Case Report

Urinary bladder radiotherapy-related chondroblastic osteosarcoma: Rare case report and review of literature

Noorah Almadani, Khaled O. Alsaad, Hamoud Al-Matrafi[1], Abdulrahman Al Hadab[2], Nouf Abdullah[3], Abdulmohsen AlKushi

Departments of Pathology and Laboratory Medicine, [2]Radiation Oncology, [3]Diagnostic Imaging and [1]Surgery, Section of Urology, King Abdulaziz Medical City and College of Medicine, King Saud University for Health Sciences, Riyadh, Saudi Arabia

Abstract

Radiation-related osteosarcomas are well described malignant mesenchymal neoplasms, yet their pathogenesis is not fully understood. They are generally classified into either skeletal osteosarcomas, or their and rare soft tissue counterpart. The occurrence of osteosarcoma in the urinary bladder (UB) following radiotherapy is exceedingly rare. To the best of our knowledge, only two cases of radiation-related urinary bladder osteosarcoma have been published; we herein describe another case of an 85-year-old man who developed post radiotherapy chondroblastic osteosarcoma of the urinary bladder four years following initial surgical resection and radiotherapy for bladder urothelial carcinoma. We believe that this is the first case of radiation-related chondroblastic osteosarcoma arising in the urinary bladder. In addition, we review the literature and explore the possible histogenesis of this rare neoplasm.

Key Words: Chondroblastic, osteosarcoma, radiation-induced, radiotherapy, urinary bladder

Address for correspondence:
Dr. Abdulmohesn AlKushi, Department of Pathology and Laboratory Medicine, King Abdulaziz Medical City, P. O. Box 22490, Riyadh 11426, Saudi Arabia.
E-mail: kushia@ngha.med.sa
Received: 08.11.2012, **Accepted:** 10.02.2013

INTRODUCTION

Extra skeletal osteosarcoma is a rare malignant mesenchymal neoplasm that has the capacity to form osseous, osteoid and chondroid matrix in soft tissue without attachment to the bone.[1] It represents 4% of osteosarcomas and 1.2% of all soft-tissue sarcomas.[2] Osteosarcoma in the UB is very rare, and about 32 cases are described in the English literature.[3] Radiation related malignancies are well documented and, in most instances, these tumors are osteosarcomas.[4] Osteosarcoma arising in the UB following radiotherapy is an exceedingly rare malignancy, and only two cases have been reported.[5,6] In this report, we describe a case of chondroblastic osteosarcoma of the UB in a patient with a history of urothelial carcinoma of the UB, treated by transurethral resection and adjuvant radiation therapy, discuss the possible histogenesis of this rare malignant tumor, and review the literature.

Access this article online	
Quick Response Code:	Website: www.urologyannals.com
	DOI: 10.4103/0974-7796.134289

CASE REPORT

An 85-year-old man, known case of long-standing diabetes mellitus, hypertension and hyperlipidemia, presented to the emergency room with a history of sudden onset of gross hematuria. His surgical history was remarkable for previous aortic valve replacement surgery and transurethral resection of right posterior lateral exophytic UB tumor 47 months prior. Pathological examination of the UB tumor showed a high-grade papillary urothelial carcinoma with deep invasion into the muscularis propria (Stage pT2b) [Figure 1]. There was no evidence of sarcomatoid differentiation. The metastatic

workup was negative. The patient was deemed a poor surgical candidate due to his medical co-morbidities, and received 66 Gy in 33 fractions of radiotherapy for seven weeks. Forty months following transurethral resection of the UB tumor, his cystoscopy and radiological workup showed no local recurrence or distant metastases.

Medical inquiry of his presenting complaint was negative for abdominal or pelvic pain, dysuria or urinary incontinence. Abdominal-pelvic non-enhanced computerized tomographic scanning revealed an asymmetrical focal thickening of the right wall of the UB with involvement of the perivesical fat strands [Figure 2]. No pelvic or retroperitoneal lymphadenopathy was detected. Transurothelial cystoscopy demonstrated a widely based, nodular fungating tumor, measuring 5 cm in maximum dimension and involving the right posterior lateral wall of the UB. Only partial transurethral resection of the tumor was performed, as complete resection was not feasible because of the extensive infiltrative growth pattern of the tumor into the UB wall.

