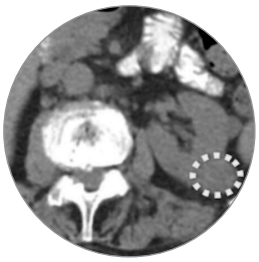

Oncocytomas: Imaging Findings and Anatomopathology Correlation

Oncocitomas: hallazgos tomográficos y correlación anatomopatológica

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Summary

Introduction: The imaging findings of oncocytomas usually coincide with renal cell carcinoma (RCC), which makes it difficult to discriminate them in imaging. ***Objective:*** To evaluate the imaging findings of a sample of oncocytomas in tomography (CT). ***Methods:*** We retrospectively selected patients with renal tumor surgery and oncocytoma anatomopathological diagnosis, who were treated between January 2015 and December 2017. Patients who underwent CT with intravenous contrast at our institution were included. ***Results:*** Of the total number of patients (n = 44), 43 had a single renal lesion while one patient presented 3 lesions. Of the total lesions (n = 47), 20 (42.55%) were diagnosed after a radical nephrectomy and 24 (51.10%) were diagnosed by a partial nephrectomy. The mean maximum diameter was 36.5 mm (RIQ 22-44, 25), of which they were grouped by tumor length into smaller or larger than 4 cm, with 22 tumors in this last group (47%). Of these, 15 tumors (31.91 %) that were larger than 4 cm had a central scar. Calcifications were evident in 3 patients (6.8 %). One tumor (2.1%) was found with the presence of inversion of segmental enhancement after administration of intravenous contrast. In this case, the oncocytoma was less than 4 cm. ***Conclusion:*** The finding of a solid mass with more enhancement than the surrounding parenchyma during the nephrographic phase makes it necessary to consider oncocytoma among the differential diagnoses.

Resumen

Introducción: En imágenes, los hallazgos del oncocitoma generalmente coinciden con el carcinoma de células renales (CCR) por lo que resulta muy poco segura su discriminación mediante imágenes. ***Objetivos:*** Evaluar el comportamiento de una muestra de oncocitoma en tomografía (TC). ***Métodos:*** Se seleccionaron retrospectivamente los pacientes con cirugía de tumor renal y diagnóstico anatomopatológico de oncocitoma, que fueron tratados entre enero de 2015 y diciembre de 2017. Se incluyeron los pacientes a quienes se les realizó TC con medio de contraste endovenoso en nuestra institución. ***Resultados:*** Del total de pacientes (*n* = 44), 43 tenían una lesión única renal, mientras que uno tenía tres lesiones. Del total de las lesiones (*n* = 47), 20 (42,55 %) fueron diagnosticadas tras una nefrectomía radical y 24 (51,10 %) fueron diagnosticadas por una nefrectomía parcial. La media de diámetro máximo fue de 36,5 mm (RIQ 22-44,25), de los cuales se agruparon en menores y mayores a 4 cm; se encontraron 22 tumores en este último grupo (47 %). De estos, en 15 tumores (31,91 %) que tenían más de 4 cm se encontró la cicatriz central. Se evidenciaron calcificaciones en 3 pacientes (6,8 %). Se encontró 1 tumor (2,1 %) con inversión de realce segmentario luego de la administración medio de contraste endovenoso. En este caso, el oncocitoma era menor a 4 cm. ***Conclusión:*** El hallazgo de una masa sólida con realce más intenso que el parénquima circundante durante la fase nefrográfica obliga a considerar al oncocitoma entre los diagnósticos diferenciales

Introducción

Renal oncocytoma is a benign tumor and represents 3-7 % of renal neoplasms (1).

Renal oncocytomas are characterized by a homogeneous hypervascular enhancement with late-stage computed tomography (CT) washing and a heterogeneous enhancement for those larger than 4 cms (2), without bleeding, calcification or necrosis (3). In large lesions it is common to find a central scar (4).

The imaging findings of oncocytomas generally coincide with renal cell carcinoma (RCC), making this method very unsafe for differentiation (3).

Methods

Patients with renal tumor surgery and anatomopathological diagnosis of oncocytoma were retrospectively selected and treated between January 2015 and December 2017. Patients who had CT scans with

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intravenous contrast medium were included. Out of 70 patients, those who did not have the four-phase protocol to evaluate renal lesions were excluded, resulting in a sample of 44 patients and 47 lesions.

