Running head: CT in EAML

The value of Computed Tomography in the Diagnostic and Prognostic Prediction of Renal Epithelioid Angiomyolipoma

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Abstract

Purpose: This study aimed to assess the importance of computed tomography (CT) imaging in the diagnostic and prognostic evaluation of renal epithelioid angiomyolipoma (EAML).

Materials and Methods: This study comprised 63 patients diagnosed with renal EAML in the First Affiliated Hospital of Soochow University during 2010-2021, who met the inclusion criteria. The clinical, pathological, and therapeutic features were analyzed to determine the optimum diagnostic and therapeutic approaches.

Results: Of the 63 participants, 20 were men and 43 women aged 24-74 years (average, 45.5 years). In 35 and 28 participants, the tumor was located on the left and right sides, respectively. All the patients underwent CT scanning. Most of the patients (54/63) with EAMLs

demonstrated hyperattenuation, one showed isoattenuation, and eight showed hypoattenuation compared with renal parenchyma on unenhanced CT images. The diameter of each tumor was 2-25 cm (average, 5.6 cm). All the participants underwent surgical treatment. Of these, 53 were followed up for 4-128 months (median, 64 months). Among the followed-up patients, one died of the tumor, one died due to acute severe pancreatitis, and two had an ipsilateral recurrence.

Conclusions: EAML is a relatively rare renal angiomyolipoma depleted in fat. A characteristic of hyperattenuation on unenhanced CT images in EAML can help distinguish this tumor from clear cell renal cell carcinoma. Surgical resection is the main treatment. Most EAMLs are benign, and only a few have malignant potential. However, post-surgery recurrence and metastasis may occur, especially in elderly patients, and thus close follow-up is recommended.

Keywords: Computed tomography; EAML; epithelioid angiomyolipoma; fat-poor AML; renal neoplasm

Introduction

Angiomyolipoma (AML) is one of the most common renal benign tumors, with an incidence of approximately 130/100,000, that originates from the mesenchymal tissue [(1)]. Epidemiological studies have revealed that AML accounts for approximately 1% of all renal tumors globally. The World Health Organization (WHO) classified AML into two types in 2016: classical and epithelioid[(2)]. The former is a benign tumor composed of various proportions of mature blood vessels with abnormally thick walls, fusiform or epithelioid smooth muscle cells, and adipocytes. Epithelioid angiomyolipoma (EAML) is mainly composed of a prominent epithelioid component, with spindle and giant cells; it occasionally contains a minimal amount of adipose tissue (tends to be < 5%) [(3,4)].

To date, most studies on malignant EAML have been case reports[5]. Therefore, our current understanding of its clinical and pathological characteristics is insufficient. Whether EAML is benign or malignant is controversial, and the WHO has not yet commented on whether malignant AML truly exists. Although the imaging features of the classical AML have been well described, the imaging appearance of EAML is relatively uncharacterized because of the rarity of the tumor. Additionally, distinguishing this tumor from clear cell renal cell carcinoma (ccRCC) is often difficult due to some of the intrinsic imaging characteristics of EAML, and thus preoperative misdiagnosis is extremely common. The main treatment of renal cancer is surgical resection, and hence some patients with EAML are over-treated, such as through radical nephrectomy, which may impair renal function. This study aimed to analyze the clinical data from 63 patients with EAML, who were treated in our hospital from 2010 to 2021, to evaluate the value of computed tomography (CT) imaging in the diagnostic and prognostic evaluation of EAML.

Materials and Methods

This study was approved by the ethics committee of the First Affiliated Hospital of Soochow University, China (2022; Approval No. 23) and carried out following the approved guidelines of the committee. Written informed consent was obtained from all patients.

