Case Report

Malignant Renal Epithelioid Angiomyolipoma with Aggressive Behavior and Distant Metastasis

Angiomyolipoma (AML) is a hamartoma and most commonly arises from kidney. It typically has a mixture of blood vessels, smooth muscle cells, and adipocytes. Some cases may show nuclear pleomorphism, mitotic activity, extension into the vena cava and multiplicity in regional lymph nodes, but without further malignant progression. However, very few cases of AML with locally aggressive behavior and distant metastases have been reported, which are therefore considered as malignant AMLs. To our knowledge, there are only seven malignant AMLs reported in the literature, and review of the literature suggests that large epithelioid subtype with tumoral necrosis may suggest the malignant change.

Key Words
angiomyolipoma; computed tomography; magnetic resonance imaging; malignant renal neoplasm

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CASE REPORT

A 58-year-old male was admitted for evaluation of a palpable mass in the right aspect of abdomen. Neither remarkable hematuria nor clinical evidence of tuberous sclerosis was present. Post-contrast abdominal CT scan revealed a huge soft tissue mass (37 × 18 × 15 cm) with heterogeneous attenuation in the upper pole of the right kidney and downward extension to pelvic cavity (Fig. 1A). The tumor showed minimal heterogeneous enhancement except for the necrotic area. Enlarged lymph nodes at the hepatic hilum and right renal hilum were also depicted. External compression of the inferior vena cava (IVC) by the tumor but with out invasion was confirmed on the digital subtracted venography. MR imaging of the tumor demonstrated hypointense signals on T₁-weighted images (T₁WI) (TR/TE: 156.2/4.1) and hyperintense signals on T₂-weighted images (T₂WI) (TR/TE: 2043/99). The gadolinium-enhanced MR imaging also depicted the tumor with minimal enhancement except at some necrotic areas (Fig. 1B). No detectable fat component was noted in the tumor on either CT or MR images. Sarcomatous tumor arising from right-sided retroperitoneum or renal cell carcinoma was primarily impressed because of the tumor size and aggressive appearance. There were no visible focal lesions in the liver. Radical nephrectomy and retroperitoneal lymph node dissection were performed. The tumor arose from the upper pole of the right kidney and compressed collecting system, duodenum and IVC. The histopathologic findings of this huge tumor demonstrated a picture of monotypic epithelioid angiomyolipoma composed chiefly of solid nests of epithelioid cells without adipose tissue and aberrant vessels (Fig. 2). No other foci of typical AML occurred in the remaining right kidney. The same histopathologic pictures were found in the resected regional lymph nodes. Tumor cells of the right renal mass and regional lymphadenopathy were both immunohistochemically positive for HBM-45 and negative for cytokeratin. These histopathologic features were consistent with a diagnosis of epithelioid angiomyolipoma.
tent with epithelioid AML, which can be differentiated from RCC or retroperitoneal sarcomaous tumor. The postoperative CT scan four months later revealed enlarged para-aortic lymph nodes and multiple low-attenuation lesions in both hepatic lobes (Fig. 3). Biopsy of the lesions in liver revealed the identical histopathologic features as that of the primary renal AML. Distinct metastases to liver and retroperitoneal met static lymphadenopathy from primary renal epithelioid AML was thus confirmed. Despite the chemotherapy, the follow-up CT scan still showed significantly progressive change of the metastatic lesions.

**DISCUSSION**

AML is the most common mesenchymal tumor of the kidney. It is typically composed of abnormal blood vessels, smooth muscle cells and adipocytes in variable proportion. The AMLs may be large, multifocal and involve both kidneys, when AMLs present as part of tuberous sclerosis. AML is generally benign even as a primary tumor even in the presence of aggressive pattern such as local invasion to nearby organs, in volve men in regional lymph nodes and lo cal invasion to IVC. The presence of pleomorphism and mitotic activity in the tumor may also be identified by typical AML. Therefore, local aggressiveness or histopathologic features of the tumor cannot solely indicate the malignancy of the AML. Malignant be havior of AML was not observed until 1991 when the first case with lung metastasis was reported.