These patients underwent multislice CT with 64- and 320-track tomographs (Toshiba Aquilion and Aquilion One, Otawara, Japan). The images were obtained in inspiratory apnea and with the following parameters: 120 kVp, variable tube current, and a 1 mm slice thickness. The study protocol consists of four phases: one phase without intravenous contrast from the lung bases to the iliac crests, injection of 100-150 mL iodinated contrast Non-ionic with a flow rate of 3 mL/s. After the administration of contrast medium, a corticomedullary (40-45 seconds), nephrographic (90-120 seconds) and excretory (7-10 minutes) phases were obtained.

For the analysis of the images, the phases were classified as: phase without contrast medium, when no intravenous contrast had been administered; corticomedullary, when the enhancement of the cortex predominated over that of the medulla (pyramids); nephrographic, when the entire renal parenchyma is homogeneous and excretory, when the contrast medium was opacifying the pyelocalytic system. The images were analyzed and interpreted at a workstation (DICOM Medical Alma 5.0).

The CT scans were reviewed by a genitourinary imaging specialist with 11 years of experience, who only had information on the age and gender of the patients. Two ROIs of between 0.5-1 cm^2 in the area of highest contrast enhancement for heterogeneous lesions and in the center for lesions with homogeneous enhancement were used for the analysis, and enhancement means were calculated. These enhancements were compared with the density of the adjacent healthy parenchyma in each of the phases (Figure 1). The maximum diameter of each lesion was measured in axial sections.

Of the 44 patients, the lesions were analyzed and evaluated according to size, enhancement pattern, magnitude of enhancement, calcifications, central scar and sign of segmental enhancement inversion; that is, sectors of the lesion that were hyperdense and hypodense in the corticomedullary phase, behaved in the opposite way in the nephrographic phase. These findings were evaluated under a system of organization of dichotomous variables.

The statistical analysis was calculated using the SPSS software (SPSS18 for Windows, SPSS, Chicago).

Results

Of the total number of patients (n = 44), 43 had a single kidney injury, while one patient had 3 injuries (Figure 2). Of the total lesions (n = 47), 20 (42.55%) were diagnosed after a radical nephrectomy and 24 (51.10%) were diagnosed by a partial nephrectomy.

Of the total, 27 patients were women (61.4%). The mean age at the time of the nephrectomy was 70 years (IQR 62.5 to 76.5). In terms of tumor characteristics, 43 were solid (91.1%), 3 were solid-cystic (6.4%) and 1 was cystic (2.2%) (figure 3).

The mean maximum diameter was 36.5 mm (IQI 22-44.25), of which they were grouped into minors (figure 4) and greater than 4 cms, with 22 tumors in this last group (47%).

The central scar was found in 15 tumors (31.91 %), all of which had a tumor larger than 4 cms (figure 5). Calcifications were evident in 3 patients (6.8%).

A tumor (2.1%) with segmental enhancement inversion was found after the administration of intravenous contrast (figure 6). In this case, the oncocytoma was smaller than 4 cms (table 1).

Table 1. Characteristics of tumors in CT

Sample	*n* = 47
Greater than 4 cm	22 (47 %)
Central Scar	15 (31,91 %)
Calcifications	3 (6,3 %)
Segmental enhancement investment	1 (2,1 %)

The mean tumor density in the non-contrast, corticomedullary, nephrographic and excretory phases was 26.8 UH (r 25.7-27.9), 150.7 UH (r 146.6-151.8), 155.6 UH (r 150.6-160.6) and 93.7 UH (r 89.8-97.6), with the highest peak in the nephrographic phase.

The relationship between tumor density and the adjacent normal parenchyma was not significant in the non-contrast phase (1 ± 2.4, p 0.42). A significant difference was found between the density of the normal parenchyma and the corticomedullary phase (25.6 ± 11.6, p 0.0001), the nephrographic phase (43 ± 10, p 0.0001) and the excretory phase (27.3 ± 5, p 0.0001) (figure 7).

Discussion

Numerous publications have reported that approximately 20% of renal masses smaller than 4 cms and between 5 and 10% of those larger than 4 cms prove to be benign lesions after surgery (5-7).

Furthermore, taking into account that nephrectomy, both radical and partial, is unnecessary in this type of lesions, numerous authors have tried to characterize them to differentiate them from the malignant ones.

Several authors, in different publications, have tried to identify distinctive characteristics of oncocytomas taking into account that they represent the second most frequent benign renal lesion. Tomographic characteristics of renal oncocytomas include defined margins, homogeneous enhancement, central scar and segmental enhancement inversion.

The enhancement with contrast medium is defined with the magnification greater than 10 UH between the image without and with contrast medium, although other authors state that the enhancement between 10-20 UH is indeterminate (8). Pseudo-enhancement of small renal masses may occur as a result of increased density of the surrounding normal renal parenchyma and should be considered especially with endophytic masses (9).

