Pathologic Quiz Case

Renal Mass in an Otherwise Healthy Man

Tara C. Rubinas, MD; Robert C. Flanigan, MD; Maria M. Picken, MD, PhD

A healthy 47-year-old man had a 5-year history of microhematuria and was found to have a right renal mass by computed tomography. A radiology report from an outside hospital documented a solid, enhancing mass measuring 4.5 × 4.5 cm at the superior pole of the right kidney (arrow, Figure 1). The patient was referred to our institution and underwent a right partial nephrectomy. The described renal mass was well circumscribed, consisting of tan and red, soft, lobulated tissue with focal areas of hemorrhage. Microscopically, the tumor consisted of pleomorphic spindle and epithelioid cells arranged in no distinct histologic pattern (Figure 2). There were scattered cells with eccentric nuclei, prominent nucleoli, and abundant amphophilic cytoplasm, reminiscent of ganglion cells. Irregular blood vessels with hyalinized vessel walls were also identified (arrow, Figure 3). Although the tumor was submitted in its entirety for microscopic examination, no other tissue elements were seen within the mass. Immunohistochemical stains were performed with appropriate controls. Epithelial markers, including cytokeratin and epithelial membrane antigen, were negative. Mesenchymal markers vimentin and actin (focal), as well as melanocytic markers HMB-45 (Figure 4) and MART-1 were positive. Additional stains including CD34, S100, c-Kit, and estrogen receptor/progesterone receptor were negative.

What is your diagnosis?

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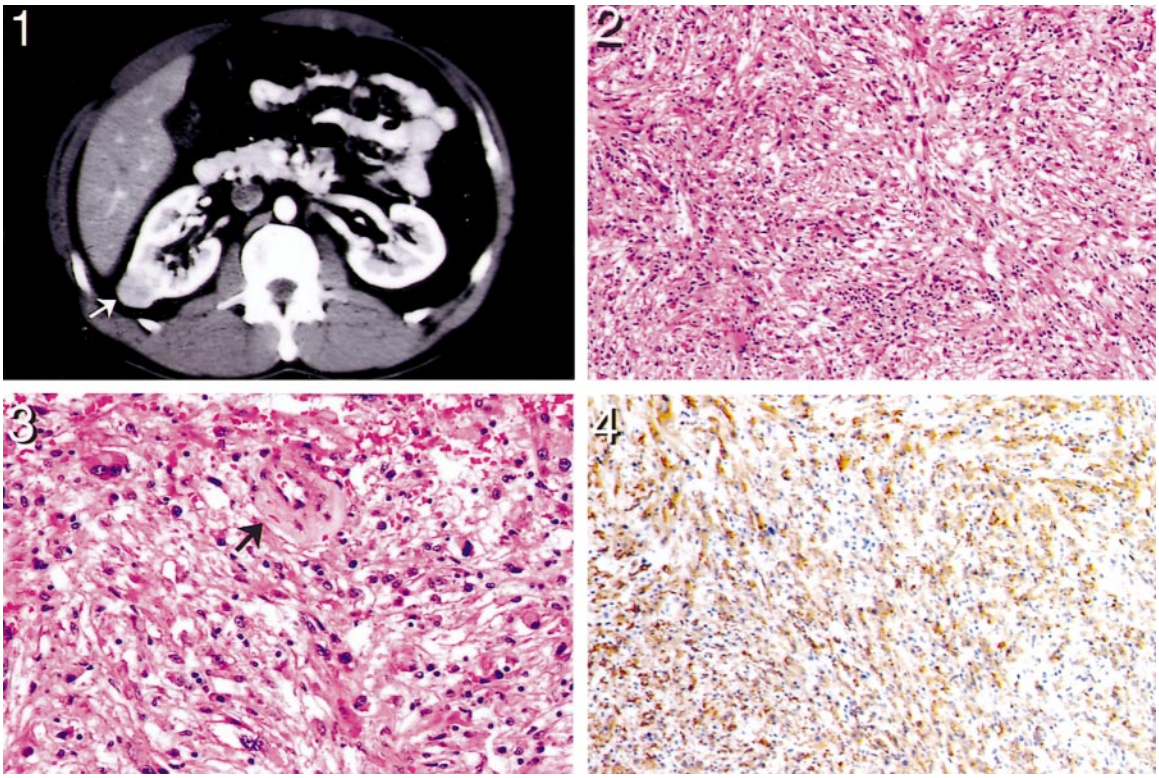
From the Departments of Pathology (Drs Rubinas and Picken) and Urology (Dr Flanigan), Loyola University Medical Center, Maywood, Ill.

