Primary osteosarcoma in a bladder diverticulum

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Osteosarcoma is a highly malignant soft tissue tumor. Bladder extra-skeletal osteosarcomas are very rare, and only few cases are reported in the English medical literature. This case is the third one of its kind to be reported consisting of a bladder diverticulum osteosarcoma. Compared to urothelial bladder carcinoma, urinary bladder osteosarcomas have a poorer prognosis. Biopsy and immunochemical staining are critical for the diagnosis. Treatment regimens vary based on the stage of the disease. However, choosing the best option for treatment is still unclear, due to the scarcity of cases available.

Key Words: bladder diverticulum, osteosarcoma, extra-skeletal, mesenchymal soft tissue tumors

Introduction

Extra-skeletal osteosarcomas are rare mesenchymal soft tissue tumors characterized by the production of osteoid or immature bone by the malignant cells.[1] They account for no more than 1% of all soft tissue sarcomas. Bladder osteosarcomas are even more uncommon, with only 35 cases reported in the literature so far, accounting for 0.04% of all extra-skeletal mesenchymal tumors. We report a case of a 65-year-old man presenting with a urinary bladder osteosarcoma within a bladder diverticulum. There are only 20 well-documented cases of diverticular sarcoma published in the literature to date.[2] Only two of those were osteosarcomas; hence we are presenting the third case of bladder diverticular osteosarcoma to ever be reported, and the second to be reported in the English literature.

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Case description

A 65-year-old hypertensive man presented with gross hematuria, dysuria and increased urinary frequency. The patient is known to have BPH and underwent TURP 3 years prior to presentation. An ultrasound of the pelvis revealed a large diverticulum on the right lateral wall of the urinary bladder, along with a 3.5 cm x 3.9 cm echogenic structure within it. Computed tomography scan, Figure 1, showed a 5.3 cm x 4.5 cm diverticulum arising from the right posterolateral aspect of the urinary bladder along with significant perivesical and peridiverticular fat streaking. Transurethral resection of the bladder diverticular tumor (TURBT), along with random bladder wall biopsies was performed. The mass appeared solid, gritty in nature, and vascular. Pathology along with immunohistochemical analysis

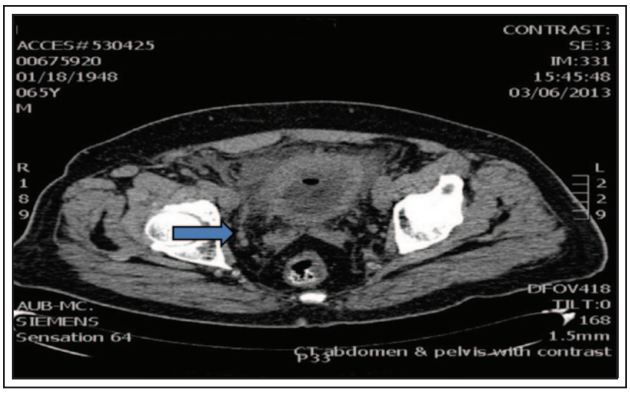

Figure 1. Pelvic CT scan demonstrating a diverticulum arising from the right posterolateral aspect of the bladder (arrow). (Courtesy of the Department of Radiology at AUBMC).

of the specimens revealed malignant sarcoma with osteoid features concurrent with vesical osteosarcoma; random biopsies were negative for malignancy. Postoperatively, 18-F FDG PET-CT scan, Figure 2, showed a hypermetabolic mass in the right posterior aspect of the bladder, compatible with malignancy, and no evidence of metabolically active disease anywhere else. At the time of surgery, the tumor had increased in size. Partial cystectomy with pelvic lymph node dissection was performed. All margins taken intraoperatively were negative for malignancy. Three months later, adjuvant chemotherapy (carboplatin and gemzar) was given. At follow up 4 months after surgery,

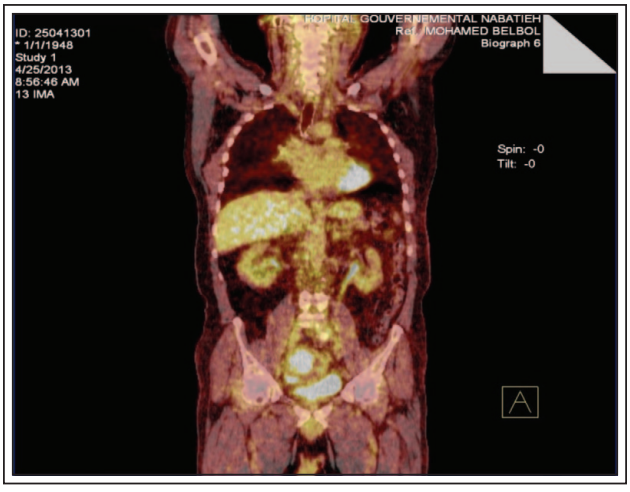

Figure 2. Whole body 18-F FDG PET-CT demonstrating a hypermetabolic mass in the right posterior aspect of the bladder without any evidence of metabolically active disease elsewhere. (Courtesy of the Nabih Berry Governmental Hospital, Nabatiyyah, Lebanon).

CT scan of the abdomen and pelvis showed local tumor recurrence with loco-regional right and left iliac and retroperitoneal lymphadenopathy, and bilateral ureteral obstruction. The patient's condition deteriorated and died 6 months postop.