Light microscopic examination was performed on 5 μ thick sections from formaldehyde-fixed, paraffin embedded tissue, and showed malignant spindle cell proliferation with neoplastic osteoid formation, surrounded by abundant malignant chondroid matrix [Figure 3]. There was no evidence of urothelial carcinoma *in situ*, or invasive papillary urothelial carcinoma. A panel of immunohistochemical stains was performed. The neoplastic spindle cells showed strong and diffuse immunoreactivity to vimentin, while the chondroid component of the tumor was positive for S100-protein. There was no staining for pan-cytokeratin, CK7, CK20 or desmin.

Due to the patient's poor clinical condition, no surgical or radiation therapy was offered as treatment options. The patient expired four months following the surgical resection due to myocardial infarction. There was no evidence of distant metastasis at the time of his death.

DISCUSSION

Sarcoma of the genitourinary tract is uncommon and comprises approximately 2% of all genitourinary malignancies.[7] Urinary bladder sarcomas account for less than 1% of malignant UB tumors; with leiomyosarcoma being the most frequent amongst adults.[8] Primary osteosarcoma originating in the UB is very rare tumor[3] and the majority of the tumors are associated with urothelial carcinoma *in situ* or papillary urothelial carcinoma. The reported cases showed a significant male predominance with a patient age range of 41 to 81 years at time of diagnosis. The most common clinical presentation is gross hematuria.[9]

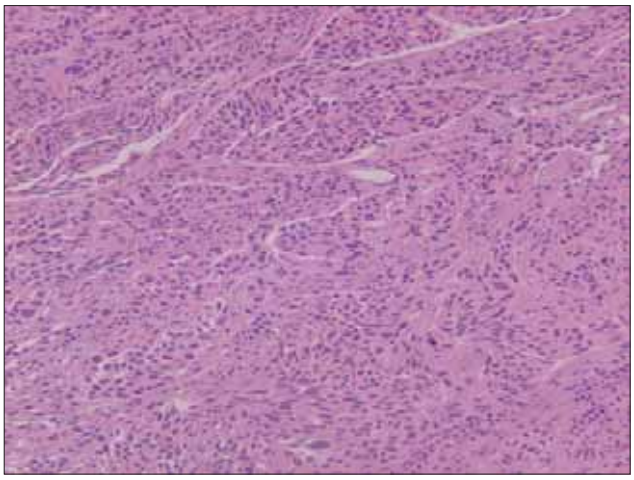

Figure 1: Solid nests of high-grade urothelial carcinoma infiltrating the muscularis propria of the urinary bladder (H and E, ×200)

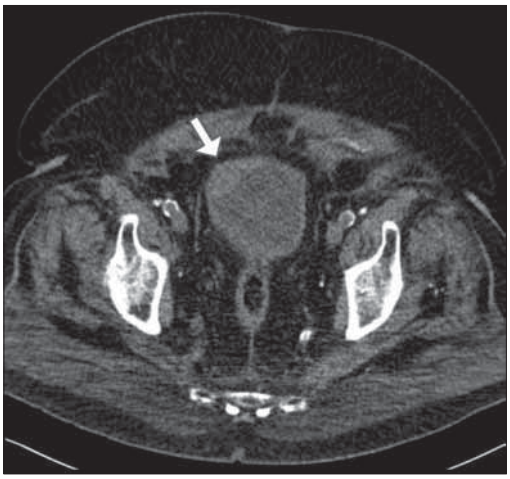

Figure 2: Computed Tomography for the abdomen and pelvis demonstrating a sessile intraluminal lesion of the right posteriolateral aspect of the UB (arrow)

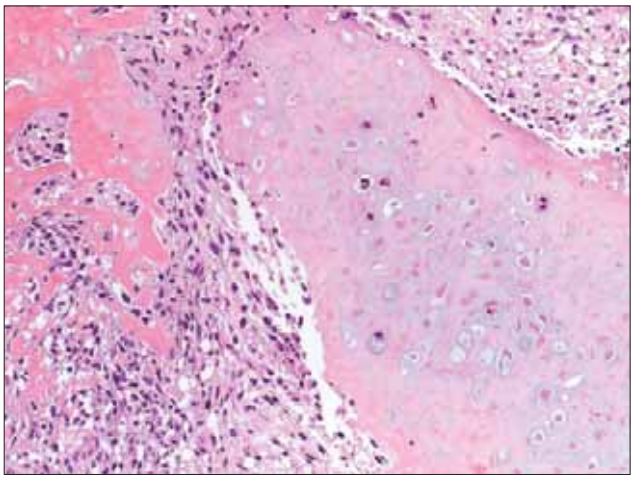

Figure 3: Osteosarcoma of the urinary bladder with malignant osteoid formation and chondroid differentiation (H and E, ×200)