The pathology database of the First Affiliated Hospital of Soochow University was retrospectively searched using the keywords "EAML" and “ccRCC” (in Chinese), and 63 cases of renal EAML, accounting for 4.7% of all the renal AML cases (1340 cases in total) in the hospital during the same period (2010-2021), were identified. EAML was defined as polygonal

cells with clear-to-eosinophilic cytoplasm and round-to-oval nuclei[6]. Atypical EAML was defined as epithelioid cells with abundant cytoplasm, vesicular nuclei, prominent nucleoli, and nuclear size more than twice the size of the nuclei of the adjacent cells. "Progressor" EAML was defined as the presence of progression, including local recurrence, distant metastasis, and death due to the disease.

The hospitalization records, including the clinical characteristics, imaging results, and treatment types, of all the eligible patients were reviewed. We extracted and analyzed the data from the medical records and postoperative pathological results of the patients, and re-examined the abdominal CT and ultrasound results of the patients in the inpatient database. Based on the findings from unenhanced CT, each tumor was classified as hyperattenuating, isoattenuating, or hypoattenuating in comparison to the renal parenchyma (cortex). The follow-up data were obtained by contacting the patients via phone call or from the Outpatient Department of Urology. The survival status of each patient was confirmed by phone call. SPSS Statistics 20.0 was used for statistical analyses. Discrete and continuous variables were compared using the chi-square and *t* tests, respectively.

Results

The detailed clinical data of all 63 patients with EAML and 64 patients with ccRCC are summarized in Table 1. Of the 63 patients with EAML, 20 were men and 43 were women aged 24-74 years (average, 45.5 years). Among these patients, 58 (92%) were asymptomatic and diagnosed with EAML during physical examination, 4 (6.3%) had waist pain and discomfort, and 1 (1.5%) exhibited hematuria as the main manifestation compared with ccRCC. Patients

with EAML were less likely to have clinical symptoms ($p < 0.05$) and an earlier age of onset ($p < 0.05$). No patient had any clinical history of tuberous sclerosis complex (TSC). All the patients underwent CT, and 10 patients additionally underwent magnetic resonance imaging (MRI). Of all the tumors, 35 and 28 were on the left and right kidneys, respectively. The clinical imaging results showed that the diameter of each tumor was 2-25 cm (average, 5.6 cm). Preoperatively, 36 cases of renal malignant tumors were misdiagnosed, including 30 cases of RCC and 6 cases of renal mesenchymal malignant tumors. Women were more common among patients with EAML (20 and 43 were male and female patients, respectively) compared with those with ccRCC (39 and 25 were male and female patients, respectively) ($p < 0.05$).

Fat components were detected on the unenhanced CT images of 8 of 63 patients. The intratumoral hyperattenuation was observed in 54 patients (Fig. 1), 1 showed isoattenuation, and 8 showed hypoattenuation (the fat component in Fig. 2) compared with the renal parenchyma. We found that the tumor in patients with EAML showed hypoattenuation on CT scans, whereas patients with ccRCC showed hypoattenuation ($p < 0.05$).

Hemorrhage and necrosis, which appeared as mildly low-density regions compared with the adjacent tumor tissues, occurred in 10 cases (Fig. 3). Heterogeneous and relatively homogenous enhancements were observed in 23 and 40 cases, respectively. Upon evaluating the pattern of the dynamic enhancement, 35 lesions were categorized as “rapid wash-in and rapid wash-out” and 28 lesions were categorized as “rapid wash-in and slow wash-out” (“wash-in enhancement pattern” meant that CT attenuation increased from the unenhanced to arterial and venous phases; “wash-out enhancement pattern” meant that CT attenuation decreased from the venous to delayed phase). Additional classical AML was detected in eight cases.

Among the 63 patients included in the study, all underwent surgical interventions. Specifically, 7 patients underwent radical nephrectomy, 7 partial nephrectomy, 10 laparoscopic radical nephrectomy, and 39 laparoscopic partial nephrectomy. Patients with EAML were more likely to choose the option of preserving the kidney unit compared with patients with ccRCC ($p < 0.05$). EAML was categorized into pure (epithelial component >80%) and partial (10% < epithelial component < 80%) EAML based on the proportion of postoperative pathological epithelioid components. Of all the cases, 39 were pure EAML and 24 were partial EAML. However, no statistically significant difference was observed in sex, age, maximum tumor diameter, and surgical methods between the pure and partial EAML cases.

