A Case of Renal Synovial Sarcoma Treated with Adjuvant Ifosfamide and Doxorubicin

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Abstract

Primary renal synovial sarcomas (SS) are rare tumors of the kidney. Faria et al first described primary renal synovial sarcoma in 1999 (Mod Pathol 12:94A). In this paper we present a primary renal synovial sarcoma case and review the 41 primary renal synovial sarcoma cases reported to date. Primary renal synovial sarcomas can exist in either a monophasic or a biphasic pattern. The monophasic variant of primary renal synovial sarcoma is more common and tends to have a better prognosis than the biphasic variant. We present in this paper, a 68-year-old woman with primary renal synovial sarcoma. She presented with right flank pain and abdominal distention. Postoperative pathology of the 20 cm mass on magnetic resonance imaging showed histologic and immunochemical features of synovial sarcoma with coexisting spindle and epithelial cells. She underwent adjuvant ifosfamide and doxorubicin chemotherapy and was free of disease at 1 year after diagnosis. As a conclusion, physicians should be aware of the possibility of malignancy in cystic renal masses and that synovial sarcoma is one of the possibilities.

Key words: kidney, neoplasm, synovial sarcoma

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Introduction

Synovial sarcoma, a rare type of soft-tissue sarcoma, occurs primarily in the extremities in young adults. Primary synovial sarcoma arising from the kidney is extremely rare (1). Renal synovial sarcoma constitutes a subtype of the cases identified as embryonal sarcoma of the kidney. The median age is 35, however age ranges between 20-72. Male cases outnumber female cases (1.7 : 1). The prognosis of primary renal synovial sarcoma is unclear due to the limited number of reported cases (2, 3). However from previously published data, renal synovial sarcomas are believed to have aggressive clinical courses and poor outcomes (4, 5).

Primary renal synovial sarcomas represent a diagnostic challenge. They are not only rare tumors, but also difficult to differentiate pathologically from adult Wilms tumors, primary renal primitive neuroendocrine tumors, congenital mesoblastic nephromas, sarcomatoid renal cell carcinoma and undifferentiated carcinoma. An accurate diagnosis is important as these unique tumors require different treatment regimens (6).

Case Report

A 68-year-old woman presented with a 1-month history of abdominal distension and right flank pain. Magnetic resonance imaging revealed a heterogeneous enhancing soft tissue mass originating from the upper pole of the right kidney which exhibited a distinct pressure on the inferior vena cava and shifted renovascular structures and aorta. On T2A images the mass consisted of cystic necrotic structures situated in a patchy manner and had a capsule. No extra-capsular extension was reported (Fig. 1, 2).

The patient subsequently underwent right nephroureterectomy. Grossly, by intraoperative observation the tumor was approximately 20 cm, and originated from the upper pole of the right kidney and adhered to the vena cava inferior. The resected tumor appeared irregular in shape, and measured 25×15×7 cm. It showed an infiltrative growth pattern into...
surrounding renal tissue.

Cut surface of the mass was grayish white colored and had with focal hemorrhage and yellow-gray necrosis.

Histological examination of tumoral tissue revealed it was composed of solid cellular conglomerates of monomorphic spindle cells with nonuniformly bounded cytoplasm in large areas and fascicles with cystic structures settled among them (Fig. 3). Active mitotic figures in tumoral tissue totaled a median of 7 per 10 high power magnification field. The tumor also exhibited necrotic and hemorrhagic areas. The inner surface of the cystic structures was lined with epithelial cells with large eosinophilic cytoplasm and apically located nuclei showing the classic hobnail appearance (Fig. 4). Immunohistochemically the tumor cells stained positive for vimentin and bcl-2, focally positive for CD 99 and EMA. There was no uptake for pancytokeratin, actin, desmin, CD 10, and low and high molecular weight cytokeratin. Based on these morphologic findings the final pathologic diagnosis was renal synovial sarcoma.

The patient underwent 4 courses of IMA chemotherapy each of which was applied in three days. Doxorubicin 60 mg/m² (70 mg) only the first day, ifosfamide 2,500 mg/m² (3,000 mg) 1-3 days and mesna 2,500 mg/m² (3,000 mg) 1-3 days. The control computed topographies after the third course showed no evidence of recurrence.

