Carcinosarcoma with a large cell neuroendocrine epithelial component: first report of an unusual biphasic tumour of the urinary bladder

Y Li, J E Outman, S C Mathur

CASE REPORT

This article describes the first reported case of carcinosarcoma of the urinary bladder with a large cell neuroendocrine epithelial component. A 61 year old man presented with gross haematuria and underwent resection of a biphasic bladder tumour. The malignant epithelial component showed large cell neuroendocrine differentiation with immunohistochemical reactivity for neuron specific enolase, synaptophysin, and chromogranin. The malignant mesenchymal component did not show specific differentiation by histological or immunohistochemical examination. The differential diagnosis of biphasic tumours in the urinary bladder is discussed, along with a review of the literature.

Malignant tumours in the urinary bladder with a biphasic pattern are rare, and include sarcomatoid carcinoma, carcinoma with pseudosarcomatous stroma, and carcinosarcoma. The epithelial components of these tumours are usually composed of transitional cell carcinoma, squamous cell carcinoma, adenocarcinoma, or undifferentiated carcinoma. Here, we report a case of carcinosarcoma with large cell neuroendocrine epithelial differentiation.

CASE REPORT

A 61 year old man presented with a two and a half month history of gross haematuria and irritative voiding symptoms. He was initially treated with a course of antibiotics and evaluated with an intravenous pyelogram, which revealed no upper or lower urinary tract pathology. Completion of his evaluation with cystourethroscopy revealed a mass on the right lateral bladder wall. The patient had no previous history of bladder or other organ neoplasia. He had a history of chronic obstructive pulmonary disease and cigarette use. He had no history of occupational exposure to known carcinogens. The patient underwent transurethral resection of the bladder tumour. Based on the pathological diagnosis of carcinosarcoma, he subsequently had a radical cystoprostatectomy specimen showed a 0.6 × 0.3 cm defect in the right lateral wall. No residual tumour was identified.

DISCUSSION

Carcinosarcoma is a rare tumour of the urinary bladder, with fewer than 100 documented cases in the literature. It occurs more frequently in men (male to female ratio of 1.7–3.0 to 1) and is generally seen in older adults, with a mean age in the 7th decade. The tumours are usually large and polyloid, and on microscopic examination contain an intimate admixture of malignant epithelial and mesenchymal elements. The epithelial components are usually transitional cell carcinoma, squamous cell carcinoma, adenocarcinoma, or undifferentiated carcinoma. The mesenchymal components may be fibrosarcoma, leiomyosarcoma, or undifferentiated sarcoma; rarely skeletal muscle, osseous, and/or cartilaginous differentiation can be seen.

Theories on the histogenesis of carcinosarcoma focus either on divergent differentiation or on “collision” tumours.
Results of immunohistochemistry have been inconclusive, because epithelial markers may or may not be expressed in the sarcomatoid component. Recent studies investigating loss of heterozygosity show overlapping shared losses between the carcinomatous and sarcomatous elements. This favours an origin from a common multipotential cell, with divergent differentiation. Similar findings have been reported in carcinosarcoma of other sites.

The differential diagnosis of carcinosarcoma includes spindle cell carcinoma (sarcomatoid carcinoma) and carcinoma with pseudosarcomatous stromal reaction. The presence of urothelial carcinoma in situ and zones of transition between epithelial and mesenchymal cells supports the diagnosis of sarcomatoid carcinoma. In addition, immunohistochemical stains show positivity for epithelial markers in the spindle cells of sarcomatoid carcinoma. Carcinosarcoma can be distinguished from carcinoma with pseudosarcomatous stromal reaction by strict application of criteria for malignancy in the stromal component. An inflammatory background is more likely in pseudosarcomatous stroma, whereas brisk mitotic activity or the presence of atypical mitoses favours a diagnosis of carcinosarcoma.

“Our case is unique in that the epithelial component exhibited large cell neuroendocrine morphology and, to our knowledge, this represents the first report of a carcinosarcoma of the urinary bladder with a large cell neuroendocrine epithelial component.”

