consent was obtained from the patient.

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