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Case report

Renal epithelioid angiomyolipoma: 2 Cases report



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Abstract

Introduction: The 2004 World Health Organization Classification of Renal Neoplasms defined epithelioid angiomyolipoma as a potentially malignant mesenchymal neoplasm, characterized by a proliferation of predominantly epithelioid cells with approximately one third of patients experiencing metastases and one half of them having a history of tuberous sclerosis complex.

Observations: We report two cases of renal epithelioid angiomyolipoma diagnosed at our institution in order to analyze their clinical behaviour and histopathological features, and insist on diagnostic pitfalls.

Conclusion: Renal tumours with certain unusual features should be investigated immunohistochemically to exclude the possibility of epithelioid angiomyolipoma. These tumours are more likely to have an aggressive behaviour when they show more morphologic features predicting malignancy.

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Introduction

Classic renal angiomyolipoma (AML) is a benign mesenchymal tumour containing fat, smooth-muscle cells and thick-walled blood-vessels. The epithelioid morphologic variant is defined by the 2004 World Health Organization (WHO) Classification of Renal Neoplasms as a potentially malignant neoplasm, characterized by a proliferation of predominantly epithelioid cells with approximately one third of patients experiencing metastases [1]. Epithelioid-AML (EAML) is included in the family of perivascular epithelioid cell tumour (PECT) which is associated genetically with tuberous scler-

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rosis complex (TSC) [2]. We herein present two cases of renal EAML.

Case reports

First case

A 28-year-old-woman having a history of TSC and bilateral dull lumbar pain was hospitalized with haematuria and acute left lumbar pain. Physical examination revealed bilateral lumbar masses. The woman then presented internal bleeding and acute severe anaemia (5 g/dl) resistant to reanimation and transfusion. Computed tomography (CT) showed bilateral renal heterogeneous masses. The biggest mass was involving nearly the whole left kidney (Fig. 1a). It was complicated by an intra tumoral and retroperitoneal haemorrhage. A radical left nephrectomy was performed immediately. Macroscopically, the tumour was yellowish non-encapsulated (Fig. 1b) measuring 16 cm × 9 cm × 7 cm and comprising areas of haemorrhage with a ruptured subcapsular haematoma. Histopathologically, the tumour was composed of epithelioid cells in sheet pattern (>80% of tumour size). These cells had often enlarged pleomorphic nuclei and abundant eosinophilic cytoplasm. Scattered multinucleated cells and mitotic figures were frequently seen

(Fig. 1c and d). A perinephric fat infiltration was identified but neither necrosis nor renal vein invasion were seen. Immunohistochemically, Human Melanoma Black 45 (HMB45) was diffusely immuno-positive. The diagnosis of EAML was made. After a 4-month follow-up, no metastases were detected. A right renal AML embolization was planned subsequently.

Second case

A 56-year-old-man, known carrying a right renal AML diagnosed on ultrasonography 12 years ago, underwent evaluation for recent right dull lumbar pain. Physical examination revealed a right lumbar mass. A control ultrasonography showed an increased-size mid-polar hyperechogenous mass concomitant with the genesis of a new low-polar heterogeneous mass both involving the right kidney. CT concluded to a suspicious low-polar tumour (Fig. 2a). No evidence of TSC or tumours in other locations was found. A radical right nephrectomy was performed. Macroscopically, two encapsulated tumours were identified. The first was brown measuring 7 cm × 6 cm × 5 cm, while the second was yellowish measuring 5 cm × 5 cm × 4.5 cm (Fig. 2b). Histopathologically, the first tumour was a classic AML whereas the second showed similar histologic findings (Fig. 2c) as the first case's tumour except necro-