The tumor profile was mainly grayish-yellow and grayish-white in 54 of 63 patients. Atypia cells (8/63) and hemorrhage and necrosis (5/63) were rare. The results of the immunohistochemical analysis (Melan-A/HMB (β-hydroxy β-methylbutyrate) 45/Ki-67/S100/SMA (smooth muscle actin)/CD34 staining) of 51 patients are presented in Table 1.

Of the 63 registered patients, we could not determine the survival status of 10 patients (they did not provide their phone numbers, or the numbers provided were outdated). The remaining 53 patients were followed up for 4-128 months (median, 64 months). Among these, 49 patients did not show disease progression. However, two patients who underwent laparoscopic partial nephrectomy had a local recurrence 18/24 months after the surgery. These patients were not treated with any additional surgery and instead received chemotherapy. Another patient died of severe cancer cachexia 12 months after the surgery. Additionally, one patient died of acute severe pancreatitis 23 months after the surgery (excluded from the follow-up).

The pathological features of the progressors and non-progressors among the 52 followed-up patients with EAML are depicted in Table 2.

No pathological or prognostic difference was found between the hyperattenuating and isoattenuating tumors.

Discussion

In 2004, the WHO defined EAML as a renal stromal tumor with malignant potential. Approximately one third of patients develop distant metastases. EAML was first reported by Mai et al. in 1996, and it accounted for 4.6%-7.7% of all AML cases globally. The average age of EAML onset has been reported as 40 years, and the incidence in men and women is approximately 1:1. In this study, the average age of the onset was 45 years, and the men-to-women ratio was close to 1:2, which was different from the reported ratio.

Clinical manifestations

Patients with EAML have an insidious onset similar to patients with classical AML, and tumors are usually detected due to physical examination or imaging. Dickinson [(7)] et al. discovered that 82%-94% of patients with lesions measuring > 4 cm complained of clinical symptoms, and 50%-60% had concomitant bleeding. Of the 63 patients in this study, 5 visited physicians because of significant symptoms; 4 had a backache, and 1 showed hematuria. All the tumors measured > 7 cm. One of the cases involving backache was proved to be malignant. These data suggested that the larger the lesion, the greater the probability of manifesting a clinical symptom.

Imaging features

Unlike typical AMLs with relatively characteristic imaging findings, EAML cases often mimic RCC, renal sarcoma, or AML, with minimal or no fat on imaging evaluation, which may lead to misdiagnosis. To date, the imaging characteristics of EAML have been much less reported than the histopathological features because most of the imaging findings are individual reports. Hyperattenuation (> 45 HU) in unenhanced CT has been regarded as a characteristic finding of EAML and entails higher density than the healthy renal parenchyma, a bulging contour of the affected kidney, markedly heterogeneous enhancement, large lesion size on presentation, a complete capsule with distinct edges, and occasionally regional lymph-node metastases [5,8]. The unenhanced CT images showed hyperattenuation in 54 of the 63 cases, isoattenuation in 1 case, and hypoattenuation (as a fat component) in 8 cases, whereas ccRCC often presented isoattenuation or hypoattenuation. The tumor components showed low intensities on T2-weighted images in 6 of the 10 cases for which MRI findings were available. Several studies have reported that AML with abundant smooth muscle and little or no fat on pathological examination (AML with minimal fat) appears as hyperattenuation and T2-low-intensity masses[9-12]. Liu [13] et al. found that most EAMLs, with or without a fat component, appeared hyperattenuated in precontrast CT images and demonstrated a dynamic enhancement pattern of rapid wash-in to slow wash-out. This phenomenon is thought to correlate with the following pathological characteristics: an abundance of abnormal vessels, higher cellular density and decreased tumor stroma, presence of a complete capsule, and lack of draining vessels.

