The authors present an interesting case of a very rare renal neoplasm, malignant epithelioid angiomyolipoma (AML), which belongs to a family of mesenchymal tumors known as perivascular epithelioid tumors (PEComas). In the modern era, benign renal AML typically presents incidentally; it is most commonly found on a CT scan obtained for other purposes. A minority of patients present with hematuria, flank pain, or a palpable mass; presentation with unexplained anemia, as in this case, is decidedly unusual. Presentation with life-threatening hematuria, the so-called Wunderlich syndrome, is fortunately very rare.

Radiographic clues include the presence of fat density on CT (any region with HU < -20) or a hypoechoic mass on ultrasonography. MRI with fat-suppressed sequences can also be considered to establish the diagnosis. All renal masses should be carefully evaluated for fat density, particularly in middle-aged women, who are most commonly affected by AML. The overwhelming majority of renal tumors with fat density are benign AMLs, although the differential diagnosis also includes malignant epithelioid versions of AML and liposarcoma. Another uncommon but well described exception is a situation in which fat density is found along with calcification; renal cell carcinoma remains a distinct possibility in such cases. Calcification and cystic degeneration are uncommon in AML. Rapid growth or substantial symptomatology may indicate an increased risk of malignancy, and while not well studied, tumor size may also be associated with malignancy (although some benign AMLs can be impressively large).

In general, most AMLs are managed with observation, particularly if relatively small (< 4.0 cm) and asymptomatic. Larger tumors appear to have an increased risk of bleeding and have traditionally been managed proactively, with either partial nephrectomy or tumor embolization. Symptomatic tumors are managed in a similar manner, with nephron-sparing approaches being preferred, particularly in patients with tuberous sclerosis (TS) who often have bilateral and multifocal disease. Considerable judgment is required in the case of large or rapidly growing tumors, and if malignancy is strongly suspected, a more radical approach should be considered—as in the current case, which required radical nephrectomy.

The diagnosis and classification of epithelioid AMLs has been variably reported in the literature. Epithelioid components are infrequently observed (they are seen in approximately 8% of renal AMLs), with pure epithelioid AMLs accounting for 1%.[1] Although there are no established diagnostic criteria, “epithelioid AML” is applied to renal AMLs that are composed exclusively or predominantly of epithelioid components. An epithelioid AML diagnosis is important for two reasons. First, approximately 25% to 35% of epithelioid AMLs are reported to be malignant, with retroperitoneal recurrence and/or distant metastasis. Several pathologic features are predictive of adverse clinical outcomes, including large size, predominance of atypical epithelioid cells (> 70% of the epithelioid cells), 2 or more mitotic figures in 10 high-power fields, atypical mitosis, and tumor necrosis.[2] However, it should be kept in mind that a minor epithelioid component in an otherwise classical AML does not adversely affect its benign clinical course.[1] The second reason a diagnosis of epithelioid AML is important is that epithelioid AMLs are more likely to be associated with TS than classic AMLs (25% vs 6.2%). In fact, epithelioid AML together with other histological features, such as epithelial cysts within AML and microscopic AML foci in a non-neoplastic kidney, strongly suggest TS.[1]

As outlined previously, a subset of AMLs is found in patients with TS. As with the association between clear-cell renal carcinoma and von Hippel Lindau (VHL) syndrome, the association of epithelioid AML with TS suggests that alterations in the TS complex (TSC) pathway are involved in the pathogenesis of epithelioid AML. TSC has been found to be uniquely associated with activation of the mammalian target of rapamycin (mTOR) pathway.[3-5] Two reports of epithelioid AMLs showed a higher incidence of TSC2 gene deletions than did benign AMLs, as well as elevated levels of phospho-70S6
kinase accompanied by reduced phospho-Akt, indicating an activated mTOR pathway.[3-4] Thus, case reports such as the one presented here have emerged in which mTOR-inhibiting therapy is applied to this rare disorder. Although anecdotal success has been reported as noted, lack of response to such therapy has also been documented.[6] Whether newer mTOR inhibitors such as everolimus (Afinitor) or temsirolimus (Torisel) are active, or whether newer agents that target multiple members of the PI3 kinase/Akt/mTOR pathway could provide additional anti-tumor activity awaits further study.

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References:

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