Urethral carcinosarcoma from bladder carcinosarcomatous lesions: analysis of clinicopathological features

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Carcinosarcoma (CS) of the bladder is a rare malignancy of the genitourinary tract that is highly aggressive with unfavorable prognoses. Data regarding the epidemiological and clinicopathological characteristics of CS of the urinary bladder have been limited due to the low reported incidence of the tumor. In particular, there is little evidence on recurrence patterns and surveillance after definitive surgical therapy. In this case report, we describe a urethral recurrence of CS after radical cystoprostatectomy for CS of the bladder. The goal of this case report is to review our current understanding of the pathological and recurrence patterns of patients with CS of the urinary bladder in order to better define postoperative care for patients with CS of the bladder.

Key Words: bladder cancer, urethra, carcinosarcoma, metastasis

Introduction

Bladder cancer is a common genitourinary malignancy with a wide variety of histological subtypes, the most common of which is urothelial carcinoma (UC). Non-UC histological subtypes comprise about 10% of reported cases and are recognized to be independent predictors of bladder cancer-specific progression and mortality following surgical treatment.[1] Non-UC subtypes include carcinosarcoma (CS), which is a rare malignancy of the urinary bladder characterized by its biphasic nature with clearly separable malignant epithelial (carcinomatous) and mesenchymal (sarcomatous) components.[1,2] The epithelial portion of such tumors is most often UC, but can also consist of squamous cell carcinoma, adenocarcinoma, or undifferentiated carcinoma. The mesenchymal portion varies more greatly, and has been reported to contain chondrosarcoma, leimyosarcoma, fibrosarcoma, osteosarcoma, rhabdomyosarcoma or undifferentiated sarcoma.[3-7]

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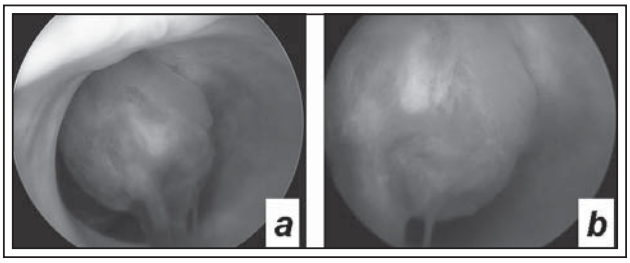
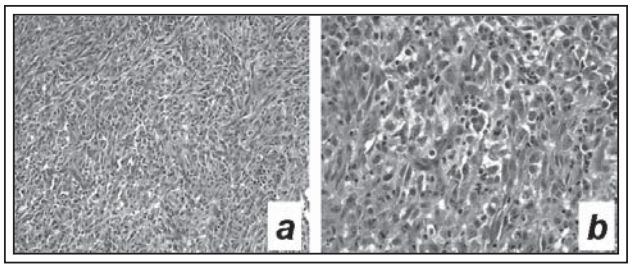
We report a case of a local recurrence of CS in the urethra after definitive surgical management of a primary CS of the bladder. In this report, we summarize our current understanding of the literature on CS of the bladder and its histopathological features with recurrence patterns.

Case presentation and management

A 66-year-old Caucasian male with an unremarkable past medical history presented with gross hematuria. A CT urogram of the abdomen and pelvis was performed and demonstrated a large bladder tumor with no evidence of hydronephrosis or extravesical invasion. Therefore, he underwent transurethral resection of the bladder tumor (TURBT) located at the trigone and right lateral wall with histopathological evaluation revealing CS with muscle invasion. Computed tomography (CT) scan of the chest, abdomen and pelvis demonstrated no evidence of metastatic disease. The patient elected to undergo radical cystoprostatectomy with orthotopic neobladder reconstruction. Final pathology demonstrated no presence of residual bladder tumor or lymph node metastasis (p0N0Mx). There was a small focus of Gleason 3 + 3 = 6 adenocarcinoma of the prostate which was organ confined. One year after his cystectomy, the patient presented with occasional blood spotting with voiding. He denied blood clots or gross hematuria. Both urine cytology and urine fluorescence in situ hybridization (FISH) analysis were negative for malignancy. A CT scan of his chest, abdomen and pelvis demonstrated no evidence of recurrent disease or lymphadenopathy. Cystoscopy revealed a mass in the pendulous urethra approximately 6 cm proximal to the urethral meatus, Figures 1a and 1b. The mass was observed to almost completely obstruct the urethra. A transurethral resection of the urethral mass was found to be recurrent osteoclast-rich undifferentiated CS, Figure 2a and 2b.



Figures 1a and 1b. Photos obtained during cystoscopy demonstrating a partially obstructing urethral mass.



Figures 2a and 2b. Photomicrograph demonstrating carcinosarcoma with streaming spindle cells. Magnification 100x (a) and 200x (b).

