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Original article

Review of the M.D. Anderson experience in the treatment of bladder sarcoma☆

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Abstract

Objective: To assess the histologic subtypes, clinical presentations, treatment approaches, and treatment-related outcomes of patients with bladder sarcoma.

Methods: Between January 1985 and July 2004, 19 patients (12 men and 7 women) with primary bladder sarcoma were evaluated at the University of Texas M.D. Anderson Cancer Center. Median follow-up duration was 72 months (range 3–141).

Results: The median age of patients at presentation was 57 years (range 22–94). The histologic subtypes of bladder sarcoma were leiomyosarcoma (N = 14), angiosarcoma (N = 3), and unclassified sarcoma (N = 2). The clinical presentation consisted of gross, painless hematuria in 79% of patients, lower urinary tract symptoms in 16%, and microhematuria in 5%. The primary treatment modalities used were surgery in 16 (84%) patients, chemotherapy in 2 (11%), and palliation in 1 (5%). The rate of local and distal recurrence was 16% and 53%, respectively. The most common sites of distant metastases were the lungs, bone, brain, and liver. The 5-year disease-specific survival rate was 59%, with a median survival duration of 6 years. There was no statistically significant difference in disease-specific survival between patients with bladder leiomyosarcoma compared to other sarcoma subtypes ($P = 0.149$). Lymphovascular invasion ($P = 0.03$) and lymphatic metastasis ($P = 0.03$) were associated with disease-specific survival, and surgical margin status was associated with recurrence-free ($P = 0.04$), disease-specific ($P = 0.03$), and overall survival ($P = 0.005$).

Conclusions: Bladder sarcoma is a highly aggressive malignancy, regardless of its histologic subtype. Surgical margin status is an important determinant of survival.

Keywords: Bladder cancer; Sarcoma; Survival

1. Introduction

Non-urothelial neoplasms of the bladder account for less than 5% of all bladder tumors in North America [1]. Sarcoma constitutes the most common mesenchymal malignancy of the genitourinary bladder [2]. Subclassification of sarcomas involves the use of histologic and special immunohistochemical staining techniques. In a recent review of the scientific literature, 192 cases of adult bladder sarcomas were identified; 50% were leiomyosarcomas, 20% rhabdomyosarcomas, and the remainder consisted of angiosarcomas, osteosarcomas, and carcinosarcomas [3]. Leiomyosarcomas are the most common type of sarcoma in adults and are characterized histologically by interwoven fascicles of malignant spindle cells. It has been reported that the incidence of leiomyosarcomas may be increased in patients receiving local pelvic radiotherapy or systemic chemotherapy as treatment for different neoplasms [4].

A study from our institution reviewed the clinical presentation and disease-specific outcome of patients with high-grade bladder leiomyosarcomas [5]. The 5-year dis-

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ease-specific survival rate in this series was 62%, and on multivariate analysis, the Memorial Sloan-Kettering Cancer Center (MSKCC) sarcoma staging system was the only predictor of survival. MSKCC reported one of the largest single-center experiences reviewing the outcomes of 10 patients diagnosed with primary bladder sarcoma [6]. The authors found that the best treatment for these tumors was radical cystectomy with negative margins of resection. In patients presenting with metastatic bladder sarcoma, multimodality treatment was often preferred, with the chemotherapeutic agents doxorubicin and ifosfamide having the greatest response. However, to our knowledge, no study has investigated whether diverse subtypes of sarcoma differ in their treatment response and disease-related outcome. In the present study, we report our experience in the treatment of the various subtypes of bladder sarcoma, focusing on disease-specific and treatment-related outcomes.

2. Materials and methods

2.1. Study design

Before conducting the present study, a retrospective chart-review study protocol was designed and approved by our institutional review board. Between January 1985 and July 2004, 21 patients were diagnosed and subsequently evaluated at the University of Texas M.D. Anderson Cancer Center for primary bladder sarcoma. All patients entered in this study were identified from our institutional tumor registry. There were 2 children with primary bladder rhabdomyosarcoma excluded. A 10-year-old boy was treated with neoadjuvant chemotherapy and cystectomy, had a distant metastasis 68 months later, and died of his disease. A 3-year-old girl was treated with chemotherapy alone, and remains alive and disease free 13 months later.

The remaining 19 patients (12 men and 7 women) constitute our patient population. The median age of patients at presentation was 57 years (range 22–94). Patient evaluation included a complete medical history, physical examination, laboratory investigations, radiologic imaging (chest x-ray, computerized tomography of the abdomen and pelvis), cystoscopy, transurethral resection of the bladder tumor, and examination under anesthesia. Bone scan and magnetic resonance imaging were performed at the discretion of the treating physician. Pathologic specimens were re-reviewed to confirm the diagnosis of bladder sarcoma in all cases. High cellular atypia, mitotic activity, and cellularity as well as necrosis and positive staining for specific immunohistochemical markers characterized bladder sarcomas (Table 1). The sarcoma subtype, stage, and grade of these tumors were noted. Pathologic stage is reported using both the T stage and the MSKCC soft tissue sarcoma staging system [6]. In the MSKCC system, stage zero indicates a low-grade tumor ≤5 cm with superficial invasion. Stage 1 indicates a low-grade tumor ≤5 cm with deep invasion. Stage 2 indicates a low-grade tumor >5 cm with deep invasion. Stage 3 indicates a high-grade tumor >5 cm with deep invasion, and stage 4 indicates metastatic disease [6].

Table 1
Immunohistochemical mesenchymal markers positive in bladder sarcoma subtypes

Immunohistochemical marker	Positive
Vimentin	All sarcoma subtypes
Actin	Leiomyosarcomas
SMA	Leiomyosarcomas
CD34	Angiosarcomas
CD31	Angiosarcomas
Myogenin	Rhabdomyosarcomas
Desmin[a]	Leiomyosarcomas
Myo-D1	Rhabdomyosarcomas

[a] Leiomyosarcomas may or may not stain positive for desmin.

2.2. Statistical analysis

The overall survival was calculated as the time from date of primary treatment until date of death from any cause or date of last follow-up. Disease-specific survival was defined as the elapsed time between the date of primary treatment to the date of death, with this diagnosis listed as the cause of death on the death certificate. Survival probabilities were calculated using Kaplan-Meier estimates [7]. For select comparisons of survival curves, we used the log-rank test [8]. Univariate analysis was conducted using the Cox proportional hazards regression model to obtain estimates of the relative risk of an event, with the *P* values based on the Wald test [9]. A log-rank test was used to evaluate the association between surgical margin status and disease-specific survival. Because of the small sample size, multivariate models were not appropriate [10]. Statistical analyses were performed using the software program STATA (version 9; StataCorp LP, College Station, TX).

3. Results

3.1. Patient population

The characteristics of the 19 patients are summarized in Table 2. Mean and median ages at presentation were 56 and 57 years, respectively. Contrary to patients with transitional cell carcinoma, tobacco use was low, with only 31.6% of the patients having a history of smoking. Leiomyosarcoma was the most common histology (74% of cases). Most patients presented with painless gross hematuria (79%), with the remaining having either local urinary symptoms (16%) or microhematuria (5%). Preoperative staging revealed that most patients (74%) had muscle-invasive disease (clinical stage T2). There were 2 patients who had metastatic disease at presentation, with the remaining having no evidence of systemic spread at onset. Preoperative upper-tract assess-