Sarcomatoid Carcinoma with a Predominant Basaloid Squamous Carcinoma Component: The First Report of an Unusual Biphasic Tumor of the Ureter

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Malignant tumors of the ureter that display biphasic patterns are very rare; they include carcinosarcomas, sarcomatoid carcinomas and carcinomas with pseudosarcomatous stroma. Although the distinction between carcinosarcomas and sarcomatoid carcinomas has been extensively discussed in the past, the recent World Health Organization classification of urinary tract tumors (2004) does not distinguish the two lesions and use the term sarcomatoid carcinoma to represent these biphasic tumors. The epithelial components of previously reported ureteral biphasic tumors comprise transitional cell carcinoma, squamous cell carcinoma, carcinoma in situ, small cell carcinoma and adenocarcinoma. In this paper, we report the first case of sarcomatoid carcinoma of the ureter with a predominant basaloid squamous carcinoma component. A 63-year-old man who had developed asymptomatic gross hematuria was diagnosed with a right ureteral tumor and underwent a right nephroureterectomy. Macroscopic examination of the excised tumor revealed a polypoid mass. Histopathologic examination exposed a tumor with malignant epithelial and sarcomatous components. The malignant epithelial component was predominantly composed of basaloid squamous carcinoma, and the sarcomatous component was mostly composed of undifferentiated spindle cells. A small focus of a chondrosarcomatous component was present. There were also transitional zones between the two components. In addition, the spindle cells of the sarcomatous component were partially positive for cytokeratin 7. We believe that the findings of this case study will increase the morphological diversity used for diagnosing malignant tumors of the ureter.

Key words: ureter – carcinoma – carcinosarcoma – immunohistochemistry

INTRODUCTION

Sarcomatoid carcinoma is a rare malignant tumor variant that involves the urinary tract (1). This type of tumor is often termed ‘carcinosarcoma’ because of its carcinomatous and sarcomatous components. Some confusion remains regarding the use of the terms carcinosarcoma and sarcomatoid carcinoma. Some authorities have differentiated between sarcomatoid carcinoma and carcinosarcoma, restricting the latter term for use when lesions with heterologous elements are present (1,2). Positive immunostaining of the sarcomatous components for epithelial markers has been emphasized in diagnosing a biphasic tumor as sarcomatoid carcinoma (3–6). However, histological distinction between carcinosarcomas and sarcomatoid carcinomas is often difficult and may be clinically meaningless. There is a growing trend toward combining these two lesions, with the term sarcomatoid carcinoma used to represent these biphasic lesions (7,8). Only 20 cases of biphasic tumors of the ureter have been documented in the English literature (3–5,9–23). The epithelial components of these biphasic tumors included transitional cell carcinoma, squamous cell carcinoma, carcinoma in situ, small cell carcinoma and adenocarcinoma. None of the reported ureteral biphasic tumors had a basaloid squamous carcinoma component. The presence of basaloid squamous carcinoma in the urinary tract itself is extremely rare. Vakar-López and Abrams (24) reported the only case of basaloid squamous carcinoma of the urinary tract that

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originated in the urinary bladder. The current report describes the first case of sarcomatoid carcinoma of the ureter with a predominant basaloid squamous carcinoma component.

CASE REPORT

A 63-year-old man with asymptomatic gross hematuria presented to our hospital. He had no past history of urinary tract disease including infection and nephrolithiasis. One week after his first visit, he experienced right flank pain. Upon examination, an intravenous pyelogram failed to visualize the right distal ureter. In addition, a computed tomography (CT) scan showed a mass in the right distal ureter (Fig. 1) and the presence of right hydronephrosis. Retrograde pyelography revealed defects in the right ureter. Cystoscopic examination revealed normal bladder mucosa. Examination of the washout fluid obtained from the right ureter revealed the presence of atypical cells. A chest CT scan and bone survey demonstrated the absence of metastatic disease. Based on the diagnosis of a right ureteral tumor, the patient underwent a right nephroureterectomy.

