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Histologic Variability and Diverse Oncologic Outcomes of Prostate Sarcomas

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Purpose: Primary prostate sarcomas are a rare type of prostate cancer that account for less than 0.1% of primary prostate malignancies. We analyzed the experience of a single institution with prostate sarcoma over 20 years.

Materials and Methods: In this case series, the medical records of 20 patients with prostate sarcoma were reviewed from June 1990 to December 2013 to identify symptoms at presentation, diagnostic procedures, metastasis presence and development, histologic subtype, French Fédération Nationale des Centres de Lutte Contre le Cancer grade, primary tumor grade and size, and treatment sequence, including surgery and preoperative and postoperative therapies. The average follow-up period was 23.6 months (range, 1.4–83.3 months).

Results: The average patient age was 46.3±16.7 years. Most patients presented with lower urinary tract symptoms (55%). The histologic subtype was spindle cell sarcoma in five patients (25%), rhabdomyosarcoma in three patients (15%), synovial sarcoma in three patients (15%), liposarcoma in three patients (15%), stromal sarcoma in three patients (15%), and Ewing sarcoma, nerve sheath tumor, and adenocarcinoma with sarcomatoid component (5% each). For liposarcoma, two patients were alive after complete surgical resection and had a good prognosis. At last follow-up, 15 patients had died of sarcoma. The 2- and 5-year actuarial survival rates for all 20 patients were 53% and 12%, respectively (medial survival, 20 months).

Conclusions: The disease-specific survival rate of prostate sarcoma is poor. However, sarcoma that is detected early shows a better result with proper management including surgical intervention with radio-chemotherapy than with no treatment. Early diagnosis and complete surgical resection offer patients the best curative chance.

Keywords: *Liposarcoma; Prostate; Rhabdomyosarcoma; Sarcoma*

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INTRODUCTION

Soft tissue sarcomas make up less than 1% of all cancers, and less than 5% of these lesions occur in the genitourinary tract [1-3]. Primary prostate sarcomas arise from non-epithelial mesenchymal components of prostate sarcoma [4]. These tumors account for less than 0.1% of primary prostate malignancies in adults [5,6]. For the prostate gland, leiomyosarcoma is the most common histological type in adults, whereas rhabdomyosarcoma is more common in pediatric patients [4,7-9]. Clinically, the tumors cause bladder outlet obstruction and often require surgical intervention to control local symptoms. Most patients present with both filling symptoms, such as frequency, urgency, dysuria, and nocturia, and voiding symptoms, such as a poor stream, hesitancy, terminal dribbling, and incomplete voiding. Less frequent manifestations are hematuria, perineal pain, rectal pain, and a burning sensation

on ejaculation. Constipation and constitutional symptoms such as weight loss may also be present [1].

Surgery has long been the mainstay of treatment for soft tissue sarcoma and usually involves cystectomy or pelvic exenteration for more locally advanced lesions. Radical prostatectomy or more conservative surgery may be an option if the sarcoma is small and is confined to the prostate but this presentation is uncommon. The long-term survival of patients with prostate sarcomas is poor owing to local recurrence after surgery and chemo-radiation therapy [4,10]. Because of the rarity of genitourinary stromal cell sarcoma, especially prostate sarcoma, clinical research on these tumors is limited and large institutional-based studies are unavailable [11]. In addition, because of the rarity of these cancers, prognosis is often considered to be unpredictable or highly variable and appears to be related to specific parameters, such as the tumor grade (high vs. low), tumor size ($\leq$5 cm vs. $>$5 cm), and anatomical site (i.e., resectability) [1]. Hence, we here report the 24-year experience of a single institution with prostate sarcoma.

MATERIALS AND METHODS

1. Patients

We retrospectively reviewed the medical records of 20 adult male patients who were diagnosed with primary prostate sarcoma and were treated at the Asan Medical Center from June 1990 to December 2013. From the patients' medical records, we extracted data on diagnostic procedures, symptoms at presentation, histological subtype, French Fédération Nationale des Centres de Lutte Contre le Cancer (FNCLCC) grade, primary tumor grade and size, treatment strategy (including surgery, chemotherapy, and radiation therapy), and outcome. All patients included in this Institutional Review Board-approved protocol-driven prospective study had a biopsy-proven prostate sarcoma.

