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Spontaneous rupture and hemorrhage of renal epithelioid angiomyolipoma misdiagnosed to renal carcinoma: a case report

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Abstract

Background Renal epithelioid angiomyolipoma is a rare and unique subtype of classic angiomyolipoma, characterized by the presence of epithelioid cells. It often presents with nonspecific symptoms and can be easily misdiagnosed due to its similarity to renal cell carcinoma and classic angiomyolipoma in clinical and radiological features. This case report is significant for its demonstration of the challenges in diagnosing epithelioid angiomyolipoma and its emphasis on the importance of accurate differentiation from renal cell carcinoma and classic angiomyolipoma.

Case presentation A 58-year-old Asian female presented with sudden left flank pain and was initially diagnosed with a malignant renal tumor based on imaging studies. She underwent laparoscopic radical nephrectomy, and postoperative histopathology confirmed the diagnosis of epithelioid angiomyolipoma. The patient recovered well and is currently in good health with regular follow-ups. This case highlights the diagnostic challenges, with a focus on the clinical, radiological, and histopathological features that eventually led to the identification of epithelioid angiomyolipoma.

Conclusions Epithelioid angiomyolipoma is easily misdiagnosed in clinical work. When dealing with these patients, it is necessary to make a comprehensive diagnosis based on clinical symptoms, imaging manifestations, and pathological characteristics.

Keywords EAML, CAML, Diagnosis, Pathology

Introduction

Renal epithelioid angiomyolipoma (EAML) is a special subtype of classic angiomyolipoma (CAML), which comprises vascular (angio-), smooth muscle (-myo-), and adipose (-lipoma) components [1]. Unlike the classical form, EAML is predominantly characterized by the presence of epithelioid cells [2].

EAML exhibits nonspecific symptoms, including abdominal pain, abdominal mass, and hematuria, or may be asymptomatic [3]. Imaging studies typically demonstrate characteristic features due to the presence of adipose tissue. However, a few atypical renal hamartomas might lack detectable adipose components on imaging, leading to misdiagnosis as RCC or CAML. Such EAML presentations often manifest as renal parenchymal masses. Due to the lack of effective diagnostic and differentiation criteria, precise diagnosis of these cases poses a significant challenge for urological clinicians [4].

In this particular patient, we mistakenly diagnosed a ruptured and bleeding EAML as a malignant renal tumor,

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resulting in radical nephrectomy. Subsequent postoperative histopathology confirmed the infiltrative growth pattern and low-grade malignant nature of the EAML.

This case report aims to emphasize the clinical, radiological, and histopathological features contributing to EAML and differentiate it from RCC and CAML. Furthermore, we summarize the current worldwide scholars' comprehensive diagnostic approaches (including imaging modalities and histological assessments) to guide appropriate management decisions and optimize patient outcomes.

Case report

The patient, a 58-year-old Asian female, was admitted due to "sudden left flank pain for one day." The patient experienced sudden and severe pain after squatting, which persisted and was unrelieved. There was no fever, hematuria, diarrhea, nausea, or vomiting. The patient had not had similar symptoms before. Then, the patient sought medical attention at a local hospital, where an abdominal computed tomography (CT) revealed a nodular lesion in the lower pole of the left kidney with a high-density subcapsular shadow, suggesting malignant renal tumor with bleeding and left renal vein tumor thrombus formation. The local hospital provided symptomatic treatment including antispasmodic and analgesic treatments. The patient's symptoms were better than before. Subsequently, the patient was referred to our hospital for further treatment. The patient was transported to our hospital on the same day with the initial diagnosis of "'left malignant renal tumor." Then she was immediately admitted for management. Physical examination indicated stable vital signs, with no abnormalities in the cardiovascular and respiratory systems. Abdominal and limb examinations showed no peculiarities, but there was positive tenderness in the left renal area. Relevant preoperative investigations showed the following results. Hematology revealed anemia with normal white blood cell count and elevated hypersensitive C-reactive protein. Biochemistry showed reduced potassium, calcium, total protein, and albumin levels, elevated homocysteine and serum amyloid A protein levels, and increased sialic acid. CT scan revealed an occupying lesion in the lower pole of the left kidney, possibly renal cancer, left renal subcapsular hematoma, right renal cyst, and normal renal artery on computed tomography angiography (CTA) (Fig. 1). Magnetic resonance imaging (MRI) showed a lesion in the lower pole of the left kidney with heterogeneous signal, possibly renal cancer with bleeding (Fig. 2). Electron capture tomography (ECT) demonstrated reduced left kidney function and normal right kidney function. Combined with the patient's symptoms and auxiliary examination results, all evidence points to the patient's diagnosis of renal tumor. The final diagnosis was a "left malignant renal tumor with bleeding and left renal vein tumor thrombus formation and left renal dysfunction."

