Case Report
Carcinosarcoma of the renal pelvis with prominent heterologous elements mimicking teratoma: a case report and literature review

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Abstract: We report a rare case of carcinosarcoma occurred in renal pelvis with prominent heterologous sarcomatous elements mimicking the renal teratoma or adult Wilms' tumor. A 56-year-old Chinese male patient who presented with right flank pain and gross hematuria was admitted to our hospital. Computed tomography after ultrasound revealed right nephrolithiasis and hydronephrosis. Percutaneous nephrostomy revealed a mass instead of renal stones in the right renal pelvis; therefore, the patient underwent subsequent radical nephrectomy. Histologically, the tumor was composed of the spindle cells, closely packed cells and foci of chondroid and osteoid components within myxoid matrix. The chondroid component showed moderate cellularity and cytological atypia. Calcification and focal osteoid matrix were identified in the periphery of these atypical cartilage islands. Of interest, focal squamous cell carcinoma was also identified in this case. These histological features mimicking the teratoma with somatic cell malignant transformation or adult Wilms' tumor. However, neither nephrogenic nests nor heterotopic organogenesis was found after the careful observation of the whole slides. Instead, we observed focal squamous cell carcinoma was also identified in this case. These histological features mimicking the teratoma with somatic cell malignant transformation or adult Wilms' tumor. However, neither nephrogenic nests nor heterotopic organogenesis was found after the careful observation of the whole slides. Instead, we observed focal squamous cell carcinoma in one of these slides. Therefore, we rendered a diagnosis of carcinosarcoma of the renal pelvis. The patient suffered from tumor recurrence 2 months after the surgery. The patient refused chemotherapy, and was dead 4 months after the recurrence.

Keywords: Adult, carcinosarcoma, renal pelvis, teratoma, Wilms' tumor

Introduction

Carcinosarcoma is a rare neoplasm that shows an admixture of epithelial and mesenchymal components. The carcinomatous component of carcinosarcoma may be represented by varying forms, including transitional cell carcinoma, adenocarcinoma or squamous cell carcinoma (SCC). The sarcomatous component shows specific features of mesenchymal differentiation, with elements that include chondrosarcoma, osteosarcoma, rhabdomyosarcoma, liposarcoma and fibrosarcoma [1]. Carcinosarcoma has been reported from a variety of anatomic organs, including esophagus, lung, pancreas, colon, ovary and uterus [2], it seldom occurred in renal pelvis [3, 4]. Sarcomatoid carcinoma or spindle cell carcinoma is the common histological subtype of the carcinosarcoma which involved the renal pelvis or urinary tract, while carcinosarcoma is relatively uncommon, if present, should be distinguished with other renal tumors with heterogeneous histological features, such as Wilms' tumor and teratoma. Immunohistochemical staining could be helpful, but with limitation, for the differential diagnosis. Sufficient sampling and trying to find the typical histological features are the key points to distinguish among them. Nephrogenic nests and heterotopic organogenesis support the diagnosis of Wilms' tumor and teratoma [5, 6], while precancerous lesion of the renal pelvic urothelium strongly supports the urothelial origin [7]. This case serves as a reminder to pathologists to be aware of this uncommon cancer to avoid a misdiagnosis and therefore inappropriate treatment.
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Case presentation

Clinical history

A 56-year-old Chinese male patient who presented with right flank pain and gross hematuria. Computed tomography (CT) after ultrasound revealed right nephrolithiasis and hydronephrosis (Figure 1A-C). The patient underwent percutaneous nephrostomy 10 days later for nephrolithiasis. During the surgery, the surgeon was aware of the probability of renal pelvic neoplasm. Considering the pyonephrosis may result in septicemia, the surgeon decided to perform selective surgery. The patient underwent radical nephrotomy in urinary surgery 20 days later, when laboratory studies showed the white blood cell count was back to normal level. Grossly, the mass (3 cm×2 cm) was hard and protruded into the pelvis and upper ureter tract, which resulted in the obstruction and the renal hydronephrosis. The minimal residual renal parenchyma was compressed into the peripheries because of the prominent hydronephrosis. The minimal residual renal parenchyma was compressed into the peripheries because of the prominent hydronephrosis. Based on the postoperative pathology results, the diagnosis was carcinosarcoma of renal pelvis. The patient suffered tumor recurrence 2 months after the surgery. The patient refused chemotherapy, and was dead 4 months after the recurrence.

