Adult Prostate Sarcoma: The Memorial Sloan Kettering Experience

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OBJECTIVE To present our institutional experience with adult prostate sarcoma over 30 years.

MATERIALS AND METHODS We reviewed 38 cases of adult prostate sarcoma diagnosed and treated at our institution between 1982 and 2012. Univariate Cox proportional hazards regression was used to determine if there was an association between specific disease characteristics (tumor size, histology, American Joint Committee on Cancer stage, and metastasis at diagnosis) and cancer-specific survival (CSS).

RESULTS A total of 38 patients were included, with a median age of 50 years (range, 17-73 years). Most men presented with lower urinary tract symptoms (45%), hematuria (24%), or acute urinary retention (21%). Diagnosis was established with prostate needle biopsy (68%) or transurethral resection of the prostate (18%). The predominant histologic subtypes were leiomyosarcoma (13 cases, 34%) and rhabdomyosarcoma (12 cases, 32%). Rhabdomyosarcoma was associated with poorer CSS (hazard ratio, 3.00; 95% confidence interval [CI], 1.13-7.92; $P = .027$) compared with leiomyosarcoma. We did not observe a significant relationship between tumor size and CSS. Overall, median CSS was 2.9 years (95% CI, 1.5-5.4), with 7.7 years for clinically localized disease (95% CI 2.5; upper bound not reached) and 1.5 years for metastatic disease (95% CI 1.1, 2.7).

CONCLUSION Adult prostate sarcoma has a poor prognosis, especially in cases of metastatic disease at the time of diagnosis. Surgery remains the standard of care, but it provides limited benefit to those with metastatic disease or as a consolidation therapy after partial response to systemic therapy. UROLOGY 84: 624–628, 2014. © 2014 Elsevier Inc.

Soft tissue sarcomas include a variety of unique neoplasms that arise from tissues of mesodermal origin. They are rare, comprising 1% of all cancers[1] and only 0.7% of primary malignancies of the prostate.[2] Twenty percent of soft tissue sarcomas arise from the abdomen or retroperitoneum.[3] Approximately 50% of patients will die of their disease by 2 years,[2] with sarcoma survival rates that have changed very little over time.[4] Sarcomas of the prostate carry a particularly poor prognosis, as the majority are fatal.[5] Significant risk factors for tumor recurrence and progression have been identified (primarily in the extremity sarcoma literature) including tumor grade, size, depth of invasion, and surgical margin status, but because sarcoma of the prostate is rare, clinical variables affecting prognosis are primarily based on single reports and small case series. Previous reports suggest that rhabdomyosarcoma (RMS) may be a favorable subtype,[2] whereas others have reported no survival difference between subtypes.[5] The largest and most recent report of prostate sarcoma had a sample size of only 25 patients, and previous series were even smaller.[2,5,6] Here, we present the largest series of adult prostate sarcomas in the literature, in an effort to identify and analyze clinical features that may be used to predict outcomes.

MATERIALS AND METHODS

Patients

After receiving institutional review board approval, we searched a prospectively maintained institutional database to identify all adult patients (aged ≥16 years) who had received a diagnosis of prostate sarcoma at Memorial Sloan Kettering Cancer Center between 1982 and 2012. This age group was used to maintain consistency with previous reports on adult prostate sarcoma. Medical records were reviewed for age at diagnosis, presenting symptoms, methods used for diagnosis, histologic subtype, tumor size, grade, treatments used, disease recurrence, and cause of death. Tumors were retrospectively staged according to contemporary American Joint Committee on Cancer (AJCC) staging for soft tissue sarcoma.[7]

Statistical Analysis

We calculated cancer-specific survival (CSS) and recurrence-free survival (RFS) as a function of tumor size, histology,

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AJCC stage, and presence or absence of metastasis at diagnosis using the Kaplan-Meier method. To determine if any of these 4 characteristics was associated with CSS or RFS, we used a univariate Cox proportional hazards regression model. Patients who did not undergo extirpative surgery (n = 11 [29%]), as well as 1 patient who did not demonstrate any response to treatment, were excluded from the recurrence analysis. Patient CSS was determined from the date of diagnosis until death from prostate sarcoma or death from other causes or until the most recent patient contact, whereas RFS was determined from date of surgery until the date of recurrence, the most recent patient contact, or date of death. All analyses were conducted using Stata 12 (Stata Corp., College Station, TX).

