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Case Report

Palladium interstitial implant in combination with external beam radiotherapy and chemotherapy for the definitive treatment of a female urethral carcinoma

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ABSTRACT

Primary urethral cancer is a rare diagnosis, especially in females. This report presents the utilization of a palladium interstitial implant and a review of the retrospective data published on the management of female urethral cancer. Excellent local control and survival has been obtained with the use of a palladium interstitial implant in combination with external beam radiotherapy and concurrent chemotherapy. This modality represents a novel and effective way to treat primary urethral cancer in females.

A 57 year-old female with a 40 pack-year smoking history presented with a three to four week history of dribbling urine and pain. Despite multiple evaluations and placement of a Foley catheter, her pain was unrelieved. A computed tomography (CT) scan of the abdomen and pelvis was obtained revealing a large mass at the base of the bladder with bladder distention and bilateral hydronephrosis. After successful placement of a Foley catheter her symptoms improved. An exam under anesthesia with cystoscopy was performed, confirming the suburethral mass approximately 4 centimeters in size. Biopsies of the suburethral mass revealed a mucin producing, poorly differentiated carcinoma and some features of adenocarcinoma with lymphovascular space invasion. The tissue showed strong cytokeratin 7 (CK7) positivity and rarely positive p63 cells. There was some controversy as to the origin of the disease and therefore prostate-specific antigen (PSA) testing was recommended. PSA positivity can confirm the origin as Skene's paraurethral glands, the homolog of the prostate gland (Wang et al., 2012). In this case, a PSA stain was negative, which is more common with mucinous adenocarcinomas and does not rule out urethral origin (Chan et al., 2000). A pelvic magnetic resonance imaging study (MRI) revealed a circumferential mass involving the entire urethra from the bladder to the introitus, measuring 40 × 37 × 40 mm, which was homogeneously enhancing and displaced the anterior vaginal wall posteriorly (Fig. 1). Notably, there were no morphologically abnormal lymph nodes, giving the final diagnosis of stage II disease; T2N0M0.

The following treatment options were presented: 1) anterior pelvic extenteration with resection of the anterior vagina, uterus, fallopian tubes, ovaries and bladder with formation of a conduit; 2) concurrent chemoradiotherapy; and 3) continued observation. The patient opted for concurrent chemoradiation with external beam radiotherapy to the pelvis, followed by an interstitial implant to the periurethral tumor. External beam radiation therapy was delivered to the pelvis using a 7 field intensity modulated radiation therapy (IMRT) plan with 6 megavoltage (MV) photons. Radiation was delivered once daily, five days per week, at 1.8 Gray (Gy) per day, for a total of 28 treatment days. The target volume, including the primary tumor and at-risk lymph nodes, was contoured to ensure adequate coverage. Concurrent cisplatin was administered weekly throughout radiotherapy. Halfway through treatment, the Foley catheter that had remained in place since diagnosis was removed without difficulty and the patient continued to void normally without complications.

At the completion of the external beam radiotherapy, both an interstitial high dose rate (HDR) treatment with a Syed template and utilization of a low dose rate (LDR) treatment with palladium-103 seeds were considered. To inform this decision, a transrectal ultrasound volume study was performed. The imaging appearance and location of the tumor bore a remarkable resemblance to a typical prostate gland, with an eccentric urethra (Fig. 2). The tumor was suitable for a palladium implant when using criteria frequently used to assess the utility of a seed implant in prostate cancer patients, namely size and lack of interference of the pubic arch. Both an LDR implant as well as an HDR

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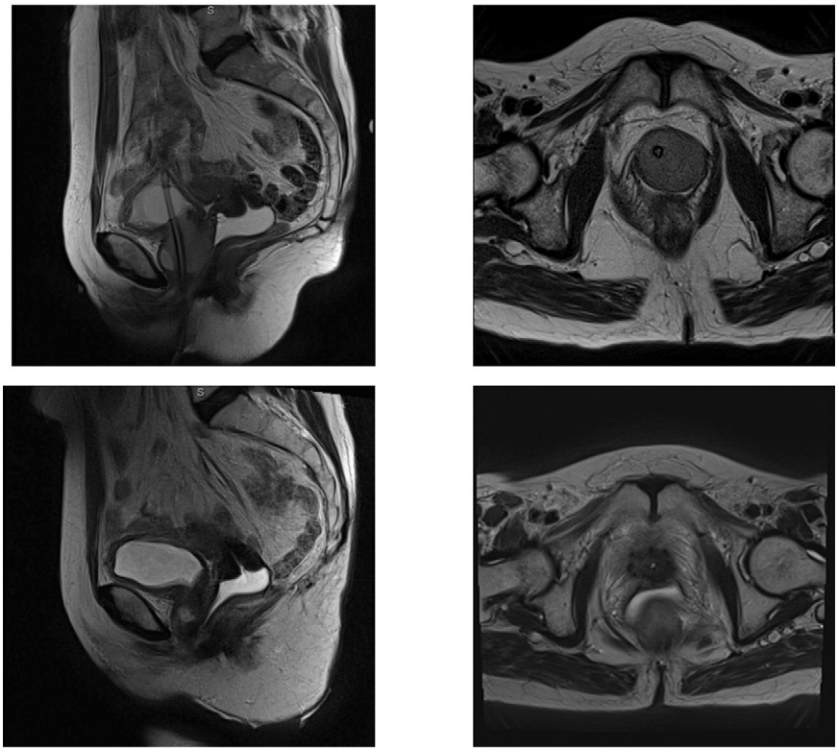

