CASE REPORT

A rare case of synchronous leiomyosarcoma and urothelial cancer of the bladder

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BAKARIS S, RESIM S, TASCI AI, DEMIRPOLAT G. A rare case of synchronous leiomyosarcoma and urothelial cancer of the bladder. The Canadian Journal of Urology. 2008;15(1):3920-3923.

We report a case of a 44-year-old woman who had coexisting distinct and separate primary tumors of the bladder: a leiomyosarcoma and a transitional cell carcinoma (urothelial cancer). The patient presented with macroscopic hematuria. A computed tomography scan of the pelvis showed a bladder mass along the left anterolateral wall. A transurethral resection of the bladder was performed. A pathological examination revealed that the mass was leiomyosarcoma. The patient underwent radical cystectomy with ileal conduit diversion. The urinary cystectomy specimen revealed an 11 cm x 6 cm x 5 cm solid mass on the left anterolateral wall and two 1-cm papillary tumors with different localization on the right and left lateral walls of the urinary bladder. Pathological examination revealed that the masses were high-grade leiomyosarcoma and urothelial cancer. Because of the differences in the histogenesis and prognosis, such cases should be differentiated from cases of carcinosarcoma of the urinary bladder. Synchronous occurrence of urothelial cancer and sarcoma as two separate primary tumors in the bladder is very rare. To our knowledge, seven cases of coexisting sarcoma and transitional cell carcinoma of the urinary bladder have been reported in the literature.

Key Words: leiomyosarcoma, urothelial cancer, multiple primary tumor, urinary bladder

Introduction

More than 80% of bladder cancers are urothelial cell carcinomas. Bladder neoplasms featuring a malignant mesenchymal component (sarcoma) are rare, accounting for only 0.38% to 0.64% of all bladder cancers.[1] Leiomyosarcoma is the most common malignant mesenchymal tumor of the urinary bladder, yet it accounts for less than 1% of all bladder malignancies, and it is most commonly seen in older patients.[2] Simultaneous occurrence of leiomyosarcoma and urothelial cancer as two separate primary tumors in the bladder is very unusual. Because of their rarity, the prognosis of these cancers is often considered to be unpredictable or highly variable, and it appears to be related to specific parameters, such as the tumor grade

Accepted for publication September 2007

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(high-grade versus low-grade) and size (< 5 cm versus > 5 cm), and the anatomical site (a resectible versus nonresectible cancer).[3]

We present a case of coexisting leiomyosarcoma and urothelial cancer (with separate neoplastic processes) in the urinary bladder of a 44-year-old woman.

Clinical summary

A 44-year-old white woman presented with a 3-month history of gross, painless hematuria with irritation upon voiding and abdominal pain; she had a palpable suprapubic mass. Hematology and biochemistry test results were normal. The patient had been treated for a presumed urinary tract infection with multiple courses of antibiotics without resolution of symptoms. A flexible cystoscopy procedure revealed a large bladder tumor arising from the left side of the bladder near the dome. Urinary ultrasonography showed a 113 mm x 82 mm x 10 mm heterogeneous soft tissue mass in the left pelvis that appeared to be on the left lateral wall of the bladder. A follow-up computed tomographic (CT) scan revealed moderate left hydronephrosis with a thickened bladder wall and a bladder mass along the left anterolateral wall. Figure 1. A CT scan of the chest revealed no metastatic pulmonary lesions. A transurethral resection of the bladder was performed. The initial pathological examination showed leiomyosarcoma with no evidence of a transitional cell carcinoma. The patient then underwent anterior exenteration (radical cystectomy, hysterectomy, and bilateral salpingo-oophorectomy) with ileal conduit diversion and bilateral pelvic lymphadenectomy.

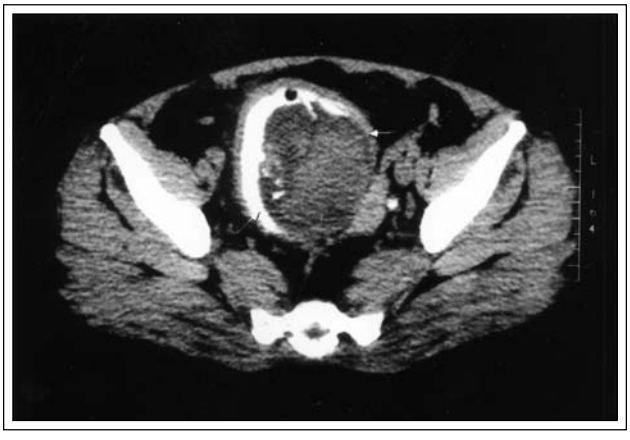

Figure 1. A computed tomography (CT) scan shows diffuse bladder wall thickening and a calcified left lateral mass lesion.

