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Teaching Case

Robotic-assisted Intraoperative High-dose Rate Remote Brachytherapy Following Laparoscopic Robotic-assisted Resection of Pelvic Recurrence of Urethral Carcinoma

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Case report

In 2014, a 64-year-old woman was diagnosed with urethral adenocarcinoma invading the anterior mid-vagina. She underwent pelvic exenteration, bilateral pelvic lymph node dissection, and ileal conduit urinary diversion in October 2014 at an outside facility. Surgical pathology results revealed pT3N0 moderately differentiated adenocarcinoma with negative margins. The patient did not receive adjuvant chemotherapy or radiation. Restaging scans in January 2015 showed a solitary enlarging right upper lobe pulmonary nodule, and a positron emission tomography (PET) scan showed intense uptake in the right upper lobe pleural-based pulmonary nodule.

The patient had a right upper lobe wedge resection on February 9, 2015, and the pathology results were consistent with metastatic adenocarcinoma, likely related to the urethral primary. The surgical margins were negative. A repeat PET scan on March 30, 2015 showed new hypermetabolic pulmonary nodules bilaterally, concerning for metastatic disease. On April 21, 2015, the patient started on carboplatin and paclitaxel and completed 3 total cycles. Because of significant side effects, including neutropenia, the patient could not tolerate the chemotherapy regimen and was switched to nivolumab. Before starting nivolumab, a computed tomography (CT) chest scan showed an interval increased size of the bilateral pulmonary nodules when compared with prior PET/CT and increased size of a precarinal mediastinal lymph node. After 15 cycles of nivolumab, the patient exhibited a partial clinical response on the basis of the Response Evaluation Criteria in Solid Tumors in the lungs and mediastinum, and she remained with stable disease while on nivolumab.

In 2016, the patient had to discontinue nivolumab because of pneumonitis. She remained off of systemic therapies with no evidence of progression until October 2017, when re-staging CT and magnetic resonance imaging showed a 3 cm mass in the pelvic floor along the right peri-vaginal area, concerning for local recurrence. The mass was just anterior to the vaginal remnant and posterior to the pubic bone (Fig 1). At that time, the patient was asymptomatic.

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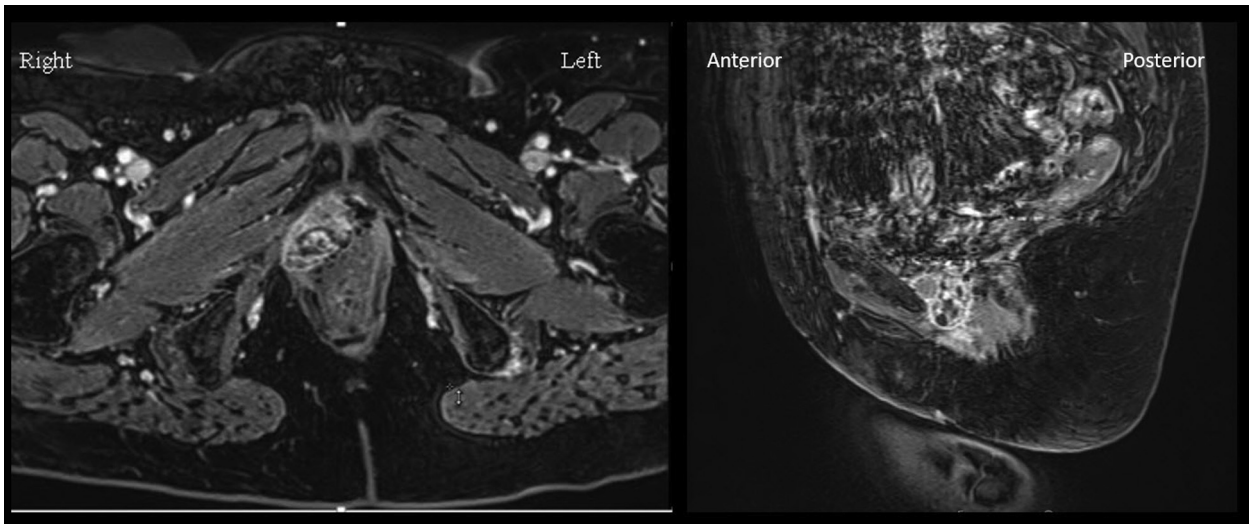

Figure 1 Magnetic resonance imaging (T1 postcontrast sequence) of recurrent urethral carcinoma. The recurrent mass was just anterior to the vaginal remnant and posterior to the pubic bone.

