CASE REPORT
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Bladder Sarcomatoid Carcinoma in an Adolescent: 10-Year Survival After Aggressive Surgical Management

Bir Ergende Mesane Sarkomatoid Karsinomu: Agresif Cerrahi Yönetimi Sonrası 10 Yıllık Sağkalım

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Abstract

Bladder cancer is a rare entity in the pediatric population. Sarcomatoid carcinoma is considered a variant histology of bladder urothelial carcinoma and is exceedingly unusual in children. We present a case of a 14-year-old black female who presented to the pediatric urology clinic with hematuria. Her history was notable for acute lymphocytic leukemia treated with cyclophosphamide, which had been in remission for four years. Subsequent workup demonstrated a large, complex bladder mass, consistent with sarcomatoid carcinoma following transurethral resection. She underwent a radical cystectomy with bilateral pelvic lymphadenectomy and ileal conduit and remains disease free 10 years after diagnosis.
Keywords: Bladder cancer, Adolescent, Radical cystectomy, Sarcomatoid

Öz

Pediatrik popülasyonda mesane kanseri nadir bir oluşumdur. Sarkomatoid karsinomda, mesane üroteliyal karsinomunun değişken histolojisi dikkate alınır ve çocuklarda son derece olağan dışıdır. Burada, pediatrik üroloji kliniğine hematuri ile başvurmuş 14 yaşındaki siyahi bir kadın olgusu sunulmuştur. Dört yıldır remisyonda olan, siklofosfamid ile tedavi edilen akut lenfositik lösemi için olgunun öyküsü kayda değerdi. Transüretral rezeksiyonu takiben yapılan tetkikler, sarkomatid karsinomu ile birbirini tutan büyük bir kompleks mesane kitlesini kanıtlamıştır. Hastaya, radikal sistektomi ile iki taraflı pelvik lenfadenektomi ve ileal konduit uygulanmıştır, tanıdan sonra 10 yıldır hastalıksız bir şekilde hayatını sürdürmektedir.
Anahtar Kelimeler: Mesane kanseri, Ergen, Radikal sistektomi, Sarkomatoid

Introduction

Sarcomatoid carcinoma is a rare variant histology of bladder urothelial carcinoma, accounting for less than 0.5% of all bladder tumors (1,2). This entity represents a biphasic tumor with epithelial and mesenchymal malignant components and is often considered synonymous with carcinosarcoma, a primary spindle cell neoplasm with epithelial elements (3). Both are rare, aggressive neoplasms typically presenting at advanced stages (1). Pathological stage is the best predictor of survival and even with aggressive treatment, the prognosis is dismal (1).

In a 2010 analysis of 221 cases, the mean age at diagnosis was 75 years, 65.2% were male, and 89.1% were Caucasian (2). We present a case of, to our knowledge, the youngest patient diagnosed with this rare histology. Diagnosed after four years of acute lymphocytic leukemia (ALL) remission and following aggressive surgical management and adjuvant chemotherapy, this patient remains disease-free 10 years after diagnosis.

In children ages 10-14, the incidence of cancer from 2003 to 2012 was 13.25 per 100.000 and the incidence of ALL was 2.14 per 100.000 (4). Childhood survivors of pediatric malignancies are at increased risk of secondary neoplasms, and the relative risk of secondary neoplasm ranges from two to eight times greater than the general population (5,6). Increased risk was also found in females and those treated with radiation or certain types of

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chemotherapy (4,7). One study reported that 7.7% of patients in remission of ALL develop second malignant neoplasms (8). The most common second malignant neoplasms present later in life and include breast, thyroid, and central nervous system tumors (8,9).

Case Presentation

A 14-year-old African-American female presented to the pediatric urology clinic with a two-month history of recurrent urinary tract infections with intermittent hematuria, dysuria and frequency. She denied recent weight loss, malaise, bone pain or other constitutional symptoms. Her past medical history was significant for ALL and family history was unremarkable. Her ALL was treated with protocol CCG 1961, consisting of vincristine, cytosine arabinoside, pegylated-asparaginase, doxorubicin, methotrexate, and cyclophosphamide. She was well hydrated per protocol, but her cyclophosphamide regimen (3 g/m^2 of cyclophosphamide given in 1 g/m^2 doses) did not necessitate the use of mesna (10,11). Additionally, she underwent cranial irradiation during the consolidation phase of her treatment. Following an uncomplicated chemoradiation course, she remained in ALL remission for four years at the time of pediatric urology consultation.