Corresponding author: Tara C. Rubinas, MD, Loyola University Medical Center, 2160 S First Ave, EMS Bldg, Room 2233, Maywood, IL 60153 (e-mail: trubina@lumc.edu).



Pathologic Diagnosis: Epithelioid Angiomyolipoma

The classic angiomyolipoma is a triphasic tumor composed of mature adipocytes, irregular blood vessels, and smooth muscle. The smooth muscle component displays the greatest variability. Morphologically, the smooth muscle can be spindled or epithelioid, with either uniform, small nuclei or pleomorphic nuclei with prominent mitoses. Characteristically, the smooth muscle has a perivascular radial arrangement; however, the smooth muscle can be admixed with the background adipose tissue or be so abundant that the diagnosis of leiomyoma is considered. Adipose tissue is abundant and in most cases is also detectable radiologically. In some instances, adipose tissue may be scanty, radiologically not apparent, and difficult to demonstrate microscopically.

Angiomyolipomas have a classic immunohistochemical staining profile, which is often helpful diagnostically. The smooth muscle (spindle and epithelioid) component stains positive with mesenchymal and melanocytic markers, which include vimentin, smooth muscle actin, muscle-specific actin, and HMB-45. Recent literature reports positive staining of angiomyolipomas with CD117 (c-Kit).[1] Epithelial markers are invariably negative in angiomyolipomas.

The epithelioid variant of angiomyolipoma is characterized by a large component of epithelioid cells. The epithelioid cells can display a range in morphology from relatively uniform, polygonal cells with mild nuclear atypia to pleomorphic cells, including multinucleated giant cells. Large mononuclear cells with eccentric nuclei, prominent nucleoli, and amphophilic cytoplasm (so-called ganglion-like cells) have been noted. Mitoses, hemorrhage, and necrosis are variable findings in the epithelioid variant of angiomyolipoma.[2] Diagnosing the epithelioid variant can be challenging, because the adipose component and characteristic vasculature identified in the classic angiomyolipoma are often absent. It is for this reason that many epithelioid angiomyolipomas have been diagnosed as renal cell carcinoma in the past.

Despite displaying features typically used to define malignancy, such as pleomorphism and mitoses, angiomyolipomas are considered benign. Twenty-one cases of angiomyolipoma with extension into the vena cava and 39 cases of spread to regional lymph nodes have been reported.[3] It remains unclear whether the concurrent presence of angiomyolipoma in regional lymph nodes represents metastasis or multicentricity. Currently the only acceptable criterion for malignancy in angiomyolipoma is distant spread.[4]

In 1995, Martignoni et al[5] suggested the concept of renal epithelioid oxyphilic neoplasms. They described 7 tumors composed of bizarre oxyphilic cells with large nuclei and prominent nucleoli, lacking adipose tissue and vasculature. Two of the 7 tumors progressed and resulted in patient death.[5] During the past 8 years the term ''renal epithelioid oxyphilic neoplasms'' has been modified and now refers to a spectrum of tumors, including epithelioid/pleomorphic angiomyolipoma and oncocytoma-like/monomorphic angiomyolipoma.

To date, epithelioid angiomyolipoma is considered a pleomorphic variant of angiomyolipoma that resembles sarcomatoid renal cell carcinoma. There is evidence that this variant poses an increased risk for recurrence and metastasis. In 1998, Pea et al[6] re-evaluated 5 cases originally thought to be epithelial renal tumors in patients diagnosed with tuberous sclerosis complex. Based on positive HMB-45 and negative keratin staining, 3 of the tumors were reclassified as epithelioid angiomyolipoma. Patient follow-up revealed that 2 of these 3 patients developed metastasis and died of their disease. The results from this study suggest that renal epithelial tumors in patients with tuberous sclerosis complex are less common than originally believed.[6]

On the other end of the renal epithelioid oxyphilic neoplasm spectrum is the oncocytoma-like angiomyolipoma. It is monomorphic and without atypical features. To date, no metastases of oncocytoma-like angiomyolipoma have been described. Recently, Martignoni et al[7] reported 2 tumors consisting of tightly arranged, large, eosinophilic cells that lacked an adipose and vascular stroma. The tumors were positive for HMB-45, whereas epithelial markers, vimentin, and desmin were negative. The 2 patients have been free of recurrence for 7 and for 10 years, respectively.[7]

The differential diagnosis of renal tumors with pleomorphic spindle cells includes sarcomatoid and eosinophilic variants of renal cell carcinoma, leiomyosarcoma, and malignant fibrous histiocytoma. The epithelioid angiomyolipoma can be differentiated from these other tumors by its characteristic immunohistochemical staining profile: positive for HMB-45 and mesenchymal markers and negative for epithelial markers.

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