After completing preoperative preparations, the patient underwent laparoscopic radical nephrectomy for renal cancer, with a smooth surgical procedure. We dissected the resected kidney after surgery and clearly saw the tumor and perirenal hemorrhage (Fig. 3). Postoperative pathology (Fig. 4) revealed "renal epithelioid angiomyolipoma" on the lower pole of the left kidney, presenting as a mass measuring 2.5 × 2.5×2 cm. Microscopic examination showed tumor cells with pleomorphic and spindle shapes, displaying cellular atypia, occasional multinucleated giant cells, rare mitotic figures, and acidophilic cytoplasm, and arranged in a sheet-like pattern. The

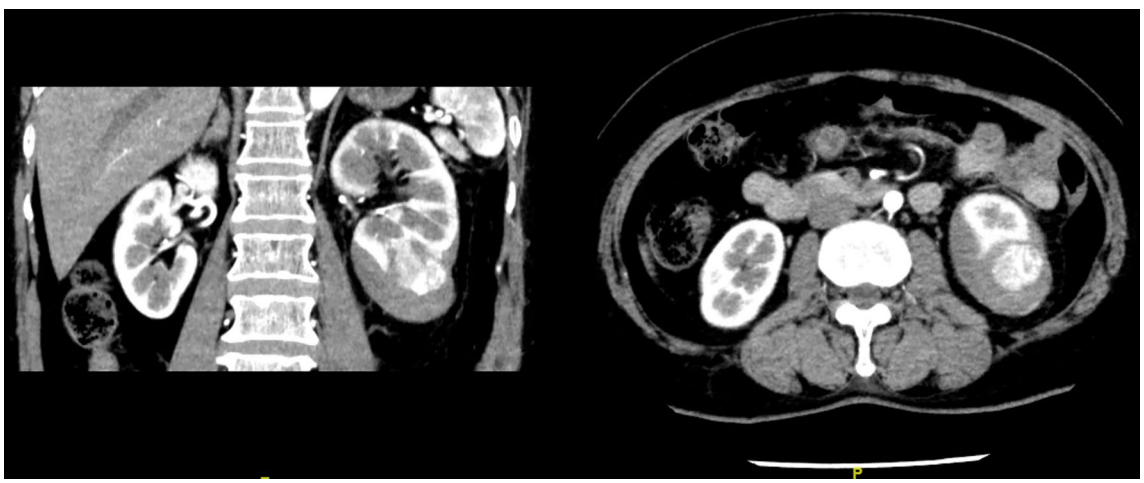

Fig. 1 Computed tomography angiography findings of the epithelioid angiomyolipoma

