Atypical renal angiomyolipoma versus renal cell carcinoma; a diagnostic dilemma. Useful Computed Tomography findings to discriminate these tumors


1Instituto GAMMA, San Miguel de Tucumán, Tucumán, Argentina
2Instituto Urológico Privado Prof. Dr. Ronald Parada Parejas, San Miguel de Tucumán, Tucumán, Argentina
3Cátedra de Bioestadísticas, Facultad de Medicina, Universidad Nacional de Tucumán, San Miguel de Tucumán, Tucumán, Argentina

Received on September 18, 2015, accepted on April 19, 2016
Available online as of May 12, 2016

KEY WORDS: Adult; Angiomyolipoma; Renal cell carcinoma; ROC Curve; Helical Computed Tomography

Abstract
Objective: To compare various computed tomographic features of atypical angiomyolipomawith those of size-matched renal cell carcinoma.
Materials and methods: A retrospective study of sixty-eight patients (17 with atypical angiomyolipomas and 51 with renal cell carcinoma) who had undergone nephrectomy due to a presumptive diagnosis of renal cell carcinoma < 45mm in diameter determined by preoperative Triphasic Computed Tomography (CT) (non-contrast corticomedullary and early excretory phases) was performed. Two radiologists who were unaware of the final diagnosis retrospectively examined the general characteristics of the tumor, their attenuation in the non-contrast phase and enhancement characteristics. A statistical analysis was performed with R software applying the Logit model to differentiate atypical angiomyolipoma from renal cell carcinoma based on the tomographic findings of a renal mass. The final model included tumor contour, attenuation features in the non-contrast scans and the enhancement pattern over time.
Results: The most valuable CT findings to differentiate atypical angiomyolipoma were the hyperdense attenuation of the tumor in the non-contrast phase and its prolonged enhancement pattern with a likelihood of 10.49 (p=0.0381) and 36.71 (p = 0.0009), respectively. Based on the value of each finding included in the model, we calculated likelihood ratios, sensitivity (0.2941) and specificity (0.9804) A ROC curve was developed to determine the optimal cut off point (0.9694) to discriminate atypical angiomyolipoma that confirmed their presence.
Conclusion: Triphasic helical CT may be useful in differentiating atypical angiomyolipoma from renal cell carcinoma in which hyperdense attenuation of the tumor in the non-contrast scans and prolonged enhancement pattern proved to be the most valuable CT features.

© 2016 Sociedad Argentina de Radiología. Published by Elsevier Spain, S.L.U. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/)

Introduction
A solid renal mass (SRM) is a macroscopic fat free lesion that enhances regardless of its pattern. It is important to detect malignant ones and differentiate them from benign lesions, particularly when they are small. **Computed Tomography (CT)** is the most sensitive technique to distinguish renal cell carcinoma (RCC) subtypes in large SRMs and for the analysis of smaller lesions. So far, the enhancement patterns to characterize malignant disease versus benign pathology and the different RCC subtypes found within small SRMs have not been rigorously assessed.**\textsuperscript{1,5,8}\**

Although most SRMs are RCC, 20-30% turns out to be benign. The treatment options of small SRMs include active surveillance, partial nephrectomy or ablation procedures. In order to maximize detection and characterization CT includes images acquired before and after the administration of intravenous contrast (phases) comparing the Hounsfield Units (HU). Although there is no consensus about a specific value as unequivocal enhancement proof, a change of 20HU...
or higher is considered strong evidence. Angiomyolipoma (AML) is the most common benign solid mass in the kidney and is present in 0.3.3% of the population. It is a hamartoma (histologically normal tissues in terms of location but in abnormal proportion) composed by varying quantities of vascular, muscle and lipid tissues. Frequent bleeding, necrosis, perirenal extension and myomatous pleomorphism may lead to a histopathological misdiagnosis of malignancy.

