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Original Article

Computed Tomography Feature Analysis Can Unravel the Confusion between Exophytic Renal Angiomyolipoma and Perirenal Retroperitoneal Liposarcoma

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Abstract

Background: exophytic renal angiomyolipoma and retroperitoneal liposarcoma has completely different management strategies. Unfortunately, confusion may occur on imaging as well as on histopathological analysis hindering definitive diagnosis. We aim to assess certain computed tomography based features which guide to optimal management protocol.
Methods: A retrospective cross sectional study performed in Radiology departments, in two different hospitals , in the period from August 2019 to January 2022. The study was approved by the research ethical committee of theirs. Two groups of computed tomography scans belong to 19 and 11 cases with exophytic renal angiomyolipoma and perirenal liposarcoma, respectively, were analyzed by two radiologists blinded to the pathological reports for a collection of CT features. These features were compared between both groups using Fisher's exact test.
Results: Renal parenchyma defects in relation to tumor and tumoral vessel connection to the renal cortex were highly suggestive for angiomyolipomas ($P < 0.001$ for both). Hemorrhage and additional angiomyolipomas are exclusive findings supporting angiomyolipoma diagnosis. Calcifications were detected by both readers only in liposarcomas ($P < 0.001$). anterior displacement of kidney is significantly higher in frequency among liposarcoma group ($P < 0.002$). The other observed features were not useful in differentiation ($P > 0.055$ for both readers)
Conclusion: Careful analysis of certain computed tomography based features of exophytic angiomyolipoma and liposarcoma can direct to definitive diagnosis and consequently to adequate management.

Keywords: CT; Exophytic; Angiomyolipoma; Perirenal; Liposarcoma.

INTRODUCTION

Renal angiomyolipoma (AML) is the most common benign renal solid tumor of mesenchymal origin. Accidental discovery of this lesion is common, while symptomatic presentation is also present. Diagnosis of angiomyolipoma is always easy by various imaging modalities, due to its abundance of fat content. It has no malignant potential. Its management is always conservative [1]. Selective embolization is an option, if the lesion undergoes hemorrhage , or increases in size , in subsequent follow up studies. Exophytic angiomyolipoma appears as a large retroperitoneal fat-containing mass related to the kidney .It is usually associated with soft tissue densities ,and vascular structures. Such imaging characteristics can cause

confusion with retroperitoneal liposarcoma [2]. Liposarcoma has a wide range of imaging appearances. It may show a variable amount of fat-content, soft tissue components ,and vascular structures regarding histological types, and degree of differentiation [3]. It necessitates a completely different aggressive approach, including wide resection with negative surgical margins and radiation therapy[4].

Large exophytic angiomyolipomas may be confused with liposarcomas even at histopathology due to sampling error at biopsy [6]. Such CT mass characteristics may be an early guide to appropriate specimen reanalysis or repetition to ensure the correct diagnosis [5].

Computed tomography is the widely available and most commonly used diagnostic tool to distinguish between these two lesions, aiding proper diagnosis, and subsequent proper management [5]. We aim to highlight CT-based characteristics differentiating between large exophytic AML and retroperitoneal liposarcoma related to the kidney. Differentiating signs are centered on findings giving clues to the exact origin of the tumor, either renal or perirenal and multiple CT characteristics of either tumor.

METHODS

This is a retrospective cross sectional study done in two radiodiagnosis departments. The study was approved by the research ethical committee of theirs . The study was done according to the code of ethics of the world medical association (declaration of Helsinki) .Written consents were waived.

All cases with contrast enhanced CT of abdomen and pelvis examinations revealing large fat-containing lesions involving the kidney or within the perirenal space in the period from August 2019 to January 2022 were enrolled in this study.