The initial plan was to treat this likely recurrent lesion with stereotactic radiation therapy (SBRT). However, the tumor mass was immediately adjacent to the small bowel (Fig 2). The patient was simulated in the prone position on a belly board, but the small bowel did not change position. Therefore, SBRT was deemed not feasible. The treatment team and patient decided to move forward with robotic surgery and intraoperative high-dose-rate remote brachytherapy.

Surgical Technique

After intravenous prophylactic antibiotics were administered, general anesthesia was induced. A pelvic examination revealed a 4 cm mass in the right pelvis invading into the proximal vagina but not into the pelvic side wall. Standard laparoscopic access was performed using the Veress needle technique. Adhesions were identified and taken down systematically. Four robotic ports and 2 assistant ports (10-12 and 5 mm, respectively) were used. The patient was placed in the Trendelenburg position, and the robot was docked. Loops of bowel were freed from the abdominal wall and the pelvis. The right pelvic mass was then resected robotically, along with part of the muscles of the pelvic floor and the right lateral vaginal cuff wall. The specimen was placed in an endobag and removed through the vagina.

After resection of the mass, the area of risk was visualized by the superior (cranial to caudal direction) robotic camera. The risk area involved the area adjacent to the right inferior pubic ramus, right anterior pubic arch, and left anterior pubic arch. The area adjacent to the left inferior pubic ramus was not at risk. Two layers of 1.65 mm of lead (1 layer folded in half) were placed through the vaginal opening. The robotic arm was utilized to position the lead over the bowel for shielding from

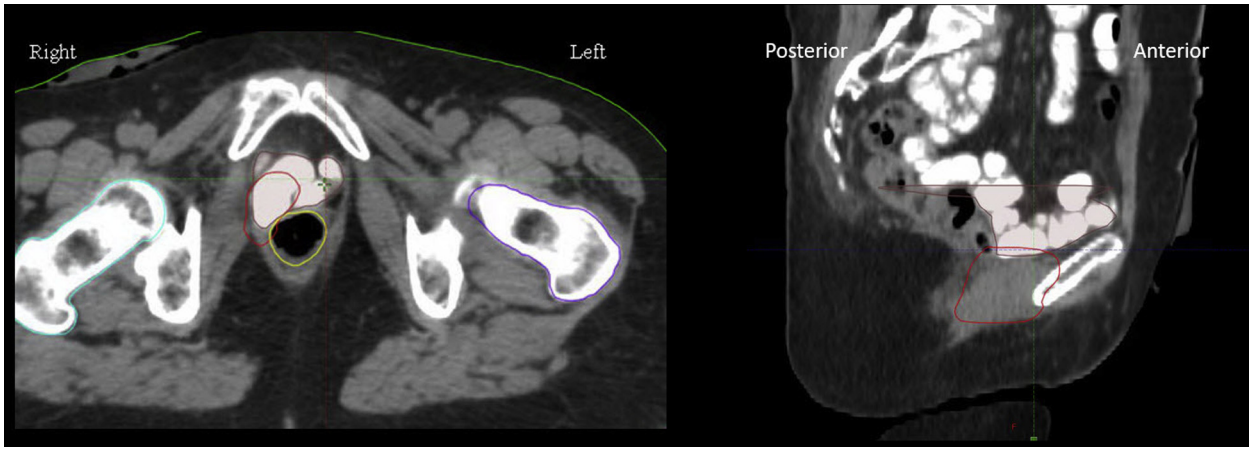

Figure 2 Stereotactic body radiation therapy planning. The planning target volume (red) extended into the small bowel (brown). The patient was flipped into the prone position on a belly board without successful movement of the small bowel out of the treatment field.

