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Sarcomas of the bladder: A case report with a review of the literature

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Sarcomas of the bladder are rare tumors with decisions about treatment and understanding of outcome based on limited reports from single institutions. Consequently, neither a standard staging system nor standard treatment exists for this disease.

A retrospective review of the medical records at our institution from January 1960 to December 1997 for sarcomas of the bladder and a review of the literature were made to better understand the natural history and treatment outcome of these tumors. We report on one case treated with curative intent and summarize the experience of other institutions.

If disease is localized to the bladder, then surgery alone, either by total or partial cystectomy or, alternatively, a multimodality approach using a combination of treatment with partial cystectomy and local radiation with chemotherapy to address risk of systemic disease can offer patients a good chance for cure

Key words: bladder neoplasms - drug therapy - radiotherapy - surgery; sarcoma

Introduction

Sarcomas are rare with an approximate incidence of only 7000 cases per year in the United States. Those involving the genitourinary tract, not including rhabdomyosarcomas, account for less than 5% of soft tissue sarcomas and only 1-2% of all genitourinary tumors. Bladder sarcomas, in particular, tend to occur at the extremes of life with a bimodal distribution of less than age sixteen and greater than age sixty.[1] Most patients present with painless gross hematuria with other common symptoms being urinary frequency, hesitancy and/or retention.[2,3-5] In adults , several histologic subtypes have been reported. The most frequent histology in adults appears to be leiomyosarcoma with other less frequent ones including malignant fibrous histiocytoma, angiosarcoma, fibrosarcoma, extraosseous osteogenic sarcoma and sarcoma NOS.[3,6-10] Rhabdomyosarcomas (RMS) are the most common pediatric blad-

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der sarcoma being clinically dissimilar from other soft tissue sarcomas and are generally managed according to national protocols. Although RMS occurs mainly in the pediatric population, forty cases were reported in a very early paper on bladder sarcomas in adults.[1]

No clear etiology exists for sarcomas of the bladder. Unlike bladder carcinomas which have several established risk factors (e.g. tobacco), sarcomas of the bladder have not been shown to have causal relationships to such factors. Very early reports have suggested that embryologic mesenchymal remnants are perhaps the origin of bladder sarcomas.[11] More recent literature has suggested a genetic link to sarcomas, including those of the genitourinary tract.[12-14] Also sarcomas arising as second malignancies have been reported from prior radiation treatment and chemotherapy treatment with the alkylating agent, cyclophosphamide.[15-18]

Its rarity prevents accruing enough patients to accurately assess treatment efficacies and to analyze characteristics of patients for prognostic indicators. Consequently, recommendations about treatment have been conflicting and based on small numbers from institutional experiences. We report a case diagnosed and treated at Roswell Park to add to the relatively few cases that have been reported and have reviewed the literature to assist in treatment decisions.

Case report

An 80 year old white male developed urinary frequency, urgency and painless gross hematuria. He underwent an intravenous pyelogram and cystoscopy. These studies revealed a mass within the bladder which was removed by partial cystectomy. The mass measured five centimeters in greatest dimension and the pathology showed it to be a leiomyosarcoma of intermediate grade. The remainder of his workup was negative for metastatic disease which included laboratory and radiographic studies. He received postoperative treatment using high energy photons to irradiate his whole pelvis to 4800 cGy to cover the bladder and its draining lymphatics and then boost treatment to the bladder only for an additional 800 cGy for a total dose of 5600 cGy. The radiation was given using 400 cGy per treatment with treatments given twice daily using an anterior-posterior field to the whole pelvis. This same treatment was used for the boost with the volume reduced to cover the bladder plus a margin. The patient remained disease free at one year follow up.

Discussion

Bladder sarcomas are rare tumors which makes treatment decisions and assessing treatment outcome difficult. Having a staging system that better characterizes bladder sarcomas would help with both treatment decisions and evaluating outcome. Currently, such a staging system is lacking. These tumors are presently staged according to the same systems utilized for bladder carcinomas, namely the Marshall-Jewet or American Joint Committee on Cancer (AJCC) TNM transitional cell bladder carcinoma systems. These staging systems are very effective with non-sarcomas of the bladder because they relate the close relationship between muscle invasion and risk of regional node and/or distant disease.[19] Bladder sarcomas, however, originate within the submucosal mesenchymal layer which would automatically stage them as invasive and place them at high risk for nodal and/or distant disease with a resulting poor prognosis. With the exception of RMS, this is not the case with sarcomas of the bladder which have a relatively low risk of regional nodal involvement. Using the AJCC soft tissue sarcoma staging system, on the other hand, would perhaps offer a better

approach since its predominate prognostic factor is grade.

However, tumor size would not adequately address bladder sarcoma. Swartz *et al.* have shown that the amount of bladder involvement is a prognostic indicator. We propose in this paper a staging system that

Table 1. Proposed staging system for sarcomas of the bladder

Histologic subtype
Leiomyosarcoma
Rhabdomyosarcoma
Other
Grade: low, intermediate, high
Size
Bulky (>30% bladder involvement)
Nonbulky
Pelvic sidewall involvement
Adjacent organ involvement
Regional nodal involvement
Distant metastasis

incorporates these apparent associated prognostic factors (Table 1) to allow better follow-up of patients and establish a multidisciplinary approach to bladder sarcomas. Specifically, mitotic activity, a major determinant of grade, has been shown to be an independent prognostic indicator and correlate well with developing metastases and overall survival.[20,21] Others include the extent of locoregional involvement and histologic subgrouping.

With respect to treatment and outcome of sarcomas of the bladder, surgery has remained the mainstay and improvements in outcome have been reported in the modern literature with survival as high as 63% at 5 years.[22] Sen *et al.* evaluated 13 patients at the Mayo Clinic between 1970 and 1985 with radical cystectomy with or without preoperative radiation.[23] They had five patients with leiomyosarcoma, three with rhabdomyosarcoma, and five with carcinosarcoma.