Histologically, osteosarcoma is classified into several types, including osteoblastic, fibroblastic, chondroblastic, and

mixed type, depending on the predominant component of the malignant extracellular matrix. Less common subtypes include small cell, giant cell, and telangiectatic variants. The pathogenesis of osteosarcoma of the UB is unclear. It is suggested that extra skeletal UB osteosarcoma originates from malignant transformation of metaplastic stromal or epithelial tissue.[10] Other hypotheses include osteosarcoma stemming from osteoblasts transferred via blood stream to the UB, or from osteoblasts that developed from immature mesenchymal tissue derived from the Wolffian body from which the trigone develops.[11] Extra skeletal osteosarcoma might also represent malignant transformation of a teratomatous component.[12] Since the majority of cases of UB osteosarcoma are usually associated with a co-existing or prior malignant urothelial neoplasm, malignant transformation from metaplastic stromal or epithelial elements most likely plays a significant role in the tumorigenesis of osteosarcoma. To the best of our knowledge, only two previous cases of post radiation therapy UB osteosarcoma were published in the English literature. Ferri *et al.,*[5] reported a case of osteogenic osteosarcoma in the trigone of the UB, with pelvic extension and uterine involvement in a 66-year-old woman 27 years following surgical excision and radiation therapy of urothelial carcinoma. Mohan *et al.,*[6] described a 27-year-old man who was diagnosed with osteogenic osteosarcoma of the UB one year following post-operative radiotherapy. The tumor invaded the pelvis and involved the sigmoid colon. No residual urothelial malignancy was detected in both these reported cases; hence they have been considered post radiation osteosarcomas of the UB. The herein described case shows a unique histogenesis as it is the first case of post-radiotherapy chondroblastic osteosarcoma of the UB reported.

Radiotherapy is a well-established modality treatment for cancer. A late effect of ionizing radiation is the development of sarcoma within the field of irradiation. Osteosarcoma, among other malignant mesenchymal neoplasms, is well known and one of the most serious complications of radiation therapy.[13] The incidence of radiation-related osteosarcoma is 0.09-0.11%, and it has a latency period ranging from three months to 53 years; however, the vast majority of the tumors occur in 10 to 20 years after radiation therapy.[14] Ionizing radiation is thought to promote tumorigenesis via genetic alteration, including mutations of TP53 and retinoblastoma tumor suppressor genes.

The differential diagnosis of osteoid-forming tumor in the UB should include urothelial carcinoma with osseous metaplastic changes, and sarcomatoid carcinoma (carcinosarcoma). In contrast to osteosarcoma, the osseous stromal component in urothelial carcinoma with osseous metaplasia exhibits mature lamellar architecture and shows no remarkable nuclear atypia. Carcinosarcoma with an osteogenic component is usually associated with malignant urothelial tumors. The most common heterologous element in carcinosarcoma is osteosarcoma; followed by chondrosarcoma, rhabdomyosarcoma, leiomyosarcoma, and rarely liposarcoma and angiosarcoma. Positive cytokeratin immunostaining and ultrastructural epithelial characteristics are retained in the malignant mesenchymal elements, indicating the likely epithelial origin of the tumor.[10] The current case showed no malignant epithelial elements or a positive immune reaction to epithelial markers.

Radical cystectomy is the standard treatment for muscle-invasive urothelial carcinoma of the UB. However, radiotherapy after transurethral cystoscopic resection could be the best alternative treatment modality offering a potential cure for poor surgical candidates.[15,16] Due to the small pool of UB osteosarcoma cases, no clear treatment guidelines are available. Osteosarcoma of the UB is a biologically aggressive tumor with poor prognosis and clinical outcome; most patients with primary osteosarcoma expire from the disease within six months of diagnosis. Although the tumor tends to be locally aggressive, distant metastases appear not to be very common.[3,9] Our patient showed no evidence of recurrent disease or distant metastasis four months after surgical resection.