Monotypic epithelioid AML is a rare subtype of AML that lacks adipose tissue and aberrant vessels. The epithelioid AML, which is hard to distinguish from renal cell carcinoma (RCC) by morphology, is characterized by its immunoactivity to HMB-45. We have re-

Table 1. Summary of the characteristics of 8 malignant angiomyolipomas

<table>
<thead>
<tr>
<th>Metastasis AML reported</th>
<th>Age/ gender</th>
<th>TSC Size (mm)</th>
<th>Classical focus of AML in the same kidney</th>
<th>Necrosis Fat component</th>
<th>Nodal involvement</th>
<th>IVC invasion</th>
<th>Histopathologic finding</th>
<th>Metastases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferry et al.</td>
<td>49/F</td>
<td>No 150</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Sarcomatous change of renal AML</td>
<td>Lung</td>
</tr>
<tr>
<td>Al-Saleem et al.</td>
<td>21/F</td>
<td>Yes NA (large mass, 5000 mg)</td>
<td>Yes</td>
<td>Yes</td>
<td>NA</td>
<td>NA</td>
<td>Epithelioid AML</td>
<td>Liver and lung, IVC thrombosis by tumor</td>
</tr>
<tr>
<td>Pea et al.</td>
<td>24/F</td>
<td>Yes NA</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>NA</td>
<td>Monotypic epithelioid AML</td>
<td>Pelvic, Liver</td>
</tr>
<tr>
<td>Pea et al.</td>
<td>29/M</td>
<td>Yes NA</td>
<td>Yes</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>Monotypic epithelioid AML</td>
<td>Liver</td>
</tr>
<tr>
<td>Christiano et al.</td>
<td>42/M</td>
<td>No 205×175×100</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Epithelioid AML</td>
<td>Lung (not biopsied)</td>
</tr>
<tr>
<td>L’Hostis et al.</td>
<td>72/F</td>
<td>No 90</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>NA</td>
<td>Monotypic epithelioid AML</td>
<td>Lung Paravertebral lymph nodes</td>
</tr>
<tr>
<td>Cibas et al.</td>
<td>49/F</td>
<td>No 40×40×30</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Epithelioid AML coexiste with typical AML</td>
<td>Liver</td>
</tr>
<tr>
<td>Current case</td>
<td>58/M</td>
<td>No 370×180×150</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Monotypic epithelioid AML</td>
<td>Liver</td>
</tr>
</tbody>
</table>

AML = angiomyolipoma; TSC = history of tuberous sclerosis complex; NA = data not available; IVC = inferior vena cava.

Fig. 3. Metastatic AML in liver. The postoperative follow-up MRI reveals multiple mass lesions in the liver and retroperitoneal lymphadenopathy (ar row heads). Biopsy of the hepatic tumors confirmed metastatic epithelioid AML.
viewed all seven malignant AMLs documented in the literature, of which were identified as epithelioid AML (Table 1). In fact, it has been speculated that some of the epithelioid AMLs must have been diagnosed as RCCs in the past.\(^\text{3-5,8}\) Malignant potential of AML may, therefore, be over looked and underdiagnosed.

Typical AML presents as a heterogeneous fat-containing tumor occasionally with hemorrhage on the CT or MRI. The size of AML is usually less than 5 cm. The presence of fat is quite specific for detecting AML on the CT scan; yet, approximately 5% AML presents with homogeneous pattern due to minimal fat component.\(^\text{9}\) Since malignant AML is rarely reported, characterization of its imaging features is necessary. In this case, we observed a huge contrast-enhanced soft tissue mass with intratumoral necrosis and cystic change but without discernible fat component. The differential diagnosis of this huge retroperitoneal lesion may include renal cell carcinoma, retroperitoneal sarcoma or even aggressive transitional cell carcinoma arising from urothelial epithelium. Although malignant AML is extremely rare, it should also be included in the differential diagnosis. How ever, in our case, the imaging findings seemed not specific for malignant renal tumors, and accurate preoperative diagnosis was difficult to be made.

In order to characterize the pattern of malignant AMLs, we also reviewed the pathologic features of 7 documented malignant AMLs in the literature (summarized in Table 1). We found that 5 out of 6 tumors with available data of tumor size were large (9-34 cm). All of the tumors presented necrosis except one that was not recorded in this respect. Except for our case, all the reported cases coexisted with other typical AML foci in the same kidney. The histopathologic findings of all these eight tumors were consistent with epithelioid AMLs, except for the one diagnosed as sarcomatoid change of renal AML. The sites of distant metastases include lung, liver and retroperitoneal lymph nodes. In contrast, tuberous sclerosis stigmas, fat component in the tumor, lymph node involvement, or IVC in vasion does not appear specific for malignant AMLs.

In conclusion, malignant AML is rarely reported and cannot be diagnosed solely on the basis of the histopathologic findings. Its imaging features of do not appear specific, either. However, we found that malignant AMLs tend to be of epithelioid subtype, coexist with typical AML, be large in size and have tumoral necrosis. Although these findings are based on limited cases, we believe this information will help understanding the malignant potential of epithelioid AMLs, raising the index of suspicion for malignant AMLs when they become large with necrosis change, so that postoperative follow-up is mandatory.

**REFERENCES**