The amount of mature fat in an EAML tumor is extremely small; still, the fat tissue can be detected in some cases. We could detect the fat tissue in the CT image of the patient, with

hyperattenuation on the edge of the tumor. This patient experienced a recurrence of the tumor after the surgery. Hence, it is important to exercise caution in diagnosing AML solely based on a CT image displaying a tumor with fat; further examination may be needed to avoid misdiagnosis. The patient currently has a postoperative recurrence, but a statistically significant analysis cannot be performed due to the small sample size of our study. Currently, no evidence indicating that EAML with additional classical AML presents a more complicated scenario than traditional AML, or that there is an increased risk of recurrence following surgery. Nevertheless, any additional risk that may be posed by the fat content should not be ignored.

We believe that small tumors, such as those sized 4-5 cm on a typical CT image, can be judged as EAML relatively accurately. However, if the tumor is > 7 cm or accompanied by necrosis, a typical image with hyperattenuation is not present. A correct diagnosis cannot be made in such cases, and a radical nephrectomy may be the optimal choice.

Pathological characteristics

Microscopically, the tumor cells were observed to be arranged in solid nests or diffuse sarcoma-like structures, and necrosis was common. Varying degrees of heteromorphism, cytoplasmic eosinophilia, and hyperchromatic nuclei were observed, and vesicles, nucleoli, and mitosis could be seen. Melanin deposition or plasma- or rhabdoid-like differentiation can easily be misdiagnosed as RCC or metastatic melanoma. Therefore, the immunohistochemical analysis plays an essential role in diagnosing EAML, which is characteristically positive for HMB 45 expression and displays SMA and melanin co-expression. S-100 and Ki-67 may also be expressed in small amounts. In this study, most patients exhibited the expression of HMB 45, S-100, and SMA. This observation was different from that of Lei et al.[14] They found that

most patients did not express S-100, and some had a slight or focal expression of Melan-A or Ki-67. Regarding the diagnostic method for EAML, Nese et al.[15]. proposed the following risk factors for malignant EAML: (1) presence of tuberous sclerosis or association with AML; (2) tumor size > 7.7 cm; (3) carcinoma-like histology; (4) extra-renal extension or renal-vein invasion; and (5) necrosis. They also proposed that tumors with 0-1, 2-3, and 4-5 risk factors should be classified into the low-, middle-, and high-risk groups, respectively.

A total of 52 patients were followed up in this study, including 37 in the low-risk group, 12 in the intermediate-risk group, and 3 in the high-risk group. Further, 1/3 of the patients in the high-risk group died during the follow-up period, 2/3 were in good physical conditions during the follow-up period, and 2/12 in the middle-risk group had ipsilateral recurrence. Other patients were in good health.

Treatment

To date, surgery has been the optimal approach to treat EAML. Many previous studies [1,16,17] reported that local recurrence or distant metastasis generally occurred 1.5–9 years after the surgery. Zomboni et al.[18] reported that EAML belonged to a family of perivascular epithelioid cell tumors (PEComa), similar to lymphagioleiomyomas and clear cell “sugar” tumors of the lung and pancreas. Of the 53 followed-up patients, only 1 died of tumor progression. The surgical method used was radical nephrectomy. Two patients experienced tumor recurrence during the follow-up period, which was not life-threatening. The surgical method used was laparoscopic partial nephrectomy. Therefore, we believed that although renal EAML was a potentially malignant tumor, nephron-preserving nephrectomy was a better choice than radical nephrectomy because the former procedure provided patients with a

relatively better quality of life than the latter.