There are typical and atypical AMLs. The classic AML accounts for the majority of the cases and is defined in the preoperative stage as an AML with typical tomographic findings of fat. Conversely, tumors with a minimal fat proportion (AMLmfc) or atypical AMLs are unusual (3-4.5%) and are characterized by the absence of fat inside a lesion that enhances with intravenous contrast. The diagnosis of a renal AML is currently made non-invasively and accurately with ultrasound (US), CT and magnetic resonance images (MRI). CT is more sensitive to detect fat within the AML due to its ability to discriminate small density differences and is useful to determine frequent complications such as perirenal extension and hemorrhage. The tomographic appearance of an AML depends to a large degree on its type which reflects its variable pathologic findings. In some cases a biopsy of the mass may be indicated (if secondary image findings are present) to ascertain the diagnosis and avoid surgery.

On the other hand, RCC accounts for almost 3% of the solid tumors. Most of the enhanced SRMs found on images are CCRs; other benign lesions are less common such as oncocytomas and atypical AMLs. Among the RCC subtypes, clear cell (cRCC), papillary RCC and chromophobe RCC (chRCC), cRCC is the most common in adults (70%) and every subtype has implications in terms of treatment and prognosis. As a result of technological advances in recent years, particularly in multidetector Helical CT (MDCT), small SRMs (<3 cm in diam.) and very small ones (<1.5 cm) have been detected. It is currently known that 20% of all the small SRMs that enhance are benign and that the tumor size by itself is not sufficient information to make treatment decisions.

The objective of this paper is to differentiate the tomography findings of an atypical AML from those of an RCC of the same size.

Materials and methods

Population

A retrospective study was conducted from May 2010 to July 2013 with the approval of the Institution’s IRB. Through a search of the digital medical records of the Urology Department, we identified patients of both genders with a preoperative presumptive diagnosis of an RCC smaller than 45 mm made by multiphasic MDCT in our institution. All the cases had undergone a total or partial nephrectomy to resect the lesion with posterior analysis of the specimen by the Pathology lab. We assessed tumors of up to 4.5 cm to compare lesions of similar sizes.

No informed consent was required for this retrospective study.

We excluded patients whose diagnoses had been made with a single phase CT (without IV contrast) or CT scans obtained in other institutions or CT scans that could not be retrieved in digital format, or with Pathology results from other centers, typical AMLs diagnosed prospectively in MDCTs based on the intra-tumor fat content or with histopathology results of the non-clear cell type (papillary and chromophobe).

Pathology reports

The Pathology lab records were analyzed to determine the diagnosis and histological characteristics of the lesions of patients subjected to partial or total nephrectomy. In every single case the material consisted in tissue section slides for microscopic assessment. All the kidney tissue slides were reviewed blindly by a single pathologist looking at a minimum of 10 fields in different tumor regions given their heterogeneous nature. The cases with diagnosed as AML were examined to determine the percentage of fat to establish if it was a typical or atypical AML.

Tomography

Multiphase CT scans were obtained with a Helical 16 row CT scanner (Phillips) using the institution’s protocol which consisted in phases with and without IV iodinated contrast. All the patients received 500-900 ml of oral contrast (2% barium sulfate suspension, EZ:CAT) 30 minutes before the tomographic exploration. The images were obtained in different phases covering the area between both diaphragm domes and the corresponding ischial tuberosity. Scanning parameters: Collimation sections: 5 mm, table speed 15 mm/rotation (18 mm/sec); 120 KVP, tube power 250-340 mA and a cycle time of 1 second. These constants were maintained in every single phase. The initial images (designated herein as non-contrast) were obtained after the intake of the oral contrast, before the administration of IV contrast and in a breath hold. For the renal enhancement phases the patients received 50-100 ml of an intravenous hydro-soluble iodinated non-ionic contrast of low osmolarity (lobitridol- Xenetix) equivalent to a dose of 2 ml/Kg of body weight and 300 mg of iodine/ml. Thus, each 50 ml bottle of contrast had 15 grams of iodide.
This was infused into the antecubital vein with an injection pump using a multiphase technique (injection rate: 3 ml/s (total infusion time of approximately 17 sec.) that was monitored visually and by palpation.