The degree of tumor enhancement and the phase of greatest enhancement is variable, as reported in different publications. In the study by Bird and collaborators (10) it was demonstrated that the oncocytoma shows greater enhancement in the corticomedullary phase while in other studies, such as that of Pierorazio and collaborators or that of Zhang and collaborators, it was observed in the nephrographic phase (11, 12). The variability reported in the enhancement with contrast coincides with our results.

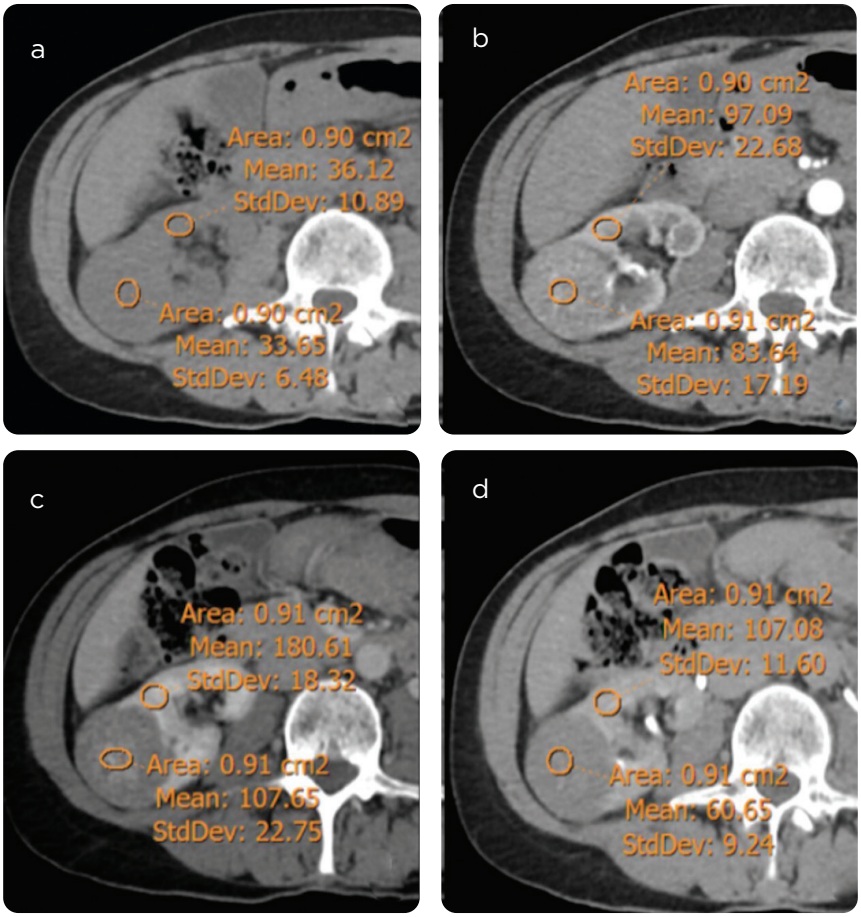

Figure 1. Multiphase CT in a 70-year-old woman. a) CT, phase without contrast medium, b) corticomedullary, c) nephrographic, and d) excretory. Heterogeneous formation in the upper pole of the left kidney. Density of the lesion and adjacent parenchyma ± SD was calculated in each phase.