Bissler et al.[19] reported 25 patients with AML who received rapamycin treatment. After 12 months of treatment, their tumor volume was reduced to 53% of the original, but the tumor volume increased to 86% of the original 1 year after discontinuing the chemotherapy. Therefore, EAML may be sensitive to chemotherapy. However, long-term follow-up is required to confirm this conclusion. Heidi et al.[20] examined 15 patients with PEComa and found that the mammalian target of the rapamycin (mTOR) cascade, which was related to tumorigenesis, was always activated in these tumors. Recently, Tomasz et al.[21] investigated the effect of sirolimus in the long-term treatment of PEComa and found that sirolimus had a definite therapeutic effect in the long-term targeted therapy of PEComa. Guo et al.[22] explored the effect of everolimus in invasive malignant renal EAML. They found that the mTOR inhibitor could effectively treat patients with invasive malignant renal EAML. Patients with TSC might benefit more from the therapy than those without TSC. This observation suggested that patients might benefit from mTOR inhibitors, but further studies should be performed to validate this observation.

Based on the current findings, we believed that nephron-preserving nephrectomy was safe for patients without lymph-node metastasis and tumor thrombosis. However, examining the long-term survival prospects requires long-term follow-up. All the therapies, including surgery, chemotherapy, and molecularly targeted drugs, may be beneficial to patients for their long-term survival.

Prognosis

Renal EAML has a certain malignant potential. Nese et al.[15] followed up with 41 patients with EAML and found that 17% and 49% had recurrence and metastasis, respectively, and 33%

died of the disease. Brimo et al.[23] found that 26% of the patients in their cohort had recurrence and metastasis. However, He et al. reported that only a small proportion of patients (5%) had tumor progression. Aydin et al.[6] found no tumor progression in 15 of 16 patients with EAML. Only one patient, with pure EAML, in their group developed lung and abdominal lymph-node metastases and then died of tumor 2 months after the surgery; no tumor progression was detected in the remaining patients during the follow-up period. Among the followed-up patients in our study, only one died of the tumor and two had an ipsilateral recurrence, accounting for a low frequency of progression among all the followed-up patients. Nevertheless, we found that elderly patients were more likely to have tumor recurrence and progression than young patients. In this study, the average age of patients in the nonprogressor and progressor groups was significantly different (45.2 and 63.7 years, respectively; $P < 0.05$).

Combining our pathology and follow-up results and comparing the CT results in a limited number of cases, we proposed the following hypothesis: (1) the mass measured > 7 cm, or the mass protruded from the kidney; (2) the CT result suggested internal necrosis; (3) patients had lymph-node or distant metastasis; and (4) patients were aged >50 years), leading to a relatively poor prognosis. This study had 12 patients with tumors >7 cm in diameter. Of these patients, one died due to the tumor (aged 74 years, and the maximum diameter of the tumor 22 cm; necrosis in the tumor and local lymph-node metastasis). Additionally, one patient (aged 67 years, and the maximum diameter of the mass 7 cm; no necrosis or metastasis) showed ipsilateral recurrence of the mass. As EAML tumors always appear enhanced in CT images, we believe that the characteristics of “rapid wash-in and rapid wash-out,” or “rapid wash-in and slow wash-out” cannot be used as the criteria for distinguishing EAML cases from renal

cancer or as prognostic factors. Many patients with no progression carried the defined high-risk factors, which will be closely examined during the follow-up with these patients.

Our findings showed that the risk of recurrence and death in EAML was relatively small, with no significant difference in prognosis between patients undergoing radical nephrectomy and those undergoing partial nephrectomy. Therefore, we believe that partial nephrectomy is a more suitable treatment option for a patient with EAML than radical nephrectomy, provided that the conditions of the patient permit. However, if the preoperative diagnosis suggests the presence of malignant tumors, radical nephrectomy may be the preferred treatment option and close follow-up is recommended.

Limitations

The present study had several limitations. First, the number of patients was not sufficient. Thus, further evaluations using a large number of patients from multiple centers are necessary to confirm our findings. Second, it was difficult to design prospective studies because of the rare nature of the disease. We could not establish uniform surgical resection standards; the histopathology of these lesions was mainly evaluated postoperatively. Elderly patients tended to have tumor recurrence and progression. Finally, most patients did not receive imaging follow-up because their tumors were misdiagnosed at that time as benign.