The exploration included the corticomedullary phase (differentiation starts at 20-30 sec post contrast), the nephrographic phase (maximum enhancement with a homogeneous nephrogram starting at 60-80 seconds post-contrast), and the early excretion phase (starting at 120 sec post contrast when contrast is cleared by the calices, infundibuli and renal pelvis). The only phase used for this study was the nephrographic phase to assess the general characteristics of the tumor. The delay in the exploration of the corticomedullary phase was 30 seconds after the injection and 120 seconds for the early excretion phase.

Image Review

All the images were reconstructed contiguously without the 5mm overlap intervals. The preoperative CT scans were reviewed by two radiologists of the team with experience in renal CT at the Extended Brilliance TM Workspace station. Although they were aware of the study design they were blinded to the final Pathology results.

First, every specialist performed a visual examination of the images of the lesion in the non-contrast phase to determine if the tumor presented areas of low attenuation associated to a negative attenuation value produced by fat content within the lesion. The tissue was considered to be fat when it had the same density as the surrounding subcutaneous or retroperitoneal fatty tissue.

The lesions in which fatty tissue was ruled out were subsequently objectively assessed by measuring the mean attenuation value of the tumor in the non-contrast, corticomedullary and early excretory phases. A work station was used to calculate the tumor diameter and to check the attenuation value through a ROI.

Image Assessment

Three features were examined in each tumor: General characteristics, its attenuation without contrast and enhancement (Table 1).

The general characteristics were studied in the nephrographic phase: margins (smooth or irregular), location of the center (extracapsular with at least 75% of the center of the tumor located beyond the kidney contour; or intracapsular with the center of the tumor located 50% or more inside the kidney contour), intra-tumor calcifications (present or absent) and perirenal changes (present or absent, that is to say, striations of attenuation of the perirenal soft tissues and thickening of the Gerota fascia).

The attenuation of the tumor in the non-contrast phase was estimated subjectively and compared to the attenuation of the surrounding kidney parenchyma. It was classified as hypovattenuation (if lower than the adjacent parenchyma), iso-attenuation (when it was similar) and as hyperattenuation (if it was stronger).

Finally the tumor enhancement characteristics were defined as an attenuation increase higher than 20HU, this included:

- Tumor enhancement distribution: “Homogeneous” (when most areas showed uniform enhancement in the cortico-medullary and early excretion phases) or as “Heterogeneous” (conversely). If attenuation was heterogeneous it was estimated subjectively using the area of higher attenuation for classification purposes.

- Enhancement pattern over time: tumor response to intra-venous iodinated contrast. It was subclassified as:
  - Early washout: when the tumor displayed a peak enhancement in the corticomedullary phase and later a washout of at least 20 HU in the early excretion phase.
  - Gradual: when the tumor attenuation value in the early excretion phase was at least 20 HU higher than in the corticomedullary phase
  - Prolonged: when the difference between the tumor attenuation values in the corticomedullary and early excretion phases ranged between -20 to 20 HU

- Degree of tumor enhancement in the corticomedullary and early excretion phases measured in HU. We considered the difference of the mean attenuation values between the images with and without contrast. Measurements were made using a round ROI of at least 1 cm² of identical location and size was used in the three exploration phases. In order to minimize the partial volume average artifact with the surrounding renal parenchyma, the ROI was placed close to the center of the tumor. The CT images selected were the scans that showed more lesion area and renal parenchyma.

Here we obtained the largest possible region of interest. The ideal ROI location was decided by consensus taking into account tumor homogeneity or heterogeneity. In the former case a solid area of enhancement was chosen in the cortico-medullary phase, whilst in the areas of heterogeneous enhancement, because they were multiple, the ROI included the largest possible number of suspicious portions (enhancing areas that measured more than 1 cm in diameter in the short axis). At least 3 ROIs were analyzed for each phase to ascertain the presence of unequivocal enhancement and then we proceeded to calculate the average values. We tried to include the largest number of enhanced areas in the ROI and to exclude the surrounding renal parenchyma and any area inside the tumor with cystic degeneration or calcifications.
Statistical methods

The statistical analysis was done with the R-project software. A multiple logistic regression was run to differentiate atypical AML from RCC based on CT findings. The exploration was used to determine the CT findings to be included in the regression model. The influence of Interaction and Confusion were looked for but neither was found. The final model included the kidney mass contour, tumor attenuation in the non-contrast phase and the enhancement pattern over time.