Diagnostic imaging included a renal/bladder ultrasound, first visualizing the bladder mass, followed by intravenous-contrasted computed tomography (CT) of the abdomen and pelvis demonstrating a complex, lobulated bladder mass with no evidence of hydronephrosis, lymphadenopathy, local extension or metastatic disease (Figure 1a). After obtaining informed consent, she underwent a transurethral resection of the bladder tumor, final pathology of which was sarcomatoid carcinoma. Metastatic workup included a positron emission tomography-CT, which was negative. After multidisciplinary consultation, discussion with the patient and family, and obtaining informed consent, the patient underwent a radical cystectomy with bilateral pelvic lymphadenectomy and ileal conduit. After 2 years with no evidence of disease, the patient made the decision to keep the conduit versus re-diversion to a neobladder. No gross extravesical involvement was noted and the urethra and reproductive organs were spared.

Pathology demonstrated a 7.1x6.5x3.9 cm tumor (Figure 1b). Histologic analysis revealed pure sarcomatoid carcinoma with heterologous mesenchymal elements in the form of chondrosarcoma. Hematoxylin and eosin staining exhibited morphologic features ranging from epithelioid to spindle to giant multinucleated cells (Figure 2a, b). Although invasion of the lamina propria was microscopically evident, no invasion of the muscularis propria was observed. Pancytokeratin staining was positive for epithelioid cells and the specimen showed

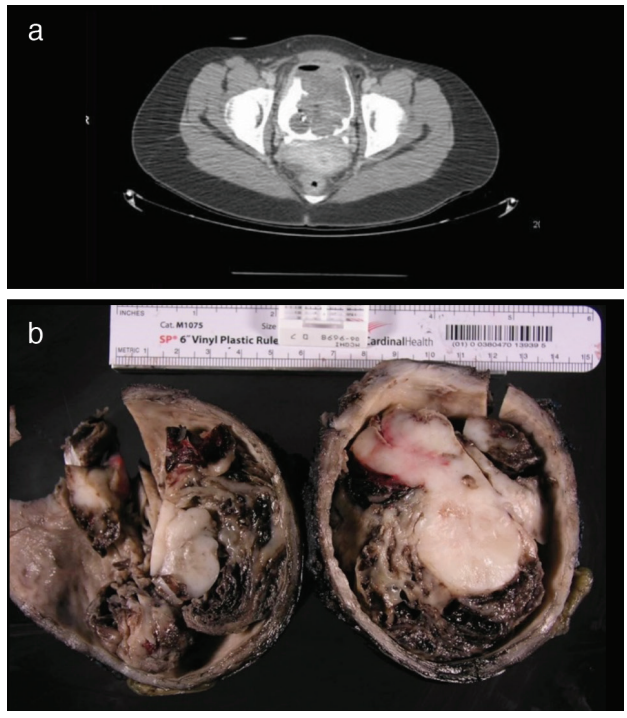

Figure 1. a) Computed tomography with intravenous contrast (transverse section), demonstrating a large volume, complex bladder mass; b) Anatomic gross representation of the bladder (bivalved) showing necrotic and viable portions of tumor, measuring 7.1x6.5x3.9 cm