Conclusions

EAML is a tumor with potential malignancy. CT can be used for the differential diagnosis of EAML and ccRCC, which are mainly detected using unenhanced CT. Once diagnosed, active treatment options such as radical/partial nephrectomy and molecular-targeted drugs

should be considered. It is crucial to closely monitor patients, especially elderly individuals, through regular follow-up examinations.

Acknowledgment

This study was supported by the Key Disciplines of Jiangsu Province (project number: ZDXKA2016012).

Conflicts of interest

None.

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Tables and Legends to figures:

Table 1. Clinical data of the patients diagnosed with EAML (*n* = 63) and ccRCC (*n* = 64)

Baseline data			
	EAML (n = 63)	ccRCC (n = 64)	*p*
Gender	male/female = 20/43	male/female = 39/25	.001
Mean age/years	45.5 (24 - 74)	58.3 (23 - 85)	<.0001
Max diameter	≤ 4cm: n = 36; 4 - 7 cm: n = 15; 7 - 10 cm: n = 5; ≥ 10 cm: n = 7;	≤ 4cm: n = 38; 4 - 7 cm: n = 18; 7 - 10 cm: n = 6; ≥ 10 cm: n = 2;	.364

Location	Upper pole: n = 15;
	middle pole: n = 20;
	lower pole: n = 28;
		Upper pole: n = 18;
		middle pole: n = 22;
		lower pole: n = 24;
			.716

CT attenuation (HU)	hyper-attenuation: n = 54;
	iso-attenuation: n = 1;
	hypo-attenuation: n = 8;
		hyper-attenuation: n = 0;
		iso-attenuation: n = 4;
		hypo-attenuation: n = 60;
			<.0001

Atypia (Yes/No)	8/57	64/0	<.0001
Necrosis (Yes/No)	5/58	12/52	.116
Cystic degeneration (Yes/No)	2/61	3/61	.508
Hemorrhage (Yes/No)	5/58	9/55	.396
Calcification (Yes/No)	0/63	2/62	.496

Associated symptoms	waist pain: n = 4;
	hematuria: n = 1;
	none: n = 58
		waist pain: n = 11;
		hematuria: n = 8;
		none: n = 45;
			.006

Involvement range			
Confined to kidney	right: n = 27； left: n = 29, (n = 56);	right: n = 31； left: n = 19, (n = 50);	.175

Beyond kidney	right: n = 1； left: n = 6, (n = 7);	right: n = 6； left: n = 8, (n = 14);	.337
Distant metastasis	0	2	-
Tumor embolus	0	4	-
Lymph nodes metastasis	2	6	-
Surgical method	radical nephrectomy: n = 17 (laparoscopic 10, traditional 7); partial nephrectomy: n = 46 (laparoscopic 39, traditional 7);	radical nephrectomy: n = 40 (laparoscopic 32, traditional 8); partial nephrectomy: n = 24 (laparoscopic 23, traditional 1);	<.0001
IHC stain			
Melan-A	29 (+); /2 (-); /32 (unclear)	-	
HMB-45	42 (+); /4(-); /17(unclear)	-	
Ki-67	45 (+, 2 - 30%); /3 (-); /15 (unclear)	-	
S100	29 (+); /16(-); /18 (unclear)	-	
SMA	46 (+); /17 (unclear)	-	
CD34	27(+); /8(-); /29 (unclear)	-	
Follow-up data			
Follow up patients	53	64	*p*
Follow up duration/month	64 (4 - 128)	68.5 (2 - 72)	-
Survival status	alive: n = 51; dead: n = 2;	alive: n = 36; dead: n = 28;	<.0001
Recurrence	2 patient suffered ipsilateral recurrence in 18/24months post-operation respectively.	6	<.0001
Death	1 patient died from serious cancer cachexia 12 months postoperatively; 1 patient died from acute severe	28	

	pancreatitis 23 months post-operation		
Metastasis	0	4	

Abbreviations:

ccRCC, Clear cell renal cell carcinoma; EAML, epithelioid angiomyolipoma; HU, Hounsfield unit. Melan-A, melanoma antigen recognized by T cells (MART-1); HMB 45, β-hydroxy β-methylbutyrate 45; SMA, smooth muscle actin.