Carcinosarcoma with neuroendocrine differentiation of the epithelial component is extremely rare, with only a few reports in the literature. Mills and colleagues studied 12 cases of small cell carcinoma of the urinary bladder and found one case with a sarcomatoid spindle cell component. However, this report did not include detailed immunohistochemical staining results on the spindle cell component. Mazzucchelli and colleagues reported two cases that had a small cell neuroendocrine epithelial component, confirmed by immunohistochemical stains, and a mesenchymal component with smooth muscle differentiation. Both cases also had foci of transitional cell carcinoma in situ. In contrast to their cases, we did not find carcinoma in situ in either the transurethral resection specimen or cystoprostatectomy specimen from our case. An ultrastructural study was performed in one case in Mazzucchelli’s report, which

<table>
<thead>
<tr>
<th>Stain (clone)</th>
<th>Source</th>
<th>Dilution</th>
<th>Epithelial component</th>
<th>Mesenchymal component</th>
</tr>
</thead>
<tbody>
<tr>
<td>CK (AE1/AE3)</td>
<td>CellMarque (Hot Springs, Arkansas, USA)</td>
<td>1/150</td>
<td>+++</td>
<td>-</td>
</tr>
<tr>
<td>CK (Cam 5.2)</td>
<td>Zymed (South San Francisco, California, USA)</td>
<td>1/100</td>
<td>+++</td>
<td>-</td>
</tr>
<tr>
<td>NSE (B85/NC/VI-H1.4)</td>
<td>CellMarque</td>
<td>1/50</td>
<td>+++</td>
<td>-</td>
</tr>
<tr>
<td>Synaptophysin (SY38)</td>
<td>Biogenex</td>
<td>Prediluted</td>
<td>+++</td>
<td>-</td>
</tr>
<tr>
<td>Chromogranin (LK2H10)</td>
<td>CellMarque</td>
<td>1/100</td>
<td>+++</td>
<td>-</td>
</tr>
<tr>
<td>PSA (ER-PR8)</td>
<td>CellMarque</td>
<td>1/100</td>
<td>-</td>
<td>+++</td>
</tr>
<tr>
<td>Vimentin (V9)</td>
<td>CellMarque</td>
<td>1/80</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>SMA (1A4)</td>
<td>CellMarque</td>
<td>1/100</td>
<td>-</td>
<td>± (wf)</td>
</tr>
<tr>
<td>MSA (HHF35)</td>
<td>DAKO</td>
<td>Prediluted</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Desmin (D33)</td>
<td>CellMarque</td>
<td>Prediluted</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>S-100 (AC4.9)</td>
<td>CellMarque</td>
<td>1/200</td>
<td>-</td>
<td>± (wf)</td>
</tr>
<tr>
<td>CD34 (QBEnd/10)</td>
<td>BioGenex</td>
<td>1/30</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

+++ strong, diffuse positive; ± (wf) weak, focal positive; – negative.

CK, cytokeratin; MSA, muscle specific actin; NSE, neurone specific enolase; PSA, prostate specific antigen; SMA, smooth muscle actin.
showed epithelial cells with irregular nuclei, clumped chromatin, and membrane limited neurosecretory granules. Ultrastructural evaluation from paraffin wax embedded tissue was unsuccessful in our case.

Our case is unique in that the epithelial component exhibited large cell neuroendocrine morphology and, to our knowledge, this represents the first report of a carcinosarcoma of the urinary bladder with a large cell neuroendocrine epithelial component. Primary large cell neuroendocrine carcinoma is extremely rare in the bladder, and has been reviewed in a recent report. Criteria for the diagnosis of large cell neuroendocrine carcinoma were proposed by Travis and colleagues for tumours of the lung. The epithelial component in our case met these criteria, with areas of nested and trabecular (neuroendocrine) growth, large cell size, coarse chromatin, and membrane limited neurosecretory granules. The clinical course and prognosis of carcinosarcoma of the urinary bladder is unknown, and our patient is alive with no evidence of disease eight months after diagnosis.

Take home messages

- We present the first reported case of carcinosarcoma of the urinary bladder with a large cell neuroendocrine epithelial component.
- This rare tumour should be included in the differential diagnosis of biphasic neoplasms of the urinary bladder.
- Although carcinosarcomas usually have an aggressive course, the prognosis of carcinosarcoma with epithelial neuroendocrine differentiation in the urinary bladder is unknown, and our patient is alive with no evidence of disease eight months after diagnosis.

Accepted for publication 21 October 2003

REFERENCES