The final logit multiple regression model was determined by the following equation:

\[
\text{Logit (AML)} = \beta_0 + \beta_1 \text{clobulated} + \beta_2 \text{smooth} + \beta_3 \text{isodense} + \beta_4 \text{hyperdense} + \beta_5 \text{gradual} + \beta_6 \text{prolonged}
\]

Table 1: Computed Tomography tumor assessment.

<table>
<thead>
<tr>
<th>General characteristics of the tumor (nephrographic phase)</th>
<th>Tumor margins</th>
<th>Smooth</th>
<th>Irregular</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central location</td>
<td>Extraduacapsular (75% or more of the center of the tumor located outside the kidney contour)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intra-tumor calcifications</td>
<td>Present</td>
<td>Absent</td>
<td></td>
</tr>
<tr>
<td>Perirenal changes (perirenal striations and thickening of the Gerota fascia)</td>
<td>Present</td>
<td>Absent</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Attenuation of the tumor</th>
<th>Hypoattenuation</th>
<th>Lower than the attenuation of the adjacent in the non-contrast phase renal parenchyma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoattenuation</td>
<td>Similar to the attenuation of the adjacent renal parenchyma</td>
<td></td>
</tr>
<tr>
<td>Hyperattenuation</td>
<td>Higher than the attenuation of the adjacent renal parenchyma</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tumor enhancement characteristics (attenuation increase above 20 HU)</th>
<th>Tumor enhancement distribution</th>
<th>Homogeneous (uniform enhancement both in the corticomedullary as well as the early excretion phase)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enhancement pattern over time</td>
<td>Early washout pattern</td>
<td>Corticomedullary phase: tumor with a peak of enhancement</td>
</tr>
<tr>
<td></td>
<td>Early excretion phase: washout &gt; 20 HU</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gradual pattern</td>
<td>Early excretion phase: Tumor attenuation increases &gt; 20 UH than in the corticomedullary phase</td>
</tr>
<tr>
<td></td>
<td>Early excretion phase: washout &gt; 20 HU</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gradual pattern</td>
<td>Prolonged pattern: (if the difference between the attenuation values of the corticomedullary and the early excretion phase ranged between -20HU and 20 HU)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tumor enhancement degree (in HU)</th>
<th>Tumor enhancement degree in the corticomedullary phase non-contrast phase – corticomedullary phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor enhancement degree in the corticomedullary phase non-contrast phase – corticomedullary phase</td>
<td>Tumor enhancement degree in the early excretion phase: non-contrast phase – early excretion phase</td>
</tr>
</tbody>
</table>
Table 2: Results of the general characteristics of the tumors.

<table>
<thead>
<tr>
<th>Gender</th>
<th>Size</th>
<th>Contour</th>
<th>Calcifications</th>
<th>Location</th>
<th>Perirenal changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>AML</td>
<td>65%</td>
<td>Smooth (100%)</td>
<td>Present</td>
<td>Absent (94%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>27%</td>
<td>Lobulated (47%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td>20-30 mm</td>
<td>Smooth (100%)</td>
<td>Present</td>
<td>Absent (94%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>27%</td>
<td>Lobulated (55%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCC</td>
<td>35%</td>
<td>30-45 mm</td>
<td>Irregular (65%)</td>
<td>Absent</td>
<td>Extracapsular (61%)</td>
</tr>
<tr>
<td></td>
<td>73%</td>
<td></td>
<td>Irregular (55%)</td>
<td>Absent</td>
<td>Extracapsular (61%)</td>
</tr>
</tbody>
</table>

The comparison was based on the tomographic findings related to contour irregularity, hypodense mass attenuation in the non-contrast phase and the early washout enhancement pattern. Statistical significance was any p value < 0.05.

Figure 1: Gender distribution according to pathology (atypical AML and RCC).

Figure 2: Tumor size distribution according to pathology (AMLmfc and cRCC).