PATHOLOGICAL FINDINGS

Grossly, the surgically resected specimen showed a well-circumscribed polypoid mass with smooth surfaces that had obliterated the distal ureter. The tumor measured 2 cm in diameter along a distal 5 cm section of the ureter (Fig. 2). Mild hydroureter and hydronephrosis were observed proximal to the tumor. The cut surface of the tumor was yellowish-white. Further, histological examination showed that the tumor had a malignant epithelial component as well as a sarcomatous component (Fig. 3A). The malignant epithelial component comprised 70% of the tumor and the remaining 30% was sarcomatous. The carcinomatous lesions focally blended into the sarcomatous lesions, and the transitional zones between the two components were clearly visible (Fig. 3B). Basaloid squamous carcinoma was the predominant epithelial component making up 60% of the whole tumor. Histologically, basaloid squamous carcinoma exhibited a variety of growth patterns. It was composed of basaloid cells that were arranged in variable-sized lobules, nests and cords (Fig. 4A). The tumor cells showed peripheral palisading (Fig. 4B). Large nests of basaloid cells showing central comedo-like necrosis and foci of pseudoglandular structures were present. The tumor cells had relatively monotonous, round and hyperchromatic nuclei with scant cytoplasm. Mitotic figures were numerous. None of the basaloid cells reacted positively with periodic acid-Schiff (PAS) or alcian blue stains. A small population of keratinizing squamous cell carcinoma, which comprised approximately 5% of the tumor, was also observed. The epithelial component had invaded deep into the muscle layer of the ureter. The neighboring mucosa showed a small amount of carcinoma in situ, some of which showed basaloid features. In contrast,
sarcomatous components were located mainly in the luminal side of the polypoid tumor and surrounded the nests of basaloid squamous carcinoma. They were mostly composed of atypical spindle cells with high mitotic activity, which revealed no specific differentiation upon histological examination (Fig. 5A). A small focus of a chondrosarcomatous component, which comprises less than 3% of the tumor, was also observed (Fig. 5B). Inflammatory changes were not prominent in the background mucosa. The renal pelvis and renal parenchyma were not affected by the disease.

**IMMUNOHISTOCHEMICAL STUDIES**

Immunohistochemistry for pancytokeratin (AE1/AE3), cytokeratin 7/8 (CAM5.2), cytokeratin 1/5/10/14 (34βE12), cytokeratin 7, cytokeratin 20, epithelial membrane antigen (EMA), α-smooth muscle actin (α-SMA), vimentin, desmin, CD34, CD68, synaptophysin, chromogranin A and Ki-67 was performed on formalin-fixed, paraffin-embedded tissue using EnVision Plus System (Dako, Glostrup, Denmark). Antigen retrieval for cytokeratin 7/8, cytokeratin 7, cytokeratin 20, vimentin, desmin, CD34, CD68, synaptophysin and Ki-67 was performed with autoclave treatment. Proteinase K epitope retrieval method was used in antigen retrieval for pancytokeratin and cytokeratin 1/5/10/14. The primary antibodies used in this study and immunohistochemical profiles of the two components of the biphasic tumor are summarized in Table 1. The epithelial component, which was predominantly composed of basaloid cells, showed positive immunostaining for pancytokeratin, cytokeratin 7/8, cytokeratin 1/5/10/14, cytokeratin 7 and EMA. The spindle cells of the sarcomatous component were positive for α-SMA and vimentin. In addition, these spindle cells were partially positive for cytokeratin 7 (Fig. 6).

On the basis of these findings, we diagnosed the tumor as sarcomatoid carcinoma with a predominant basaloid squamous component. The post-operative course was uneventful and the patient was well and without tumor recurrence at 10 months.

**DISCUSSION**

Malignant tumors of the ureter that display a biphasic pattern are extremely rare. In total, only 20 cases have been documented in the English literature (3–5,9–23). These tumors include sarcomatoid carcinomas, carcinosarcomas and carcinomas with pseudosarcomatous stroma. The nomenclature used for these biphasic tumors is sometimes confusing, and it is often difficult to assess all cases of biphasic tumors due to the vague diagnostic criteria used in each report. Some authorities have distinguished sarcomatoid carcinoma and carcinosarcoma (1,2). Eble and Young classified malignant tumors with both epithelial and spindle cell components as follows. The term ‘carcinosarcoma’ is used if heterologous differentiation of the sarcomatous components exists, and the term ‘sarcomatoid carcinoma’ is used when the epithelial component merges imperceptibly with the sarcomatous component; this is in contrast to a carcinosarcoma wherein the interphases between the two components are sharp (2).

