Sarcomatoid urothelial carcinoma of the bladder: a contemporary clinicopathologic analysis of 37 cases

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Introduction: *Sarcomatoid urothelial carcinoma is a dedifferentiated biphasic tumor that exhibits morphological and/or immunohistochemical evidence of epithelial and mesenchymal differentiation. In this series, we analyzed the clinicopathologic features of this rare variant of urothelial carcinoma.*

Materials and methods: *A search was made through our surgical pathology files and consultation files of the senior author for cases of sarcomatoid urothelial carcinoma of the bladder from 2005-2014. All the slides were retrieved and re-reviewed, and clinical data was also obtained including follow up.*

Results: *Thirty-seven cases of sarcomatoid urothelial carcinoma of the bladder were identified. Mean patient age was 71 years (range: 51 to 88 years). Twenty-six of 37 (70%) patients were male and 11/37 (30%) patients were female. Twenty-five cases were from cystectomy/cystoprostatectomy specimens, 8 cases from transurethral resection of bladder tumor specimens and 4 cases were from biopsy specimens. The mean tumor size was 5 cm (range: 1.4 cm to 13.0 cm). Four of 37 (10%) cases had focal heterologous components; 1 case with both chondroid and osteoid, 2 cases with chondroid and 1 case rhabdoid elements. Twenty-one of 37 (56%) patients died within a year of presentation.*

Conclusions: *Sarcomatoid urothelial carcinoma of the bladder is more prevalent in males, with the mean age of 71 years in our series. Smoking is an important risk factor. Sarcomatoid urothelial carcinoma is an aggressive variant of urothelial carcinoma which commonly presents at an advanced stage, and over 50% of patients in our series died of disease within 1 year of presentation.*

Key Words: urothelial carcinoma, sarcomatoid differentiation, clinicopathologic analysis, follow up, prognosis

Introduction

Sarcomatoid urothelial carcinoma of the bladder is a rare, dedifferentiated tumor, characterized by the presence of biphasic malignant neoplastic components exhibiting morpho-logical and/or immunohistochemical evidence of epithelial and mesenchymal differentiation. The malignant spindle cell component is usually an undifferentiated high grade sarcoma. Heterologous components may be seen in the form of rhabdomyosarcoma, chondrosarcoma, liposarcoma and osteosarcoma.[1] Foci of sarcomatoid differentiation have been identified in conventional urothelial carcinoma as well as variants of urothelial carcinoma, including with micropapillary, villoglandular and plasmacytoid variants.[2-4] In addition, adenocarcinoma, squamous cell carcinoma and small cell carcinoma have been described in some studies on sarcomatoid urothelial carcinoma.[5] Ikegami et al analyzed 14 cases of sarcomatoid urothelial carcinoma of

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the urinary bladder, and 2 of these cases had squamous differentiation as epithelial components.[6] Torenbeek et al reported 3 of 18 cases of sarcomatoid urothelial carcinoma with squamous differentiation, 1 case each with adenocarcinoma, combined adenocarcinoma and squamous differentiation, and small cell carcinoma in the epithelial components.[7]

The pathogenesis of sarcomatoid urothelial carcinoma is somewhat controversial. Different theories exist based on clonality, to explain the origin of these morphologically diverse and biphasic tumors. Some studies based on morphologic analysis, propose a theory of collision tumor of two independent, monoclonal tumors occurring simultaneously.[8,9] Others however suggest a common clonal origin with divergent differentiation into carcinomatous and sarcomatoid components.[10-12]

Sarcomatoid urothelial carcinoma represents only 0.1% to 0.3% of all histologic types of bladder carcinoma.[13] Because of the rarity of this biphasic tumor, uncertainty still exists regarding the prognosis and therapeutic implications. In this study, one of the largest to date, we analyzed the clinicopathologic features of sarcomatoid urothelial carcinoma.

Material and methods

A search was made through our surgical pathology files, and consultation files of the senior author for cases of sarcomatoid urothelial carcinoma from 2005-2014. All the slides were retrieved and re-reviewed, and clinical data was also obtained including follow up from comprehensive electronic medical records. This study was completed following the guidelines of, and with approval from, our Institutional Review Board.