Pathology findings

The cystectomy specimen contained a thick, white-gray, 11 cm x 6 cm x 5 cm tumor that extended from the left anterior bladder wall through the bladder dome and into the posterior bladder wall. Gross examination revealed a well-circumscribed mass with areas of gross hemorrhage and necrosis, with mucosal ulceration. In addition, two 1-cm smooth polypoid masses with intact surface were determined in different localizations on the right and left lateral walls of the urinary bladder. A microscopic examination of the solid tumor for leiomyosarcoma showed a fascicular, highly cellular growth pattern, Figures 2a, 2b. The periphery of the tumor showed irregular infiltration of muscularis propria, Figure 2c. The tumor cells had elongated, blunt-ended nuclei and acidophilic fibrillary cytoplasm. There was marked nuclear pleomorphism with atypia and a high mitotic rate (more than 22 mitoses/10 high-power fields), Figure 2d. Necrosis was present in more than 25% of the tumor, and vascular invasion was not seen. The tumor was classified as high-grade based on nuclear atypia, mitotic activity, and the percentage of tumor necrosis.

Histologic findings in the cystectomy specimens were similar to findings from a previous transurethral resection. Immunohistochemical staining showed that the spindle cells reacted with antibodies to smooth muscle actin (SMA Ab-1 Clone1A4-Neomarkers), Figure 2e and vimentin, and did not react with antibodies to cytokeratin, S-100 protein, CD68, and, in the present case, desmin. Additional histologic elements were identified in the resection specimen.

Another two polypoid masses of the specimen contained a urothelial cancer. Histological examination revealed that the tumor was a typical, high-grade papillary transitional cell carcinoma characterized by fibrovascular papillae. The papillae were lined with urothelial cells with nuclear pleomorphism. A pathology examination showed invasion into the lamina propria; invasion into the muscularis propria, however, was not seen, Figure 2f. Immunohistochemical tests showed that the urothelial carcinoma stained positive for cytokeratin.

Dissection of the uterus revealed well-circumscribed, tan-pink, firm leiomyomas in the myometrium that were 0.5 cm in diameter. No atypia or mitosis was noted. The remaining uterus, cervix, ovaries, and fallopian tubes were otherwise unremarkable. No tumor was detected in the right or left pelvic lymph nodes. She had no clinical evidence of recurrent or metastatic disease. The patient was followed up postoperatively with radiotherapy. She died of metastatic disease 1 year after the initial diagnosis.

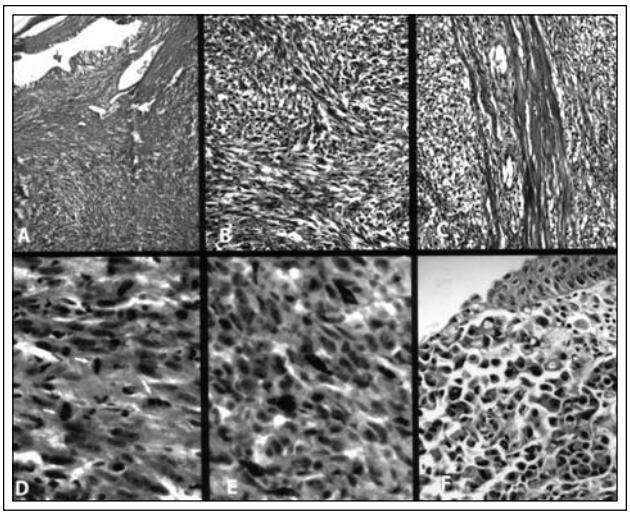

Figure 2a, b, c, d, e, f. Microscopic findings of the vesical tumor. a) Normal urothelium is shown in the left upper corner. Low-power view of the leiomyosarcoma of the urinary bladder (hematoxylin-eosin, magnification X100). b) The tumor consisting of fascicles of spindle cells arranged in interlacing bundles (hematoxylin-eosin, original magnification X200). c) Leiomyosarcoma consisting of spindle cells irregularly infiltrating the muscularis propria (H&E, magnification X200). d) High-power view of the tumor cells showing marked pleomorphism with atypia and many mitotic figures (arrows) (H&E, original magnification X400). e) Immunoperoxidase staining of tumor cells that are positive for smooth muscle actin (Immunohistochemical staining, magnification X400). f) Conventional papillary transitional cell carcinoma. These cells had hyperchromatic, pleomorphic nucleus (H&E, magnification X200).