Fig. 1. Upper row: T2-weighted sagittal and axial MRI at initial diagnosis revealing a 4 cm periurethral mass with a Foley catheter traversing the lesion. The lesion is diffusely enhancing with some areas of hyperintensity. Lower row: T2-weighted sagittal and axial MRI at 5 months post-treatment, revealing no discrete or identifiable periurethral mass, and no regional lymphadenopathy to suggest recurrence.

implant were considered good treatment options, but we had no data or experience to support the idea that either an LDR or HDR technique had superiority for control or toxicity. Given our large institutional experience treating men with LDR implants with pelvic external beam radiotherapy for prostate cancer, we felt confident that we could predict the probability of toxicities to the rectum, bladder and urethra using an LDR implant in this case. Although we were concerned about the possibility of seed aggregation in a rapidly responding tumor, which would favor an HDR technique, we felt this was unlikely to be the case in this patient. Even so, we used palladium-103, which has a shorter half-life than iodine-125, to reduce the risk of overdose to the urethra if the tumor responded rapidly. HDR would have been the preferred treatment in cases where rapid regression of tumor was anticipated, or in cases where the disease was more irregularly shaped, or in a distribution that less resembled the anatomy of a prostate gland.

Seventeen days after completion of the external beam portion of the radiotherapy treatment, the patient was implanted with fifty palladium-103 interstitial seeds to a total dose of 100 Gy. Intra-operative fluoroscopy is displayed in Fig. 3. The total activity was 105.955 millicurie (mCi). The gross tumor volume (GTV) was 18.11 cc, the volume receiving 100% of the dose (V100%) was 17.48 cc (96.49%) and 90% of the volume (D90%) received at least 117.63 Gy (117.63%). Thirty percent of the urethra (D30%) received 150.7% of the dose, and 5% of the urethra (D5%) received 163.3% of the dose. The bladder V100% was 4.05 cc, the dose to 3 cubic centimeters (cc) (D3cc) was 118.33 Gy, and the dose to 1 cc (D1cc) was 179.75 Gy. The rectum V100% was 0.09 cc, the D3cc was 27.69 Gy, and the D1cc was 45.48 Gy. Fig. 4 shows a representative cross section of the post-implant dosimetry.

Five months later, as part of routine follow-up, a pelvic MRI revealed a significant response to therapy with no discrete residual

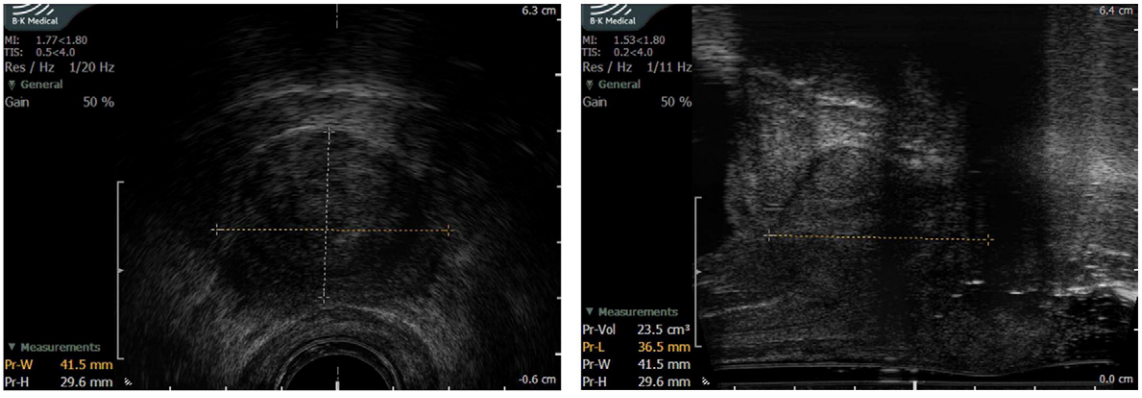

Fig. 2. Transrectal ultrasound volume study pre-implantation axial and coronal images. The urethral tumor displays a remarkable resemblance to a typical prostate gland. The dimensions of the tumor are displayed in the lower left of the images.