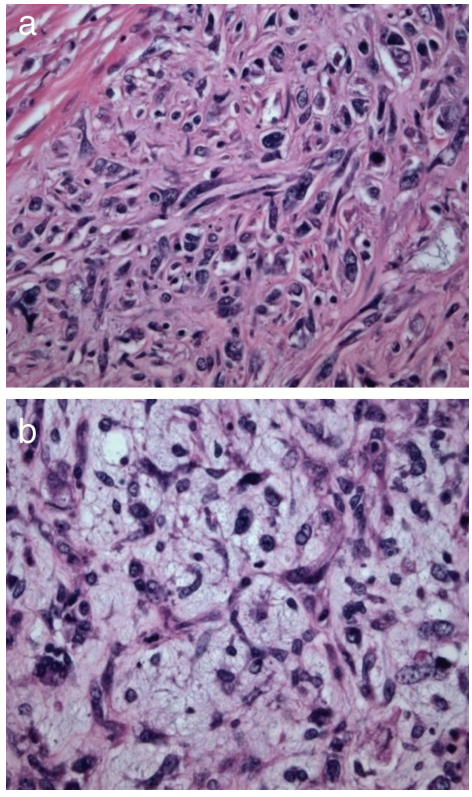

Figure 2. Hematoxylin and eosin stains of tumor at 10x, a) demonstrating T1 lamina propria invasion (muscle layer, left upper corner), spindle, and multinucleated cells. b) 40x representation demonstrating large multinucleated sarcomatoid malignant cells

diffuse positivity with vimentin staining. The final pathologic staging of the tumor was pT1N0MX with 0 of 8 lymph nodes positive.

Secondary to the patient's age and aggressive nature of the tumor, after further multidisciplinary discussion it was decided to administer adjuvant adult-dose chemotherapy (four cycles of standard adjuvant gemcitabine and cisplatin). Ten years following the aggressive management, surveillance imaging remains free of disease recurrence. Although at last follow-up she has not attempted to become pregnant, she expresses a desire for children in the future.

Discussion

This case represents the first report of an adolescent with bladder sarcomatoid carcinoma, an aggressive and rare neoplasm. The largest case series reported to date, reports the mean age at diagnosis to be 75 years (2). Given the dismal 1-, 5-, and 10- year survival rates of patients, 53.9%, 28.4%, and 25.8% respectively, aggressive surgical management and adjuvant chemotherapy are typically required and have remarkably allowed this patient to remain disease-free for 10 years post-treatment (2).

The initial treatment protocol for this patient's ALL included cyclophosphamide, which is metabolized to acrolein, a known urotoxin associated with hemorrhagic cystitis and bladder cancer. Mesna can be added to the cyclophosphamide treatment regimen to reduce associated urothelial toxicity. Mesna is classically reserved for patients receiving high-dose cyclophosphamide, typically defined as 50 mg/kg or 3 gm/m^2 (10,11,12,13). Based upon this recommendation, our patient's cyclophosphamide dose did not necessitate the use of mesna (10,11). Given the inherent risks of secondary bladder malignancy with cyclophosphamide use, readdressing the minimum cyclophosphamide dose requiring concomitant mesna administration may be necessary, especially in children.

Although rare in children and adolescents, bladder cancer outcomes are poorer in females than males and surgical management traditionally includes bladder, reproductive organ, and anterior vaginal vault removal (14,15). This patient's sarcomatoid carcinoma, age, and gender highlight the importance of considering the risks and benefits of disease recurrence versus subsequent fertility, particularly when assessing the aggressive nature of this tumor and benefits of radical extirpative surgery. This compels urologists to consider reproductive organ sparing extirpative surgery for invasive bladder cancer in appropriate young females desiring preservation of fertility. Further follow-up of this patient will be enlightening to assess reproductive capabilities, particularly in the setting of two previous aggressive chemotherapy regimens.

This case demonstrates a rare, aggressive bladder sarcomatoid carcinoma secondary malignancy following ALL that was treated aggressively with reproductive organ sparing surgery, adjuvant chemotherapy and long-term survival. An increased index of suspicion for secondary malignancies allows timely diagnosis, aggressive treatment and the best opportunity for long-term survival.

Ethics

Informed Consent: A consent form was completed by all participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: P. F., S.B., Z.K., A.S., J.D., Concept: P.F., S.B., Z.K., A.S., J.D., Design: P.F., S.B., Z.K., A.S., J.D., Data Collection or Processing: C.C., P.F., S.B., Z.K., Analysis or Interpretation: C.C., P.F., S.B., Z.K., A.S., J.D., Literature Search: C.C., P.F., S.B., Z.K., A.S., J.D., Writing: C.C., P.F., S.B., Z.K.