Figure 3: Tumor contour according to pathology (AMLmfc and cRCC).

Figure 4: Tumor location according to pathology (AMLmfc and cRCC).
Results

The study found 68 adults with renal masses under 45 mm in diameter (average: 27 mm range 11-45 mm) diagnosed by MDCT as RCCs, there were 43 males and 25 females with ages ranging from 30-83 years (mean age: 57) (Table 2). The Pathology lab results were: 17 atypical AMLs and 51 RCCs.

There was a predominance of females in the atypical AML group (65% of the total; n: 11) and males predominated in the RCC group (73%; n = 37) (fig. 1).

In terms of size most of the RCCs measured 30-45 mm and the atypical AMLs ranged from 20-30 mm (fig. 2).

All the AMLs had smooth contours and intratumor calcifications, while most had an intracapsular location (65%) and...
absence of perirenal changes (94%). The majority of the RCCs had irregular contours (65%), extracapsular location (61%), perirenal changes (94%) and absence of intra-tumor calcifications (88%) (figs. 3-6). Atypical AMLs were Hyperdense in 59% of the cases in the non-contrast phase and the RCCs were Isodense or Hypodense in similar proportion: 43% and 45%. On the other hand, atypical AMLs had a homogeneous enhancement distribution in 82% of the cases and a prolonged enhancement pattern in 59% while the RCCs showed a heterogeneous enhancement in 96% and early washout enhancement in 94%. Atypical AMLs had an average tumor attenuation in the non-contrast phase of 32 HU (range: 21-42 HU) 79 HU in the corticomedullary phase (range: 54-111 HU) and 67 HU (range: 49-75 HU) (figs. 8 & 9) in the early excretion phase. The RCCs had an average tumor attenuation value in the non-contrast phase of 26 HU (range: 21-35 HU), it was 100 HU (range: 81-143 HU) in the corticomedullary phase and 72 HU (range: 54-112 UH) in the early excretion phase (fig. 10).

Figure 9: Enhancement pattern over time (AMLmfc and cRCC).

Figure 10: Average tumor attenuation (HU) in each phase according to each tumor type (AMLmfc and cRCC).

Figure 11: Average enhancement (HU) in each phase according to tumor pathology (AMLmfc &cRCC).

Figure 12: Pathology results of the Solid Renal Masses (n = 68).
enhancement of the atypical AMLs was 46 HU during the corticomedullary phase and it was 35 HU in the CCRs. Additionally, a dramatic difference was observed in enhancement during the early excretion phase between the atypical AMLs (74 HU) and the RCCs (47 HU) (fig. 11; Table 3).

The biopsies of the resection specimens (partial/total nephrectomies) performed at the same center revealed 17 cases of atypical AML (26%) and 51 cases of RCC (74%). These 17 cases had not been diagnosed in the preoperative period and were presumed to be RCC on the basis of tomographic findings but they were subsequently diagnosed as atypical AMLs at the Pathology lab. The MDCT images of these 17 atypical AMLs were reviewed.

Out of the 68 patients, 51 (74%) had an RCC. When subjected to the histological examination, 47 cases were exclusively or predominantly formed by clear cells (fig. 12) and the other four were papillary RCCs.

The CT findings found to be significant were: hyperdense tumor attenuation in the non-contrast phase and the prolonged enhancement pattern. Meaning that if there is a hyperdense attenuating tumor in the non-contrast phase the odds ratio for it to be a true atypical AML is 10.49; but if the enhancement pattern is prolonged over time this odds ratio raises to 36.71 (Table 4).

Table 3: Attenuation and tumoral enhancement.