2. Pathologic review

At diagnosis, electron microscopy and immunohistochemical staining were performed to confirm that the tumors were of mesenchymal origin and to determine the prostate sarcoma subtype. Patient tumors were retrospectively staged according to the American Joint Committee on Cancer staging for soft tissue sarcoma. FNCLCC grade was determined on the basis of the degree of differentiation, degree of tumor necrosis, and the number of mitoses per high-power field.

3. Surgical review

Complete resection was defined as the absence of gross residual disease after surgical excision of the tumor. A microscopically negative margin was defined as no tumor at the inked specimen margin. In all cases, transurethral resection of the prostate, retropubic radical prostatectomy, and radical cystectomy with radical prostatectomy was performed. Surgical intervention was performed by multiple surgeons, not only from urology, but also from general surgery departments.

4. Statistics

Freedom from local recurrence, metastasis-free survival, and disease-specific survival were the study end points. The actuarial probability of these end points was modeled by the Kaplan-Meier method. Local recurrence was defined as the first recurrence of disease of the same histological type at the primary tumor site. Distant metastasis was defined as recurrent disease at a distant site or multiple intra-abdominal recurrences. Deaths caused by disease were the only end points for disease-specific survival.

RESULTS

1. Patient characteristics

The average age (±standard deviation) of the 20 patients was 46.3±16.7 years. Patient symptoms are listed in Table 1. Most patients presented with dysuria and lower urinary tract symptoms (55%). Rectal examination revealed nonspecific enlargement of the prostate. Diagnosis of prostate sarcoma was performed via transrectal ultrasound-guided biopsy in 17 patients, transurethral prostatic resection in 4 cases, and suprapubic prostatectomy in 2 cases. Staging evaluation usually involved computed tomography (CT), magnetic resonance imaging (MRI), chest radiography, and a bone scan. The size of the mass ranged from 45 to 150 mm (average, 90.4 mm). Eight patients presented with metastatic disease. Metastatic lesion types are listed in Table 2.

Prostate-specific antigen (PSA) data were available for 18 patients, and only 1 had increased PSA (39.5 ng/mL). The PSA value for 18 patients ranged from 0.05 to 2.4 ng/mL (median, 1.4 ng/mL). Table 3 lists the disease characteristics, treatments, and outcomes in the 20 patients.

TABLE 1. Symptoms at presentation

Symptom	No. of patients (%)
Urinary obstruction	8 (40)
Pelvic, perineal pain	1 (5)
Urinary frequency	2 (10)
Urinary retention	1 (5)
High prostate-specific antigen	2 (10)
Incidental	1 (10)
Hematuria	4 (20)
Hemospermia	1 (5)

TABLE 2. Lesions at metastasis

Lesion	No. of patients (%)
Cancer with metastasis	8 (40)
Bone	4 (20)
Lung	3 (15)
Cancer with distant lymph node (inguinal)	1 (5)

