Epithelioid Angiomyolipoma of Kidneys

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Abstract

Renal angiomyolipoma (AML) is a benign tumor composed of fat cells, smooth muscle cells, and thick-wall blood vessels. Epithelioid angiomyolipoma (EAML) is a variant of AML and is composed of purely epithelioid cell with melanogenesis markers. Neither adipocytes nor abnormal blood vessels are noted. Pathologically, tumor cells have nuclear atypia and eosinophilic cytoplasm. EAML has a malignant tendency and is difficult to differentiate from renal cell carcinoma (RCC). We report two cases in this study. The patients had no medical and family histories of tumor. The first patient, a 50-year-old woman, had no symptoms and a renal tumor mass was noted incidentally in a healthy examination. Computer tomography of the abdomen showed a heterogeneous mass with slight calcification, and a blunt contour rising from the right kidney was noted. Initially RCC was diagnosed, thus this patient received a nephrectomy. The second patient, a 54-year-old woman, had left flank soreness and body weight loss of about 4 kgs over two months. Abdominal CT and ultrasound revealed a well-defined soft tissue lesion in the left retroperitoneal region and we suspected it from the left kidney. This patient received excision of the retroperitoneal tumor. Positive staining for HMB-45 (Human Melanoma Black-45) was noted in the pathological reports of both cases. EAML was the final diagnosis. Thus, we concluded EAML was required to confirm by pathology.

KEY WORDS: epithelioid angiomyolipoma, renal cell carcinoma, human Melanoma Black-45

Case Presentation

Case 1

A renal mass was found incidentally on a renal ultrasound (Fig. 1a) in a 50-year-old woman in a healthy examination. The medical and family histories were unremarkable. Her urinalysis and renal function were in a normal range. Computerized tomography (CT) scan of the abdomen (Fig. 1b) noted a heterogeneous mass with slight calcification and blunt contour rising from the right kidney. No definite evidence of bone metastasis was demonstrable at Tc-99m MDP. She received a right, radical nephrectomy. The pa-
Two Case Reports of Epithelioid Angiomyolipoma

Case 1

A pathology report showed EAML. This $8 \times 5 \times 3.5$ cm tumor from the renal parenchyma was gray white, solid, and firm. The tumor was composed of spindle cell with positive immunostaining for vimentin, smooth muscle actin, desmin, and HMB-45, but negative for cytokeratin (Fig. 2). No recurrent tumor was noted on follow-up after twenty months.

Case 2

A 54 year-old female women had menopause syndrome with estrogen 0.625 mg used. No systemic disease was noted. She had poor appetite and general malaise for 5 months, left flank soreness, and a 4 kg body weight loss over two months. Initially, she went...
to the Gastrointestinal outpatient department. Her urinalysis and renal function were normal, but an intra-abdominal mass was noted on abdominal ultrasound (Fig. 3). Abdominal CT scan revealed a well-defined soft tissue lesion in the left retroperitoneal region and this lesion was close to the left kidney (Fig. 4). Thus, we suspected it from the left kidney. She received excision of the retroperitoneal tumor. The pathology report revealed perivascular epithelioid cell tumor (PEComa). Microscopically, the tumor was composed of polygonal or spindle cells with eosinophilic or clear cytoplasm. Vascularity was high. The tumor cells showed immunoreactivity for HMB45, smooth muscle actin, and neuron-specific enolase. They were focally stained for CD117 but not stained for chromogranin A, synaptophysin, desmin or S-100 protein. No recurrent tumor was found after follow up of one year.

**Discussion**

Renal angiomyolipoma (AML, also called renal hamartoma) is a benign tumor, which includes two types. The first type, sporadic AML, often occurs in middle-aged women. Most patients are asymptomatic, but some patients have flank pain, hematuria, and a palpable tender renal mass. The second type is inherited AML, which is often associated with tuberous sclerosis. The clinical presentations of inherited AML are similar to that of sporadic AML, but also include neurologic symptoms of tuberous sclerosis: mental retardation, seizure and adenoma sebaceum (3). Additionally, the inherited AML is usually bilateral, small, and multifocal, but the sporadic AML is single, unilateral, and larger in size. Enlarged AML can develop micro-/macro-aneurysm with a risk of rupture. Aneurysm rupture leads to acute bleeding and hypovolemic shock. Risk factors for bleeding are a larger tumor size (≥ 4 cm) and vascular anomalies. Surgical intervention or transcatheter arterial embolization is needed to arrange for this complication. Histologically, AML is composed of thick-wall blood vessels, smooth muscle cells, and mature or immature fat tissue. AML can easily be diagnosed with imaging because of its fat content.