<table>
<thead>
<tr>
<th></th>
<th>Attenuation</th>
<th>Enhancement distribution</th>
<th>Enhancement pattern</th>
<th>Avg. tumor attenuation</th>
<th>Tumor enhancement degree</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>NCP</td>
<td>CMP</td>
<td>EEP</td>
</tr>
<tr>
<td>Atypical AML</td>
<td>Hyper 59%</td>
<td>Homogeneous 82%</td>
<td>Prolonged 59%</td>
<td>32 HU (range: 21-42 HU)</td>
<td>79 HU (range: 54-111 HU)</td>
</tr>
<tr>
<td>RCC</td>
<td>Iso (43%)</td>
<td>Heterogeneous 96%</td>
<td>Early washout 94%</td>
<td>26 HU (range: 21-35 HU)</td>
<td>100 HU (range: 81-142 HU)</td>
</tr>
<tr>
<td></td>
<td>Hypo 45%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NCP: non contrast phase      CMP: corticomedullary phase      EEP: Early excretion phase

Table 4: Multiple logistic regression model results.

<table>
<thead>
<tr>
<th>Finding</th>
<th>Coefficient</th>
<th>Odds ratio</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-20.5708</td>
<td>1.16471e-09</td>
<td>0.9942</td>
</tr>
<tr>
<td>Lobulated contour</td>
<td>1.1276</td>
<td>3.08390e+00</td>
<td>0.9998</td>
</tr>
<tr>
<td>Smooth contour</td>
<td>18.0759</td>
<td>7.084029e+07</td>
<td>0.9949</td>
</tr>
<tr>
<td>Isodense Att.</td>
<td>-0.4006</td>
<td>6.699450e-01</td>
<td>0.7199</td>
</tr>
<tr>
<td>Hyperdense Att.</td>
<td>2.3502</td>
<td>1.048747e+01</td>
<td>0.0381*</td>
</tr>
<tr>
<td>Gradual p</td>
<td>2.8248991</td>
<td>1.685924e+01</td>
<td>0.603</td>
</tr>
<tr>
<td>Prolonged p</td>
<td>3.6031</td>
<td>3.671046e+01</td>
<td>0.009*</td>
</tr>
</tbody>
</table>

*Significant p value (p ≤ 0.05).
The next step was to calculate the probability of having an atypical AML based on the value of each tomographic finding included in the statistical model. Sensitivities and specificities were calculated for each parameter and a ROC curve developed to determine the optimal cutoff point to discriminate an atypical AML (fig. 13) that was 0.9694 since it maximizes specificity (0.9804) has a sensitivity of 0.2941 and a positive likelihood ratio of 15.

Given a pretest probability of 0.25 it is possible to calculate the post-test probability through the positive likelihood ratio. If you want to establish the probability for a lesion to be an atypical AML the post-test probability is 0.83.

Discussion

Tumors of the renal parenchyma are a group of neoplasms that may range from benign to very aggressive. Therefore, morphological characteristics, enhancement degree and pattern vary substantially according to their architecture and subtype. Thus, the characterization of renal parenchyma tumors with imaging techniques poses difficulties.

Although it is important at the pre-surgical stage to differentiate solid renal masses to plan treatment and council patients, there are no clearly defined image criteria to classify the different histological subtypes. Diagnosis defined on the basis of a biopsy is also a challenge considering it is hard to differentiate a chromophobe RCC from an oncocytoma or an RCC with a sarcomatoid component from an AML with a spindle cell component.

Atypical AMLs are the most important masses to differentiate from RCC through images. A study proved that 6.9% of patients who underwent a partial nephrectomy under the suspicion of an RCC with an average diameter of 2.3 cm (range: 1.2-4.3 cm) had the Pathology confirmation that it was an AML. This entity accounts for 1% of all the kidney tumors explored surgically. They present as single lesions or associated to tuberous sclerosis and are found incidentally in US or CT scans; or present itself as chronic pain, acute retroperitoneal hemorrhage, shock, a palpable mass or hematuria.

They appear in Ultrasound as round or oval shaped lesions well circumscribed and highly echogenic (iso or hyperechoic). When they are located in the renal sinus, typical AMLs are hyperechogenic whilst the atypical ones present a homogeneous isoechogenicity and therefore it is important to consider RCC as a differential diagnosis. Although hyperechogenicity of a kidney mass is highly suggestive of an AML, it is not pathognomonic. For this reason it is important for CT to confirm the presence of fat to be able to rule out a potentially curable RCC.