Discussion

Sarcomas originating from the kidney are extremely rare and are classified according to histologic type: leiomyosarcoma, liposarcoma, rhabdomyosarcoma, fibrosarcoma, malignant fibrous histiocytoma, hemangiopericytoma and osteosarcoma (7, 8). Leiomyosarcoma is the most common renal sarcoma, which accounts for 40-60% of reported cases, followed by rhabdomyosarcoma, malignant fibrous histiocytoma, fibrosarcoma, angiosarcoma, hemangiopericytoma, liposarcoma, chondrosarcoma and osteosarcoma (9-12). Although the origin is unknown, synovial sarcoma is a well
defined clinical and pathologic tumor type that mainly develops in juxtaarticular soft tissue or in the limbs of young people and adults (1). Synovial sarcoma has 3 histologic subtypes: unidirectional, bidirectional, and poorly differentiated. Because of epithelial and spindle cell components, bidirectional differentiated synovial sarcoma is easy to diagnose; however sometimes it is difficult to distinguish unidirectional synovial sarcoma from other spindle cell sarcomas. Primary renal synovial sarcoma needs to be differentially diagnosed from leiomyosarcoma, fibrosarcoma, malignant peripheral nerve sheath tumors, primitive neuroectodermal tumors, solitary fibrous tumors, hemangiopericytoma, mixed epithelial and mesenchymal tumors, Wilms’s tumors, and renal sarcomatoid carcinoma.

Leiomyosarcoma and fibrosarcoma are also rare in the kidney, and are solid, have no small cysts with a spike shaped cell lining, and few hemangiopericytoma shaped structures, often express SMA, but do not express BCL2, CD99, or CD56. Hemangiopericytoma and solitary fibrous tumors occasionally occur in the kidney, and only a few cases have been reported (13, 14). Though synovial sarcoma has hemangiopericytoma shaped structures, it is difficult to discriminate from hemangiopericytoma and solitary fibrous tumors. However, in synovial sarcoma cells, pleomorphism and heteromorphism are obvious and cells in the mitotic phase are more common. Moreover, lacunae with a spike shaped cell lining can be observed, while for hemangiopericytoma, the irregular antler shaped blood vessel are more visible, the cells have no obvious heteromorphism, and no small cysts with cube or spike shaped cell linings exist. Also the immunohistochemistry is different. The expression of CD34 is diffuse and strongly positive in hemangiopericytoma and solitary fibrous tumors, and no epithelial markers are detected (15). Argani et al (1) reported on 15 patients with renal primary synovial sarcoma, where the majority of the tumors had small visible cavities with smooth inner walls, which were different from the pseudo cavities of tumor necrosis. Since 1987, when t (X; 18) translocation was found, this abnormality has been considered as the genomic character of synovial sarcoma, which can be detected in approximately 90% of synovial sarcomas (16–18). In general, synovial sarcomas are found in close association with joint capsules and tendons in the extremities. However, on rare occasions they may be found without association to a joint space, as in primary renal synovial sarcoma. Argani et al examined embryonal sarcomas of the kidney and sought to determine if embryonal sarcomas and renal synovial sarcomas were similar entities. They performed polymerase chain reaction in four cases of embryonal sarcoma. The SYT-SSX fusion gene was present in all four cases. The other 11 embryonal sarcomas were pathologically similar (1). Fifteen of the 16 previous cases of primary renal SS were diagnosed using reverse-transcription polymerase chain reaction to detect the SYT-SSX gene fusion transcript caused by the t(X; 18) translocation (1, 8) whereas in the one remaining case a SYT-SSX gene fusion transcript caused by the t(X; 18) translocation was identified by cytogenetic analysis but no further karyotypic details were published (1).

We present a case of primary renal SS assessed by standard cytogenetic analysis, which confirms a karyotype that is characteristic of SS as opposed to RCC with or without further genetic aberrations (5). More recently, an additional two cases of primary synovial sarcoma were confirmed by the molecular detection of the SYT-SSX fusion transcripts (8). Thus, classic embryonal sarcomas and primary renal synovial sarcomas appear to be the same entity. As for the differential diagnosis of renal synovial sarcoma; adult Wilms tumor, clear-cell sarcoma of the kidney, primitive neuroendocrine tumor of the kidney, congenital mesoblastic nephroma, sarcomatoid renal cell carcinoma and undifferentiated carcinoma must be taken into account. Immunohistochemical staining helps to differentiate these tumors. Synovial sarcomas usually stain positive for cytokeratin, vimentin, bcl2, epithelial membrane antigen and do not take up stain for actin, desmin, S-100 or CD-34. Clear-cell sarcoma of the kidney does not stain for epithelial markers (cytokeratin) (19). Polymerase chain reaction testing has greatly aided in confirming the diagnosis of renal synovial sarcoma by detecting the SYT-SSX fusion gene (20).