Blinded to CT images, our search yielded 19 cases, whose radiology reports contained exophytic angiomyolipoma ,and 13 cases contained retroperitoneal liposarcoma related to either kidney. In exophytic AML cases, 11 cases were provided with their histopatholgy reports, either post-operative (n=2), or needle biopsy (n=9). Four cases were reported, associated with other AMLs ,either in the same kidney, or the contralateral kidney (n = 4), and four cases with sequential follow up reports indicating stable size and appearance. All 13 cases reported as retroperitoneal liposarcomas were confirmed with their pathology reports.

Patients were examined with (Philips Ingenuity Core 128, Philips Healthcare, The Netherlands). And GE LightSpeed Ultra(General Electric Healthcare; Milwaukee, WI). Supine positions were used for the CT scan. The used beam collimation was 0.625 mm. All patients received 150 ml of non-ionic intra-venous contrast media (Ultravist or Omnipaque, 370 mg I/mL or 350 mg I/mL concentration). Injection was performed using an automatic injector ,at a rate of (2 to 3 ml/s). Examinations were acquired in precontrast, corticomedullary phase (25 to 30 second delay time) ,and nephrographic phase (100 second delay time).

Two consultant radiologists separately ,and randomly examined all thin sections axial CT images and multiplanar images using PAXERA PACKS system without clinical history, or pathological results for the following points:

- Location of lesions, fat content within lesion (≤ -10 HU), additional fat containing lesions in either kidney, renal cortical defects in relation to the lesion, anterior renal displacement, presence of calcifications, intralesional soft tissue nodules , and associated hemorrhage.
- Intra-tumour vessels; enlarged intralesional vessels, tracing these visible intralesional vessels' origins(If they are derived directly from the renal hila or passing to or through the renal parenchyma)

Each reader commented on each point for each case, whether it was present or absent.

Statistical Analysis

Enrolled cases were divided in to two groups; exophytic angiomyolipoma group and perirenal liposarcoma group. Descriptive statistics were performed for each group , regarding their age and sex in the form of mean, standard deviation and percentages. Frequency and percentages of each character in used image analysis method for mass and vascular characters were demonstrated for our both readers. Analytical statistics using Fisher exact test were used to compare frequency of imaging characteristics between both groups. Data analysis was performed with SPSS 13.0 software (SPSS Inc. Chicago, IL). A P value of < 0.05 was considered

statistically significant and P value of < 0.001 was considered highly significant.

RESULTS

Our study is a cross sectional study included 32 patients(20 females and 12 males) .Nineteen patients were diagnosed with exophytic AMLs (14 females and 5 males) .The mean of their ages was 41.8 years, while 13 patients were diagnosed with retroperitoneal perinephric liposarcomas (6 females and 7 males), The mean of their ages was 54.7 years (Table 1).

Studied CT features, their frequencies ,and P-value of their statistical significance are demonstrated in (Table 2). Similar fat containing lesion in ipsilateral kidney, or the contralateral kidney was a feature exclusive for angiomyolipoma. In our study multiple angiomyolipomas (one of them was exophytic) were detected in four cases (4/19, 21.1%). No similar finding was detected in cases diagnosed as liposarcoma .

Renal parenchymal defect sign was detected in all AML cases (19/19, 100%) with p value <0.001 for both readers. Both readers reported renal parenchymal defect in one case of retroperitoneal sarcoma. Post-operative histopathology reported a breach in renal capsule with actual infiltration of renal parenchyma at site of contact with the mass.

Non-Fat attenuation components were either hemorrhage, soft tissue nodules, or calcifications. Hemorrhage was a finding of AML cases (4/19, 21.1%), while intratumor soft tissue nodules other than fat were more frequent in cases diagnosed with liposarcoma (7/13, 53.8%) ,with no statistically significant difference between both groups.

Intra-tumor calcification was present only in liposarcoma cases (9/13, 69.2%). p value <0.001 for both readers.

Anterior displacement of the kidney was detected in 8 cases of liposarcoma (8/11, 61.5%) compared to only 2 cases of exophytic AML (10.5%) with P value of 0.002 for both readers.

