Angiomyolipoma (AML) is a common benign renal tumor composed of thick-walled blood vessels, smooth muscle, and adipose tissue, but the malignant epithelioid variant is extremely rare. A 78-year-old woman presented with fever and left flank pain for 3 days. Computed tomography showed a heterogeneously enhanced mass without fat density in the left kidney. Radical nephrectomy was performed and pathology showed malignant epithelioid AML with regional lymph node metastases. The tumor cells were positive for human melanosome-associated protein (HMB-45) on immunohistochemical staining. The patient died of disseminated metastases (lungs and bones) 5 months postoperatively. Epithelioid AML is a potentially aggressive tumor. The prognosis is poor in metastatic disease. HMB-45 immunoreactivity is a useful marker to make diagnosis. [J Formos Med Assoc 2007;106(2 Suppl):S51–S54]

Key Words: human melanosome-associated protein, malignant epithelioid angiomyolipoma

Angiomyolipoma (AML) is a common benign renal tumor that is composed of thick-walled blood vessels, smooth muscle, and adipose tissue, but the malignant epithelioid variant is extremely rare. Here, we report a case of a 78-year-old woman who had malignant epithelioid AML with regional lymph node metastases.

Case Report

A 78-year-old woman presented with fever and left flank pain for 3 days. She was diagnosed with urinary tract infection, and oral antibiotics were given at local clinics. On admission, her fever had subsided. Physical examination found no evidence of tuberous sclerosis complex. Renal echo showed a heterogeneously hypoechoic tumor in the lower pole of the left kidney. Contrast-enhanced computed tomography (CT) confirmed the presence of a heterogeneous mass occupying the lower middle portion of the left kidney. No fat density was discernible and renal cell carcinoma was suspected. Paraaoortic lymph nodes were also noted (Figure 1). Radical nephrectomy was performed. Pathology showed malignant epithelioid AML with regional lymph node metastases. Grossly, the mass measured 12.5 × 7.5 × 8.5 cm in size. On sectioning, the tumor was found to be well demarcated. The cut surface was brown and yellowish with focal hemorrhage and necrosis (Figure 2). Microscopically, the tumor was composed of predominantly pleomorphic polygonal epithelioid cells with abundant eosinophilic cytoplasm in a sheet or thick trabecular pattern, separated by vascular structures. The cells had bizarre nuclei with increased mitotic figures. Areas of necrosis and hemorrhage associated with hemosiderin
depositions were seen. Tumor emboli in lymphatic or vascular spaces were discernible. Paraaortic lymph nodes revealed metastases from the tumor cells (Figure 3). Scanty adipose tissue and abnormal blood vessels characteristic of classic AML were found. Immunohistochemical (IHC) staining showed that the tumor cells were melanosome-associated protein (HMB-45) positive, but negative for cytokeratin and smooth muscle alpha-actin (SMA). So the pathologic diagnosis of malignant epithelioid AML with regional lymph node metastasis was made. A postoperative bone scan showed multiple bony metastases 4 months later. The patient died of disseminated metastases (lungs and bones) 5 months postoperatively.

**Discussion**

AMLs arise mainly in the kidney and almost always have a benign clinical course. The typical AML is regarded as a benign lesion, despite the presence of nuclear pleomorphism and mitotic activity. Extension to the surrounding tissue or local recurrence of AML is considered to be multifocal lesions rather than metastasis. A rare variant of atypical AML is described as epithelioid AML with predominant epithelioid smooth muscle cells, which is distinctly different from typical AML. Among them, only sporadic cases have been reported to have malignant clinical courses.
Microscopically, epithelioid AML consists of sheets of polygonal cells with abundant eosinophilic cytoplasm and pleomorphic nuclei. HMB-45 immunoreactivity is a useful tool for the diagnosis of AML. Some reports have hypothesized that AML is a member of the perivascular epithelioid cell tumor family (PEComa) as an explanation of the unique pattern of immunoreactivity that shows the coexpression of muscle-specific actin such as SMA and melanocytic markers such as HMB-45 and melan-A. Positivity for HMB-45 and negativity for most other markers, including cytokeratin and epithelial membrane antigen, are characteristics of PEComa. However, it is still difficult to diagnose epithelioid AML because the mature adipose cells and blood vessels that comprise typical AML are not evident. In our case, IHC staining showed that the tumor cells were HMB-45 positive, but negative for cytokeratin and SMA. Only scanty adipose tissue and abnormal blood vessels characteristic of classic AML were found.

Limited numbers of malignant epithelioid AML had been reported in the literature. A definitive diagnosis is difficult to make preoperatively. Strict criteria in the diagnosis of malignant epithelioid AMLs have not been established, which include HMB-45-positive tumors of an epithelioid nature, and significant pleomorphism, mitotic activity, and tumor necrosis. However, not all cases with cytologic atypia correlate with poor prognosis. The diagnosis of malignancy can be made only by the presence of metastases. The differential diagnosis from renal cell carcinoma in those epithelioid AMLs with cellular atypia and scanty fat tissue is still difficult. Sometimes, the diagnosis of epithelioid AML can only be done after surgery or autopsy. Some researchers have reported that fine needle aspiration cytology with immunostaining is helpful in the diagnosis.

It is difficult to differentiate malignant epithelioid AML from other solid renal tumors such as oncocytoma, renal cell carcinoma, and sarcomatous lesions by imaging study alone. CT or magnetic resonance imaging is most often used to detect foci of fat, whose presence is overwhelmingly characteristic of AML. However, the diagnosis of epithelioid AML is difficult since the mature adipose cells and abnormal blood vessels that comprise typical AML are usually not evident in epithelioid AML. No specific characteristics of malignant epithelioid AML in imaging modalities have been described in the literature.

Our patient had a more rapidly progressive course compared with other reported cases. She died 5 months after presentation due to disseminated metastases. There are no reliable morphologic criteria of malignancy for these tumors, other than the presence of metastasis. Kawaguchi et al reported a case of renal epithelioid AML with malignant transformation and detected p53 mutations, which suggests that p53 mutation might play a role in malignant transformation. According to scattered reports, the disease-specific survival for malignant epithelioid AMLs vary greatly. However, the prognosis in metastatic disease is poor on average. Radical surgical resection seems to yield a beneficial result. If disseminated disease is noted, adjuvant chemotherapy should be given. However, the response is not so good.

In conclusion, epithelioid AML is a rare variant of AML, which behaves aggressively. It is difficult to distinguish from renal cell carcinoma preoperatively. We should keep in mind that careful interpretation of histopathologic and IHC features are necessary to accurately classify the tumor.

References