Materials and methods

The tumor tissues were fixed in 10% formalin and embedded in paraffin. Four-micrometer sections were cut from each paraffin block. One section was stained with hematoxylin-eosin (H&E); the others were stained for immunohistochemistry using the streptavidin-peroxidase system (Ultrasensitive; Mai Xin Inc., Fuzhou, China) according to the manufacturer’s instruction. Commercially available, prediluted monoclonal antibodies against the following antigens were used to evaluate the specimen: pan-cytokeratin (AE1/AE3), CK5/6, p63, CK7, CK20, GATA3, vimentin, WT-1, SALL4, synaptophysin, CD56, neuron specific enolase (NSE), CD34, S100, PAX8, GFAP, olig2, Desmin, MyoD1, INI-1 and Ki-67. For the negative controls, the primary antibody was replaced with PBS.

Microscopic features

Microscopically, the tumor was composed of the spindle cells (Figure 2A and 2B), closely packed cells (Figure 2C and 2D) and foci of chondroid and osteoid components within myxoid matrix (Figure 2E and 2F). The spindle cells within myxoid matrix (Figure 2G) were positive for vimentin (Figure 2H) and p63, while negative for AE1/AE3. The closely packed cells with scant cytoplasm formed obscure nodular structures and showed moderate to severe cytological atypia with obvious atypical mitoses (Figure 2I). The cells in this area were focal positive for AE1/AE3 (Figure 2J) and diffusely positive for p63 (Figure 2K). The Ki-67 labeling index was approximately 60% and 20% in closely packed cells area and spindle cells area. The chondroid component showed moderate cellularity and cytological atypia (Figure 3A). Calcification and focal osteoid matrix were identified in the periphery of these atypical cartilage islands (Figure 2E and 2F). In focal area, the isolated squamous epithelium and immature cartilage with osteoid matrix mimicking teratoma (Figure 3B), but no heterotopic organogenesis was found in the whole sections. Foci of hemangiopericytoma-like pattern and infarction were also identified in this case (Figure 3C). Focal SCC was also identified in this case (Figure 3D-F). The stroma surrounding the nests of SCC was sarcomatous, containing numerous atypical non-cohesive spindle cells with a high mitotic activity. The carcinomatous lesions focally blended into sarcomatous areas, generating transitional zones between the two tumor components (Figure 3D and 3E). An examination of the slides led to the identification in one of them of the squamous metaplasia and severe atypical hyperplasia (Figure 3E-I) of renal pelvic urothelium. The urothelium underwent squamous metaplasia (Figure 3J) was
negative for PAX8 and GATA3 (Figure 3K), while positive for p63 (Figure 3L) and CK5/6.

**Immunohistochemical staining**

The mesenchymal component shows focal positive for pan-cytokeratin (AE1/AE3) and show diffuse and strong positive for vimentin and p63, but negative for pan-cytokeratin (AE1/AE3), WT-1, GFAP, olig2, PAX8, S100, CD34 Desmin, HMB45, Melan-A, TLE-1, MyoD1, INI-1 and SALL4. The closely packed cells show positive for NSE CD56 and synaptophysin. The SCC component showed the typical immunohistochemical results which were diffusely positive for p63, CK5/6, and negative for CK7, CK20 and GATA3. The Ki-67 labeling index was approximately 60%.

**Discussion**

Carcinosarcoma is a high-grade neoplasm of the renal pelvis in which the malignant epithelial components, usually recognizable as such (of transitional, glandular, squamous, or undifferentiated type), coexists with foci of mesenchymal differentiation, such as rhabdomyosarcoma, chondrosarcoma, osteosarcoma, liposarcoma, or so-called malignant fibrous histiocytoma [1]. According the heterogeneous structures, carcinosarcoma of the renal pelvis should be distinguished with other tumors such as, teratoid Wilms’ tumor, teratoma, synovial sarcoma and PEComa. In the current case, making a reasonable explanation of these heterogeneous structures within the tumor is the key to render a correct diagnosis.