Intra-tumor vessels were detected in either AML and liposarcoma groups. On tracing origins of these vessels to detect their connection to renal parenchyma or renal pedicle; Intra-tumor vessel connected to/or passing through renal parenchyma was a special finding for AML group for both readers with (P<0.001). Our reader 1 detected both types of vascular communications in the same case.

Intra-tumor vessel extending to renal hilum was a feature of both groups with no statistical difference between both groups according to both readers.

We verified final diagnosis for each group differently. Histopathology was performed for 11 case of exophytic AML and all cases diagnosed with perirenal liposarcoma. Other cases of AML final diagnosis were verified upon imaging. Presence of other AML in 4 tuberous sclerosis cases , typical CT feature of AML, and stability over consequent follow up studies were enough to establish diagnosis of AML.

Table (1): Baseline characteristics of the studied groups:

Variable	Angiomyolipoma group (N=19)	Liposarcoma group (N=13)
Age: Mean ± SD	41.8 ± 13.2	54.7 ± 9.2
Sex: Female: Male:	14 (73.7%) 5 (26.3%)	6 (46.2%) 7 (53.8%)

Table (2): CT features of the studied groups:

CT feature	Reader 1		P value	Reader 2		value
	Angiomyolipoma group (N=19)	Liposarcoma group (N=13)		Angiomyolipoma group (N=19)	Liposarcoma group (N=13)	
Additional fat containing lesions	4 (21.1%)	0 (0%)	0.077	4 (21.1%)	0 (0%)	0.077
Renal parenchyma defect	19 (100 %)	1 (7.7%)	**<0.001 ****	19 (100 %)	1 (7.7%)	**<0.001 ****
Non-fat attenuation components:						
Soft tissue nodules	4 (21.1%)	7 (53.8%)	0.055	4 (21.1%)	7 (53.8%)	0.055
Hemorrhage	4 (21.1%)	0 (0%)	0.077	4 (21.1%)	0 (0%)	0.077
Connected to/passing through renal parenchyma	17(89.4%)	0 (0%)	**<0.001 ****	16 (84.2%)	0 (0%)	**<0.001 ****
Directly connected to renal hilum	3 (15.8%)	5 (38.5%)	0.145	3 (15.8%)	4 (30.8%)	0.316
Anterior displacement of kidney	2 (10.5%)	8 (61.5%)	**0.002***	2 (10.5%)	8 (61.5%)	**0.002***

Test: Fisher-exact test. *: significant difference (p<0.05).
**: Highly significant difference (p<0.001).