To conclude, osteosarcomas of the UB occurring after radiation therapy are exceedingly rare tumors with local, aggressive biological behavior. Pure post radiotherapy osteosarcoma should be differentiated from urothelial carcinoma with osseous metaplastic changes and sarcomatoid differentiation. Along with recurrence of the disease, urologists and oncologists should also consider the complications of radiotherapy, including malignancies, in all patients exposed to radiotherapy.

REFERENCES

1. McCarter MD, Lewiss JJ, Antonescu CR, Brennan MF. Extraskeletal osteosarcoma: Analysis of outcome of a rare neoplasm. Sarcoma 2000;4:119-23.
2. Ahmad SA, Patel SR, Ballo MT, Baker TP, Yasko AW, Wang X, *et al*. Extraosseous osteosarcoma: Response to treatment and long-term outcome. J Clin Oncol 2002;15:521-7.
3. Baydar DE, Himmetoglu C, Yazici S, Kiziloz H, Ozen H. Primary osteosarcoma of the urinary bladder following cyclophosphamide therapy for systemic lupus erythematosus: A case report. J Med Case Rep 2009;3:39.
4. Lagrange JL, Ramaioli A, Chateau MC, Marchal C, Resbeut M, Richaud P, *et al*. Sarcoma after radiation therapy: Retrospective multi-institutional study of 80 histologically confirmed cases. Radiology 2000;216:197-205.
5. Ferrie BG, Imrie JE, Paterson PJ. Osteosarcoma of bladder 27 years after local radiotherapy. J R Soc Med 1984;77:962-3.
6. Mohan H, Ahla S, Nada R, Jogai S, Attri AK. Osteosarcoma of the bladder-a case report. Indian J Pathol Microbiol 2001;44:451-52.
7. Russo P, Brady MS, Conlon K, Hajdu SI, Fair WR, Herr HW, *et al*. Adult urological sarcoma. J Urol 1992;147: 1032-6; discussion 1036-7.
8. Labanaris AP, Zugor V, Meyer B, Nützel R, Helmus S, Labanaris PG, *et al*. Urinary bladder leiomyosarcoma in adults. Int Urol Nephrol 2008;40:311-6.

9. Godlewski J, Maslowski Z, Tenderenda M. Primary osteosarcoma of the urinary bladder. C E J Urol 2009;62:37-8.
10. Akoluk A, Barazani Y, Slova D, Shah S, Tareen B. Carcinosarcoma of the bladder: case report and review of the literature. Can Urol Assoc J 2011;5:E69-73.
11. Chitiyo ME. Primary osteogenic sarcoma of the urinary bladder. J Pathol 1973;111:53-6.
12. Fine G, Stout AP. Osteogenic sarcoma of the extraskeletal soft tissue. Cancer 1956;9:1027-43.
13. Virtanen A, Pukkala E, Auvinen A. Incidence of bone and soft tissue sarcoma after radiotherapy: A cohort study of 295,712 Finnish cancer patients. Int J Cancer 2006;118:1017-21.
14. Amendola BE, Amendola MA, McClatchey KD, Miller CH Jr. Radiation-associated sarcoma: a review of 23 patients with post radiation sarcoma over a 50-year period. Am J Clin Oncol 1989;12:411-5.
15. Stenzl A., Cowan NC, De Santis M, Kuczyk MA, Merseburger AS, Ribal MJ, *et al*. Treatment of muscle-invasive and metastatic bladder cancer: update of the EAU guidelines. Eur Urol 2011;59:1009-18.
16. Tran E, Souhami L, Tanguay S, Rajan R. Bladder conservation treatment in the elderly population: Results and prognostic factors of muscle-invasive bladder cancer. Am J Clin Oncol 2009;32:333-7.

How to cite this article: Almadani N, Alsaad KO, Al-Matrafi H, Al Hadab A, Abdullah N, AlKushi A. Urinary bladder radiotherapy-related chondroblastic osteosarcoma: Rare case report and review of literature. Urol Ann 2014;6:247-50.

Source of Support: Nil, **Conflict of Interest:** None.