Case Report

Sarcomatoid Carcinoma of the Urinary Bladder: A Clinicopathological Study of 4 Cases and a Review of the Literature

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Sarcomatoid carcinoma (SC) of urinary bladder is a rare tumor exhibiting aggressive behavior. Here we are reviewing the pathologic and clinical characteristics of 4 consecutive cases of this rare tumor. Three out of 4 patients were males and one female. The median age was 72.8 years (range, 60-79 years). Patients underwent transurethral resection of bladder tumor and the diagnosis of bladder SC was established on the pathologic examination of the resected bladder tissue. Despite treatment all patients died within 22 months of the diagnosis of SC. SC of the bladder are true biphasic malignant neoplasm exhibiting morphologic and immunohistochemical evidence of epithelial and mesenchymal differentiation with the presence or absence of heterologous elements. The aggressive of the tumor precludes radical therapy whenever possible, since adjuvant therapy seems to have little effect.

Key Words: *Transitional cell carcinoma; Urinary bladder neoplasms*

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Sarcomatoid carcinoma (SC) of the urinary bladder is a very rare variant of transitional cell carcinoma (TCC) that accounts for 0.3% of all histologic subtypes. Less than 100 cases have been reported in the literature until now [1]. Most cases have been reported as single case reports and small series; only one study examining 41 consecutive cases from a single institute exists in the literature [2].

This type of tumor is often termed "carcinosarcoma" (CS) because of its carcinomatous and sarcomatous component. Although the distinction between SC and CS has been extensively discussed in the past, the most recent World Health Organization classification of urinary tract tumors does not distinguish between SC and CS and uses the term "sarcomatoid carcinoma" to denote all of these lesions [1]. The epithelial component may be TCC, squamous cell carcinoma, carcinoma in situ, small cell carcinoma, and adenocarcinoma, whereas the sarcomatous component could consist of leiomyosarcoma, chondrosarcoma, rhabdomyosarcoma, and rarely liposarcoma. More than one type of heterologous differentiation may be present [2].

In the present study, we present 4 cases of SC of the urinary bladder that were diagnosed and treated in our in-

stitute and discuss the morphogenesis and histologic features of this rare entity.

CASE REPORT

Four specimens of SC of the bladder were obtained between 1995 and 2009 and all were received via consultation with one of the authors. The sections were fixed in 10% buffered formalin, processed in the standard fashion, embedded in paraffin, cut at 4 µm intervals, and stained with H&E. Immunohistochemical staining was performed by the standard immunoperoxidase technique. The antibodies used included cytokeratin, AE1/AE3, 34BE12, vimentin, muscle-specific actin (HHF-35), smooth-muscle-specific actin, prostate-specific antigen (PSA), prostate alkaline phosphatase (PSAP), monoclonal carcinoembryonic antigen (mCEA), chromogranin, P63, CD31, and factor VIII. Cases were scored for the percentage of sarcomatoid component, necrosis, and heterologous elements.

1. Presentation of cases

1) Patient demographics and prior history: Three of the

4 patients were males and one was a female. Their median age was 72.8 years (range, 60-79 years), and most of the patients were older than 70 years. Two patients presented with de novo bladder cancer. In one of them, the tumor was found accidentally by abdominal ultrasound, whereas in the remaining patient, the tumor was diagnosed by cystoscopy upon investigation of gross hematuria.

Two patients had a prior history of TCC of the urinary bladder. In one of these two patients, the tumor was diagnosed by cystoscopy during regular follow-up, whereas in the remaining patient, the tumor was diagnosed before the scheduled follow-up cystoscopy.

All patients underwent transurethral resection of the bladder tumor (TUR-BT) for diagnostic and staging purposes (involvement of bladder muscularis). The diagnosis of bladder SC was established by the pathologic examina-

tion of the resected bladder tissue in all patients.

2) Detailed clinical features

(1) **Case 1:** A 76-year-old man with no prior history of bladder cancer presented with gross hematuria. Upon ultrasound investigation, he was found to have a large bladder mass arising from the right lateral wall. He reported a history of recurrent hematuria in the last 6 months. Cystoscopy showed that the tumor protruded in the bladder lumen, covering the orifice of the right ureter. It had a partly typical papillary appearance and was partly solid, invading most of the right lateral wall. A computed tomography (CT) scan of the abdomen revealed a mild dilatation of the right renal pelvis and regional lymphadenopathy. No metastatic disease was found.