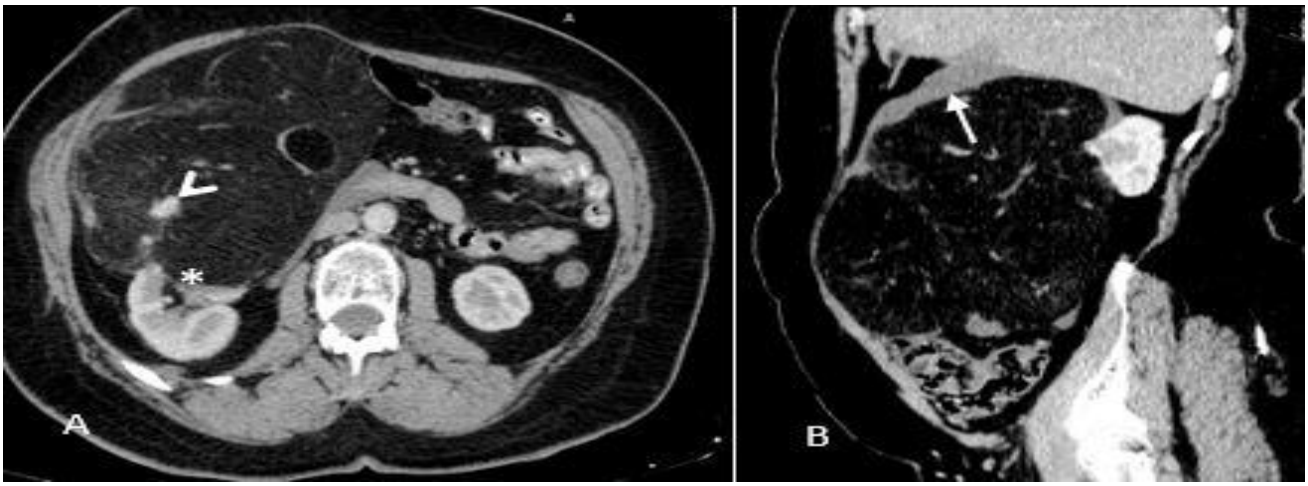
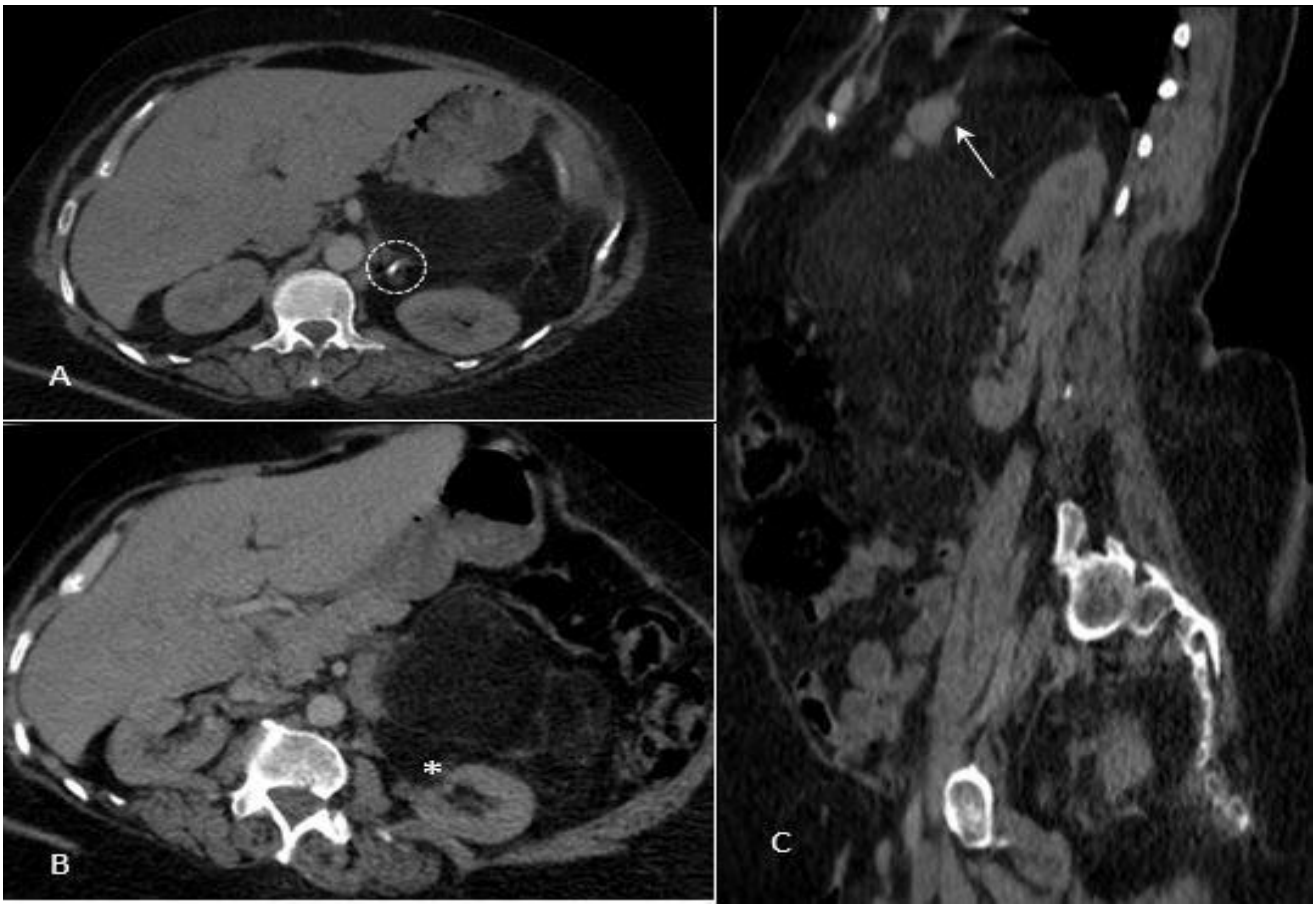