Results

Thirty-seven cases of sarcomatoid urothelial carcinoma were identified, Figures 1a-1d. Mean patient age was 71 years (range: 51 to 88 years). Twenty-six of 37 (70%) patients were male and 11/37 (30%) patients were female. Twenty-five cases were from cystectomy/cystoprostatectomy specimens, 8 cases from transurethral resection of bladder tumor specimens and 4 cases were from biopsy specimens. The mean tumor size was 5 cm (range: 1.4 cm to 13.0 cm). 4/37 (11%) cases had focal heterologous components (1 case with both chondroid and osteoid, 2 cases with chondroid, Figures 2a and 2b, and 1 case with rhabdoid elements). Other variants of urothelial carcinoma present were; squamous differentiation 7/37 (19%) cases, glandular differentiation 4/37 (11%) cases, plasmacytoid differentiation 2/37 (5%) cases and 1/37 (3%) case each of micropapillary and lymphoepithelioma-like differentiation. In the cystectomy/cystoprostatectomy cases, the trigone was the most frequently involved area (13/25, 52% cases) followed by lateral and posterior walls (10/25, 40% and 8/25, 32%, respectively), with some tumors being multifocal. Fifteen of 25 (60%) cystectomy/cystoprostatectomy cases were pT3a (3 pN2, 3 pN1, 8 pN0, 1 pNX), 7/25 (28%) cases were pT4a (2 pN2, 3 pN1, 2 pN0) and 3/25 (12%) cases were pT2b (1 pN1, 2 pN0). Thirteen of 30 (43%) cases with a surface component had

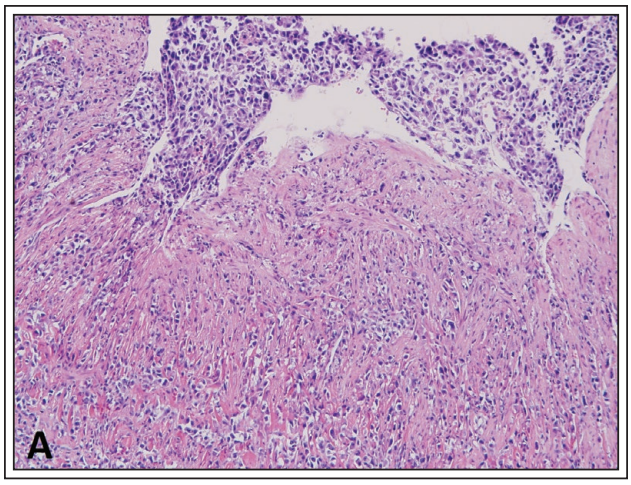

Figure 1a. Sarcomatoid urothelial carcinoma with overlying conventional high grade urothelial carcinoma.

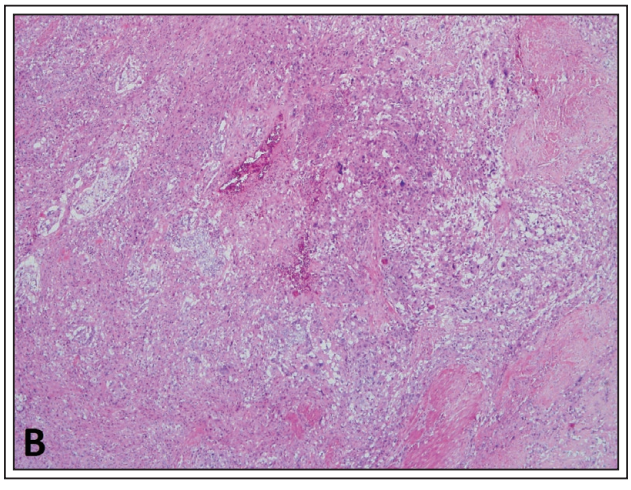

Figure 1b. Sarcomatoid urothelial carcinoma invading muscularis propria (detrusor muscle). Note nests of non-sarcomatoid urothelial carcinoma with focal clear cell change (low magnification).