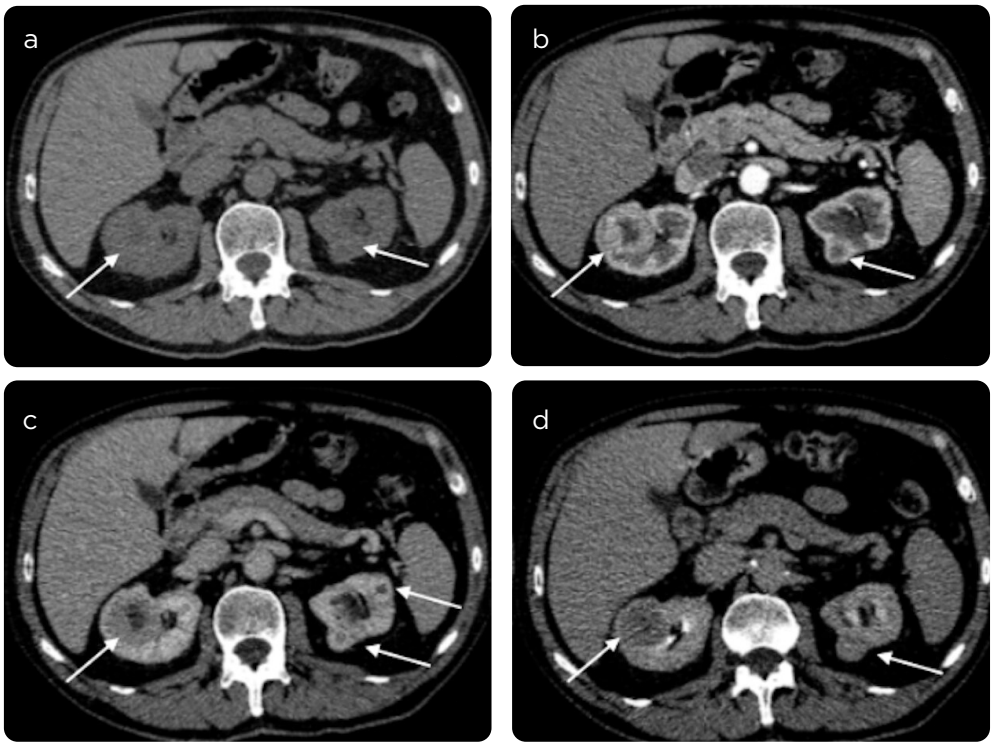

Figure 2. Bilateral oncocytomas. a) CT, phase without contrast medium, b) corticomedullary, c) nephrographic and d) excretory, in both kidneys, with early peripheral enhancement, while the central sector of the tumors has less enhancement, in relation to the central scar. The tumors show less relative enhancement with respect to the healthy renal parenchyma, the central area cannot be differentiated from necrosis that could present a renal cell carcinoma.