TABLE 3. Characteristics in 20 patients with prostate sarcomas

Pt. No.	Age (y)	PSA (ng/mL)	Histologic type	Grade	Size (mm)	Metastasis	FNCLC Grading	Surgical intervention	Surgical margin	CTx	RTx	Current status	Survival (mo)
1	30	0.95	RMS	High	56.6	Yes	3	No	-	Yes	Yes	Expired	17.6
2	24	0.50	RMS	High	76	Yes	3	No	-	Yes	Yes	Expired	44.7
3	20	0.57	RMS	High	64	No	2	No	-	Yes	No	Expired	8.4
4	56	0.50	Spindle	High	49	No	2	Yes	Negative	No	No	Expired	5.7
5	31	1.20	Spindle	High	120	No	3	Yes	Positive	Yes	No	Expired	5.9
6	56	2.40	Spindle	High	140	Yes	3	Yes	Negative	Yes	Yes	Expired	31.3
7	49	1.00	Spindle	High	45	No	1	No	-	No	No	F/U loss	1.4
8	30	0.69	Spindle	High	120	No	1	No	-	Yes	Yes	F/U	33.2
9	54	2.24	Synovial	High	39.5	Yes	3	Yes	Negative	No	Yes	Expired	4.7
10	61	0.33	Synovial	High	150	No	3	Yes	Negative	No	Yes	Expired	18.3
11	28	1.30	Synovial	High	100	Yes	3	Yes	Positive	Yes	No	Expired	30.5
12	71	2.10	Pleomorphic	High	250	No	1	Yes	Negative	No	Yes	F/U	83.3
13	51	0	Pleomorphic	High	61	No	3	No	-	No	Yes	expired	3.3
14	39	0.63	Pleomorphic	High	110	No	1	Yes	Negative	Yes	No	F/U	35.1
15	36	0.23	Stromal	High	98.5	Yes	3	Yes	Negative	No	Yes	Expired	6.0
16	41	0.99	Stromal	High	110	No	3	Yes	Negative	No	Yes	Expired	32.3
17	75	39.5	Stromal	High	100	Yes	3	Yes	Negative	No	No	Expired	37.1
18	72	-	Adenocarcinoma with sarcoid component	High	46	No	1	Yes	Negative	No	No	Expired	27.6
19	42	-	Stromal hyperplasia with sarcomatoid component	Low	65	No	1	Yes	Negative	No	No	F/U	39.0
20	60	0.05	Nerve sheath	High	100	No	3	Yes	Negative	No	No	Expired	7.4

F/U, follow-up; Pt., patient; PSA, prostate-specific antigen; FNCLCC, Fédération Nationale des Centres de Lutte Contre le Cancer; CTx, chemotherapy; RTx, radiotherapy; RMS, rhabdomyosarcoma.

The histologic subtype was spindle cell sarcoma in five patients (25%), rhabdomyosarcoma in three patients (15%), synovial sarcoma in three patients (15%), liposarcoma in three patients (15%), stromal sarcoma in three patients (15%), and Ewing sarcoma and adenocarcinoma with sarcomatoid component in one patient each. For spindle cell sarcoma, chemotherapy was performed with surgical therapy and three patients died of sarcoma. For rhabdomyosarcoma, chemotherapy rather than surgical therapy was mainly performed and three patients died of sarcoma. In the liposarcoma group, two patients are alive after complete surgical resection and have a better prognosis than that in the patients with other pathologic results.

2. Treatment

Surgery was the initial treatment in 12 patients: 6 underwent retropubic radical prostatectomy with radical cystectomy, 5 underwent retropubic radical prostatectomy only, and 1 underwent transurethral resection of the prostate. All excisional surgeries were margin-negative. Gross examination revealed an ill-defined mass with a fleshy to firm consistency with focal areas of hemorrhage, necrosis, and cystic degeneration. The majority of prostate sarcomas have a high-grade appearance microscopically, with areas of viable tumor showing hypercellularity, variable degrees of nuclear atypia, and mitotic activity. Necrosis and cystic degeneration was sometimes prominent.

The majority of the remaining patients (eight cases) were first treated with chemotherapy. For rhabdomyosarcoma, all three patients initially received chemotherapy, which consisted of vincristine, doxorubicin, cyclophosphamide, ifosfamide, and etoposide. For the other histologic subtypes, such as spindle cell sarcoma, synovial sarcoma, and Ewing sarcoma, four patients initially received chemotherapy, which consisted of doxorubicin and ifosfamide. Thirteen patients received radioactive therapy after surgery or chemotherapy.

3. Survival

At the last follow-up, four patients had no evidence of disease after treatment, with a median survival of 47.6 months (range, 33–83 months). The remaining 15 patients died of sarcoma. For spindle cell sarcoma, four patients died after treatment and one patient survived. For rhabdomyosarcoma, all patients died after treatment. All treated synovial sarcoma patients expired. Two-thirds of liposarcoma patients survived after treatment. Both patients who survived after surgery were diagnosed with nonmetastatic prostate cancer. This result shows that proper management at a curable state can have a survival benefit.

No patients died of causes not related to sarcoma or as a consequence of treatment. The median survival of all 15 patients was 17.6 months (range, 3.3–44.7 months).

A total of 14 patients underwent initial or delayed surgical extirpation of the prostate sarcoma and involved local structures. None of the patients in our series had clinically abnormal pelvic lymph nodes. Therefore, pelvic lymphadenectomy was not routinely performed. Microscopically negative surgical margins were achieved in 11 patients and grossly positive margins were present in 2. The 2- and 5-year actuarial survival rates for all 20 patients were 53% and 12%, respectively (medial survival, 20 months).