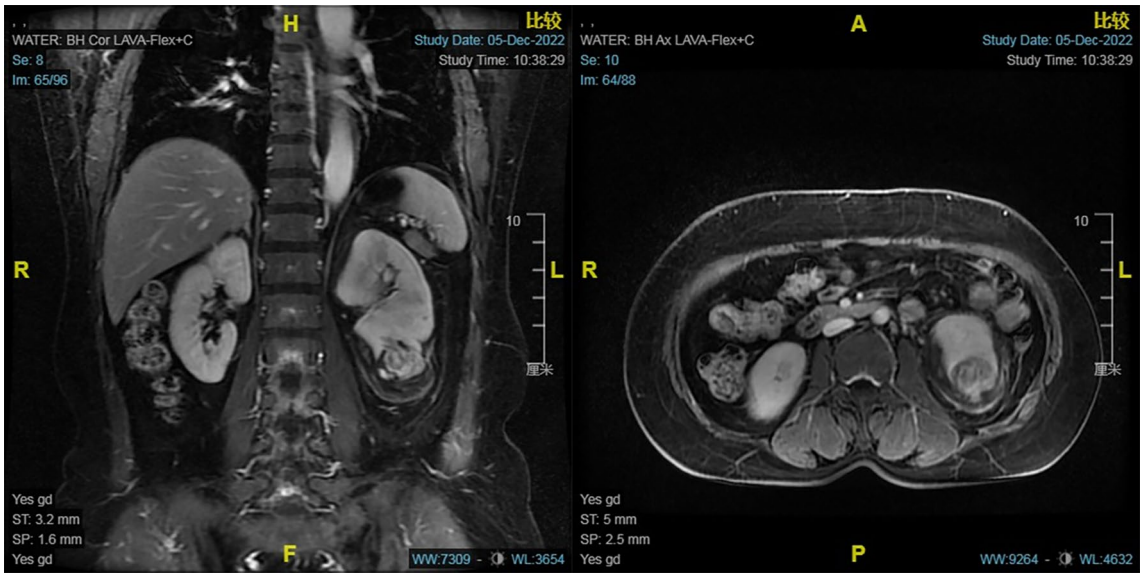

Fig. 2 Magnetic resonance imaging (MRI) findings of the epithelioid angiomyolipoma

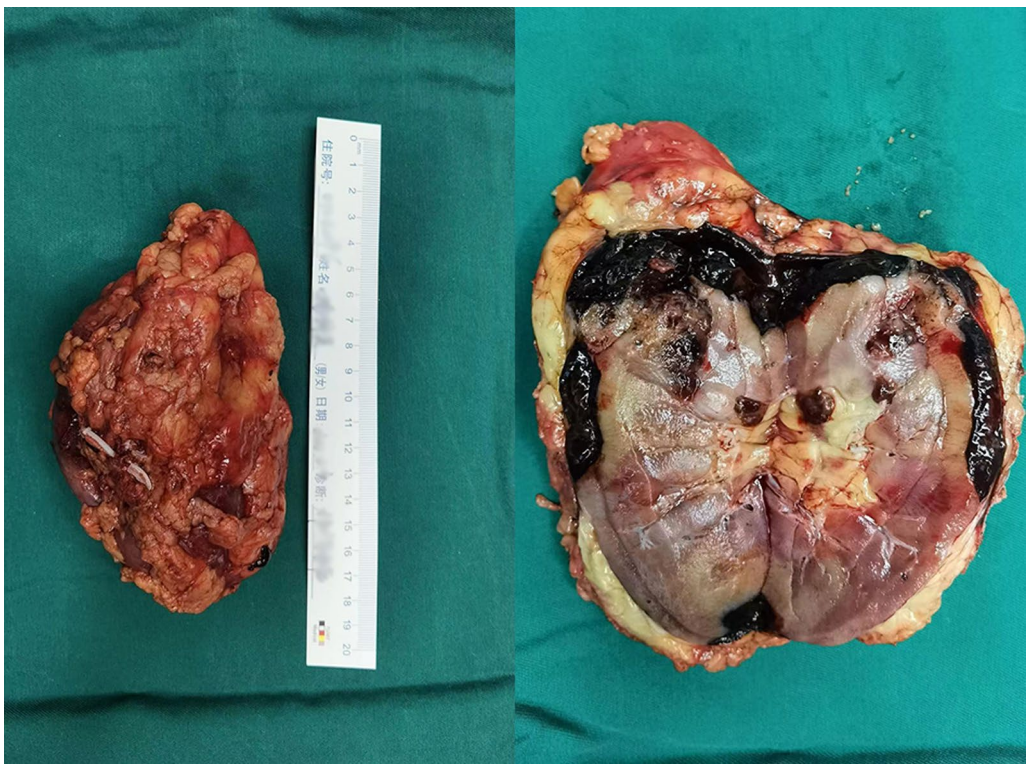

Fig. 3 Postoperative specimen

tumor exhibited infiltrative growth with intravascular tumor thrombi, negative resection margins on the renal hilum and the ureter. Immunohistochemistry staining results indicated Ki-67 (5%+), P53 (occasional+), CK7 (−), CD10 (−), P504S (−), CK34βE12 (−), RCC (−), TFE3 (−), CAIX (−), Vim (+), CD34 (endothelial+), E-cad (+), EMA (−), PAX-8 (−), HMB-45 (+), MelanA (+), CAM5.2 (−), and D2-40 (lymphatic vessels+). After surgery, the patient experienced no complications during the postoperative recovery period and was discharged 1 week after