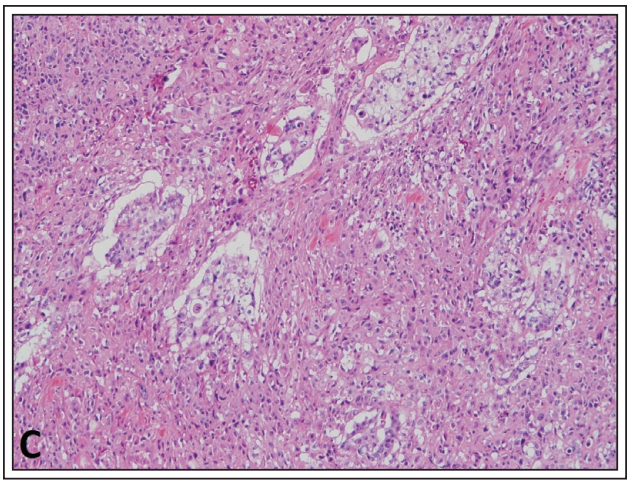

Figure 1c. Sarcomatoid urothelial carcinoma with adjacent nests of non-sarcomatoid urothelial carcinoma with focal clear cell change (high magnification).

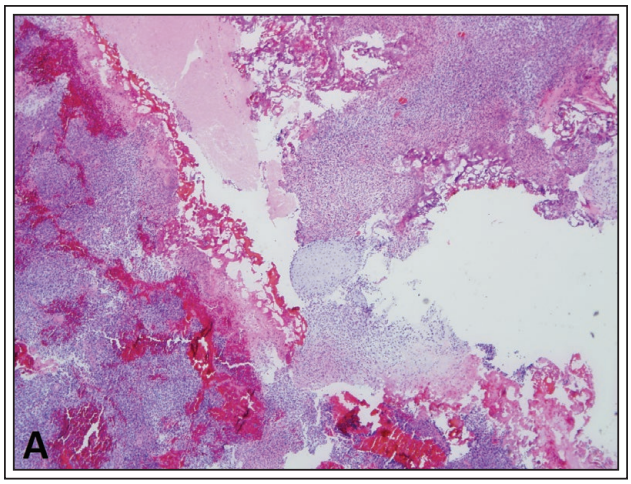

Figure 2a. Sarcomatoid urothelial carcinoma with focal heterologous (chondroid) differentiation (low magnification).

associated overlying urothelial carcinoma in situ. Six of 8 (75%) transurethral resection and 3 of 4 (75%) biopsy specimens had invasion into lamina propria. Three of 8 transurethral resection (37%) specimens and 1 of 4 biopsy (25%) specimens had invasion into muscularis propria (detrusor muscle). Ten of 25 patients (40%) received chemotherapy, of which 2/10 patients (20%) had neoadjuvant chemotherapy and 8/10 (80%) had adjuvant chemotherapy. All patients with available history presented with hematuria. Twenty-one of 29 (72%) patients with available social history had a significant history of smoking. Twenty-one of 37 (57%) patients died within a year of presentation. Nine of the 21 (43%) patients were pT3, 7/21 (33%) patients were pT4 and 5/21 (24%) were pT2. Five of the 10 patients (50%) that got chemotherapy died within a year of presentation.

Discussion

Over the years, different nomenclature have been used in literature to describe these biphasic tumors, including carcinosarcoma, pseudosarcomatous transitional cell carcinoma, malignant mesodermal

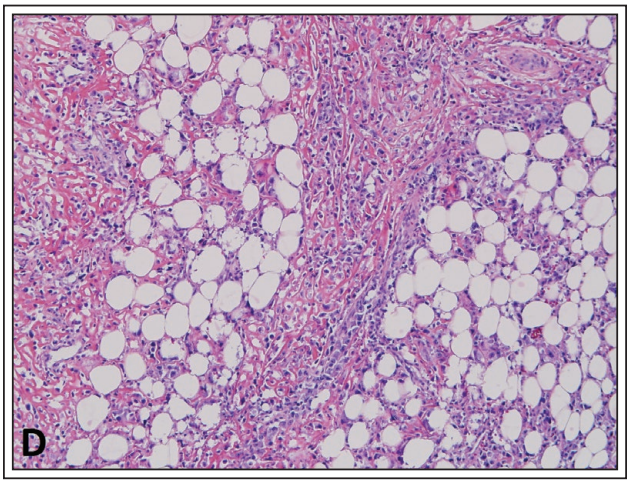

Figure 1d. Sarcomatoid urothelial carcinoma with invasion of perivesical fat.

