Epithelioid angiomyolipoma with tumor thrombus

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Epithelioid renal angiomyolipoma is a rare malignant variant of angiomyolipoma (AML); the latter being a well-characterized, benign kidney tumor derived from various connective tissue elements. In this case report, we describe a patient with an epithelioid AML and renal vein thrombus.

Key Words: angiomyolipoma, renal vein thrombus

Introduction

Angiomyolipoma (AML) is a well-known, benign mesenchymal neoplasm of the kidneys composed of adipose tissue, smooth muscle-like cells and thick walled vessels. It comprises approximately 1%-6.4% of all renal tumors and is benign in the majority of cases.[1,2] In rare circumstances, malignant variants known as epithelioid AMLs (eAMLs) have been described, characterized by their pathological characteristics of severe epitheliolid atypia and high mitotic count.[3] These eAMLs tend to behave aggressively, however due to their rarity, most of what is known stems from case series and reports. Herein we describe a case of a malignant AML with renal vein involvement. To our knowledge, this is one of less than 20 definitive cases reported in the literature.

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Case report

A 75-year-old male was referred from the emergency department for an episode of painless, gross hematuria. He had no other symptoms other than nocturia once per night. There was no known history of tuberous sclerosis. Laboratory tests were within normal limits, with the exception of mild thrombocytopenia (platelets = 105) and 2+ blood/1+ protein on urine dipstick. Cytology revealed atypical urothelial cells. Subsequent CT urogram demonstrated an ill-defined hypoenhancing lesion within the interpolar and lower pole region of the left kidney. A 13 cm abdominal aortic aneurysm was discovered incidentally, for which a follow up CT angiogram was obtained. This demonstrated heterogeneous appearance of the left renal vein, suspicious for thrombus, Figure 1.

He was referred for hospitalization due to his concurrent vascular findings, and underwent subsequent MRI of the abdomen to better characterize his renal abnormality. This MRI confirmed an infiltrative appearing left renal mass with renal vein

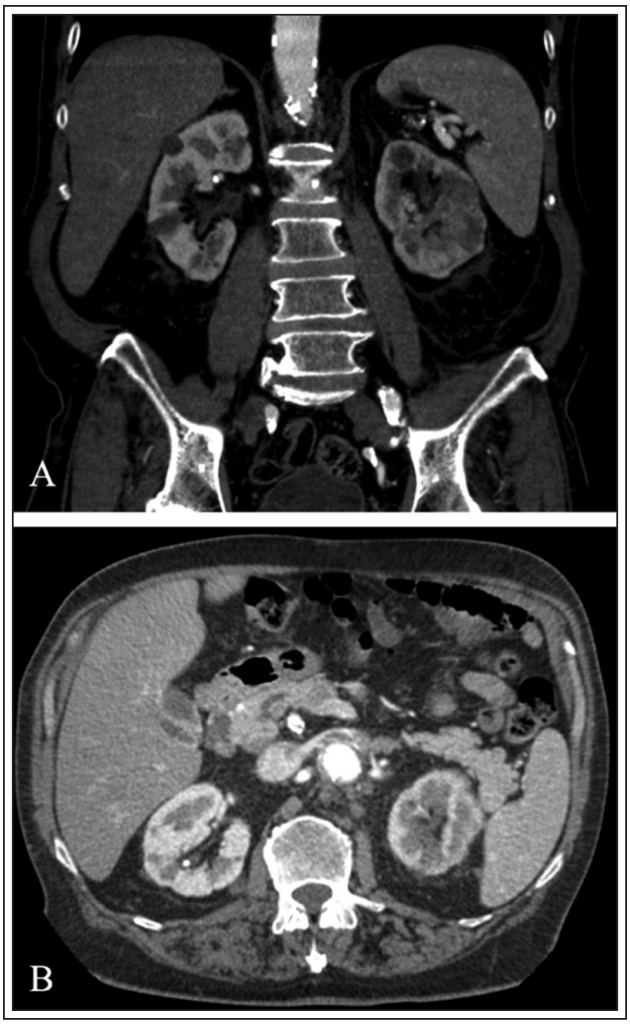

Figure 1. A) CT urogram demonstrating hypoenhancing lesion of left kidney. **B)** CT angiogram with heterogeneous appearance of left vein suggestive of thrombus.

tumor thrombus and multiple enlarged retroperitoneal and peri-aotic lymph nodes, Figure 2. The patient underwent a combined open abdominal aortic aneurysm repair and nephrectomy with lymphadenectomy.