Comparison of pathological features between the EAML and ccRCC. The chi-square test was used for the Gender, Max diameter, Location, CT attenuation (HU), Atypia, Necrosis, Cystic degeneration, Hemorrhage, Calcification, Associated symptoms, Surgical method, Survival status; the *t* test was used for the other parameters.

Table 2. Comparison between nonprogressors and progressors

Mean	Non-progressors (n = 49)	Progressors (n = 3) *	*p*
Age/years	45.2	63.7	.024
Ratio of male/female	0.36 (13/36)	2 (2/1)	.196
Max diameter/cm	5.827 ± 0.835	10.17 ± 5.019	.228
CT attenuation (HU)	Hyper/non-hyper (44/5)	Hyper/non-hyper (3/0)	1.0
Percentage of epithelioid cells	Pure/partial (27/22)	Pure/partial (3/0)	.253
necrosis	3/46	1/3	.217
Percentage of atypia cells	8/49	1/3	.442

Of the 63 patients, 53 were followed up for 4-128 months (median, 64 months). Among these, 49 had no progression, 2 had disease recurrence in 18/24 months postoperatively, 1 died of the tumor, and 1 died of acute severe pancreatitis 23 months after the surgery (we ruled out this patient).

Comparison of pathological features between the non-progressors and progressors. The chi-square test was used for the male/female ratio, CT attenuation (HU = Hounsfield units), and percentages of epithelioid, necrotic, and atypia cells; the *t* test was used for the other parameters.

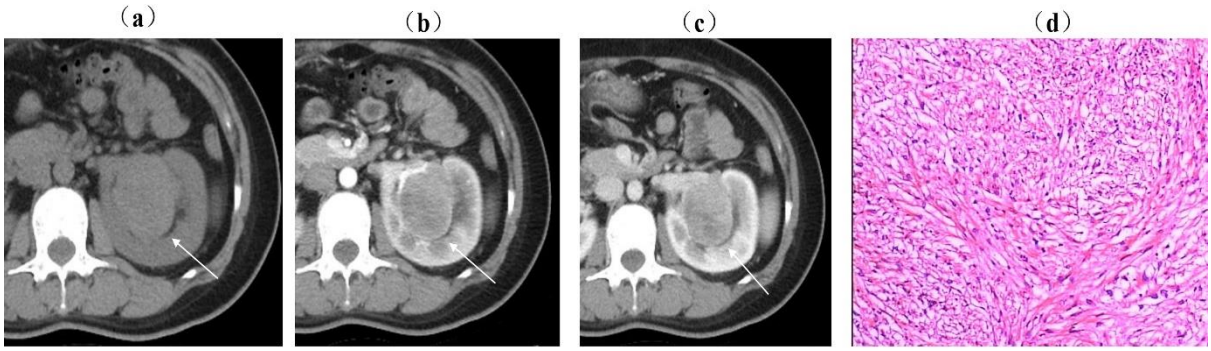

Figure 1. A 63-year-old woman with a homogeneous solid lesion. (a) Unenhanced CT image showed a hyperattenuating mass in the right kidney (*arrows*). No fat density was detected. (b and c) Dynamic contrast-enhanced CT image showed a homogeneously enhanced tumor in the corticomedullary and early excretory phases (*arrows* in b and c, respectively).

(d) Hematoxylin-and-eosin staining. The visual field is abundant with epithelioid cells, containing red cytoplasm and large nuclei; nucleoli are visible, with a certain degree of pleomorphism and mitotic figures (original magnification, ×100).

