CASE REPORT

Epithelioid angiomyolipoma: imaging appearances

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ABSTRACT. Epithelioid angiomyolipoma is a recently described rare variant of renal angiomyolipoma. It can occur in patients with or without tuberous sclerosis, and may potentially be malignant. We report the imaging findings from two cases of epithelioid angiomyolipoma: the first in a patient with tuberous sclerosis complex, arising in a horse-shoe kidney and growing into the inferior vena cava and right atrium; the second in a 62-year-old hypertensive man.

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Angiomyolipomas (AMLs) are the most common mesenchymal renal neoplasm, and are now included under the umbrella term “neoplasms of the perivascular epithelioid cells”, also referred to as “PEComas”. These tissues show co-expression of both melanocytic (HMB-45 and/or Melan-A) and smooth muscle (actin and/or desmin) markers [1, 2]. Renal AMLs consist of two distinct histological subtypes: classic triphasic and monotypic epithelioid AML. Classical AMLs are benign and composed of a proliferation of blood vessels, smooth muscle and adipose tissue in variable proportions. Epithelioid AMLs, described in 1998 by Pea et al [3], are composed purely of epithelioid cells arranged in sheets and are characterised by the absence of both adipocytes and abnormal vessels. This rare subtype of AML is potentially malignant and may exhibit aggressive biology, including recurrence and metastasis. Although the imaging features of classical AML are well described in the radiology literature [4–6], there are only a few case reports describing the imaging appearances of primary malignant epithelioid AMLs [7] and their metastatic deposits [8, 9]. Here, we report a case of epithelioid AML in a patient with tuberous sclerosis complex (TSC), arising in a horse-shoe kidney and growing into the inferior vena cava (IVC) and right atrium, and a second case in a 62-year-old hypertensive man.

Case 1

A 33-year-old man with known tuberous sclerosis presented with shortness of breath, pain in the left groin and macroscopic haematuria. Renal tract ultrasound demonstrated a mass arising from the lower pole of the right kidney that did not have typical ultrasonographic

features of an AML. A CT was performed to further characterise this lesion and demonstrated a horseshoe kidney with a thin connecting isthmus and a 9 cm × 6 cm heterogeneous mass in the lower pole (Figure 1). In addition, a tumour thrombus was seen to extend into the right renal vein and along the IVC. An MRI scan confirmed the CT findings of a large mass occupying the mid and lower poles of the right side of a horseshoe kidney. MRI also showed a tumour thrombus protruding into the right atrium and extending further into the right ventricle, with atrial contraction (Figure 2).

The patient underwent surgery for removal of the tumour mass, the right part of the horseshoe kidney and the tumour thrombus from the IVC and right atrium. Pathological assessment demonstrated a 10 cm × 12 cm mass lesion occupying the lower pole and hilum of the right kidney and extending into the right renal vein with a number of 5 mm satellite nodules adjacent to the main tumour. There were no lymph nodes identified in the perinephric fat but tumour was seen to extend into the right renal vein and IVC, with evidence of invasion into the vessel wall. Histology revealed a tumour composed of sheets of round/polygonal epithelioid cells containing abundant granular cytoplasm and many bizarre multinucleated cells (Figure 3). Immunohistochemical staining confirmed the diagnosis of malignant epithelioid AML.

Case 2

A 62-year-old man with hypertension was found to have bilateral renal masses on investigation of his hypertension. Diagnostic CT demonstrated bilateral solid renal lesions, a well-circumscribed right-sided lesion measuring 2.3 cm and a lobulated left-sided lesion measuring 3.2 cm (Figure 4). On subsequent imaging, the right-sided lesion remained stable, whereas the left-sided lesion had increased in size.

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Figure 1. Axial post-contrast CT image demonstrating a heterogeneous mass lesion at the lower pole of the right side of a horseshoe kidney (arrow). A thin isthmus connecting to the left lower pole is also seen (arrowhead).

