Review

Sarcomatoid Carcinoma of the Urinary Bladder

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Abstract

Sarcomatoid carcinoma of the urinary bladder (SCUB) is a rare and aggressive subtype of bladder cancer that has a poor prognosis. Limited information is available regarding its clinical features and appropriate treatments. A systematic literature search for published reports on SCUB was performed in the MEDLINE database using the key words "bladder cancer," "sarcomatoid carcinoma," and "carcinosarcoma.". The search resulted in the identification of 276 reports published from January 1960 to January 2014, of which 40 were ultimately included in the present review. No prospective study or clinical trial of SCUB was reported in English language studies. Of these studies, 2 cancer registry studies and 13 large case series, which had included $\geq$ 8 cases were identified. Seven single-institution studies contained adequate clinical follow-up information, and the rest had mainly focused on the pathologic features of the disease. Both the registry and the single-institution studies showed that patients with SCUB presented with a high histologic grade, advanced-stage disease, and a poor prognosis. Comparing the single-institution studies to the Surveillance, Epidemiology, and End Results cohorts, significant differences were found in the age at diagnosis, male-to-female ratio, tumor stage, treatment pattern (cystectomy, radiation, and chemotherapy), and outcomes, likely reflecting differences in referral and practice patterns. The tumor stage was identified as a significant predictor for cancer-specific survival. The results of the present study suggest that SCUB is not as rare as previously thought. Patients with SCUB should be referred to specialists or centers with extensive experience with this rare and serious disease.

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Introduction

Sarcomatoid carcinoma (SC) of the urinary bladder (SCUB) is an unusual malignancy containing both carcinomatous and sarcomatous components. It is a rare, but aggressive, form of bladder cancer, comprising < 1% of all bladder cancers.[1] In most reported cases of SCUB, the epithelial component will be urothelial carcinoma (UC), although squamous cell and small cell carcinoma components have often been reported.[2-7] The mesenchymal component varies from homogeneous sarcoma to more heterotopic elements, such as malignant bone, cartilage, and other mesenchymal tissues.[4,7] It tends to present at an advanced stage and be associated with a poor prognosis.[8] The current body of data of SCUB is limited to case reports and small case series. Little is known about the biology of its aggressiveness and underlying mechanism of chemotherapy resistance and rapid progression. No specific treatment guidelines are available for SCUB owing to the rarity of the disease.

In the present report, we have summarized the current understanding of SCUB and provide an overview of the epidemiology, clinical features, and management of this rare variant of bladder cancer.

Materials and Methods

Search Strategy and Inclusion Criteria

A systematic literature search for published reports on SCUB was performed in the PubMed database using the key words "bladder cancer," "sarcomatoid carcinoma," and "carcinosarcoma." The reference lists from the relevant reports were inspected and cross-referenced and any other pertinent publications added to our review. The exclusion criteria included metastatic lesions to the bladder and studies in languages other than English.

Data Extraction and Analysis

Data extraction from the included studies was performed by 2 investigators. For the reports for which the full text was not available; data in abstract form were also reviewed. The data collected included the year of publication, patient age, patient gender, tumor grade, stage at treatment of SCUB, and survival outcome.

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Descriptive statistics, such as frequency counts, medians, and ranges, were used to characterize the pooled sample.

Results

A total of 67 reports satisfied the inclusion criteria, including 52 case reports and 15 retrospective studies. Fifteen reports on SCUB were identified in PubMed and were incorporated in our analysis, including 2 Surveillance, Epidemiology, and End Results (SEER) registry studies[9,10] and 13 retrospectives studies with $\geq$ 8 patients.[2-7,11-17] The final cohort for our study included 835 patients: 522 from 2 published SEER registry studies and 313 from the 13 largest case series. Of these, 7 single-institution studies[5,7,11-13,15,17] contained adequate clinical follow-up information, and the remainder had mainly focused on the pathologic features of the disease.

The demographic features, presenting symptoms, and clinicopathologic features of 835 patients from 15 reports are summarized in Table 1. SCUB has been more common in men than in women (male-to-female ratio, 1.3-16:1), most frequently occurring in patients in their sixth to seventh decades of age (range, 30-91 years). The most common symptom at presentation has been gross hematuria (70%-100%). The tumors are usually large and, on microscopic examination, contain an intimate admixture of malignant epithelial (eg, transitional cell carcinoma, squamous cell carcinoma, adenocarcinoma, or undifferentiated carcinoma) and mesenchymal elements. The average tumor size was 4.5 cm (median, 3.45 cm; range, 1-9.1 cm).