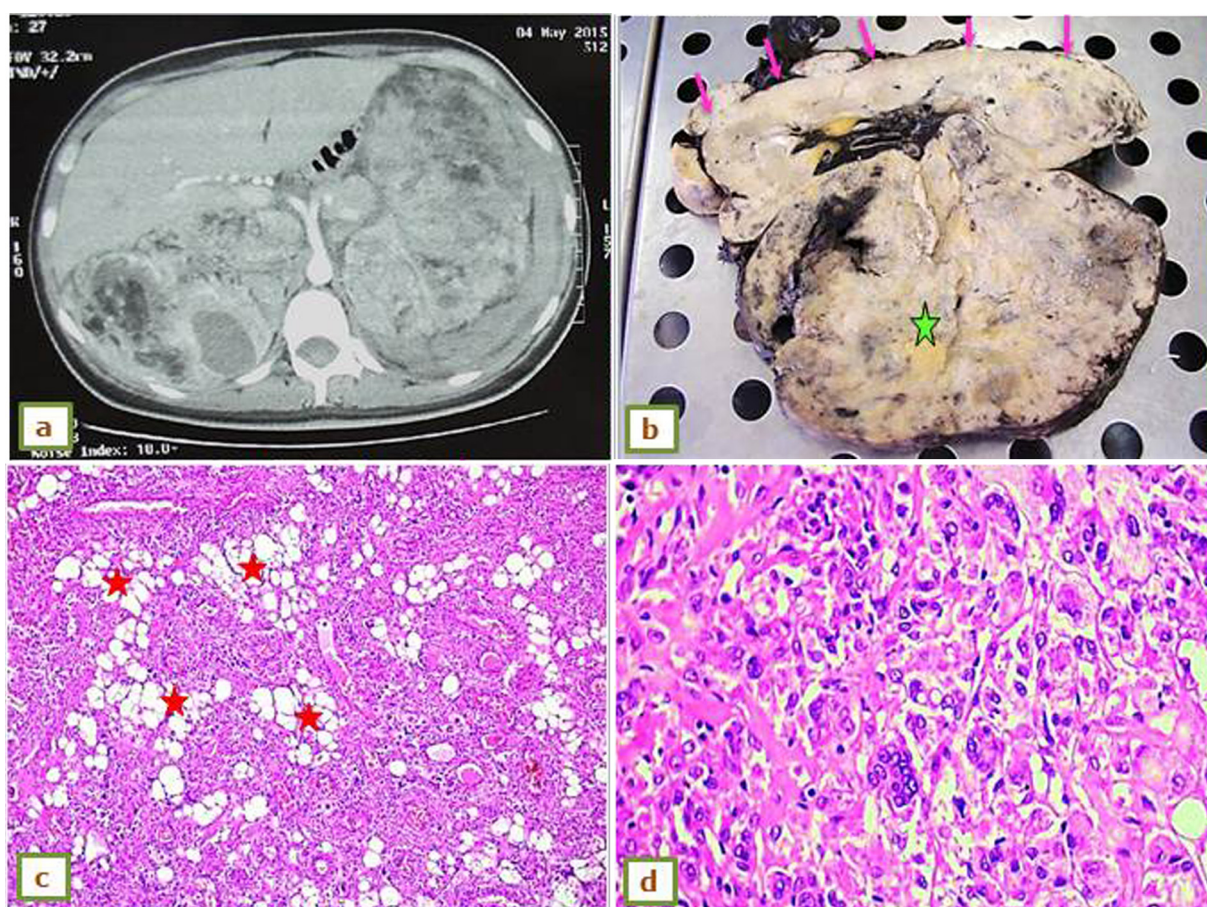


Figure 1 (case 1) (a) CT scan: multiple heterogeneous masses of both kidneys with an intra-tumoral haemorrhage in the left kidney extending to the retro peritoneum (b) Gross appearance in EAML: a lobulated white yellowish tumour (green star) with areas of haemorrhage. The tumour pushes to the periphery the normal renal parenchyma (pink arrows). (c) Histologic features of EAML: mature fat (red stars) and smooth muscle cells (haematoxylin and eosin, original magnification 20×). (d) Histologic features of EAML: Epithelioid cells with abundant eosinophilic cytoplasm (haematoxylin and eosin, original magnification 40×).