DISCUSSION

The rarity of adult prostate sarcoma is a major obstacle in the clinical research of this cancer, and contemporary data are therefore scarce [1,3,12]. Sexton et al. [4] reported 21 cases and Wang et al. [11] reported 25 cases of prostate sarcoma in reviews that spanned 3 decades, but these data included only adult prostate sarcoma, whereas our current data included pediatric to adult patients [2]. Russo [13] and Mondaini et al. [1] reported their experience with genitourinary sarcoma, but accurate comparison with our research was difficult because their prostate sarcoma patients were analyzed together with patients with other genitourinary sarcomas, including those of renal, bladder, seminal vesicle, and paratesticular origins.

Most prostate sarcomas cause urinary obstruction, and transurethral prostate resection performed because of symptoms of bladder outlet obstruction without elevation of PSA may reveal prostate sarcoma [7,14]. Unlike renal sarcoma [15], prostate sarcoma is often suspected before surgery, especially when a young man presents with lower urinary tract obstruction, a markedly enlarged prostate, and a normal PSA value. In contrast with prostate adenocarcinoma, the PSA level is generally not elevated in patients with prostate sarcoma, which can be explained by the nonepithelial origin of sarcoma [16]. For most patients, the initial diagnosis can be preoperatively established by using image-guided needle biopsy, which is well tolerated, requires no anesthesia, and often provides adequate tissue for a histological diagnosis.

Clinical staging is further enhanced by cross-sectional pelvic imaging. MRI is the imaging modality of choice for extremity sarcomas [5]. For large prostate sarcomas, we believe MRI facilitates surgical planning by providing multiplanar images, better delineation of the soft tissue plane, and superior assessment of the relationship between the tumor and adjacent viscera and neurovascular structures. Various histological subtypes have been found. The most common subtype is spindle cell sarcomas. Other subtypes are rhabdomyosarcomas, synovial sarcoma, liposarcoma, Ewing sarcoma, stromal sarcoma, and nerve sheath tumor [17]. Comparison of the relationship between prognosis and the various subtypes has been difficult because of their rarity.

The overall survival rate for patients with prostate sarcoma is poor. Owing to the lack of an early screening method, specific clinical symptoms result in more advanced disease at presentation. The overall 5-year actuarial survival rate for our patients was 12%, compared with a range of 0% to 60% in other series [18-20]. However, comparison of data from various series is difficult because of a nonuniform method of reporting patient and pathological characteristics, changes over time in radiographic staging, and the relatively small number of patients with prostate sarcoma.

We determined whether various factors, including patient age, tumor grade, size, metastasis, and therapeutic procedures affected survival. However, we found no survival differences between patient groups in our study. We checked the overall survival of patients by use of univariate and multivariate analyses but found no valuable results owing to the various histologies and limited number of patients.

The prognosis is poor for patients with prostate sarcoma who are treated with surgery alone, and a multimodality therapy is thus strongly recommended [21]. The rare occurrence of prostate sarcoma has limited the critical evaluation of treatment strategies and patient survival to anecdotal experiences. However, our results suggest that there may be a survival advantage of treatment with a combined multimodality approach [22,23]. Although there is no definite treatment strategy for prostate sarcoma, multimodality treatments that are likely to be more effective for patients with prostate sarcoma can be derived from existing protocol-based strategies for other sarcomas, such as retroperitoneal and pelvic sarcomas [24,25]. Innovative, combined multimodality treatment strategies may help to improve prognosis for patients with these generally poor prognosis tumors.

CONCLUSIONS

Prostate sarcoma is a rare neoplasm that accounts for only 0.1% of prostate cancer cases. This cancer usually follows an aggressive clinical course, and the prognosis is generally poor, with a medial overall survival of 20 months in our series. Owing to a lack of screening for prostate sarcoma, early image-guided needle biopsy is recommended for patients with a suspected prostate sarcoma. With existing protocol-based strategies, proper management is needed for curative intent. Additional collaborative large-scale studies are necessary for appropriate management of this undesirable disease.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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