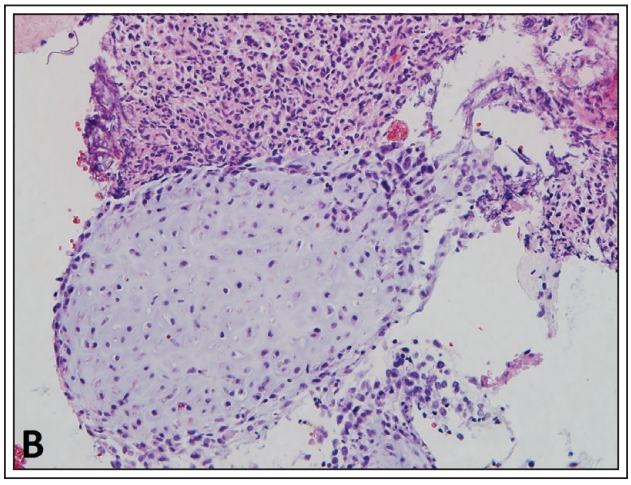

Figure 2b. Sarcomatoid urothelial carcinoma with focal heterologous (chondroid) differentiation (high magnification).

mixed tumor, spindle cell carcinoma, giant cell carcinoma, and malignant teratoma. However, 2004 World Health Organization classification of urothelial neoplasms has defined sarcomatoid carcinoma as all biphasic malignant neoplasms with evidence of epithelial and mesenchymal differentiation.[14]

In the past, there was a great deal of confusion and inconsistencies in the literature regarding the nomenclature and histopathogenesis of these tumors. In some series, "carcinosarcomas" and "sarcomatoid carcinomas" were regarded as separate entities. However, there is now overwhelming consensus amongst Urologic Pathologists that the term "sarcomatoid carcinoma" should be used for all biphasic malignant neoplasms of the bladder (including cases previously referred to as "carcinosarcomas") exhibiting morphologic and/or immunohistochemical evidence of epithelial and mesenchymal differentiation (with the presence or absence of heterologous elements documented in the diagnosis)".

Sarcomatoid urothelial carcinoma of the urinary bladder predominantly affects elderly patients, with male predilection.[13] Commonly reported risk factors include tobacco smoking, previous urothelial carcinoma, recurrent cystitis, diabetes, neurogenic bladder, and bladder diverticulum.[7] Previous history of radiation or cyclophosphamide therapy has also been reported to be associated with this variant of urothelial carcinoma.[15,16]

Young et al in 1988 reported 12 cases of sarcomatoid urothelial carcinoma arising in 7 male and 5 female patients with a mean age of 71.5 years (range: 60 to 83 years). Seven tumors were sessile and five were polypoid, and all patients presented with hematuria.[5] Torenbeek et al in 1994, studied 18 cases of sarcomatoid urothelial carcinoma, and found that the distribution of age, sex, and clinical symptoms are similar to conventional urothelial carcinoma (mean age of 71 years, male predominance, and initial presentation with hematuria). The tumors were located most frequently in the lateral wall in 9/18 (50%) patients, followed by posterior wall in 4/18 (22%) patients. All tumors in their series were broad based solid masses with a mean size of 4.5 cm (range: 2 cm to10 cm), with surface ulceration. All tumors presented with advanced stage; 8/18 (44%) cases at pT2, 7/18 (39%) cases at pT3, and 3/18 (17%) cases at pT4. Metastatic spread was present in 8/18 (44%) patients. Eleven of 18 (61%) patients died of disease within a mean duration of 12 months (range: 2 to 34 months) after the initial diagnosis. They concluded that sarcomatoid urothelial carcinoma behaves as a high grade malignancy with advanced initial stage and unfavorable outcome.[7]