Final pathology revealed a 7.8 cm epithelioid angiomyolipoma with tumor necrosis, 9/10 mitotic figures per HPF, atypical mitosis and sarcomatoid features. Vascular invasion was also present. Stains for Melan A and HMB-45 were positive, while epithelioid stains were negative, confirming the diagnosis, Figure 3. The tumor extended into renal vein, with positive vein margin. No lymph node specimens were positive for malignancy.

The patient was last seen 15 months after surgical resection. He was doing well at the time, without evidence of metastatic disease on MRI.

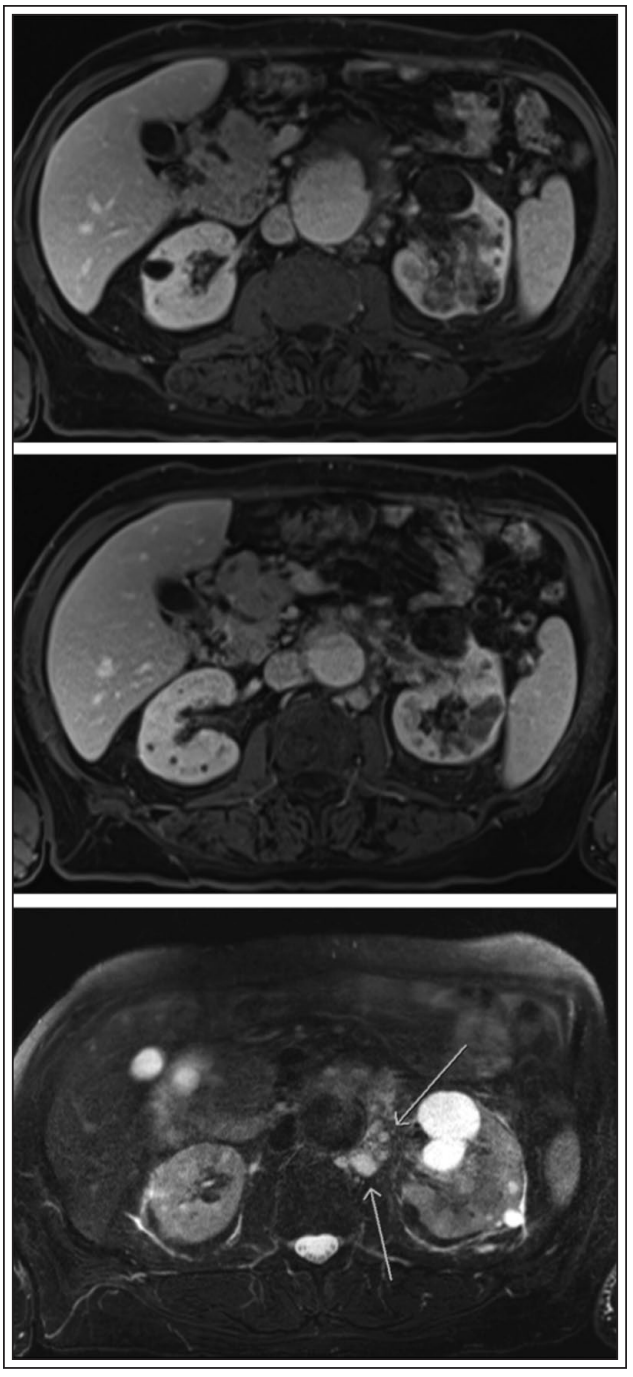

Figure 2. MRI with and without contrast demonstrating infiltrative left renal mass with vein thrombus and peri-aortic lymphadenopathy.