EAML is a variant of angiomyolipoma. Histologically, pure epithelioid cells with positive melanogenesis markers are noted but adipocytes and vascular tissue are not present (1, 2). EAML consists of cells with abundant eosinophilic cytoplasm, and pleomorphic and hyperchromatic nuclei. Intraductal hemorrhage and necrosis are more common in EAML than classic AML (4). Because of deficient fat content, EAML is difficult to diagnose with preoperative radiological studies (5). Additionally EAML has a malignant tendency (6, 7), so differentiating it from other renal neoplasms, such as renal cell carcinoma (RCC), is important (8-10).

Park et al. (11) reported two important clinical clues for EAML: [1] the tumor contains epithelioid cells which stain positive for melanoma markers such as HMB-45, melan-A, smooth muscle cells markers such as HHf-35, SMA and caldesmon, but negative for epithelial markers, [2] tumors without fat content in CT or MRI study.

RCC and AML have similar symptoms, such as flank pain, hematuria, a flank mass. Other symptoms of RCC included weight loss, anemia, fever, hypertension, hypercalcemia, and hepatic dysfunction (Stauffer syndrome). The RCC has a male predominance and its peak incidence is in the sixth and seven decades (12). On CT image, the typical RCC is generally greater than 4 cm in diameter, shows heterogenous density, and can be enhanced with contrast. EAML showed uniform, prolonged contrast enhancement and a higher signal intensity index on double-echo, chemical shift FLASH MRI (5, 13). Hélénon et al. reported the malignant characteristics of renal tumor included intratumoral calcification, large, irregular tumor with invasion to the perirenal or sinus fat.
tissue, large necrotic tumor with small foci of fat, and nonfatty lymph nodes or venous invasion (14).

CT scan in our two cases revealed slight intra-tumor calcification and the tumors were initially diagnosed as RCC. However, the pathology report showed EAML. Therefore, EAML requires pathological diagnosis. At pathology, immunochemical stains are important to discriminate between RCC and EAML. Renal cell carcinoma contains cytokeratins or epithelial membrane antigen, or both. EAML contains HMB-45, and is negative for cytokeratins and epithelial membrane antigen.

In managing AML, renal ultrasound should be arranged at regular intervals for one to three years. If malignancy transformation is noted (such as EAML), the tumor mass becomes larger than 4 cm or the symptoms worsen, CT or MRI should be performed. TAE or nephrectomy is needed for complication of AML. Total nephrectomy is indicated for a nonfunctioning kidney causing hypertension, local tissue invasion, tumor in the renal vein, and very strong evidence of malignancy. Because EAML is in the family of perivascular epithelioid cell tumor, EAML may respond to chemotherapy. Cibas E.S. et al. described a 49-year-old female with renal EAML. The tumor cells had characteristic morphology and immunohistochemical features of both classic and epithelioid AML. Initially, this patient received nephrectomy, however the liver metastasis was noted after 3 years, and the metastatic tumor was identical to epithelioid foci in the resected kidney. Then the patient’s symptoms were relieved after receiving doxorubicin (dose: 60 mg/m²). Thus, Cibas E.S. et al. confirmed EAML was malignant. Ferry et al. reported a case which didn’t respond to dacarbazine, ifosfamide and mesna for two cycles. Lowe et al. showed a patient with ascites receiving doxorubicin, cyclophosphamide, dacarbazine, ifosfamide/sodium α-mercaptoetane-sulfonate and onartopirenone cisplatin. The ascites resolved after treatment. Unfortunately, her symptoms recurred about 1 month later and she died after 3 months (6, 15, 16).

In conclusion, AML is a benign renal tumor, but epithelioid angiomyolipoma, which is a variant of AML, has a malignant tendency. However, the pre-operative diagnosis is difficult for EAML. The imaging characteristics of EAML are similar to RCC in our two cases, thus EAML is still needed to diagnose by pathology.

References