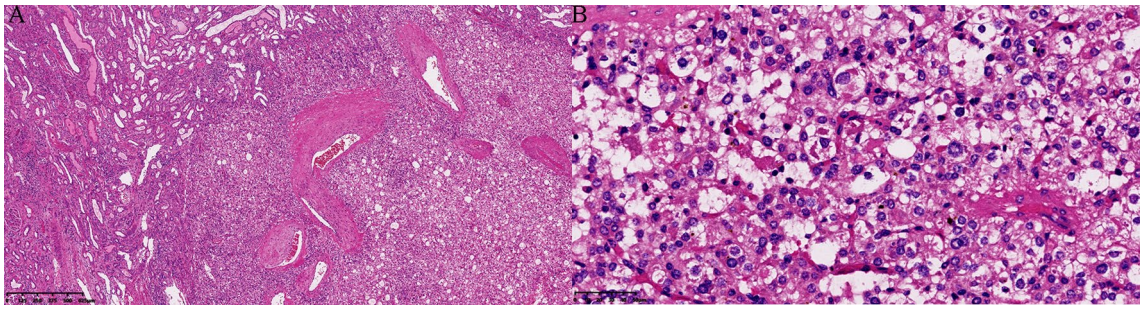

Fig. 4 Histopathological image of the epithelioid angiomyolipoma. **A** ×4, **B** ×40

surgery. The patient is currently in good health and is regularly followed up with the outpatient department of our hospital.

Discussion

EAML is a unique subtype of angiomyolipoma, characterized by the presence of various cytoplasm-rich, acidophilic epithelioid cells, in addition to mature adipose cells, thick-walled vessels, and smooth muscle-like spindle cells [5]. EAML is a rare renal epithelial tumor, accounting for less than 1% of all renal epithelial tumors and approximately 7.7% of renal angiomyolipoma [6]. Previous literature reports indicate that EAML can exhibit invasive growth, recurrence, metastasis and intravascular tumor thrombi [7], rendering it a potentially malignant tumor with a metastatic rate of about one-third [8]. In our case, as a potentially malignant tumor, EAML demonstrated its invasiveness into surrounding tissues. When the patient experienced severe lumbar pain, CT results showed a local filling defect in the renal vein, indicating vascular invasion by the tumor. In recent years, due to the lack of typical clinical and radiological features, preoperative accurate diagnosis of EAML is challenging, leading to misdiagnosis and missed diagnosis. Currently, the definitive diagnosis mainly relies on postoperative histopathological examination. Although advances have been made in pathological diagnosis techniques, comprehensive understanding of EAML among clinical practitioners remains lacking. Therefore, we report this patient, which is the first case report on the whole network in which a ruptured and bleeding renal epithelioid angiomyolipoma was misdiagnosed as kidney cancer. We published our diagnosis and treatment process to remind colleagues to pay attention to such cases. Our case report, combined with other studies, will aid in comprehensively summarizing the diagnosis and treatment norms of EAML.

Based on our patient and extensive literature review, we summarize the clinical characteristics of EAML. In the early stages of the disease, EAML often lacks specific clinical symptoms and is usually incidentally detected during physical examinations or follow-up of patients with tuberous sclerosis complex (TSC) [9]. As the tumor enlarges, patients may experience localized discomfort due to traction on the renal capsule, presenting clinical symptoms such as lumbar pain, abdominal pain, and abdominal mass. Further progression of the tumor, involving adjacent blood vessels or causing ruptured hemorrhage, can lead to sudden severe pain and hematuria [10]. When a patient with a renal mass experiences acute bleeding, clinical practitioners should consider EAML in the diagnostic process.