(2) **Case 2:** A 77-year-old male smoker with a history of recurrent non-muscle-invasive grade 3 urothelial carcino-

FIG. 1. (A) Transitional cell grade 3 carcinoma. Beneath that can be seen a spindle cell neoplasm with a sarcomatous appearance (H&E, x100). (B) Immunoperoxidase stain with vimentin showing immunoreactivity in the spindle cell component (Vim, x100).

FIG. 2. (A) A chondrosarcomatous area with atypical and pleomorphic chondrocytes (H&E, x200). (B) Transitional cell grade 3 carcinoma: epithelial component admixed with chondromatous areas (H&E, x100)

ma and multiple TUR-BTs presented with gross hematuria and anemia. Cystoscopy showed the tumor to appear as a solid mass located mainly in the bladder base. A CT scan of the abdomen was suspicious for locally advanced disease (invasion of the vesical fat). CT scans of the abdomen, chest, and brain as well as a bone scan were negative for metastatic disease.

(3) Case 3: A 79-year-old man who was a heavy smoker, suffering from diseases that seriously influenced his quality of life, and with a history of recurrent bladder cancer and subsequent TUR-BTs was found to have a recurrent tumor during follow-up cystoscopy. The radiologic evaluation was not considered suspicious for metastatic disease.

(4) Case 4: A 60-year-old woman who presented with frequency, urgency, and persistent dysuria was found to have a suspicious lesion on abdominal ultrasound. Cystoscopy

showed a tumor arising from the bladder base. No regional lymphadenopathy or metastatic disease was shown on a CT scan.

3) Histologic features

(1) Case 1: The biopsy specimen had an overall volume of 70 cc. It consisted partly of papillary and partly of solid, transitional cell grade 3 carcinoma. Beneath that was a spindle cell neoplasm with a sarcomatous appearance (Fig. 1A). The spindle cell component showed mild nuclear pleomorphism and severe mitotic activity. In immunohistochemistry, the epithelial component was stained for P63. The spindle cell component was positively stained for vimentin (Fig. 1B) with a small subset of these cells being at least focally positive for cytokeratin. The stains for HHF-35, SMA, and desmin were negative.

(2) Case 2: The biopsy specimen had an overall volume

FIG. 3. (A) Spindle cell-like appearance of the sarcomatous component with numerous mitoses (H&E, x200). (B) Immunoperoxidase stain with desmin showing immunoreactivity in some spindle cell components (Desm, x200).

FIG. 4. (A) Sarcomatoid component of the tumor characterized by spindle cells with elongated and blunt nuclei (H&E, x100). (B) Immunoperoxidase stain with cytokeratin showing immunoreactivity in the spindle cell component (Cyt, x100).

of 35 cc. It mainly consisted of sarcomatous elements that had morphologic characteristics of chondrosarcoma (Fig. 2A). The epithelial component was a solid, grade 3 TCC with large areas of necrosis (Fig. 2B). In immunohistochemistry, the epithelial component was focally positively stained for P63. The cartilaginous element was positively stained for S100p.

(3) Case 3: The biopsy specimen had an overall volume of 0.5 cc. The tumor was characterized by a biphasic proliferation of malignant epithelial and sarcomatoid elements. The epithelial component was a solid, invasive, grade 3 TCC. The sarcomatous component had a spindle cell-like appearance and was characterized by severe nuclear pleomorphism. Mitoses were numerous (Fig. 3A). In immunohistochemistry, spindle cells were positively stained for vimentin, whereas a small subset of these cells were positively stained for desmin (Fig. 3B). Focally, spindle cells were positively stained for cytokeratin.

(4) Case 4: The biopsy specimen had an overall volume of 3 cc. The tumor mainly consisted (up to 80%) of sarcomatous elements with a spindle cell-like appearance (Fig. 4) and a large areas of necrosis. Immunohistochemically, the epithelial component was positively stained for cytokeratin and P63. Spindle cells were positively stained for vimentin and negatively for actin and Melan A. A small subset of these cells was positively stained for cytokeratin (Fig. 4B).

(4) Patient treatment and outcomes: Patients unfit for radical surgical treatment (cases 1, 2 and 3) were advised to receive radiotherapy and adjuvant chemotherapy.

Case 1 patient received radiotherapy and adjuvant chemotherapy consisted of 4 cycles of cisplatin, methotrexate, vinblastine (CMV) regiment. Although he was alive with CS at the point of final follow-up (18 months after diagnosis), he died 3 months later.