Two of the 5 patients with leiomyosarcoma were treated with preoperative irradiation. One (pathologic stage B1) of these two patients was treated with radical cystectomy and preoperative irradiation of 5000 cGy and died at sixteen months after developing local and distant disease. The other (PS B1) was treated preoperatively with 6000 cGy and is free of disease seventy-eight months after completion of treatment. Two of the five were treated with radiation alone with doses of 6500 cGy and 6000 cGy and died at eighteen months and forty-six months respectively after developing both local and distant disease. No clinical stage was given for either but neither was felt to be surgical candidates. One patient (PS A) had a radical cystectomy alone and is free of disease at eighty-six months. The authors conclude from their experience that those patients felt to be curative should be treated with radical cystectomy with or without preoperative irradiation regardless of histology and that with modern techniques for staging and treatment, patients have a much better prognosis today than patients described in the older literature.

Another series by Swartz *et al.* on leiomyosarcoma of the bladder reported on ten cases. Pathologic staging was not indicated in the paper so that no correlation of pathologic stage and treatment outcome can be made. One patient treated with partial cystectomy and postoperative radiotherapy (dose not given) for inadequate margins has remained alive without disease at 5 years of follow-up.[12] Three others treated with partial cystectomy alone with adequate margins are alive without disease at 6, 6 and 9 years. Only one patient was treated with definitive radiotherapy after an initial misdiagnosis of squamous cell carcinoma and recurred locally after 4 years. The other patients in the series had either radical cystectomy (n=3), partial

cystectomy with chemotherapy (n=1), ileal conduit (n=1), or biopsy alone (n=1), and all are dead of either postoperative complications or disease progression. The authors in this paper felt that if adequate margins can be obtained, then partial cystectomy is the treatment of choice, and that radical cystectomy should be performed only for more extensive lesions where adequate margins are not obtainable.

They did not feel that enough information exists on the role of either postoperative radiation or adjuvant chemotherapy with this disease to justify their use as part of initial curative treatment but rather could be utilized in the setting of recurrent and/or metastatic disease.

Eleven patients with leiomyosarcoma were reported by Ahleringer *et al.*[2,] 7 of whom had bladder as the primary site and 4 with prostate. Patients with nonbulky disease of the bladder were treated with surgical resection and given adjuvant chemotherapy and external beam irradiation if the margin or nodes were positive. Bulky disease, defined as greater than 30% of bladder involvement, received preoperative chemotherapy with or without postoperative irradiation. None of their patients had pathologically positive nodal disease. Six of the 7 bladder patients are alive without evidence of disease (range of 35-97 months) with 1 lost to follow-up. The authors concur with Swartz *et al.*[12] in suggesting that partial or subtotal cystectomy for smaller tumors to avoid urinary diversion is justified as long as negative margins are achieved, and that, based on the 3 patients treated for stage C prostate involvement, radiotherapy with doses of between 4500 cGy and 5000 cGy be used for microscopic residual disease after removal of bulky disease. They also further suggest adopting preoperative chemotherapy for cytoreduction using agents such as cisplatin and doxorubicin for bulky or transmural disease and postoperative chemotherapy for either responsive tumors to preoperative chemotherapy or pathologic 3A patients.

A series from Memorial Sloan Kettering reviewing their experience with urologic sarcomas between 1982 and 1989 found 6 cases of leiomyosarcomas of the bladder.[24] The authors discuss the local and distant recurrences as well as survival data according to histologic grade, size and margin status after surgery, but they make no distinction between the different subtypes of bladder sarcoma.

Thus no conclusions as to differences in outcome between leiomyosarcomas and other histologies can be made. No patient received irradiation as part of their treatment but two had treatment with surgery and chemotherapy. The 3 rhabdomyosarcomas were treated on a rhabdomyosarcoma protocol with multimodalities of surgery, chemotherapy and radiation. Two patients with small (< 2 cm) leiomyosarcomas, 1 of which was a low grade and the other a high grade tumor, underwent complete transurethral resection alone with local control reported with 7 years follow-up. As a group, when compared with other urologic sites, sarcomas of the bladder had the highest 5-year survival at 80%. The authors show that urologic sarcomas in general share similar prognostic indicators as with sarcomas at other sites; namely, with increasing grade, size and depth, both local recurrences and metastases increase.

Our review of the literature shows that varying modes of managing these rare tumor exists. This is not surprising since personal experiences and extrapolation of treatments tend to control management decisions when there is little data available to assist in the decision making process. The location of the tumor would seem to occur anywhere within the bladder by the published reports, although the trigone region appears to have the highest predilection.[25,26-29] This may account for the varying results that are achieved with using a partial resection alone.

Despite the differences that exist in the outcome between series, most series seem to suggest that a subtotal cystectomy as opposed to a radical cystectomy can achieve good results as long as adequate margins are achievable. More aggressive surgery appears to be indicated for large, bulky tumors. However, the addition of radiation for positive margins after partial cystectomy and/or chemotherapy also appears to offer good results and thus avoid the need for removing the bladder.[2] The results of Russo *et al.* and Suit *et al.* would suggest that, like sarcomas at other sites, a multimodality approach for urologic sarcomas may provide better functional outcome and durable local control.[24,30] The case we present in this paper, although with short follow-up, is a clear example of how properly selected patients can undergo conservative management with this disease involving the bladder, as has been shown with transitional cell tumors of the bladder, having disease controlled without the need for removing the bladder.[31] Adopting a standard staging system would allow for optimizing treatment in a multidisciplinary fashion by basing treatment decisions on prognostic factors and aid in the design of future treatment protocols.

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