When establishing the diagnosis of sarcomatoid carcinoma, the presence of carcinoma in situ and transitional zones between the epithelial and mesenchymal cells have been emphasized. In addition, immunoreactivity for epithelial markers such as cytokeratins and EMA in the spindle cells of sarcomatoid carcinoma has often been demonstrated (3–6,25). However, even the heterologous components of
the reported carcinosarcoma may immunohistochemically express epithelial markers (1). Moreover, overlapping shared losses of heterozygosity between the carcinomatous and heterologous elements of the bladder biphasic tumor have been shown by Gronau et al. (26), suggesting a monoclonal origin of the two elements. Furthermore, similar clinical characteristics of biphasic tumors with or without heterologous components have been reported in the prostate, urinary bladder and renal pelvis (1,8,27). These reports are strong supportive evidence in favor of combining sarcomatoid carcinoma and carcinosarcoma into a single entity in these organs. In fact, the recent World Health Organization classification of tumors of urinary tract (2004) does not distinguish between the two lesions, and uses the term sarcomatoid carcinoma to represent biphasic tumors with or without a heterologous component as we do in this manuscript (7).

Carcinoma with pseudosarcomatous stroma should clearly be distinguished from sarcomatoid carcinoma by applying a strict criterion to diagnose malignancy in the stromal component. An inflammatory background is usually observed in pseudosarcomatous stroma, whereas brisk mitotic activity or the presence of atypical mitoses is indicative of sarcomatoid carcinoma (28).

In our case study, all of the features that we observed support the diagnosis of sarcomatoid carcinoma, including the following: the presence of basaloid squamous carcinoma in situ, zones of transition between the epithelial and spindle cells and positive immunostaining of the spindle cells for cytokeratin. First, the presence of basaloid squamous carcinoma in situ in the neighboring mucosa shows that this tumor originated in the ureteral epithelium. Second, zones of transition between the two components and positive cytokeratin staining of the spindle cells suggest the possibility of epithelial components showing metaplastic differentiation toward the sarcomatous components. Although the spindle cells were diffusely positive for vimentin and α-SMA, their histology differed from that of typical leiomyosarcoma. Similar undifferentiated spindle cell components that express α-SMA have also been observed in several other sarcomatoid carcinomas of the ureter (3,5). On the basis of these findings, we believe that basaloid squamous carcinoma arose in the right distal ureter and showed focal transformation toward sarcomatous components.

To the best of our knowledge, this is the first documented case of a biphasic ureteral tumor with a basaloid squamous component. Among the previously reported biphasic tumors of the ureter, five cases were reported as sarcomatoid carcinoma (3–5,10). The epithelial components of these tumors were composed of transitional cell carcinoma in one case, squamous cell carcinoma in another case and both transitional and squamous cell carcinoma in two cases. The histology of the carcinomatous components was not specified in one of the cases (3–5,10). The epithelial components of the reported ureteral carcinosarcoma were composed of transitional cell carcinoma, carcinoma in situ, small cell carcinoma and adenocarcinoma and squamous cell carcinoma (9,11–22).

The term ‘basaloid squamous carcinoma’ was first proposed by Wain et al. (29) in 1986 to describe a variant of squamous cell carcinoma. This type of lesion most commonly arises in the upper aerodigestive tract with a predisposition for the hypopharynx, the base of the tongue and the larynx (29–32). Other reported sites of occurrence include the esophagus, bronchus, lung, vulva, anal canal, thymus, cervix, prostate and salivary gland (33–42). The basaloid squamous carcinoma of the urinary bladder reported by

Table 1. Antibodies used for immunohistochemical studies and findings of both the epithelial component and the sarcomatous component