Review of Published Data

Terminology

Research on SCUB has been hampered by the tumor's rarity, which has precluded the possibility of collecting large series of cases and gathering significant clinical follow-up information. Performing a review of the published data for these tumors has also been challenging because of the continuous changes in the terminology and diagnostic criteria. We found that older case series of this tumor were associated with uncertainties in tumor classification; thus, the disease management could have differed from contemporary standards.

Multiple terms have been used to describe SCUB, including malignant mesodermal mixed tumor, spindle cell carcinoma, giant cell carcinoma, SC, carcinosarcoma (CS), pseudosarcomatous transitional cell carcinoma, and malignant teratoma.[4,11,18,19] The current World Health Organization classification has recommended the use of the term "sarcomatoid carcinoma" for all biphasic malignant neoplasms of the urinary tract, exhibiting morphologic and/or immunohistochemistry evidence of epithelial and mesenchymal differentiation.[1]

Epidemiology

In studying the incidence of this rare tumor, the single-institution and registry studies both have limitations. Nevertheless, we postulated that the incidence of this tumor and the clinical effect of this subtype have likely been underestimated and underreported.[10] Evidence from the contemporary cohort has shown that this variant of bladder cancer can increase over time, likely owing to the heightened awareness of the aggressive subtype and improved immunohistochemistry techniques.[20] A better understanding of SCUB can only be achieved by international collaboration to improve tissue availability and accessibility to allow the study of the true incidence and clinical effect of this rare tumor subtype.

Although the reported incidence of SCUB in single-institution studies has ranged from 0.3% to 4.3% of all the histologic types of bladder carcinoma,[2,21] the incidence reported in an analysis of the SEER database was much lower.[9,10] Wright et al[9] identified 135 cases of SC and 166 cases of CS of bladder from a total of 182,283 patients identified with primary bladder cancer. The greater incidence rate of SCUB and younger age at presentation observed in single-institution studies likely reflect the referral patterns to large tertiary-care referral centers.[10] Younger patients with rare tumors are most likely to visit referral centers for a second opinion. Compared with their community counterparts, pathologists from centers of excellence are more likely to have the expertise to identify this rare histologic subtype.[22]

Similar to conventional UC, SCUB is a disease of advancing age. Wang et al[10] reported a large cohort of 221 patients, with a median age at diagnosis of 75 years (range, 41-96 years). The male-to-female ratio was 1.9:1. Most patients (89.1%) were white; African American and other ethnicities accounted for 6.8% and 4.1%, respectively.[10] Comparing the single-institution studies to the SEER cohorts, significant differences were found in the demographic characteristics, including age at diagnosis, male-to-female ratio, and tumor stage.

Both population and single-institution studies showed that patients with SCUB presented with high histologic grade and advanced-stage disease and had a dismal prognosis.

Etiology and Histogenesis

Although no definite risk factors for SCUB have been identified to date, it has usually been associated with cigarette smoking; 50% to 79% of patients with SCUB have been current or former smokers.[4,12,13] Previous treatment with intravesical cyclophosphamide and radiation therapy for previous conventional UC has been reported to result in sarcomatoid transformation.[2,23]

The histogenesis of SCUB remains uncertain. Several theories exist regarding the origin of these tumors. Some investigators have suggested that these tumors might develop as a result of undifferentiated, totipotent neoplastic cells that undergo multiple pathways of terminal differentiation into either mesenchymal or epithelial elements.[24] Others have concluded that SCUB might be the result of true "collision" tumors, cases in which different components share no common features on immunohistochemistry and electron microscopic examinations and both malignant epithelial and mesenchymal components arise independently of each other.[25] Recently, the results of molecular genetic studies have provided strong support for a common monoclonal origin of both epithelial and mesenchymal components in SCUB.[14,26,27] Armstrong et al[14] examined TP53 mutation status and p53 protein expression in both the sarcomatoid and the epithelial components of cases of sarcomatoid UC. The investigators found that the mutations identified in the microdissected epithelial and sarcomatoid components were identical in all 5 cases.[14] In addition, the sarcomatoid and epithelial tumor components in all cases showed concordant p53 expression patterns.[14] These data suggest a common clonal origin of the phenotypically different tumor components. The TP53 mutations probably occurred early in the