Case 2 patient refused any intervention and discharged home. He died within 1 year of the diagnosis of SC.

Case 3 patient received radiotherapy only. Despite treatment he developed metastatic disease to the sacrum and liver 6 and 9 months after the diagnosis of SC respectively. He was started chemotherapy however he died 1 month after the diagnosis of liver metastases.

The remaining patient (case 4) underwent radical cystectomy. Although surgical margins were disease free in pathology report she developed local recurrence involving rectum and liver metastases 8 months after surgery and she died 6 months later.

DISCUSSION

Malignant tumors that display a biphasic pattern are relatively unusual. They are more commonly observed in the female genital tract but may also be encountered in other locations, including the male genital system, lower and upper respiratory tract, and urinary tract [3]. Although their existence was recognised as early as the mid 19th century, the exact histogenesis of these neoplasms remains a con-

troversial issue in tumor pathology. According to the most widely accepted theories, these tumors may develop from a pluripotent neoplastic cell or may be true collision tumors, in which both malignant epithelial and mesenchymal components arise independently of each other [4,5]. Histologically, the first theory is supported by the presence of ultrastructural features (desmosomes or tonofilaments) of epithelial differentiation in sarcomatoid elements. Genetic and molecular studies argue for a monoclonal origin of both the epithelial and mesenchymal components in SC of the urinary bladder [6]. Interestingly, Sung et al found that a subset of tumors displayed discordant allelic losses associated with advanced urothelial carcinoma, which may reflect genetic divergence during the clonal evolution of SC [6].

SCs of the bladder are true biphasic malignant neoplasms exhibiting morphologic and immunohistochemical evidence of epithelial and mesenchymal differentiation with the presence or absence of heterologous elements [1]. Microscopically, the sarcomatoid component is composed of a urothelial glandular or small cell component showing a variable degree of differentiation. The most common is urothelial carcinoma (80%), followed by squamous cell carcinoma (32%), adenocarcinoma (26%), and small cell carcinoma (5%). The mesenchymal component most frequently observed is osteosarcoma (97%), followed by chondrosarcoma (30%), rhabdomyosarcoma (20%), undifferentiated high-grade spindle cell neoplasm (17%), leiomyosarcoma (7%), liposarcoma, angiosarcoma, and other mixed types of mesenchymal differentiation [1]. By immunohistochemistry, the epithelial component reacts with cytokeratins. Mesenchymal cells react with vimentin or specific markers corresponding to mesenchymal differentiation. SC does not pose diagnostic difficulties to pathologists. In most cases, the diagnosis can be established by conventional H&E examination. Differential diagnosis should include pure sarcoma, particularly in cases composed exclusively of spindle cells; leiomyosarcoma; carcinoma with pseudosarcomatous stroma; and sarcomas with pseudoepitheliomatous hyperplasia [7]. Pseudosarcomatous stroma and other morphologic forms of pseudosarcomatous proliferations (such as inflammatory pseudotumors and postoperative spindle cell nodules) are usually highly vascularized with numerous small slit-like vessels. The cells show minimal reactive-type atypia and atypical mitotic figures are absent. Pseudoepitheliomatous hyperplasia associated with sarcoma of the urinary bladder can resemble the architecture of malignant epithelial proliferation on low-power examination. More detailed examination shows a less intimate association between the two components with a more abrupt interface between true malignant sarcomatous elements and epithelial elements of purely hyperplastic nature. According to the literature, these tumors occur predominantly in male smokers, with a mean age of 72 years. Usual signs and symptoms include hematuria, dysuria, and urinary tract infection [2,8]. Less often, SC arises in patients with a history of radiotherapy, chemotherapy, or

conditions that cause cell replication abnormalities [1]. In our cases, the patients had no such history; however, a progression of the preexisting grade 3 urothelial carcinoma to a sarcomatoid tumor at the time of diagnosis cannot be excluded (Case 2, 3).

The appropriate treatment for such rare tumors has not yet been defined; however, the aggressive behavior suggests radical therapy whenever possible [9]. Total cystectomy often followed by radiation therapy and/or chemotherapy seems to be the preferred treatment [10]. The effectiveness of these treatments is not known because of the varying results of each case. The only factors predictive of long-term survival are negative surgical margins and the absence of metastatic disease at the time of presentation [1]. Unfortunately, cases with metastasis, such as our case 3, have a very poor prognosis. Further study with more cases and experience would be of great value both pathologically and clinically.

Conflicts of Interest

The authors have nothing to disclose.

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