Multimodal Therapy in the Treatment of Prostate Sarcoma: The Johns Hopkins Experience

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Abstract

Prostate sarcoma is an aggressive malignancy. Because the disease has poor outcomes when treated with surgery alone, we evaluated the effect of neoadjuvant chemoradiation on survival. Compared with surgery alone, patients who received neoadjuvant chemoradiation had improved overall, cancer-specific, and recurrence-free survival. These preliminary data support the continued investigation of neoadjuvant therapy in patients with prostate sarcoma.

Background: The objective of this study was to evaluate the use of neoadjuvant chemoradiation in patients with prostate sarcoma treated at our institution and report oncological outcomes. **Materials and Methods:** The records of patients with intermediate- or high-grade prostate sarcoma treated with curative intent at our institution from 1993 to 2013 were reviewed. Patient demographic information, tumor characteristics, and treatment modalities used were assessed. Overall survival (OS), cancer-specific survival (CSS), and recurrence-free survival (RFS) were calculated. **Results:** Eight patients met inclusion criteria. The mean age at presentation was 64 years, and urinary obstruction was the most common presenting symptom. All patients underwent surgical resection and neoadjuvant radiation and 6 had concurrent chemotherapy. Four patients received intraoperative radiation. With a median follow-up of 36 months, there were no local recurrences, 6 metastases, 4 deaths from disease, and no deaths from other causes. The median OS and CSS was 67.8 months, with actuarial OS and CSS rates of 100% at 1 year, 75% at 2 years, 62.5% at 3 years, and 62.5% at 5 years. Median RFS was 14.2 months, with actuarial RFS rate of 75% at 1 year, 37.5% at 2 years, and 25% at 3 years. **Conclusion:** Prostate sarcomas are rarely cured using surgical resection alone. Our cohort treated with a multimodality approach had favorable CSS and RFS compared with historic and contemporary series of surgery alone and no local recurrences. Most patients developed metastatic recurrence, highlighting the aggressive nature of this disease

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Introduction

Prostate cancer is the most commonly diagnosed malignancy in men, with an estimated 233,000 new cases in 2014.[1] Most of these cases are adenocarcinoma, and nonepithelial neoplasms account for < 1% of prostatic tumors.[2] Among the rarest prostatic tumors are sarcomas of the prostate, which arise from the prostatic stroma and represent < 0.1% of prostate malignancies.[3] Because of the rarity of these tumors, there is a paucity of evidence regarding an optimal treatment approach.

Soft tissue sarcomas develop from mesenchymal-derived tissues. Although sarcomas have heterogeneous biologic potential, intermediate- and high-grade sarcomas often present with locally

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advanced disease and behave aggressively.[4,5] Although it was generally accepted that complete surgical excision (R0) afforded the best opportunity for long-term survival for patients with retroperitoneal sarcomas (RPS),[6] randomized trials have demonstrated superior local control when preoperative radiation was used.[7,8]

Prostate sarcomas have traditionally been treated with radical surgery—either cystoprostatectomy or pelvic exenteration.[9] Despite aggressive management, local control and survival has historically been poor.[10,11] Although case series of prostate sarcoma have included patients treated with multimodal therapy, there have been no reports that have explicitly evaluated the use of adjuvant therapies in addition to surgery.

Extrapolating findings from the RPS literature,[4,7,12,13] we have instituted a multimodality approach including chemotherapy and radiation therapy before surgery for the treatment of prostate sarcomas. Herein, we report our experience using this approach and the effect that this treatment modality has had on long-term local and distant cancer control.

Materials and Methods

Patient Selection

Our Institutional review board-approved prostate cancer database (1993-2013) was queried for cases of prostate sarcoma. Pediatric patients, patients with carcinosarcoma, those in whom malignancy did not arise in the prostate, and those seen for pathologic consultation but treated elsewhere were excluded. A total of 15 cases were identified. Of those, 5 patients with low-grade stromal sarcoma or phyllodes tumor were excluded because these tumors behave indolently.[14] Additionally, 1 patient who was treated with palliative intent only and 1 patient with incomplete pathologic data were excluded, leaving 8 patients to form our study cohort. All patients were treated from 2006 to present. Medical records were reviewed to examine clinicopathologic characteristics at presentation, treatment regimens, survival, local recurrence, metastases, and death.