The imaging features of EAML often resemble those of RCC or CAML. The lack or minimal presence of adipose tissue on imaging is one of the important reasons for misdiagnosis [11]. Previous studies have shown that EAML typically appears as a high-density solid lesion on CT, and its extrarenal growth often leads to changes in the renal contour. Most lesions have a smooth interface with the renal parenchyma, forming the "cup sign" or "split sign" [12]. The patient's CT coronal image showed a clear "cup sign." In MRI images, the solid components of EAML usually present as low signals on T2-weighted images [13]. One-third of EAML cases may also exhibit malignant behavior on MRI, such as local invasion and distant metastasis. The renal capsule, perirenal fat, and renal vein are the most susceptible tissues to invasion [14]. The identification of such features on MRI should prompt consideration of EAML in the diagnosis. In recent years, deep learning has introduced many new methods to address various computer vision problems [15]. Many medical imaging problems have also adopted deep neural network structures, achieving excellent results [16]. From our perspective, collecting sufficient EAML imaging data and using residual neural networks and dilated convolutions for network training and local prediction may enable the discovery of new features for precise EAML diagnosis that cannot be discerned by the naked eye.

Due to the lack of specific clinical manifestations and radiological features, EAML is often prone to misdiagnosis in clinical practice. Histopathological examination of tumor tissues remains an essential means for confirming the diagnosis. On cytological morphology, Caliò summarized two presentations of EAML under the microscope. One of the presentations is EAML consisting of atypical large acidophilic cells with prominent nuclei, exhibiting a cancer-like appearance. The intranuclear inclusions are often present (neuroblastoma-like appearance) and arranged together. Multinucleated giant cells can resemble the atypical mononuclear cells in the background and may display areas of necrosis. The other presentation comprises epithelioid and enlarged spindle cells, arranged diffusely. Compared with cancerous tumors, these tumors show uniform growth patterns, less cellular atypia, clearer cytoplasm, and intranuclear inclusions [17]. Additionally, the mesenchymal component of EAML primarily exhibits large acidophilic pleomorphic cells with prominent nucleoli, while the CAML show more bland spindled cells. The presence of atypical mitoses and necrosis also supports the diagnosis of EAML [18].

With the rapid development of next-generation sequencing (NGS) and whole-exome sequencing (WES) technologies, researchers have made further progress in understanding the relationship between the disease and molecular biomarkers. Pathway inactivation due to P53 mutations is a key genetic step in many tumor types [18]. The clinical significance of Ki-67 as a proliferation marker and prognostic indicator has been extensively studied in human tumors [19]. Li found that EAML commonly exhibits higher expression levels of P53 and Ki-67 compared with CAML [20], which aligns with the results of this patient. Moreover, studies have shown EAML is related to high expression of MDM2 [21] and TFE3 [22]. This research provide new insights into potential molecular biomarkers for the diagnosis and differentiation of EAML.

EAML, as a relatively rare subtype of renal angiomyolipoma, has garnered increasing attention from researchers and clinical practitioners in recent years. However, due to its overlapping clinical features and radiological findings with renal cancer and CAML, EAML is prone to misdiagnosis preoperatively. Although there is currently no standard diagnostic guideline for EAML, with the popularization of diagnostic techniques, continuous accumulation of cases, and rapid development of molecular biology techniques, it is believed that future clinical diagnoses and treatments of EAML will advance to a higher level.

Conclusion

This case underscores the clinical impact of EAML and its potential for misdiagnosis. It draws attention to the need for heightened awareness among clinicians about this rare entity. It is necessary to make a comprehensive diagnosis based on clinical symptoms, imaging manifestations, and pathological characteristics to avoid unnecessary radical surgeries and optimize patient outcomes.

Abbreviations

EAML	Renal epithelioid angiomyolipoma
CAML	Classic angiomyolipoma
RCC	Renal cell carcinoma
CT	Computed tomography
CTA	Computed tomography angiography
MRI	Magnetic resonance imaging
ECT	Electron capture tomography
TSC	Tuberous sclerosis complex
NGS	Next-generation sequencing
WES	Whole-exome sequencing

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Author contributions

Wenhao Zhang: writing—original draft, conceptualization. Xiaodong Jin: visualization. Chundan Wang: formal analysis. Shaobo Jiang: writing—review and editing. Jiasheng Yan: investigation. Yubing Li: conceptualization, supervision.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Declarations

Ethical approval and consent to participate

Not applicable.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

Not applicable.

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