Adult Wilms tumor will also show primary spindle cell predominance as renal synovial sarcomas, however, the SYT-SSX gene fusion will be absent which confirms PRSS (21).

Surgical resection and ifosfamide-based chemotherapy are approved as the mainstay for the management of renal synovial sarcoma (22, 23). In a case reported by Schaaf et al response to ifosfamide and adriamycin is demonstrated (24). However, in surgical managing cystic renal mass, extreme care must be taken to avoid cyst puncture during tumor mobilization or excision and adequate margin of normal parenchyma must be maintained (25).

The treatment protocol of renal synovial sarcomas consists of adjuvant ifosfamide-based chemotherapy mostly adjuvant to radical nephrectomy. High-dose ifosfamide-based chemotherapy is also advocated by some clinics as neoadjuvant and adjuvant therapy for patients with localized or advanced soft tissue synovial sarcomas, and favorable results are reported (22, 23). Kampe et al (22) reported tumor-free survival in 13 patients with localized soft tissue synovial sarcoma after a 37-month-follow-up. Park et al (26) reported complete remission using a doxorubicin and ifosfamide protocol in a PRSS patient developing metastases in the lung in the fourth month following radical nephrectomy. However, currently, there is no definite consensus regarding the use of chemotherapy as an adjuvant modality in these cases.

The previously published 41 cases are analyzed below in terms of epidemiological properties, clinical presentation, immunohistochemical staining features, adjuvant therapy and follow-up with tables which summarize the analysis.

Twenty-one of the cases (51.2%) were female. The mean age of the whole group was 37 (15–67). The two most common clinical symptoms at presentation were hematuria and
renal mass followed by right lower quadrant pain totally seen in 26 of patients. As far as it is reported 7.3% of patients had metastasis on admission. Advanced local extension was reported in 19.5%. Mean tumor volume was 11 cm (3-21). Detailed immunohistochemical staining features and results of SYTSSX gene fusion are seen in Table 1, 2, respectively.

Adjuvant therapy is known to have been given to 8 (19.5%) patients. As an adjuvant therapy 2 patients had chemotherapy and radiotherapy where 5 patients had only chemotherapy and 1 patient had stereotactic body radiotherapy.

The details of chemotherapy regimens applied and follow-up of 7 patients who underwent adjuvant therapy are seen in Table 3.

Final status of 26 patients is not reported. Seven (17.9%) patients died, 2 died because of postoperative sepsis. The 6 (14.6%) of 8 living patients were free of disease whereas disease in the other 2 (4.9%) recurred. Most common metastatic localization is the lung (17.1%) followed by the liver (9.8%).

In conclusion, primary renal synovial sarcoma is an extremely rare neoplasm which was first reported by Faria in

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### Table 1. Immunohistochemical Staining Features of Previously Published Cases