RESULTS

Patient characteristics have been summarized in Table 1. Additional detailed characteristics are presented in the Supplementary Table 1. Of 38 patients overall, 26 (68%) died of their disease, with a median follow-up of 1.8 years (interquartile range, 1.3-4.2 years). The median follow-up for patients who did not die of their disease was 4.1 years (interquartile range, 1.0-7.6 years). The median CSS among all patients was 2.9 years (95% CI, 1.5-5.4). Among patients with localized disease, median CSS was 7.7 years (95% CI, 2.5; upper bound not estimable), whereas for patients with metastatic disease at diagnosis, median CSS was 1.5 years (95% CI, 1.1-2.7 years).

Primary treatment strategies used depended on whether metastatic disease was present at the time of diagnosis. Twenty-one patients (55%) had no clinical evidence of metastatic disease at time of diagnosis; of these, 19 were treated with extirpative surgery including cystoprostatectomy (n = 9), radical prostatectomy (n = 6), or pelvic exenteration (n = 4), whereas 2 refused surgery. Figure 1 shows an example of imaging and endoscopic appearance of 7-cm clinically localized prostate sarcoma, which was managed with cystoprostatectomy. Seven also received neoadjuvant systemic chemotherapy and radiation and another 4 received adjuvant chemotherapy, whereas 8 were treated with surgery alone. Agents most commonly used for neoadjuvant therapy included combination gemcitabine and docetaxel; doxorubicin with ifosfamide; or cyclophosphamide, vincristine, and doxorubicin. Of the 19 patients treated surgically, 8 remained disease free after treatment, with a median follow-up of 81 months. Three patients had positive surgical margins, all of whom experienced recurrence and died as a result of disease progression (local disease in 1 and systemic in all 3). Of the 2 patients with clinically localized disease who were managed without surgery, 1 remained free of disease 55 months after treatment with chemotherapy and radiation, whereas the other progressed systemically and died of the disease 14 months after diagnosis.

Seventeen patients (45%) had metastatic disease identified at the time of diagnosis, including 6 with limited nodal disease only. Chemotherapeutic regimens used most commonly included combination protocols VAC (vincristine, dactinomycin, and cyclophosphamide), or MAID (mesna, Adriamycin [doxorubicin], ifosfamide, and dacarbazine). Durable response in the setting of systemic disease was not seen with any regimen. Fifteen of the 17 died of their disease, with a median CSS of 1.5 years (95% CI, 1.1-2.7), whereas the remaining 2 had progressive disease but were lost to follow-up at 11 and 13 months. Eight of the patients with metastatic disease had extirpative surgery, including 4 with limited nodal disease, 2 after a partial response to upfront systemic therapy, 1 with a solitary pulmonary metastasis that was resected, and 1 for palliation of local symptoms. Two had positive surgical margins. All 8 of these patients progressed systemically and died of their disease at a median of 1.7 years (95% CI, 0.7-3.6) after surgery.

Figure 2 displays Kaplan-Meier curves for the probability of CSS stratified by tumor histology. The Supplementary Figures display Kaplan-Meier curves for the probability of CSS stratified by tumor stage, primary tumor size, and presence or absence of metastasis at

Table 1. Patient and disease characteristics: Values are displayed as median (interquartile range) or frequency (percentage)

Characteristics	No. (%)
No. pts	38 (100)
Age at diagnosis, y	50 (27-57)
Tumor diagnosis modality	
Prostate biopsy	26 (68)
TURP	7 (18)
Other	5 (13)
Tumor size	
<5 cm	7 (19)
5-10 cm	19 (53)
>10 cm	10 (28)
Tumor histology	
Leiomyosarcoma	13 (34)
Rhabdomyosarcoma	12 (32)
Other sarcomas*	13 (34)
Tumor grade	
High grade	35 (92)
Low grade	3 (8)
AJCC stage IV	10 (26)
No. pts with metastasis at diagnosis	17 (45)
Total PSA (ng/mL)	1.0 (0.8-2.2)
Radiation	24 (77)
Unknown	7 (18)
Chemotherapy	31 (86)
Unknown	2 (5)
Surgical approach	
Cystoprostatectomy†	13 (48)
Pelvic exenteration†	8 (30)
Prostatectomy†	6 (22)
No surgery	11 (29)
Positive surgical margins†	5 (22)
Unknown	4 (15)
Progressed through treatment‡	5 (13)

AJCC, American Joint Committee in Cancer; No, number; PSA, prostate-specific antigen; Pts, patients; TURP, transurethral resection of prostate.

* Includes osteosarcoma, synovial, undifferentiated, and mixed sarcomas.

† Values include only those who underwent surgery.

‡ Patients who progressed through treatment were excluded from the recurrence analysis.