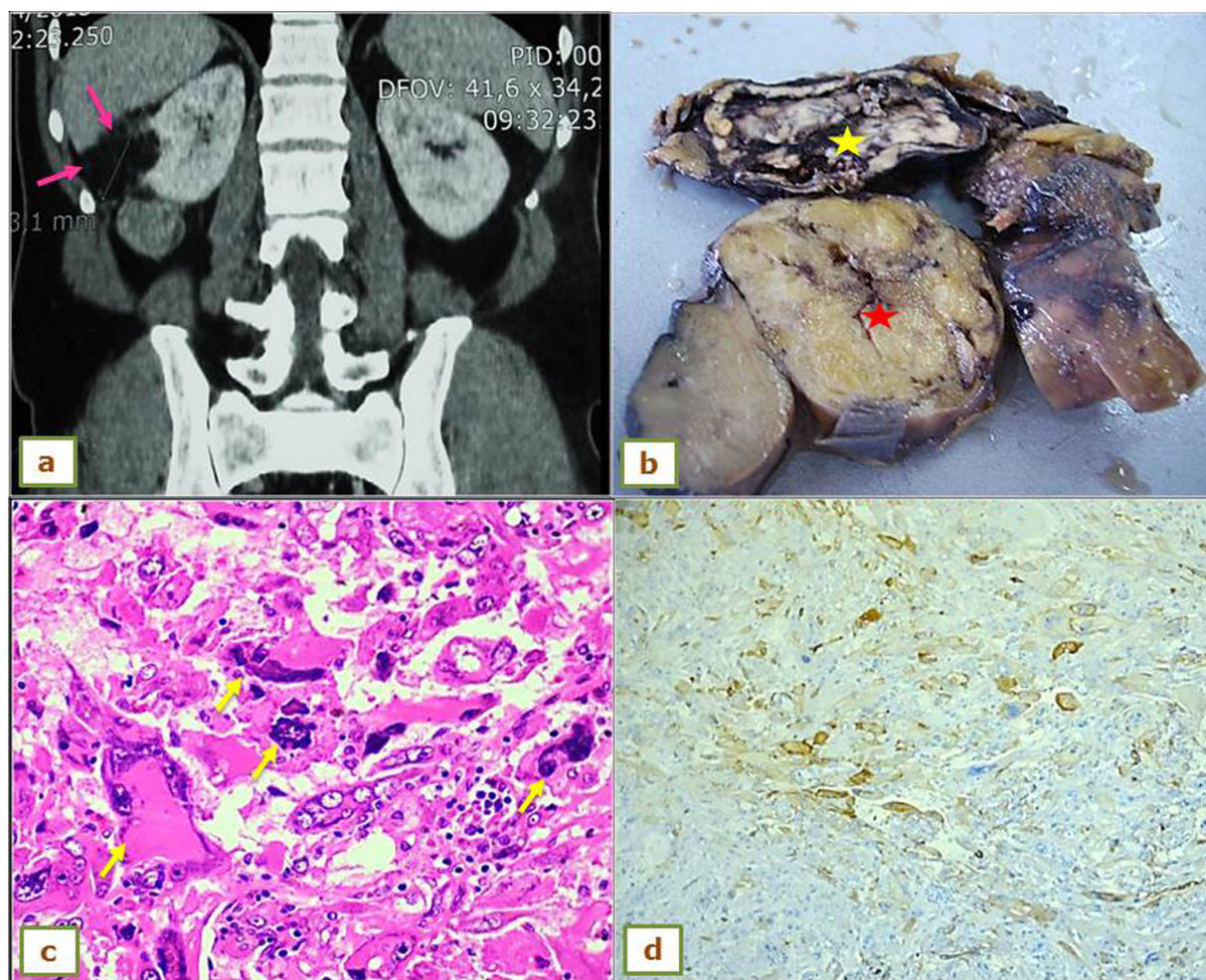


Figure 2 (case 2) (a) CT scan: an hypodense mass of 5.3 cm in the lower pole of the right kidney (pink arrows). (b) Gross appearance: the first tumour (yellow star): a brown lobulated encapsulated mass, the second tumour (red star): a white yellowish mass (c) Histologic findings in EAML (second tumour): Epithelioid cells with enlarged pleomorphic vesicular nuclei and abundant eosinophilic cytoplasm; scattered multinucleated tumour cells (yellow arrows) were often seen (haematoxylin and eosin, original magnification 40 \times). (d) Immunostain for HMB45 in renal tumour cells (original magnification 40 \times).

sis which was observed in this case. Immunohistochemically, both tumours showed HMB45 diffuse positivity (Fig. 2d). Two AMLs were diagnosed: a classic one and an epithelioid one. The patient was lost of sight within 6-month follow-up with no metastasis objectified.