Discussion

Although multifocal involvement is a well-known feature of urethelial carcinoma, the coexistence of two or more primary urinary bladder tumors of different histologic types is very rare. The literature includes reports of cases with two or more different types of bladder carcinomas, cases of bladder carcinoma and benign mesenchymal tumors, and cases, such as the present one, with both carcinoma and sarcoma of the bladder.[5,6] To our knowledge, seven cases of coexisting sarcoma and transitional cell carcinoma of the urinary bladder have been reported in the literature.[7-13] Of these seven cases: the carcinomas were transitional cell carcinoma in all cases; and the sarcomas were leiomyosarcoma in six cases and osteogenic sarcoma in one case. These cases differ from cases of carcinosarcoma in that the sarcomatous element and carcinomatous element do not admix. Chen suggested that "unlike the dismal outcome of most cases of bladder carcinosarcoma, the prognosis of cases with multiple primary tumors may be favorable, especially if the coexisting tumors are all well differentiated".[6] The presenting features of these coexisting tumor are similar to those of conventional bladder tumors: hematuria, dysuria, pollakiuria, and urinary tract infection. The etiology and risk factors for the development of malignant, mixed epithelial-mesenchymal tumors in the urinary bladder are largely unknown. Partly due to its rarity, the etiology of bladder sarcoma remains unknown. In one study, an association was reported between long-term chemotherapy with cyclophosphamide and urinary bladder sarcoma.[13] Other investigators found an association between previous radiation exposure and the development of leiomyosarcomas in the urinary bladder.[14] We could not discern any etiologic or predisposing factor in our patient. There was no known association with other bladder pathology or systemic disease.

Leiomyosarcoma must be differentiated from reactive spindle-cell proliferation of the urinary bladder, including inflammatory pseudotumor and postoperative spindle-cell nodules. Inflammatory pseudotumor is a myofibroblastic proliferation in a myxoid and inflammatory background that lacks the cytologic atypia of leiomyosarcoma. A postoperative spindle-cell nodule is associated with a history of recent surgery or trauma, particularly transurethral resection, and again, this spindle-cell proliferation lacks the atypia of leiomyosarcoma. Leiomyosarcoma exhibits greater cytologic atypia, abnormal mitoses, and an arrangement in compact cellular fascicles in contrast to reactive spindle-cell proliferations, which have a loose vascular myxoid background. Sarcomatoid carcinoma can resemble leiomyosarcoma, but it is usually associated with a malignant epithelial component, or it exhibits cytokeratin positivity. It is important to distinguish leiomyosarcoma from rhabdomyosarcoma with the aid of immunohistochemical markers.[15] Leiomyoma can be morphologically separated from leiomyosarcoma based on its small size, low cellularity, circumscription, and lack of cytologic atypia.[5]

Wide local excision is considered as the treatment of choice, and radiation and chemotherapy are then offered to patients with positive margins, nodes, or bulky disease. If locally advanced or metastatic disease is noted, the administration of neoadjuvant chemotherapy should be considered. The role of postoperative radiotherapy and/or adjunctive chemotherapy for leiomyosarcomas has not been studied to a great extent.

Alabaster et al reported urethral recurrence after radical cystectomy for a leiomyosarcoma.[16]

Conclusion

This was a case of leiomyosarcoma occurring in conjunction with urothelial cancer of the bladder. Radical cystectomy was performed, and the patient received postoperative radiotherapy. Immunoperoxidase staining for actin and cytokeratin revealed that the tumors were multicentric. Because of the differences in the histogenesis and prognosis, such cases should be differentiated from cases of carcinosarcoma of the urinary bladder. Further collaborative large-scale studies are needed to better understand the major prognostic determinants of these tumors and to identify specific treatments. □

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