Discussion

Data regarding the epidemiological and clinicopathological characteristics of CS of the urinary bladder have been limited due to the low reported incidence of this tumor subtype. Recently, Wright and colleagues investigated 166 cases of CS using the National Cancer Institute's population based Surveillance, Epidemiology and End Results (SEER) database.[8] Until this review, fewer than 70 cases of bladder CS were reported in the literature.[1-7,9-13] Patients with CS of the bladder presented at similar ages as urothelial carcinoma patients but at a higher T stage with more frequent regional and distant metastases.[8] On multivariate analysis, patients with CS were at higher risk for death compared to those with urothelial carcinoma.[8] Risk factors for the development of bladder CS are generally accepted to be similar to those for UC and include smoking;[5,6] male sex, and age in the sixth or seventh decade, although cases have been reported in age ranging from 21-91 years old.[2-4,6] Analysis of occupation has yielded no association with tumor development.[4] CS of the urinary bladder has also been noted to arise in patients following radiation therapy to the pelvis in a small minority of cases (with an interval usually > 10 years following therapy), presumably due to affected cell replication abnormalities.[5,14] Of note, cyclophosphamide has been hypothesized to transform urothelial carcinoma into CS.[4,12]

Diagnosis of CS can be made by histological analysis with conventional hematoxylin and eosin stains of tumor sections.[6] Special care should be taken to distinguish CS from a true sarcoma, urothelial carcinoma with benign metaplasia, or from a distant metastases.[5] Immunohistochemical analysis and electron microscopy are particularly useful to differentiate CS from sarcomatoid tumors, although it should be noted that adequate tissue sampling is necessary for such analysis. However, the presence of

epithelial markers which distinguish the sarcomatoid tumors from CS may only present focally.[4,7,8]

Radiographic imaging of the bladder for the diagnosis of CS versus UC's has been investigated.[2] T1-weighted magnetic resonance (MR) imaging is often not helpful in distinguishing CS tumors from UC. The biphasic nature of the tumors can be reflected more efficiently by heterogenous signal intensity on T2-weighted and contrast enhanced MR imaging. Additionally, another radiographical aspect of CS tumors of the bladder is the lack of arterial enhancement for CS with gadolinium-enhanced imaging. In contrast, UC tumors of the bladder have significant early enhancement with MRI, which may make it another useful modality to differentiate CS from UC.[2]

It is generally accepted that CS of the urinary bladder has an at least partly monoclonal origin. This is supported by the often gradual transition observed in tumor histopathology and more notably by loss of heterozygosity and comparative genomic hybridization analyses, which reveal strikingly similar patterns between the two phenotypic components.[9,10] Some analyses further suggest that perhaps the sarcomatous component is a metaplasia of carcinatomatous cells towards mesenchymal differentiation, citing methylation as a possible signaling mechanism to downregulate E-cadherin and facilitate such conversion.[10] However, the monoclonal origin of these tumors has been debated, with some studies demonstrating the existence of lesions with distinct genetic changes between the histological components, implying possible existence of separate clones of origin or at least a divergent course of tumor development.[7,9,10]

Presenting signs and symptoms of this malignancy are similar to other types of bladder cancer, with the most common being new or recurrent hematuria of short duration. Dysuria, pollakisuria, and urinary tract infections are other potential presenting signs or symptoms.[3-5] In contrast to the histological appearance of these tumors, which more commonly varies, on gross appearance, these tumors are generally large (up to 12 cm), and present as single, exophytic, polypoid or nodular, ulcerated masses. Their predominant location is most commonly the bladder base, followed by the trigone and lateral walls of the bladder. Location, size, shape, and multiplicity should not be used to differentiate these tumors from UC.[2-6]

Due to the low incidence of the disease and the lack of a large multi-institutional series, there is no established treatment or surveillance protocol for CS of the bladder. The majority of treated cases reported in the literature have undergone radical cystectomy as a single therapeutic modality. However, in recognition of the aggressive nature of this malignancy, the most recommended treatment in the literature has been radical cystectomy with adjuvant radiotherapy.[1,4-6,8,11] Such intervention has especially been emphasized for CS found in bladder diverticulum. Due to the reduced amount of muscle fibers in the bladder wall of a diverticulum, there may be increased likelihood of extravesical invasion and quicker systemic dissemination. These cases have furthermore also been noted to pose diagnostic uncertainty, due to noted difficulties in distinguishing an exophytic growing tumor of the bladder diverticulum from an extravesical mass on imaging studies.[7]

For patients with CS of the bladder, prolonged survival is uncommon after surgical intervention (cystectomy or TURBT).[3,4] Prognosis is poor for patients with these rare and highly aggressive tumors of the urinary bladder, which generally present as high stage tumors with muscularis propria involvement and increased likelihood for extravesical extention and metastases.[2-6,8,15] Similar to UC, pathological stage is the best predictor for survival following cystectomy for patients with CS of the urinary bladder.[7] Various series have reported mean survival from 8-17 months after treatment with radical cystectomy with or without adjuvant radiation therapy. Long term survival analyses have consistently revealed an approximately 50% survival rate at 1 year and 14%-17% survival rate at 4-5 years follow-up after treatment.[4,6,8] On multivariate analysis, patients with CS were found to have a two-fold risk of death at 1 year compared to patients with UC of the bladder, even after adjusting for stage of disease at presentation.[8]

To our knowledge there is no previously reported recurrence pattern of CS to the urethra. However, given the aggressive nature of the disease, urethrectomy should be considered in patients with tumors at the bladder neck or involving the prostatic urethra. As for surveillance, depending on the pathological stage of the disease and choice of urinary diversion, we would recommend aggressive screening for local recurrence and distant metastasis in patients who have undergone definitive management for bladder CS. As for our patient, we recommended total urethectomy with conversion of his ileal orthotopic neobladder into either a catheterizable stoma, or a new ileal conduit, or an Indiana pouch. However, the patient elected to follow-up with his local radiation oncologist and refused further surgical intervention.