In terms of CT, a typical AML has enough fat content to be recognized and in general terms RCC can be ruled out. In the phase with no contrast this solid renal mass is hypodense because it contains macroscopic fat (like the normal subcutaneous or retroperitoneal fat) with negative attenuation values (between -10 and -120 HU) intercalated with soft tissue.
density elements as striations that represent smooth muscle, blood vessels or hemorrhage. Some authors consider that absolute CT values are only relatively reliable because they may be affected by other factors such as analysis parameters (kilovolts and milliamps) ROI orientation and values of the surrounding tissues. These lesions enhance in the post-contrast phases\textsuperscript{12, 14-20, 34}.

Likewise, atypical AMLs are difficult to diagnose with CT because of the impossibility to detect intra-tumoral fat (absent macroscopic fat or minimal quantities of fat). It may be missed if not all the solid renal masses are examined meticulously and they might not be distinguishable from other renal tumors (including RCC) this leads to unnecessary surgery and finally the surgical specimen is diagnosed by the Pathology lab as an atypical AML. In such cases if the preoperative CT is retrospectively reviewed, a fat free enhanced renal mass is

---

Figure 15: CT of an atypical renal angiomyolipoma (arrows). Pattern and enhancement over time.

Figure 16: CT of an atypical renal angiomyolipoma (arrows). Pattern and enhancement over time.
seen. CT in the non-contrast phase always shows these lesions as hyperdense compared to the renal parenchyma but after contrast is administered they have a homogeneous and prolonged enhancement that reveals vascular structures or relevant fibro-muscular elements or conversely, they do not enhance proportionately with the fat content and diminished vessel pattern (all nonspecific findings to be able to ascertain a diagnosis of atypical AML).

Fat is not detectable in axial images because it is obscured by intra-tumor bleeding or the mass is mainly composed by muscle tissue, vascular structures or immature fatty tissue or due to a minimal amount of scattered fat in the midst of other components.

The most important role of the Radiologist is to differentiate atypical AMLs from RCC and other malignant tumors using preoperative CT, in a non-invasive and reliable manner since it is vital to make therapeutic decisions as asymptomatic AMLs are managed conservatively (watched) but RCCs depending on their size and location require surgery (radical or partial nephrectomy) or else angiographic embolization.

Magnetic Resonance shows typical AMLs as hyperintense in T1 weighted images without contrast because of their fatty component with a signal that is similar to perirenal fat in the T2 weighted images, whilst the atypical AMLs are hypointense in T2 weighted images with a remarkable decline of signal intensity that is focal or diffuse in opposed-phase secondary to intracellular fatty content. This does not necessarily mean it is an AML because some RCCs may also present these features due to abundant microscopic fat content. Nonetheless there are some imaging features that differentiate RCCs from AMLs both in the non-contrast as the IV contrast phases. Many papers have discussed the scarcity or absence of fat in certain AMLs defined histologically and so such authors recommend that faced with the suspicion that a SRM has a small amount of fat, CT should be used adjusting collimation and the table advance to obtain an effective section thickness (1.5-5 mm). In this line some authors propose recording the attenuation value in the pre-contrast stage (HU sampling using the ROI) if required whilst other authors suggest using a multiphase acquisition to improve detection. Sant et al.36 determined that a negative attenuation coefficient is characteristic of a kidney AML with mature fat elements whilst a positive attenuation, in spite of it being suggestive of RCC may also be found in AMLs with low mature fat content or with a high proportion of immature fetal fat. CT has a relative inability to identify the latter which may be deemed as a limitation for the preoperative diagnosis of AML.

The positive attenuation coefficient of an atypical AML is explained by the fact that its fat fraction is only 5 – 15% of the tumor mass and/or by the proportion of fetal or immature adipocytes with respect to mature fat.

In this regard Winkler considers that when the fat fraction is higher than 50% of the mass it allows a reliable diagnosis of a typical AML. In terms of the non-contrast phase, our study found that hyperdense attenuation was a significant tomographic finding for the diagnosis of atypical AML (figs. 14-16).