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References

1. Lopez-Beltran A, Pacelli A, Rothenberg HJ, Wollan PC, Zincke H, Blute ML, Bostwick. Carcinosarcoma and sarcomatoid Carcinoma of the bladder: Clinicopathological study of 41 cases. J Urol 1998;159:1497-1503.
2. Wang J, Wang FW, Lagrange CA, Hemstreet Iii GP, Kessinger A. Clinical features of sarcomatoid carcinoma (carcinosarcoma) of the urinary bladder: Analysis of 221 cases. Sarcoma 2010:2010.
3. Wick MR, Swanson PE. Carcinosarcomas: current perspectives and an historical review of nosological concepts. Semin Diagn Pathol 1993;10:118-127.
4. Surveillance Epidemiology and End Results, National Cancer Institute, U.S. National Institute of Health, www.cancer.gov [Accessed August 20, 2016].
5. American Cancer Society 2007 childhood cancer statistics, www.cancer.org [Accessed August 20, 2016].
6. Guerin S, Hawkins M, Shamsaldin A, Guibout C, Diallo I, Oberlin O, Brugières L, de Vathaire F. Treatment-adjusted predisposition to second malignant neoplasms after a solid cancer in childhood: a case-control study. J Clin Oncol 2007;25:2833-2839.
7. Neglia JP, Friedman DL, Yasui Y, Mertens AC, Hammonds S, Stovall M, Donaldson SS, Meadows AT, Robison LL. Second malignant neoplasms in five-year survivors of childhood cancer: Childhood cancer survivor study. J Natl Cancer Inst 2001;93:618-629.
8. Hijiya N, Hudson MM, Lensing S, Zacher M, Onciu M, Behm FG, Razzouk BI, Ribeiro RC, Rubnitz JE, Sandlund JT, Rivera GK, Evans WE, Relling MV, Pui CH. Cumulative incidence of secondary neoplasms as a first event after childhood acute lymphoblastic leukemia. JAMA 2007;297:1207-1215.
9. MacArthur AC, Spinelli JJ, Rogers PC, Goddard KJ, Phillips N, McBride ML. Risk of a second malignant neoplasm among 5-year survivors of cancer

in childhood and adolescence in British Columbia, Canada. Pediatr Blood Cancer 2007;48:453-459.

10. Hensley ML, Schuchter LM, Lindley C, Meropol NJ, Cohen GI, Broder G, Gradishar WJ, Green DM, Langdon RJ Jr, Mitchell RB, Negrin R, Szatrowski TP, Thigpen JT, Von Hoff D, Wasserman TH, Winer EP, Pfister DG. American Society of Clinical Oncology clinical practice guidelines for the use of chemotherapy and radiotherapy protectants. J Clin Oncol 1999;17:3333-3355.
11. Hensley ML, Hagerty KL, Kewalramani T, Green DM, Meropol NJ, Wasserman TH, Cohen GI, Emami B, Gradishar WJ, Mitchell RB, Thigpen JT, Trotti A 3rd, von Hoff D, Schuchter LM. American Society of Clinical Oncology 2008 clinical practice guideline update: use of chemotherapy and radiation therapy protectants. J Clin Oncol 2009;27:127-145.
12. National Cancer Institute: PDQ® Bladder and Other Urothelial Cancers Screening. Bethesda, MD: National Cancer Institute. Available at: http://www.cancer.gov/types/bladder/hp/bladder-screening-pdq.[Accessed August 16, 2016].
13. Schuchter LM, Hensley ML, Meropol NJ, Winer EP; American Society of Clinical Oncology Chemotherapy and Radiotherapy Expert Panel. 2002 update of recommendations for the use of chemotherapy and radiotherapy protectants: Clinical practice guidelines of the American Society of Clinical Oncology. J Clin Oncol 2002;20:2895-2903.
14. Messer JC, Shariat SF, Dinney CP, Novara G, Fradet Y, Kassouf W, Karakiewicz PI, Fritsche HM, Izawa JI, Lotan Y, Skinner EC, Tilki D, Ficarra V, Volkmer BG, Isbarn H, Wei C, Lerner SP, Curiel TJ, Kamat AM, Svatek RS. Female gender is associated with a worse survival after radical cystectomy for urothelial carcinoma of the bladder: A competing risk analysis. Urology 2014;83:863-867.
15. Klaassen Z, DiBianco JM, Jen RP, Evans AJ, Reinstatler L, Terris MK, et al. Female, black, and unmarried patients are more likely to present with metastatic bladder urothelial carcinoma. Clin Genitourin Cancer 2016;14:489-492.