<table>
<thead>
<tr>
<th>Antigen</th>
<th>Clone</th>
<th>Source</th>
<th>Dilution</th>
<th>Epithelial component</th>
<th>Sarcomatous component</th>
</tr>
</thead>
<tbody>
<tr>
<td>CK</td>
<td>AE1/AE3</td>
<td>DAKO, Glostrup, Denmark</td>
<td>1:300</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>CK 7/8</td>
<td>CAM5.2</td>
<td>Becton-Dickinson, San Jose, CA, USA</td>
<td>1:10</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>CK 1/5/10/14</td>
<td>34βE12</td>
<td>DAKO, Glostrup, Denmark</td>
<td>1:50</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>CK 7</td>
<td>OV-TL 12/30</td>
<td>DAKO, Glostrup, Denmark</td>
<td>1:100</td>
<td>+</td>
<td>+ (Focal)</td>
</tr>
<tr>
<td>CK 20</td>
<td>Ks 20.8</td>
<td>Novocastra, Newcastle upon Tyne, UK</td>
<td>1:200</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>EMA</td>
<td>E29</td>
<td>DAKO, Glostrup, Denmark</td>
<td>1:100</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>α-SMA</td>
<td>1A4</td>
<td>DAKO, Glostrup, Denmark</td>
<td>1:50</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>Vimentin</td>
<td>V9</td>
<td>DAKO, Glostrup, Denmark</td>
<td>1:1000</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>Desmin</td>
<td>D33</td>
<td>DAKO, Glostrup, Denmark</td>
<td>1:200</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>CD34</td>
<td>QBE-10</td>
<td>Immunotech, Marseille Cedex, France</td>
<td>1:50</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>CD68</td>
<td>PG-M1</td>
<td>DAKO, Glostrup, Denmark</td>
<td>1:100</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Synaptophysin</td>
<td>SY38</td>
<td>DAKO, Glostrup, Denmark</td>
<td>1:20</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Chromogranin A</td>
<td>DAK-A3</td>
<td>DAKO, Glostrup, Denmark</td>
<td>1:100</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Ki-67</td>
<td>MIB-1</td>
<td>Novocastra, Newcastle upon Tyne, UK</td>
<td>1:200</td>
<td>+ in 42% of the cells</td>
<td>+ in 45% of the cells</td>
</tr>
</tbody>
</table>

CK, cytokeratin; EMA, epithelial membrane antigen; SMA, smooth muscle actin; +, positive; –, negative.
Vakar-López and Abrams (24) is the only case that originated in the urinary tract. Common histopathologic features of these tumors include nests of small basaloid cells with hyperchromatic nuclei, scant cytoplasm and brisk mitotic activity. Additionally, the cells often show peripheral palisading. Coexistence of conventional squamous cell carcinoma is frequently observed in other anatomic sites (29–32,34). Immunohistochemically, 34B E12 antibody, which recognizes cytokeratin 1/5/10/14, has been reported as a specific marker for basaloid squamous carcinoma (30,41).

Few documented reports exist of basaloid squamous carcinoma with a spindle cell component. Muller and Barnes (43) studied 30 cases of basaloid squamous carcinoma of the head and neck and found only two cases (6.6%) that exhibited this biphasic feature. One tumor arose from the tonsil, and the other from the larynx. Recently, Amatya et al. (44) reported the first case of esophageal carcinosarcoma with a predominant basaloid squamous carcinoma component. The sarcomatous component of the tumor exhibited rhabdomyosarcoma differentiation. Our case shows that coexistence of spindle cell components and basaloid squamous carcinoma can also be observed in the urinary tract.

Sarcomatoid carcinomas of the ureter are generally considered to be highly aggressive tumors with a poor prognosis (5,12), and no effective adjunctive therapy has been reported (19). Furthermore, basaloid squamous carcinoma, a predominant component of this tumor, has exhibited an aggressive clinical course and poor outcome in other anatomic sites (29,30,32,34). Although the patient in this report is free of disease at 10 months, we believe that careful monitoring is necessary.

In conclusion, we report the first case of ureteral sarcomatoid carcinoma with a predominant basaloid squamous carcinoma component. This rare tumor should be included in the differential diagnosis criterion of biphasic tumors of the ureter.

Conflict of interest statement
None declared.

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