The patient underwent a partial nephrectomy on the right side, revealing an oncocytoma. A further partial nephrectomy was planned for the left side almost 3 months after the initial imaging. However, during the operation, the lesion was found to be more extensive

than originally anticipated, and a full nephrectomy was performed. Pathological assessment of the sample demonstrated a 7 cm × 6 cm exophytic mass lesion at the interpolar region of the left kidney, with no evidence of extension into the left renal vein. There was, however, extension of disease into the perinephric fat and extramural tumoural emboli. Histological analysis revealed tumour cells with abundant eosinophilic cytoplasm, vesicular nuclei and prominent nucleoli (appearances similar to those in Figure 3). Immunohistochemistry confirmed the diagnosis of epithelioid AML with focal positivity for HMB45 and Melan A.

Discussion

TSC is an autosomal dominant genetic disease characterised clinically by mental retardation and seizures that manifest in infancy or early childhood. Renal pathology is encountered in approximately 60% of these patients [10] and includes renal cysts, AMLs, oncocytomas and renal cell carcinoma (RCC).

Renal AMLs can occur sporadically or in association with TSC [11]. 20% of AMLs are associated with TSC, whereas 50% of patients with TSC have AMLs, which tend to be multiple and bilateral [12, 13].

(a)

(b)

Figure 2. (a) Coronal and (b) sagittal true-FISP (true fast imaging with steady state precession) MR images. Tumour occupies the lower pole and hilum of the right side of the horseshoe kidney. A tumour thrombus is seen to extend into the right renal vein, inferior vena cava and right atrium (white arrowheads). Gated cardiac MRI shows the mobile tumour thrombus extending into the right ventricle with atrial contraction (black arrow).

Figure 3. Malignant epithelioid angiomyolipoma. Photomicrograph (magnification $\times 40$; haematoxylin and eosin stain) showing sheets of epithelioid cells with abundant granular cytoplasm and bizarre multinucleated cells, which characterise this tumour.

A subgroup of epithelioid AMLs can be aggressive and are termed “malignant epithelioid AMLs”. Histologically, they can closely resemble high-grade or sarcomatous RCC, which has resulted in misdiagnosis [3, 14]. Pea et al [3] reassessed the histology of five tumours previously reported as RCC and found that three showed a phenotype compatible with the epithelioid

Figure 4. Axial post-contrast CT image demonstrating a lobulated exophytic mass arising from the interpolar region of the left kidney (black arrow).

variant of AML and that two of these patients had subsequently died from metastatic disease (only one of the five cases was confirmed to be a true RCC on review). Patients with TSC have often been considered at a higher risk of developing RCC; it has been postulated that this increased risk results from the fact that epithelioid AML has previously been misinterpreted as a carcinoma. The percentage of cases of renal malignancy in patients with tuberous sclerosis that is, in fact, due to epithelioid AML is not known. Although some, or even many, of the reported cases of RCC in TSC patients are in fact epithelioid AML, it is unlikely that all such cases are epithelioid AML. In some cases, RCC can also arise in the simple renal cysts seen in TSC.

Epithelioid AML can recur locally, metastasise [8, 15] and cause death [16]. It is difficult to diagnose malignancy in epithelioid AML based on histology alone, as not all cases with cytological atypia are malignant. However, the criteria for malignancy are still being developed [5].

Classical AMLs, with their fat component, are relatively easy to characterise on imaging, and unnecessary surgery can be avoided [4, 17]. Failure to detect intratumoural fat in a renal mass in patients with TSC can be caused by [7]:

- Minimal fat AML, which is predominantly composed of smooth muscle cells.
- Intratumoural haemorrhage, which obscures the normal fat attenuation/signal.
- The mass representing more suspicious pathology, such as a RCC or malignant epithelioid AML.

Epithelioid AMLs, with their high cellular content and lack of fat, cause diagnostic difficulty. They appear as hyperattenuating masses with variable enhancement on CT (as in our patient). On MRI, they also demonstrate a high cellular content with no evidence of fat — features that should raise a suspicion of RCC. Consideration of this diagnosis is important because non-cystic renal masses in patients with TSC may be managed without surgical resection in an attempt to preserve normal renal parenchyma in a patient group who typically have multiple bilateral tumours.

In summary, epithelioid AMLs are a recently described rare variant of renal AML that may occur in patients with or without TSC. These are potentially malignant tumours that have imaging appearances similar to RCC. In a patient with TSC, any renal mass that is clearly not a simple renal cyst, does not contain fat or does not have the characteristic features of a smooth muscle-predominant AML should be considered suspicious for malignancy.

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