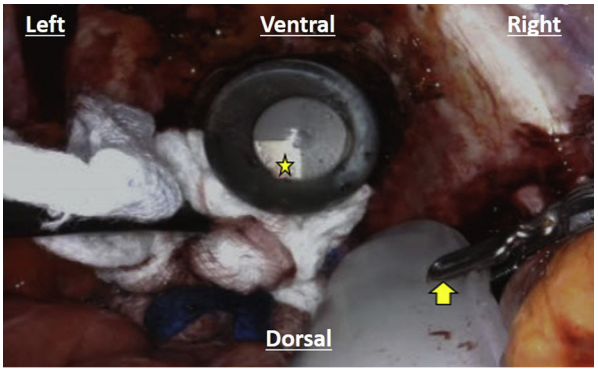

Figure 3 Intraoperative view from superior robotic camera. Two layers of 1.65 mm of lead (1 layer folded in half) were placed through the vaginal opening. The surgeon positioned and secured the lead over the bowel with the robotic arms (⇧). The vaginal cylinder (3.5 cm diameter) was placed through the vaginal remnant opening. Cerrobend shielding (☆) was placed in the cylinder to protect the left inferior pubic ramus area. A surgical sponge was placed in the left lower quadrant to further protect these tissues and position the implant against the right pubic arch (highest risk area). The high-dose-rate remote brachytherapy afterloader unit was used to deliver 7.5 Gy (at 0.5 cm tissue depth) to a length of 4 cm (2 cm of pubic arch + 2 cm of vaginal cuff).

intraoperative radiation. The vaginal cylinder (3.5 cm diameter) was placed through the vaginal remnant opening to the area of risk as described, using direct visualization from the superior robotic camera. The area of risk extended superiorly 2.0 cm from the vaginal cuff opening (Fig 3).

A Cerrobend shield was placed in the left posterior quadrant of the cylinder to shield the uninvolved left inferior pubic ramus area. The surgeon placed sterile gauze packing posterior to the left posterior quadrant of the cylinder, using the robotic arm, to decrease the distance from the tip of the cylinder to the right anterior pubic surgical margin. This surgical maneuver increased the dose to the highest risk area during brachytherapy by decreasing the distance from the tissue to the radioactive source. Next, the tandem was inserted into the cylinder, and the transfer cable was connected to the tandem. Dosimetry was performed to optimize the dose to the risk areas, using a high activity (7.25 Ci) Iridium-192 source. The prescribed dose was 7.5 Gy at 0.5 cm depth to a 4 cm length (2 cm of the pubic arch and 2 cm of the vaginal cuff; red line in Fig 4 corresponds to prescription isodose). The high-dose-rate remote brachytherapy unit was then connected to the transfer cable, and treatment was delivered over 525.4 seconds. After completion of the intraoperative remote brachytherapy, the patient was surveyed and tested negative for radioactivity. The vaginal cuff was reconstructed using 0 V-loc sutures in running fashion.

The final pathology report revealed a 2.4 cm infiltrating moderately differentiated adenocarcinoma

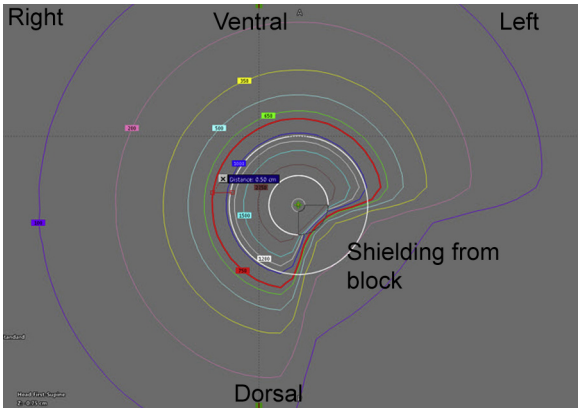

Figure 4 The high-dose-rate afterloader delivered 7.5 Gy at 0.5 cm tissue depth to 2 cm of the pubic arch + 2 cm of the vaginal cuff.

involving the vaginal wall. The surgical margins were negative for adenocarcinoma.

Follow-up

The patient tolerated the procedure with no immediate intra- or postoperative complications, and she was discharged with only mild nausea on postoperative day 2. The patient was seen in follow-up 4 weeks after the procedure and reported moderate perineal pain that was controlled with pain medications. She was simulated for external beam radiation to the pelvis, including the surgical bed and iliac/obturator lymph nodes, to a planned dose of 45 Gy in 25 fractions, using 10 MV photons and volumetric arc therapy. Soon after CT simulation, the patient was admitted with uncontrolled pelvic pain and constipation. She was worked up for septic arthritis of the pubic symphysis; however, bone biopsy results of the pubis and infectious disease work-up both were negative.