The typical Wilms’ tumor was triphasic with undifferentiated blastema, mesenchymal (stromal) components, and epithelial components. The mesenchymal components usually have a spindle cell fibroblast-like configuration but may also exhibit chondroid and osteoid differentiation. In the current case, the spindle cells, chondroid and osteoid structures in the myxoid stroma (Figure 2A-F) mimic the mesenchymal components of Wilms’ tumor; the closely packed cells with scant cytoplasm mimic the...
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The primitive, irregular renal glomerular tufts or tubules were absent in this case; however, the mesenchymal components of Wilms’ tumor may be prominent and predominate almost to the exclusion of others in extreme cases [8]. Therefore, the biphasic Wilms’ tumor seems a plausible diagnosis with these histological structures. However, how to explain the focal SCC within Wilms’ tumor seems a problem. Although squamous or transitional epithelium [1, 9, 10] can be encountered in Wilms’ tumor and the variety of tissues may cause the confusion to distinguish with teratoma, the malignant transformation of these metaplastic epitheliums is never reported in the literature. Moreover, the squamous differentiation of the epithelial component in Wilms’ tumor is a sign for mature differentiation and often indicates the favorable prognosis. In addition, the squamous metaplasia and severe atypical hyperplasia of the renal pelvic urothelium (Figure 3G-L) strongly support the carcinoma of renal pelvis instead of the Wilms’ tumor. Neither the typical Wilms’ tumor nor the nephrogenic nests were found after the careful examination of the whole slides. The immunostaining results, that the closely packed cells with rare cytoplasm were negative for WT-1, do not support the diagnosis of Wilms’ tumor, neither. Therefore, we exclude Wilms’ tumor based on these reasons.

Initially, we also try to use the renal teratoma with somatic cell malignant transformation to explain the focal SCC, when we did not find the squamous metaplasia and severe atypical hyperplasia of the renal pelvic urothelium. Renal teratoma is a rare entity, and has strict criteria. For a primary renal teratoma, Beckwith has put forth the following criteria: (i) The primary tumor should be definitely of renal origin, which means that the entire neoplasm must be confined within the renal capsule and no teratomas in remote sites. (ii) The tumor should exhibit definitely heterotopic organogenesis, with clearly recognizable evidence of attempt to form organs other than kidney. Definite organogenesis can be defined as the presence of immature or mature tissue arranged in a manner mimicking the ‘normal’ development of the organ or the mature appearance of the organ [11]. The presence of bone, cartilage, muscle, fat, neuroglial tissue, and mature epithelium on their own is not the convincing evidence for organogenesis. Indeed, all of these tissues can be observed in both teratomas and

Figure 3. Histological features and the squamous metaplasia and severe atypical hyperplasia of the renal pelvic urothelium. (A) The chondroid component showed moderate cellularity and cytological atypia (magnification X100). (B) The isolated squamous epithelium and immature cartilage with osteoid matrix mimicking teratoma (magnification X100). (C) Hemangiopericytoma-like pattern (magnification X100). (D-F) The stroma surrounding the nests of SCC was sarcomatous, containing atypical spindle cells with a high mitotic activity. The carcinomatous lesions focally blended into sarcomatous areas (D: magnification X40; E: magnification X100; F: magnification X400). (G-J) The squamous metaplasia and atypical hyperplasia of the urothelium (G: magnification X40; H: magnification X200; I: magnification X400; J: magnification X100). (K) Urothelium underwent squamous metaplasia was negative for GATA3. (L) Urothelium whether underwent squamous metaplasia or not were positive for p63 (magnification X100). (G-J) Severe atypical hyperplasia of the renal pelvic urothelium (magnification X100). (A-J) HE slides. (K-L) IHC slides.
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Table 1. Summary of previously reported carcinosarcoma of the renal pelvis in the literature