Figure (1); (A and B): 45-year-old female with a large exophytic angiomyolipoma (A); axial CT image showing anterior renal parenchymal defect with beak sign (asterisk),multiple linear vascular structures and central intralesional non-fat attenuating nodule (arrow head). (B); sagittal reformatted image shows a peripheral rim of blood density (white arrow). Hemorrhage is common in AML cases not in liposarcoma cases



- **Figure (2) Figure (2);** 65-year-old male with perirenal liposarcoma. (A and B); axial CT images reveals interalesional calcification (dashed circle) and anterior small renal parenchymal defect (Asterisk) (C); sagittal reformatted image shows non-fat attenuation nodules (white arrow).

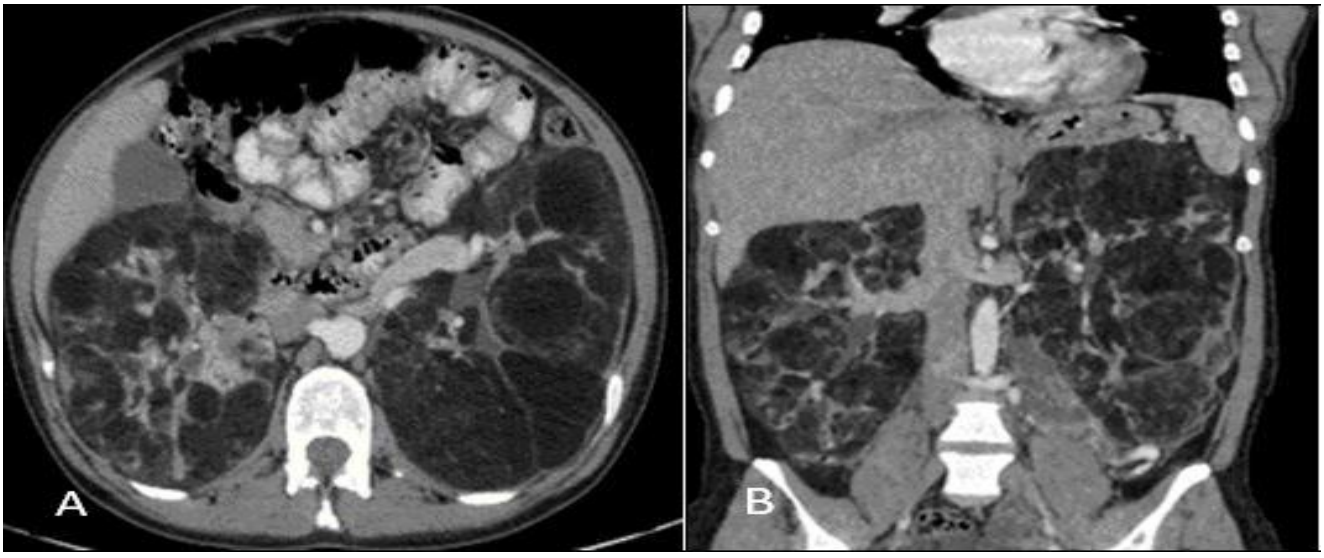
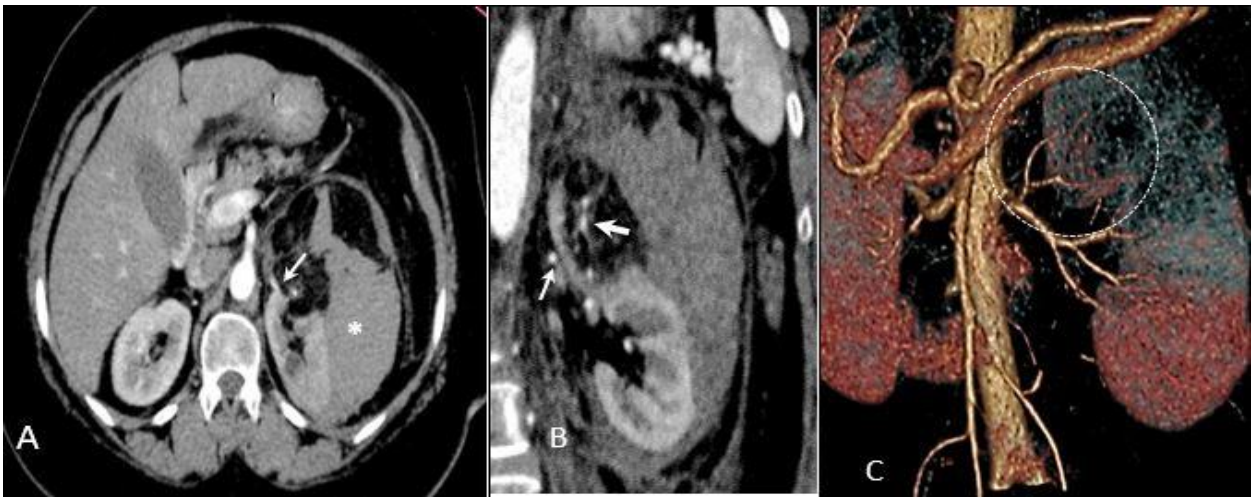
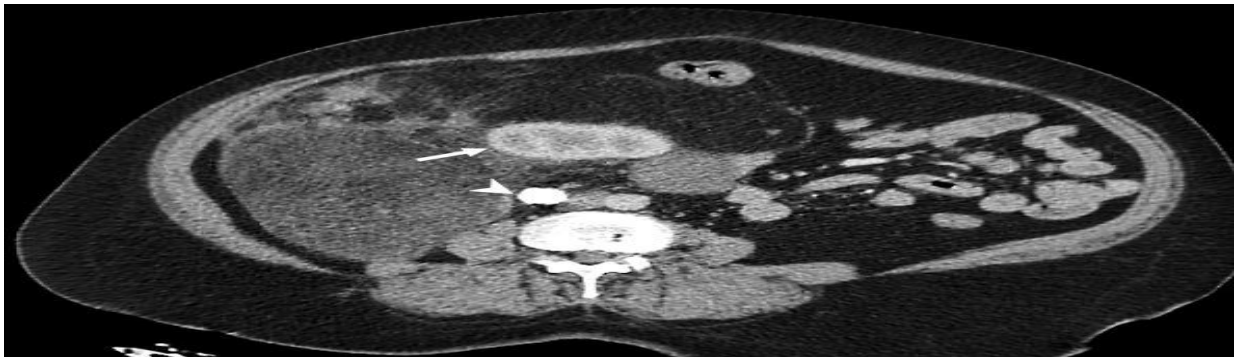


Figure (3); 32-year-old female (A) axial and coronal (B) CT images show large bilateral multiple and variable sized renal angiomyolipomas in a case of tuberous sclerosis.



- **Figure (4):** 39-year-old female with left renal exophytic AML, (A)axial and (B) coronal CT cuts (cortico-medullary phase) show parenchymal defect, fat content of the lesion and associated hemorrhage (astrisk). Multiple vascular structures seen connected to both renal parenchyma and also extending to hilar vessels (arrow heads). vascular connections are confirmed on CT angiography (C) volume rendered image (dashed circle).



- **Figure (5):** 50-year-old male with perirenal liposarcoma. Axial CT image demonstrates heterogeneous fat containing mass with anterior renal displacement, rotation (arrow) and lesion calcification (arrow head).