Tumor enhancement has also been compared between AMLs and CCRs. The usefulness of different parameters in the detection of SRMs varies according to different authors. Some consider that the nephrographic phase is superior because it achieves maximum, homogeneous enhancement of the kidney parenchyma and more difficult in the corticomedullary and early excretion phases. Other authors like Smith et al. detected 20-30% more solid renal masses using the early excretion phase than the corticomedullary phase but a recent review found comparable sensitivities for SRM detection in both the corticomedullary and the early excretion phases.

In this regard Cohen et al.45 detected 1.5 times more SRMs when they interpreted the non-contrast images in the
nephrographic phase together with the non-contrast images in the corticomedullary phase.

Millet et al. determined there were no useful CT criteria either morphological or related to enhancement to differentiate small malignant tumors from benign ones. Discrepancies also persist in terms of attenuation value and enhancement pattern to differentiate these tumors. In our experience the CT finding that proved to be significant was Prolonged Enhancement over time for atypical AMLs. Additionally, crRCCs displayed an enhancement above 87 HU in the corticomedullary phase and above 54 in the early excretion phase in agreement with Kim et al. The Hosokawa et al. paper stated that hyperdense renal tumors in the non-contrast phase with moderate enhancement and without demonstration of any fat component suggested that it was an atypical AML. Pierorazio et al. determined that a small SRM with high and early enhancement has a higher probability of being a crRCC than an oncocytoma, a chromophobe RCC an AML or a papillary RCC. In their study, as in our series (fig. 17) higher enhancement values during the corticomedullary phase increased the likelihood of crRCC. Conversely and contrary to our findings, Bird et al. showed that crRCCs displayed a 50% washout. As other papers did, we included morphometric and enhancement features to provide clues on tumor histology. Although Pierorazio et al. could not determine CT usefulness, probably as a result of the small sample size or because it reflected differences in the biology of the small SRMs (generally more homogeneous) and the larger ones included in prior studies, in this case practically all of the atypical AMLs had smooth edges, an intracapsular location, no perirenal changes or intra-tumor calcifications while the RCCs mostly had irregular borders, extracapsular location, perirenal changes and no intra-tumor calcifications. Among the strengths of our study, it is worth mentioning the strict application of a standard CT protocol (acquisition time and technique) that avoided extrinsic factors that could affect results. Additionally, like Zhang et al, we minimized the partial volume artifact in the areas with cystic or necrotic changes thus reflecting the actual tumor vasculature by measuring the areas of greater enhancement in the heterogeneous SRMs instead of doing so in the whole tumor. Meanwhile, most of the analysis only include malignant tumors or its subgroups while our study took into account both the benign and the malignant neoplasms, as did Jinzaki et al. (although his cohort was relatively small [n = 40]). On the other hand the limitation of our study lies in the small number of cases although other series had the same disadvantage due to the rarity of atypical AMLs.

Secondly, although our Radiologists were unaware of the pathology results, this study should be conducted prospectively and truly blinded. We should also mention the retrospective nature of the study and that the rate of malignant lesions (88%) is probably higher than in the general population because our institution is a referral tertiary care center for oncology patients. However, even in the general population, the incidence of malignant kidney lesions is much higher than the incidence of benign solid tumors. Lastly, we should not fail to highlight that our sample included a relatively small number of benign lesions and other small, benign kidney masses of a different histology that were not included.

Conclusion

Triphasic helical CT is the standard imaging method to assess solid renal masses of less than 4 cm. It is useful to differentiate atypical AMLs from RCCs and the most valuable CT findings were “hyperdense tumor attenuation without IV contrast” and the “prolonged enhancement pattern”. However, future studies should include larger populations, prospective multiobserver measurements and improvement in the actual value of the enhancement pattern in predicting histology diagnoses.

Ethical responsibilities

Protection of human subjects and animals

The authors declare that no experiments were done in human subjects or animals for this research

Confidentiality

The authors declare that they have observed the protocols of their center related to the publication of patient data

Privacy Rights and Informed Consent

The authors declare that no patient data are disclosed in this article

Conflict of interest

The authors declare that they have no conflict of interest

References

4. Warshauer DM, McCarthy SM, Street L, Bookbinder MJ, Glickman MG,