<table>
<thead>
<tr>
<th>Antigen</th>
<th>Frequency</th>
<th>Positive (%)</th>
<th>Frequency</th>
<th>Positive (%)</th>
<th>Not done</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vimentin</td>
<td>25</td>
<td>61</td>
<td>2</td>
<td>4.9</td>
<td>14</td>
</tr>
<tr>
<td>desmin</td>
<td>-</td>
<td>-</td>
<td>23</td>
<td>56.1</td>
<td>18</td>
</tr>
<tr>
<td>S100</td>
<td>-</td>
<td>-</td>
<td>21</td>
<td>51.2</td>
<td>20</td>
</tr>
<tr>
<td>EMA</td>
<td>14</td>
<td>34.1</td>
<td>11</td>
<td>26.8</td>
<td>16</td>
</tr>
<tr>
<td>SYTSSX1</td>
<td>11</td>
<td>26.8</td>
<td>6</td>
<td>14.6</td>
<td>24</td>
</tr>
<tr>
<td>SYTSSX2</td>
<td>13</td>
<td>31.7</td>
<td>4</td>
<td>9.8</td>
<td>24</td>
</tr>
<tr>
<td>NSE</td>
<td>1</td>
<td>2.4</td>
<td>1</td>
<td>2.4</td>
<td>38</td>
</tr>
<tr>
<td>WT1</td>
<td>1</td>
<td>2.4</td>
<td>2</td>
<td>4.9</td>
<td>38</td>
</tr>
<tr>
<td>BCL2</td>
<td>18</td>
<td>43.9</td>
<td>-</td>
<td>-</td>
<td>23</td>
</tr>
<tr>
<td>CK</td>
<td>11</td>
<td>26.8</td>
<td>9</td>
<td>22</td>
<td>21</td>
</tr>
</tbody>
</table>

### Table 2. SYT-SSX Fusion Gene Detection Results of Previously Published Cases

<table>
<thead>
<tr>
<th>SYTSSX1</th>
<th>Frequency</th>
<th>Positive (%)</th>
<th>Frequency</th>
<th>Positive (%)</th>
<th>Not done</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>13</td>
<td>31.7</td>
<td>4</td>
<td>9.8</td>
<td>24</td>
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</table>

### Table 3. Follow Up and Final Status of 8 Previous Patients who Underwent Adjuvant Therapy

<table>
<thead>
<tr>
<th>ADJUVANT THERAPY</th>
<th>FOLLOW UP</th>
<th>FINAL STATUS</th>
<th>REFERENCES</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 cycles of Imatinib + Vincristine + Adriamycin + Cyclophosphamide alternated with cisplatinum + etoposide</td>
<td>Pulmonary metastasis after 6 months</td>
<td>Died 12 months after initial diagnosis</td>
<td>5</td>
</tr>
<tr>
<td>2 cycles of ifosfamide - cisplatinum followed by radiotherapy</td>
<td>Disease free 5 months after surgery</td>
<td>not known</td>
<td>21</td>
</tr>
<tr>
<td>5000 cGy RT and 4 cycles of ifosfamide and Adriamycin</td>
<td>Metastasis to lomber vertebra 6 months after surgery</td>
<td>Disease free 7 months following vertebrectomy</td>
<td>31</td>
</tr>
<tr>
<td>6 cycles of vincristine-doxorubicine-etoposide-ifosfamide followed by radiotherapy</td>
<td>Sepsis and severe pancytopenia</td>
<td>Died 1 month after surgery</td>
<td>32</td>
</tr>
<tr>
<td>Ifosfamide (2.4 g/m² per day for 5 days) and etoposide (60 mg/m² per day for 5 days)</td>
<td>Adult Wilms' tumor with favorable histology was diagnosed. Adjuvant treatment was not carried. On 33 months follow-up CT scan revealed a recurrent tumor in the renal fossa. Underwent adjuvant chemo for his recurrent tumor. Three months later, the patient developed rapid growing liver metastasis</td>
<td>Died 4 years after the first surgery.</td>
<td>34</td>
</tr>
<tr>
<td>Ifosfamide (2000 mg/day [day 1–5], every 28 days) and etoposide (100 mg/day [day 1–5])</td>
<td>Lung metastasis 4 months after surgery. Underwent chemo after metastasis</td>
<td>Complete remission</td>
<td>26</td>
</tr>
<tr>
<td>6 cycles doxorubicin and ifosfamide</td>
<td>Metastatic at presentation. 4 years disease free after 8 courses of chemotherapy SBRT for lung recurrence</td>
<td>Not known</td>
<td>33</td>
</tr>
</tbody>
</table>
Renal synovial sarcoma is rare and its prognosis is poor. Most patients die within the first decade after diagnosis due to tumor recurrence or metastasis. In our analysis of previous studies, the longest survival time reported was 48 months. Its morphologic and immunohistochemical characteristics may be related to other spindle cell tumors of the kidney. Therefore, a diagnosis of primary renal synovial sarcoma needs to exclude other similar diseases and confirm the SYTSSX gene fusion by molecular analysis.

Conclusion

The authors state that they have no Conflict of Interest (COI).

References