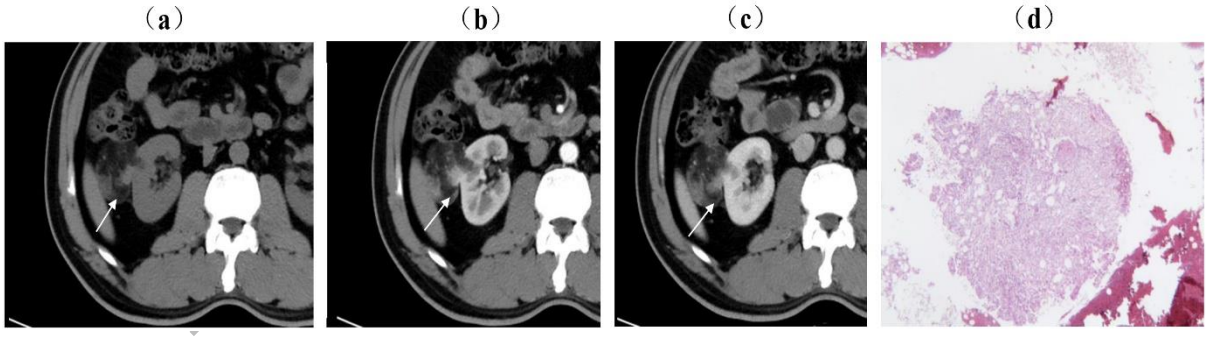

Figure 2. A 50-year-old man with a heterogeneous solid lesion, who suffered from an ipsilateral recurrence 18 months after the surgery.

(a) Unenhanced CT image showed a hypoattenuating mass in the right kidney (the *arrows* show the fat-enriched regions), with a hyperattenuating part on edge. (b and c) Dynamic contrast-

enhanced CT image showed a heterogeneous enhanced tumor in the corticomedullary and early excretory phases (*arrows* in b and c, respectively).

(d) Hematoxylin-and-eosin staining. The epithelioid cells were diffuse and surrounded by many fatty cells (original magnification, ×100).

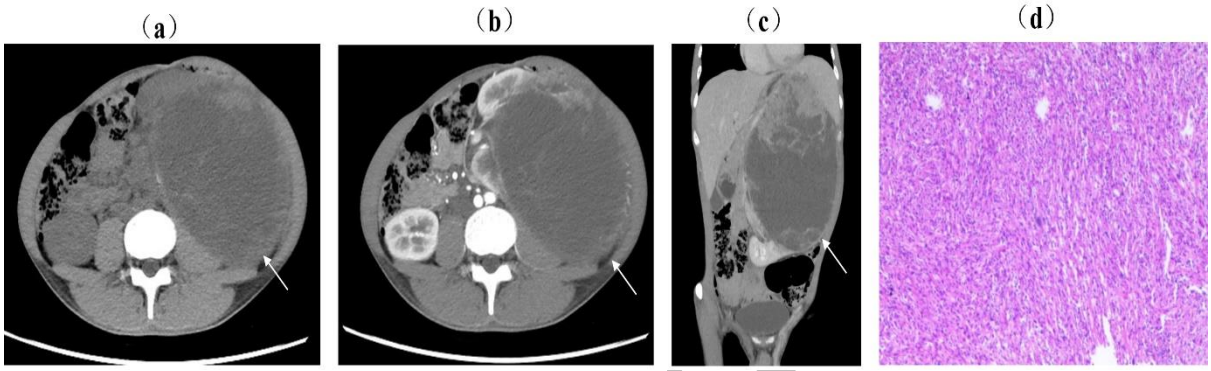

Figure 3. A 74-year-old man with a heterogeneous solid lesion, who died 12 months after the surgery. (a) An unenhanced CT image showed a heterogeneous solid-type lesion, with a hyperattenuating part on the edge. (b and c) Dynamic contrast-enhanced CT image showed a heterogeneous solid-type lesion-enhanced tumor in the corticomedullary and early excretory phases (*arrows* in b and c, respectively). (d) Hematoxylin-and-eosin staining. Consistent with EAML, the tumor was massive with hemorrhagic necrosis. The tumor cells invaded the perirenal fat tissue, and some of them contained large atypia, prominent nucleoli, and a few pathological mitotic figures (original magnification, ×100).