Conclusion

CS of the urinary bladder is an exceedingly rare and highly aggressive tumor with unfavorable

prognosis due to its high stage presentation and high recurrence rate following treatment. Although there is a consensus that this tumor requires multimodality therapy, there is no established treatment protocol due to the lack of prospective evaluation of treatment with neoadjuvant/adjuvant chemotherapy and/or radiation therapy. Until such data becomes available, aggressive surveillance is indicated which should include the pendulous urethra in male patients. □

References

1. Rogers CG, Palapattu GS, Shariat SF, Karakiewicz PI, Bastian PJ, Lotan Y, Gupta A, Vazina A, Gilad A, Sagalowsky AI, Lerner SP, Schoenberg MP. Clinical outcomes following radical cystectomy for primary nontransitional cell carcinoma of the bladder compared to transitional cell carcinoma of the bladder. *J Urol* 2006;175(6):2048-2053.
2. Tekes A, Kamel IR, Szarf G, Chan TY, Schoenberg MP, Bluemke DA. Carcinosarcoma of the urinary bladder: dynamic contrast-enhanced MR imaging with clinical and pathologic correlation. *Am J Roentgenol* 2003;181(1):139-142.
3. Young RH. Carcinosarcoma of the urinary bladder. *Cancer* 1987;59(7):1333-1339.
4. Lopez-Beltran A, Pacelli A, Rothenberg HJ, Wollan PC, Zincke H, Blute ML, Bostwick DG. Carcinosarcoma and sarcomatoid carcinoma of the bladder: clinicopathological study of 41 cases. *J Urol* 1998;159(5):1497-1503.
5. Perret L, Chaubert P, Hessler D, Guillou L. Primary heterologous carcinosarcoma (metaplastic carcinoma) of the urinary bladder: a clinicopathologic, immunohistochemical, and ultrastructural analysis of eight cases and a review of the literature. *Cancer* 1998;82(8):1535-1549.
6. Baschinsky DY, Chen JH, Vadmal MS, Lucas JG, Bahnson RR, Niemann TH. Carcinosarcoma of the urinary bladder--an aggressive tumor with diverse histogenesis. A clinicopathologic study of 4 cases and review of the literature. *Arch Pathol Lab Med* 2000;124(8):1172-1178.
7. Sousa Escandón A, Garcia R, Argüelles M, Maceiras F, Perez-Valcarcel J. Carcinosarcoma in a bladder diverticulum. A case report and literature review. *Urol Int* 2000;65(3):169-172.
8. Wright JL, Black PC, Brown GA, Porter MP, Kamat AM, Dinney CP, Lin DW. Differences in survival among patients with sarcomatoid carcinoma, carcinosarcoma and urothelial carcinoma of the bladder. *J Urol* 2007;178(6):2302-2306.
9. Gronau S, Menz CK, Melzner I, Hautmann R, Möller P, Barth TF. Immunohistomorphologic and molecular cytogenetic analysis of a carcinosarcoma of the urinary bladder. *Virchows Arch* 2002;440(4):436-440.
10. Halachmi S, DeMarzo AM, Chow NH, Halachmi N, Smith AE, Linn JF, Nativ O, Epstein JI, Schoenberg MP, Sidransky D. Genetic alterations in urinary bladder carcinosarcoma: evidence of a common clonal origin. *Eur Urol* 2002;37:350-357.
11. Hoshi S, Sasaki M, Muto A, Suzuki K, Kobayashi T, Tukigi M, Ono K, Sugano O, Saso S. Case of carcinosarcoma of urinary bladder obtained a pathologically complete response by neoadjuvant chemoradiotherapy. *Int J Urol* 2007;14(1):79-81.
12. Sigal SH, Tomaszewski JE, Brooks JJ, Wein A, LiVolsi VA. Carcinosarcoma of bladder following long-term cyclophosphamide therapy. *Arch Pathol Lab Med* 1991;115(10):1049-1051.
13. Damiano R, D'Armiento M, Cantiello F, Amorosi A, Tagliaferri P, Sacco R, Venuta S. Gemcitabine and cisplatin following surgical treatment of urinary bladder carcinosarcoma. *Tumori* 2004;90(5):458-460.
14. Sreenan JJ, Hart WR. Carcinosarcomas of the female genital tract. A pathologic study of 29 metastatic tumors: further evidence for the dominant role of the epithelial component and the conversion theory of histogenesis. *Am J Surg Pathol* 1995;19(6):666-674.
15. Renan MJ. How many mutations are required for tumorigenesis? Implications from human cancer data. *Mol Carcinog* 1993;7(3):139-146.