Discussion and literature review

A bladder diverticulum is an outpouching of the bladder mucosa through weakened muscular areas of the bladder wall.[11] It is acquired as a result of increased intravesicular pressure in patients with bladder outlet obstruction or those who have neurogenic bladder.[1] The most common location is the posterior bladder wall. Macroscopically, a bladder osteosarcoma is gritty, polypoid, variably hemorrhagic, and often deeply infiltrative.[3,4]

Histology and immunohistochemistry are essential at arriving at the definitive diagnosis of extra-skeletal osteosarcoma. Microscopically, malignant lace-like osteoid produced by the spindled sarcomatous cells, is seen along with chondroid matrix, in the absence of concurrent epithelial malignancy.[5] Important to note is that if a recognizable malignant epithelial component is detected, then that is diagnostic of sarcomatoid carcinoma even when osteoid is present. Moreover, the presence of cytologic atypia helps differentiate osteosarcoma from stromal osseous metaplasia.[3] The diagnosis of bladder osteosarcoma should only be made after excluding these possibilities.

Several immunohistochemical markers also exist to help distinguish osteosarcomas from other similar pathologies. Papandreou et al[5] analyzed their paraffin-embedded tissue sections by applying primary antibodies to cytokeratin 7 and 20, epithelial membrane antigen (EMA), smooth muscle actin, desmin, CD34 and CD68. All those markers turned out to be negative in bladder osteosarcoma. Vimentin and p53, on the other hand, are strongly expressed in the neoplastic cells and thus help arrive at the definitive diagnosis.

Microscopically, the tumor that we resected was composed of malignant spindle cells containing hyperchromatic nuclei, along with osteoid deposition, but no malignant epithelial component, Figure 3. The neoplastic cells were diffusely positive to vimentin and negative to CKAE1/3, CK7, CK20, Desmin, SMA, and MSA, therefore consistent with the diagnosis of osteosarcoma. The random bladder biopsies, however, were negative for malignancy and showed only mild inflammation.

The prognosis of vesical osteosarcoma is dismal. According to a review by Ghalayini et al, 22 of 25 patients with vesical osteosarcoma who were left untreated, died at 6 months follow up, most as a result of local

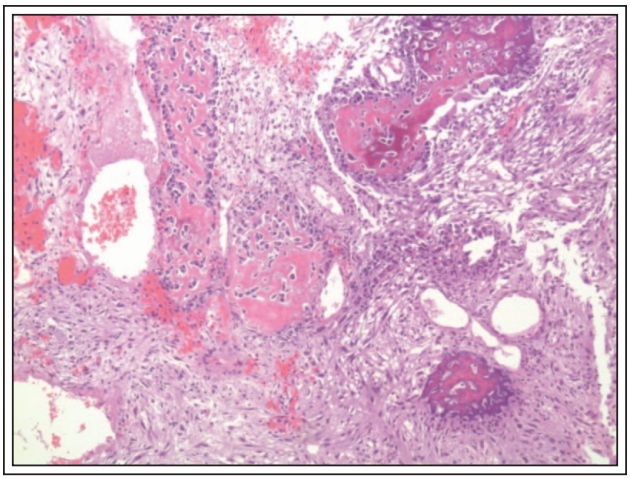

Figure 3. H&E stain showing malignant spindle-shaped cells along with osteoid and ossified bony centers consistent with osteosarcoma.
(Courtesy of the Department of Pathology & Laboratory Medicine at AUBMC).

spread with urinary tract obstruction and secondary infection.[4] Consequently, it is of prime importance to distinguish osteosarcoma from other related diagnoses, like sarcomatoid urothelial carcinoma and urothelial carcinomas with osseous metaplasia, especially when the latter two carcinomas are low grade. Those tumors do not require aggressive therapy like osteosarcoma and have a much better prognosis. According to Allan et al, to diagnose an extra-skeletal osteosarcoma, several criteria[6] must be met, namely: production of malignant osteoid or bone by the sarcomatous tissue; presence of a uniform morphological pattern of sarcomatous tissue that excludes the possibility of malignant mesenchymoma; ready exclusion of an osseous origin.

Due to the paucity of cases encountered so far, there is not yet a standard of care for the treatment of vesical osteosarcomas, let alone those occurring in bladder diverticuli. However physicians have tried several options, with minimal success, due to the aggressive nature of the disease. In general, the treatment protocol depends on the depth of invasion of the tumor, which is categorized as superficial, muscle invasive, or hyperinvasive.[3] Superficial malignancies may be treated either with cauterization or instillation of Bacille Calmette-Guérin. Hyperinvasive tumors require radical cystectomy with chemo and radiation.[7] For muscle-invasive tumors, radical cystectomy with or without chemotherapy has been the traditional standard treatment.[3]

Papandreou et al reported the case of a primary bladder osteosarcoma treated with transurethral resection and external beam radiotherapy (EBRT). The patient died 8 months later, and the authors' conclusion was that EBRT with transurethral resection provide no benefit in patients with primary osteosarcoma of urinary bladder and are associated with a poor quality of life.[5]

However, multiple publications claim that large muscle-invading osteosarcomas can be successfully treated with radical cystectomy and combination chemotherapy. A 54-year-old woman who underwent this protocol remained free of disease on follow up, 56 months after cystectomy. Hence, all patients found to have advanced disease should be considered for this approach.[8]

Conclusion

Osteosarcoma in the urinary bladder is an extremely rare entity with a dismal prognosis as compared to urothelial bladder carcinoma. Biopsy and immunochemical staining are crucial in arriving at the definitive diagnosis. Treatment regimens vary based on the stage of the disease; however, the patient's comorbidities and life expectancy must be taken into account when choosing the best option for treatment. The exact management of such an extra-skeletal osteosarcoma is still unclear, due to the paucity of cases available to date; however, we believe that surgery is the mainstay, with adjuvant chemotherapy/EBRT in selected patients. □

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