Discussion

Epithelioid angiomyolipomas remain a complicated entity. One third of eAMLs have showed aggressive clinical features, such as local recurrence and distant

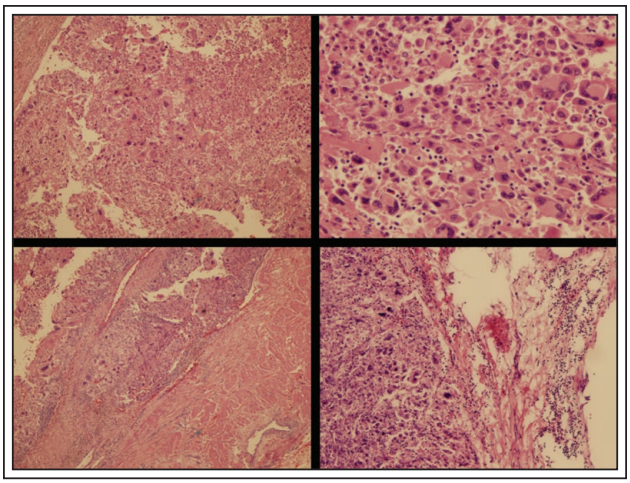

Figure 3. HE staining demonstrating pleomorphic malignant cells with multinucleated giant cells. Nuclei are irregular with irregular nuclear membrane. The giant cells are eosinophilic, occasionally vacuolated, and contain abundant cytoplasm. There are also smaller fusiform and epithelioid cells; both cell types show irregular nuclei with hyperchromatic chromatin and prominent nucleoli. There are abundant mitosis and atypical, bizarre mitotic figures.

metastasis.[3] In a meta-analysis by Faraji et al, 38% of patients developed an unfavorable outcome, defined as distant/lymph node metastasis, local recurrence, adrenal involvement or death over a mean follow up of 23 months (range 3-60 months).[4] In contrast, there have been reports of traditional AMLs with local invasive growth and renal vein thrombus that follow a benign course.[3,5]

Within malignant eAMLs, vascular invasion is rare and extensive literature on the subject is lacking.[6,7] Demographics and outcomes are difficult to quantify due to the lack of details within available reports. It is important to note that the true incidence of this condition is unknown, as only case reports and small series exist. Additionally, there have been reports of eAMLs previously misdiagnosed as various other malignancies.[8] While over half of all eAML cases have been reported with an association with tuberous sclerosis, there have also been reports in non-affected patients.[9]

Histopathologically, eAML may resemble sarcomatoid renal cell carcinoma (RCC) or high grade RCC and is comprised of medium to large epithelioid cells, spindle cells and numerous giant multinucleated cells.[2,9] Tumor cells are noted to be round or polygonal with prominent nucleoli.[9] Immunologically, these tumors are notable for (+) HMB-45 and/or (+) Melan-A and typically (-) cytokeratin/S100 staining.[2,3]

In an attempt to predict clinical outcomes, Brimo et al classified epithelioid AMLs into those with and without atypia. They developed a predictive model of 4 atypical features including 1) ≥ 70% atypical epithelioid cells, 2) ≥ 2 mitotic figures per 10hpf, 3) atypical mitotic figures and 4) necrosis. Using these 3 out of 4 of these criteria, they were able to accurately identify 78% of malignant eAMLs and 100% of benign eAMLs.[3]

No established treatment regimen exists, however surgical resection is considered gold standard for eAMLs due to its aggressive behavior.[2] Case reports utilizing doxorubicin showed some reduction in tumor size, however other case reports have shown negative outcomes with various chemotherapy regimens.[5] Activation of mTOR is thought to be common in non-TSC related eAMLs, and there is evidence that mTOR inhibitors (everolimus, sirolimus and temsirolimus) may have role in metastatic disease and reducing tumor size.[7] □

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