The patient's symptoms improved, so she started external beam radiation and received 14 of 25 planned fractions. She subsequently developed a urinary tract infection, pneumonia, ileus, heart failure, and fungemia. At that time, radiation therapy was discontinued. She recovered slowly, and at her 9-month follow-up appointment, she was feeling well. Her symptoms of fatigue, pain, and nausea had all resolved. The 9-month postoperative surveillance CT scans of her abdomen, pelvis, and chest showed no evidence of local recurrence of disease or metastases.

Discussion

Urethral carcinomas are extremely rare, with an annual incidence of 0.73 per 100,000 person-years.[1] Male to female incidence is about 3:1 and female urethral carcinomas account for only 1% of cancers in the female genitourinary tract.[2] In females, squamous cell is the most

common histology at 70% followed by transitional cell at 20% and adenocarcinomas at 10%.[2] The majority of patients with urethral cancers are treated with surgical resection. In a Surveillance, Epidemiology, and End Results (SEER) database study, 42% of the 722 women identified with urethral cancers were treated with radiation as part of their treatment course.[3] The treatment of recurrent urethral cancers is difficult and the use of chemotherapy and radiation is normally for palliation.

The use of brachytherapy for women with urethral carcinoma is a treatment option in the primary tumor setting. For primary urethral carcinoma, small lesions <4 cm can be treated with brachytherapy alone, but larger lesions should be treated with a combination of external beam radiation therapy (EBRT) and brachytherapy. Interstitial brachytherapy using a catheter in men or a vaginal applicator in women is the primary modality for tumors >5 mm. Doses typically used for low-dose-rate monotherapy are 60 to 65 Gy in 3 to 5 days or 20 to 25 Gy if given as a boost to EBRT.[4]

Milosevic et al reported outcomes for 34 women treated for primary urethral carcinoma with primary radiation therapy, either EBRT alone or EBRT plus brachytherapy boost. The combination of EBRT and brachytherapy reduced the local recurrence by a factor of 4.2. Overall survival (OS) was 41% at 7 years, and 15% of patients developed fistulas. Brachytherapy had the most benefit in this study for patients with bulky primary disease.[5]

In a case series by Eng et al, 8 patients with high-stage disease treated with surgery alone had a disease-free survival of 23.3 months compared with 45.2 months in patients treated with surgery and chemotherapy and/or radiation.[6] In our case, the patient had primary pT3 disease and was treated with surgery alone. She developed metastatic disease 6 months after surgery and recurrent disease 3 years after surgery.

The optimal salvage treatment for recurrent urethral carcinoma is not well established. Gakis et al addressed the impact of salvage surgery or radiation for recurrent urethral cancer and reported a series of 139 patients (43 women) with primary urethral carcinoma. Fifty-nine patients (42.5%) were recurrence-free after primary treatment. The researchers reported survival outcomes of 80 patients with any recurrences based on salvage therapy. The 3-year OS for patients treated with salvage surgery versus salvage radiation therapy was similar at 84.9% and 71.6%, respectively, compared with the 3-year OS for patients without any recurrence (86.7%; $P = .65$). The 3-year OS for patients who did not undergo surgery or radiation for recurrence was significantly lower (38%; $P < .01$). In general, radiation therapy was given as 40 to 45 Gy to the pelvic region over 4 to 5 weeks with a 20 to 24 Gy boost to the primary tumor by either intensity modulated radiation therapy (over 2-2.5 weeks) or brachytherapy (over 1-2 days).[7]

Conclusions

We report on the use of robotic-assisted laparoscopic surgical resection of a patient's pelvic recurrence from urethral carcinoma and the use of the da Vinci robot to assist with the delivery of intraoperative high-dose-rate remote brachytherapy. This approach may provide a safe option for some patients with recurrent pelvic neoplasms without the need for an open laparotomy. This technique also allows direct visualization (through the robotic camera) of the implant and surrounding normal tissues that need to be displaced or shielded.

This radiation technique could be an option for patients with organs at risk near the disease where large doses of radiation (EBRT or SBRT) would not be tolerated. Our patient was started on external beam radiation therapy after the procedure, but because of side effects from the surgery as well as other comorbidities, she only received 14 of the 25 planned fractions. At 9-month follow-up the patient had no long-term side effects and no evidence of disease recurrence or metastases.

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