Discussion

PECT represent a family of tumours including classic AML and clear epithelioid cell tumours reported under a variety of names such as EAML and clear cell sugar tumour [3]. The WHO has recently introduced this unifying term of “PECT” and defined it as “a mesenchymal tumour composed of histologically and immunohistochemically distinctive perivascular epithelioid cells [1].”

There is a strong association between PECT and genetic alterations of TSC, an autosomal dominant genetic disease due to loss of heterozygosity in the TSC1 region (9q34) or TSC2 region (16p) [2,3]. In fact, nearly one half of patients diagnosed with AML have a history of tuberous sclerosis complex [1,4]. Classic AMLs are often

discovered incidentally on imaging due to the presence of fat in them. Owing to their indolent behaviour, they are rarely resected or embolized until they reach a size where the possibility of haemorrhage is significant as happened in our first case.

Classic AMLs represent 1% of surgically removed renal tumours [1], while EAMLs are extremely rare accounting for 4.6% of consecutively resected AMLs [5].

EAML’s mean age is 40 years with an even sex predisposition. No specific features of EAML in terms of clinical manifestations or imaging modalities comparing to classic AML have been found.

Grossly, these tumours are solid often haemorrhagic. Microscopically, EAML had two architectural patterns: AML with carcinoma like growth pattern characterized by large cells arranged in cohesive nests, and AML with epithelioid spindled cells organized in diffuse growth pattern [2]. In 2004 WHO considered AML as epithelioid when epithelial morphology is predominant [1]. In our two cases, the epithelioid component represents more than 80% of the tumour size. Histologically, EAML may be confounded with renal cell car-

cinoma or melanoma, particularly when epithelioid component and nuclear atypia are evident.

AML shows strong immunostaining by melanocytic marker (HMB45, melan-A) and smooth muscle actin (SMA) but neither epithelial markers nor S-100 protein were immunopositive.

Radical tumour resection could be important in the treatment. Adjuvant radiochemotherapy may be beneficial, but their effects need further investigation.

Recurrence was seen in around 17% of patients and metastasis in about 30% of patients [6]. The commonest metastatic sites were lymph nodes, liver, lung and peritoneum. The meantime to metastases in patients developing metastatic disease during follow-up is 17–31 months [2]. The prognostic factors predicting malignancy in EAML are not well-defined. They include associated TSC, tumour size (>7.7 cm), extrarenal extension or renal vein invasion, carcinoma like growth pattern, tumour necrosis, percentage of atypical epithelioid cells $\geq 70\%$, >2 mitotic figures/10HPF and atypical mitoses [5,7–9]. The frequency of these adverse prognostic parameters was correlated with disease progression. In our two cases, none showed evidence of malignant clinical behaviour at the available follow-up period although they contained, each, six of the above-mentioned criteria; therefore, the diagnosis of malignancy should be made only on the basis of the presence of metastases. P53 gene mutation, detected in EAML but not classic AML, is suggested to have a role in the malignant nature of EAML [1].

Conclusion

EAMLs have significant overlap in morphology with more commonly occurring renal neoplasms. Appropriate diagnosis requires adequate immuno-staining with melanocytic makers. EAML can behave aggressively and even metastasize. Disease progression seems to be correlated with the number of poor prognosis's parameters encountered. Surgical resection alone may not be sufficient and adjuvant therapy may be needed. A multimodality treatment approach needs to be explored in order to settle a standardized therapy for this newly recognized variant of AML.

Authors' contribution

Ons Boudaouara designed and wrote the article.

Rim Kallel made its critical revision.

Walid Smaoui collected and analysed clinical and radiological data.

Slim Charfi interpreted anatomopathological data.

Saadi Makni furnished some pathological illustrations.

Mohamed Nabil Mhiri contributed to the interpretation of clinical data.

Hela Mnif provided the article conception and other pathological illustrations.

Tahya Sellami Boudawara intervened in the drafting of the article.

Conflict of interest

None declared.

Source of funding

None declared.

Ethical approval

Not applicable.

Patients consent

Written informed consent was obtained from the two patients for publication of this case report and any accompanying images.

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