In 1998, Perret et al reviewed 8 cases of sarcomatoid urothelial carcinoma with heterologous elements and reported similar results. There were 5 males and 3 females with median age of 70 years, and patients presented with hematuria and dysuria. Tumors were solitary in all cases and located in the right lateral wall in 6/8 (75%) cases. Tumors had a mean size of 5 cm (range: 2 cm to 12 cm). Four of 8 (50%) patients died of disease within a mean duration of 17 months postoperatively (range: 2 to 42 months). They also reviewed 55 cases from the literature and reported that primary heterologous carcinosarcoma of the urinary bladder is a highly malignant neoplasm occurring predominantly in elderly male population at advanced stage on presentation and rapidly become lethal.[9]

Lopez-Beltran et al in 1998 analyzed the clinicopathologic features of 41 cases of carcinosarcoma and sarcomatoid carcinoma of the bladder. All 41 patients presented at a high stage. Treatment included cystectomy in 11 patients with (4/11) and without (7/11) radiation therapy, and transurethral resection in 4 with (1/4) and without (3/4) radiation therapy. A total of 11 patients died of disease within a mean of 17.2 months (range: 1 to 48 months). They concluded that carcinosarcoma and sarcomatoid carcinoma are highly aggressive malignancies with a similar outcome regardless of histological findings and treatment, and also concluded that the pathological stage is the best predictor of survival.[17]

In 2000, Ikegami et al analyzed 14 cases of sarcomatoid carcinoma of the bladder. Most patients in their series presented with an advanced stage disease, pT2 (7/14, 50%) and pT3 (5/14, 35%). Six of 14 (43%) patients died of disease between 5 and 36 months after the initial diagnosis was made.[6]

Wright et al in 2007, on multivariate analysis, reported overall unadjusted survival rates for 46,515 patients with urothelial carcinoma using the SEER registry, 135 with sarcomatoid carcinoma and 166 with carcinosarcoma were 77%, 54% and 48% at 1 year, and 47%, 37% and 17% at 5 years, respectively. Sarcomatoid carcinoma presented at a similar age but at a higher T stage and with more frequent regional and distant metastases compared to conventional urothelial carcinoma.[13]

In 2010, a series of 221 cases using the Surveillance, Epidemiology and End Results (SEER) Program database reported median age of the patients with sarcomatoid carcinoma of the bladder as 75 years (range: 41 to 96 years). Of the patients with a known tumor stage (n = 204), 72.5% had a regional or distant stage; 98.4% of patients with known histology grade (n = 127), had poorly or undifferentiated histology. Multiple primary tumors were indentified in about

40% of study subjects. The majority of patients (95.9%) received cancer directed therapy, 35.8% had radical or partial cystectomy, 15.8% of patients received radiation therapy combination with surgery. The median overall survival was 14 months (95% CI 7-21 months). One, 5, and 10 year cancer specific survival rates were 53.9%, 28.4% and 25.8%, respectively. They concluded that in a multivariate analysis, only tumor stage was found to be a significant prognostic factor for disease-specific survival.[18]

Atilgan et al in a recent case report proposed that although sarcomatoid carcinoma is very aggressive and lethal tumor, disease-free survival times could be enhanced with radical combination therapies.[19] Transurethral resection and partial cystectomy carry the inherent risk of incomplete tumor resection. Radical cystectomy with pelvic lymphadenectomy is the treatment option of choice for those who are candidates for surgery. However, despite radical surgery, local recurrence and/or metastasis has been reported.[13] Complete responses have been reported after neoadjuvant chemoradiation therapy.[20] Although different therapeutic options have been described, it is very likely that optimum therapy should include multimodality treatment protocols including surgery, radiation and adjuvant chemotherapy, when feasible. We need multi-institutional randomized clinical trials to make any definitive progress in dealing with these uncommon aggressive variants of bladder cancer.

Conclusions

In conclusion, on the basis of our contemporary series of 37 cases of sarcomatoid urothelial carcinoma at our institution, we have confirmed the previously reported characteristics and behavior of this biphasic tumor. We also recommend using the term sarcomatoid urothelial carcinoma in the description of this entity. In our series, these tumors are also more prevalent in males, with a mean age of 71 years. Smoking is an important risk factor, similar to conventional urothelial carcinoma. Sarcomatoid urothelial carcinoma is an aggressive variant of urothelial carcinoma which commonly presents at an advanced stage, and over 50% of patients in our series died of disease within 1 year of presentation. □

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