DISCUSSION

Exophytic AML may be superficially similar to retroperitoneal perirenal liposarcoma regarding their fat content. Certain computed tomography (CT)-based features help radiologists to reach a definitive diagnosis, to make a proper clinical decision, either conservative management, or surgical option with postoperative treatment. Also, these features can resolve posed confusion in histopathology between the two lesions ,which may occur due to erroneous sampling ,and when smooth muscles element of angiomyolipoma is scanty or atypical.

Those CT features are centered on the identification of the exact origin of the tumor, either renal ,or from retroperitoneal /perinephric fat ,and analysis for certain morphological characteristics of each lesion.

Renal AMLs were more common in 5th decade and in females. Khaddam et al., studied epidemiology of renal AMLs, also declared similar results of higher female prevalence and tendency to occur in 4th or 5th decades [7]. Retroperitoneal liposarcoma showed almost similar incidence regarding patients sex with mean age of 54.7 years. In agreement with Stoeckle et al., who reported 56 years as median age and Gronchi et al., who reported equal sex distribution [8-9].

In our opinion renal parenchyma defect is the most important feature in the determination of renal origin of the lesion and is diagnostic in cases of AML, but this single CT sign must be used with caution, because it can also occur in cases of aggressive liposarcomas.

A definite parenchymal defect was demonstrated in all patients with exophytic AMLs ,and in only one case of liposarcoma, with a statistically significant difference between both groups (p value <0.001) (Fig.1). This results are enhanced with Israel et al. [5], Woo et al. [10] and Wang et al. [11] studies. They reported that all their exophytic AML cases displayed renal parenchymal defects.

Our study, detected renal parenchymal infiltration in one case of liposarcoma . Woo et al. [10], Ellingson et al. [12] both had similar findings at their studies, while Tateishi et al. [12] detected two cases of dedifferentiated liposarcoma that were invading the kidneys (Fig.2). Our single case and their cases as well ,were confirmed on post-operative histopathological examination.

Wang et al. [11] detected a renal parenchymal defect in a case of liposarcoma encasing the kidney, but stated that it was not a true invasion, and the defect was at the site of renal cyst which was misinterpreted as a cortical defect.

Israel et al.[5] reported a case of liposarcoma with questionable invasion of renal parenchyma which was not established on pathological evaluation and referred that to thick slice sections (10 mm) used for images analysis and concluded that this factor could result in false image evaluation. We overcame such factor with a standardized protocol used in our institutions. 0.625 mm beam collimation was used for yielding thin section images and multiplanar reformation to evaluate the renal parenchyma- tumor interface for any defect accurately. Thin sections (3-5 mm slice thickness) also enabled Woo et al. [10] and Ellingson et al. [12] for detection renal parenchyma invasion in liposarcoma cases.

Additional AMLs were clues to solve confusion between the two lesions if present and indicate exophytic AML diagnosis. We detected additional AMLs in four cases of AML (21.1% of AML group) and none of liposarcoma cases. All our four cases were diagnosed with tuberous sclerosis (Fig.3). No sporadic AMLs cases were detected. Israel et al. [5] and Woo et al. [10] also detected multiple AMLs in 27% and 28.6% of their AML cases, respectively, and both also admitted that no similar finding was depicted in their liposarcoma cases. There is only one case report described by Sekido et al., who detected an additional renal fat-containing lesion in a retroperitoneal liposarcoma case [10]. Pathological analysis of that case reported intrarenal metastasis from liposarcoma. No other studies to date described associated AML with liposarcoma.

The presence of other non-fat attenuation components within the examined lesion, such as soft tissue nodules, hemorrhage ,and calcification was analyzed in our study. Intratumoral nodules of non-fat attenuation were detected in both AML and lipoarcoma groups, with no statistical difference between the two groups (Fig 1 and 2). This finding tended to be more frequent in the liposarcoma group (53.8%) than in the AML group (21.1%). Ellinson et al. had similar results [12]. Woo et al. reported frequencies in both groups were 78.6% and 75% in AML and liposarcoma groups, respectively [10]. Such results lead to careful use of this finding. The wide variation of liposarcoma histopathological types and the heterogeneity of large exophytic AML make such character debatable.