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>No. of cases</th>
<th>Age/sex</th>
<th>Follow-up (months)</th>
<th>Outcome</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parikh et al. [4]</td>
<td>2015</td>
<td>1</td>
<td>45/M</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Wu et al. [3]</td>
<td>2014</td>
<td>1</td>
<td>65/F</td>
<td>34</td>
<td>NED</td>
<td>No</td>
</tr>
<tr>
<td>Nicolas et al. [16]</td>
<td>2014</td>
<td>1</td>
<td>63/M</td>
<td>16</td>
<td>Dead</td>
<td>Recurrence after 6 months, and died 16 months after the initial diagnosis.</td>
</tr>
<tr>
<td>Dong et al. [17]</td>
<td>2014</td>
<td>1</td>
<td>73/F</td>
<td>8</td>
<td>NED</td>
<td>No</td>
</tr>
<tr>
<td>Vermeulen et al. [18]</td>
<td>2000</td>
<td>1</td>
<td>77/M</td>
<td>8</td>
<td>NED</td>
<td>No</td>
</tr>
<tr>
<td>Dimitriou et al. [7]</td>
<td>2000</td>
<td>1</td>
<td>84/M</td>
<td>6</td>
<td>Dead</td>
<td>NA</td>
</tr>
<tr>
<td>Lopez-Beltran et al. [19]</td>
<td>1996</td>
<td>5</td>
<td>65-to-82 years-old (mean 71.6; three males and two females)</td>
<td>6-20</td>
<td>All Died of disease</td>
<td>NA</td>
</tr>
<tr>
<td>Tarry et al. [20]</td>
<td>1982</td>
<td>1</td>
<td>67/M</td>
<td>NA</td>
<td>Dead</td>
<td>NA</td>
</tr>
</tbody>
</table>

NA, not available; NED, no evidence of disease.

Teratoid nephroblastomas. The following structures such as skin with the dermal appendages, bronchial structures with bronchial glands and cartilage, brain (neuroglial tissue), and teeth, if present, can be regarded as the evidence of organogenesis [6]. Therefore, no heterotopic organogenesis is found in the current case, and the tumor is mainly located in ureteropelvic area, which do not support the diagnosis of renal teratoma. Again, the squamous metaplasia and carcinoma in situ of the renal pelvic mucosa indicates the urothelial origin of this tumor.

Renal synovial sarcoma and renal PEComa should be considered as differential diagnosis for the renal tumor with the biphasic structures. Essentially, both of them are malignant mesenchymal tumors with epithelioid differentiation instead of the real epithelial tumors. In the current case, the carcinoma in situ indicates the SCC with in the tumor is the invasion of the urothelial carcinoma, but not the epithelioid differentiation from the mesenchymal components. In addition, a panel of immunohistochemical staining (CK, EMA, Vimentin, S-100, Melan-A, HMB45 and TLE-1) will be helpful for the differential diagnosis. S-100, Melan-A and HMB45 are always positive in PEComa, while renal synovial sarcoma usually expresses TLE-1 and harbors the translocation t(X;18) (p11.2/q11.2).

In this case, the sufficient sampling and the identification of precancerous lesion are key points for the final diagnosis, although we discussed so many probabilities to distinguish with other tumors. The squamous metaplasia and severe atypical hyperplasia of the renal pelvic urothelium strongly support the urothelial origin of this tumor. Therefore, the SCC can be explained as the urothelial carcinoma with squamous cell differentiation or metaplastic carcinoma; the spindle cell and chondroid areas can be explained as the sarcomatous region. Considering above, we render the final diagnosis of carcinosarcoma of renal pelvis.

The histogenesis of carcinosarcomas remains controversial and there are two predominant theories. As a representative, Völker et al. [12] thought that carcinosarcomas may originate from a common pluripotent progenitor cell which undergoing epithelial and mesenchymal differentiation, while Perret et al. [13] proposed that certain carcinosarcomas should be regarded as a variant of sarcomatoid carcinoma which shows prominent heterologous differentiation. The phenomenon of squamous metaplasia in the current case seems support the latter hypothesis. It is important to detect and diagnose carcinosarcoma as earlier as possible, because of the aggressive behavior and bad prognosis of this tumor [14, 15]. We reviewed literature for previously reported carcinosarcoma of the renal pelvis and summarized them in Table 1. The patient in the current case suffered from tumor recurrence only 2 months after the surgery and died of the disease also demonstrate this phenomenon.

Conclusion

This case serves as a reminder to pathologists of the need to be aware of this uncommon histological pattern to avoid a misdiagnosis of this
aggressive cancer as teratoma or Wilms’ tumor
and therefore inappropriate treatment.

Acknowledgements

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Disclosure of conflict of interest

None.

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References