Multimodal Approach

Patients with a histologically confirmed diagnosis of prostate sarcoma meet with a multidisciplinary team consisting of a urologic oncologist, medical oncologist, radiation oncologist and, if needed, a surgical oncologist. Cross-sectional imaging is obtained to evaluate the extent of local disease and to assess for the presence of metastatic disease. All patients receive neoadjuvant radiation with goals of tumor shrinkage and improved respectability.[4,7] In patients with adequate renal function who are eligible for chemotherapy, concurrent radiosensitizing chemotherapy is administered, with a preference for MAI (mesna [2-mercaptoethane sulfonate Na], doxorubicin, ifosfamide) based on its efficacy for soft tissue sarcomas.[15,16] Restaging imaging is obtained after completion of chemoradiation to assess disease response and for surgical planning. The goal of surgery is an R0 resection and a surgical oncologist is recruited in cases when a total pelvic exenteration is needed. In patients with disease who might have close surgical margins because of the proximity to the iliac vessels and pelvic side wall, intraoperative radiation (IORT) is administered at the time of surgical resection with a goal to improve local control.[17]

Chemoradiation

Neoadjuvant radiotherapy was used in all cases. Intensity-modulated radiotherapy was delivered in 1.8 to 2 Gy/d fractionated doses to a total of 45 to 50.4 Gy in 7 cases. In a case when previous prostate brachytherapy had been used to treat previous prostate adenocarcinoma (patient 5), a reduced intensity-modulated radiotherapy dose of 36 Gy was administered.

Concurrent radiosensitizing chemotherapy was given in 6 cases. Chemotherapy was not used in 1 patient because of renal insufficiency and in 1 because of patient preference. Five patients received intravenous MAI in a 5-day inpatient regimen. Mesna was administered on days 1 to 4, doxorubicin on days 1 to 3 for a total of 60 mg/m^2 per cycle, and ifosfamide on days 1 to 3 for a total of 7500 to 10,000 g/m^2 per cycle. Subcutaneous pegfilgrastim 6 mg was administered on day 5. Two cycles were administered when tolerated. One patient (patient 6; Table 1) who required hospitalization for neutropenia after the first cycle received doxorubicin only in the second cycle. Patient 3 with angiosarcoma received 2 cycles of doxorubicin, paclitaxel, and cisplatin based on reports of efficacy for epithelioid angiosarcoma of the seminal vesicle.[18]

In 4 cases, an IORT boost of 10 Gy was delivered to the resection bed via brachytherapy catheters in a silicone Freiburg flap applicator (Figure 1).[17]

Surgical Resection

All 8 patients underwent complete resection of the prostate sarcoma. In each case, the goal of resection was complete macroscopic removal, including adjacent organs as indicated based on intraoperative findings. In patients in whom the urinary bladder was removed, a urinary reconstruction was also performed.

Statistical Analysis

Overall survival (OS) and cancer-specific survival (CSS) were determined from the date of diagnosis until date of death from prostate sarcoma (CSS) or other cause (OS). Recurrence-free survival (RFS) was determined from the date of diagnosis until local or metastatic recurrence. Survival curves were plotted using the Kaplan−Meier method and compared with log-rank tests. All statistical analyses were performed with Stata 13 (StataCorp, College Station, TX). Two-sided P values $< .05$ were considered significant.

Results

Patient Characteristics

Patient demographics are shown in Table 2. The mean age at presentation was 65 (range, 41-73) years. Seven patients (87.5%) were Caucasian and 1 (12.5%) was Asian. The presenting symptoms were urinary obstruction in 4 patients (0%), rectal pain in 3 (37.5%), and abnormal digital rectal examination alone in 1 (12.5%). Prostate-specific antigen levels ranged from 0.5 to 3.4. Metastatic survey was negative in 7 patients (87.5%), and positive for retroperitoneal and supraclavicular adenopathy in 1 patient (12.5%) (patient 2; Table 2). The diagnosis of prostate sarcoma was made using transrectal ultrasound-guided biopsy of the prostate in 5 patients (62.5%), transurethral resection of the prostate in 2 patients (25%), and after subtotal suprapubic simple prostatectomy in 1 patient (12.5%). Because ours is a tertiary comprehensive cancer