Angiomyolipoma contains intra-tumoral vessels with incomplete internal elastic lamina predisposing hemorrhage. Incidence of hemorrhage increases specially when AML reaches a large size. Regarding our results, Israel et al. [5], Woo et al. [10] and Wang et al. [11]; hemorrhage was present only in cases of exophytic AML group (fig.1and 4), not in a case diagnosed with liposarcoma.

We detected intralesional hemorrhage in 4 cases of AML (21.1%). According to the concordant studies, 28.6%,35.6%, and 6% were the reported frequencies of AML associated with hemorrhage, respectively. Ellinson et al. study reported associated hemorrhage in both AML and liposarcoma groups in first reader reading, but not in second reader reading, who did not detect hemorrhage in liposarcoma cases [12].

No intra-tumor calcification was detected in our cases of AML. Schieda et al. also agree that calcification is

unusual for AML[15]. We collected only five case reports detected AML calcifications [16-20].

Intratumor calcifications detected in 69% of our liposarcoma cases, with a statistically significant difference between both groups (P< 0.001) (Fig. 2 and 5). Ellingson et al. [12] and Wang et al. [11] also reported calcifications only in their liposarcoma groups, with a significant difference P<0.05 and P< 0.001, correspondingly. Tateishi et al. described how calcification and ossification are features of dedifferentiated liposarcoma and were detected in 30% of their liposarcoma cases.

Regarding intratumoral vessels, our results revealed that both lesions may contain vascular structures. Origin tracing of these vessels was found as an effective tool to point out the origin of the tumor.

A vascular connection to/through renal parenchymal was found in only in AML group (Fig. 4). 3 AML cases (15.8%) and 5 liposarcoma (38.5%) cases revealed vascular connections to renal hilum. Liposacoma vascular connection to renal parenchymal vessel was not detected, which was a rational finding due to its extra renal origin. Compatible with our results, the frequency of vascular connection of AML to renal parenchyma or through renal parenchyma was 71% and 77.7% in Woo et al. [10] and Ellingson et al. [12] studies, respectively, compared to 0% for liposarcoma cases in both studies.

Direct AML vascular connection to the hilum was detected in 28.6% and 33.3% for the same studies, compared to 18.8% and 33.3% of liposarcoma cases. No statistically significant difference was achieved between both groups in our study (P=0.1) and in these two studies (P=0.6 and P=0.99) as well.

Anterior renal displacement is an expected finding with large exophytic angiomylipoma originating from the posterior cortex and liposarcoma in the posterior perinephric region. We detected anterior renal displacement in two cases of AML (10.5%) and eight cases of liposarcoma (61.5%) (P=0.002). We also noted that liposarcoma displaces the kidney beyond the anterior margin of the vertebral column with or without renal rotation (Fig.5). In cases of AML, anterior renal displacement was milder with no evidence of rotation.

Woo et al. and Wang et al. results showed parallel statistically significant differences between their studied exophytic AML group and liposarcoma group regarding renal displacement, with similar notes regarding the extent of renal displacement and rotation [10-11].

Histopathology verified the CT diagnosis for all biopsied lesions in this study. Ellinson et al. [12] were confronted with a case diagnosed on a CT basis as AML while histopathology reported it as liposarcoma. Re-reading of the specimen admitted the CT AML diagnosis and attributed it to sampling error.

In conclusion, analysis of thin section images of contrast enhanced CT in the evaluation of a fatty perinephric mass leads to an exact diagnosis. The presence of a renal parenchyma defect and an intra-tumoral vessel extending to, or passing through the renal parenchyma looks to reliably distinguish the diagnosis of exophytic angiomyolipoma, but the presence of calcifications strongly suggests liposarcoma.

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