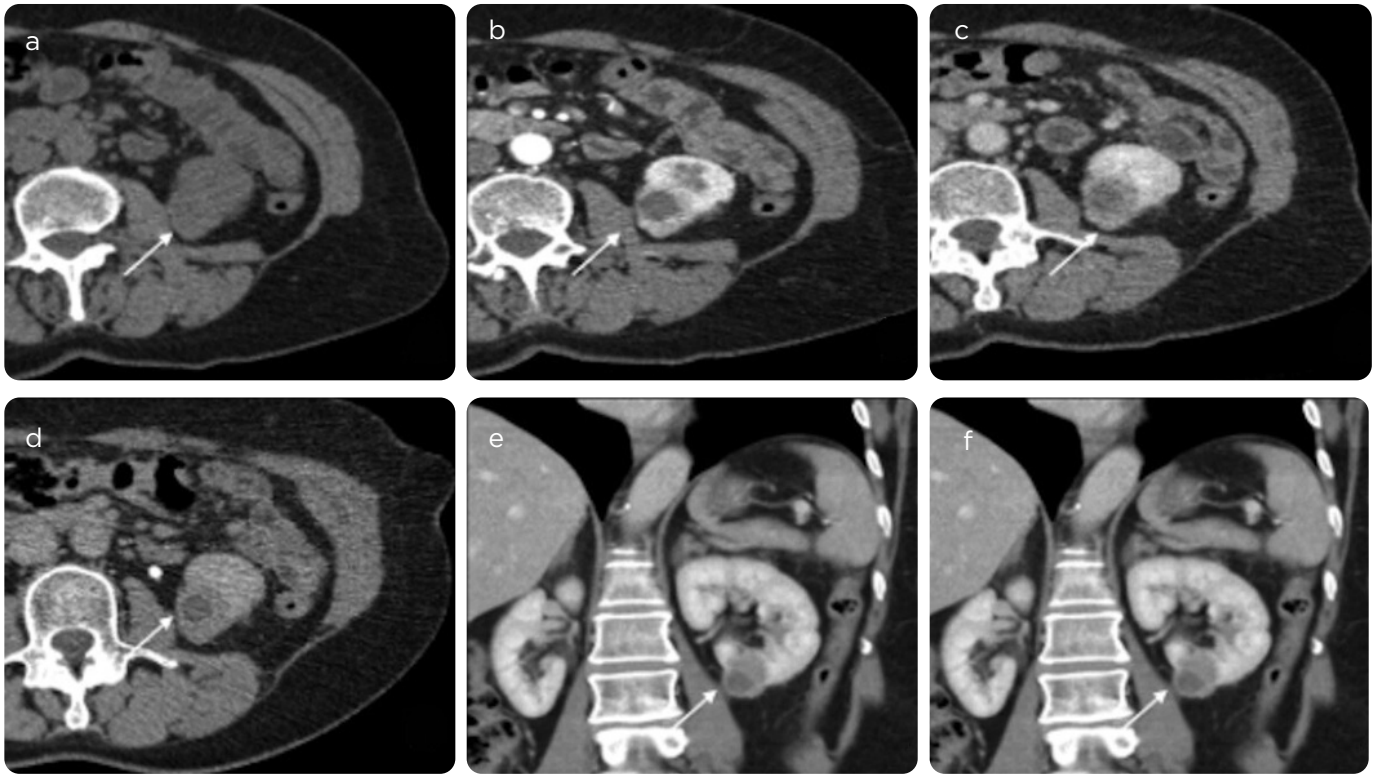

Figure 3. Solid cystic oncocytoma. CT scan, a) phase without contrast medium, corticomedullary (b axial, e coronal and f sagittal), c) axial nephrographic and d) axial excretory. Solid-cystic formation in the lower pole of the left kidney. Central region of low density that does not enhance in the phases with contrast medium and the rest of the tumor enhances especially in the corticomedullary phase (b), although to a lesser extent in relation to the adjacent parenchyma. The unenhanced area cannot be differentiated from necrosis which could be found in renal carcinoma with necrosis or cystic varieties.

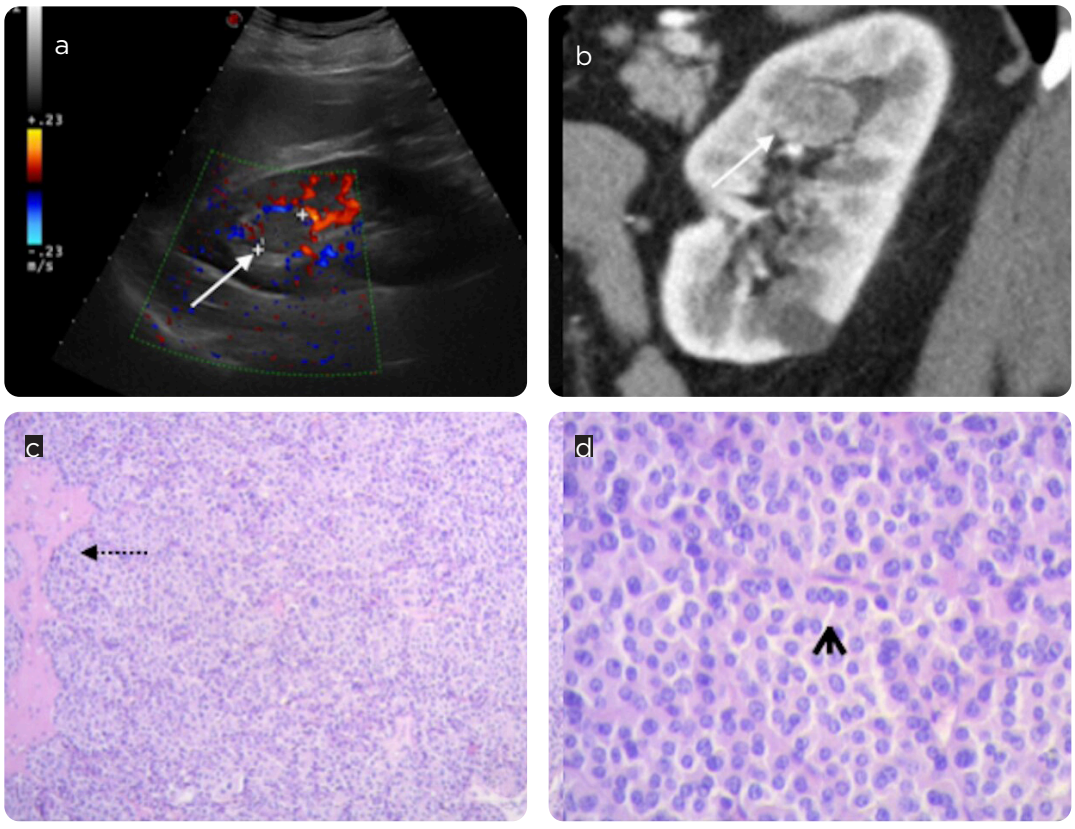

Figure 4. Correlation between ultrasound and CT. a) Renal ultrasound and CT in corticomedullary phase (b) sagittal reconstruction). Nodular formation less than 4 cms that is insinuated in the renal sinus (arrow), which presents Doppler flow in its interior and peripheral (a). In CT it is evidenced the formation (arrow) that slightly displaces the upper calitic group and presents heterogeneous enhancement after the administration of intravenous contrast. c) Histology with hematoxylin and eosin 100x and d) 400x, which evidences a solid pattern with vascular structures (black dotted arrow) and oncocytic cells with nuclei with degenerative atypia (black arrowhead).

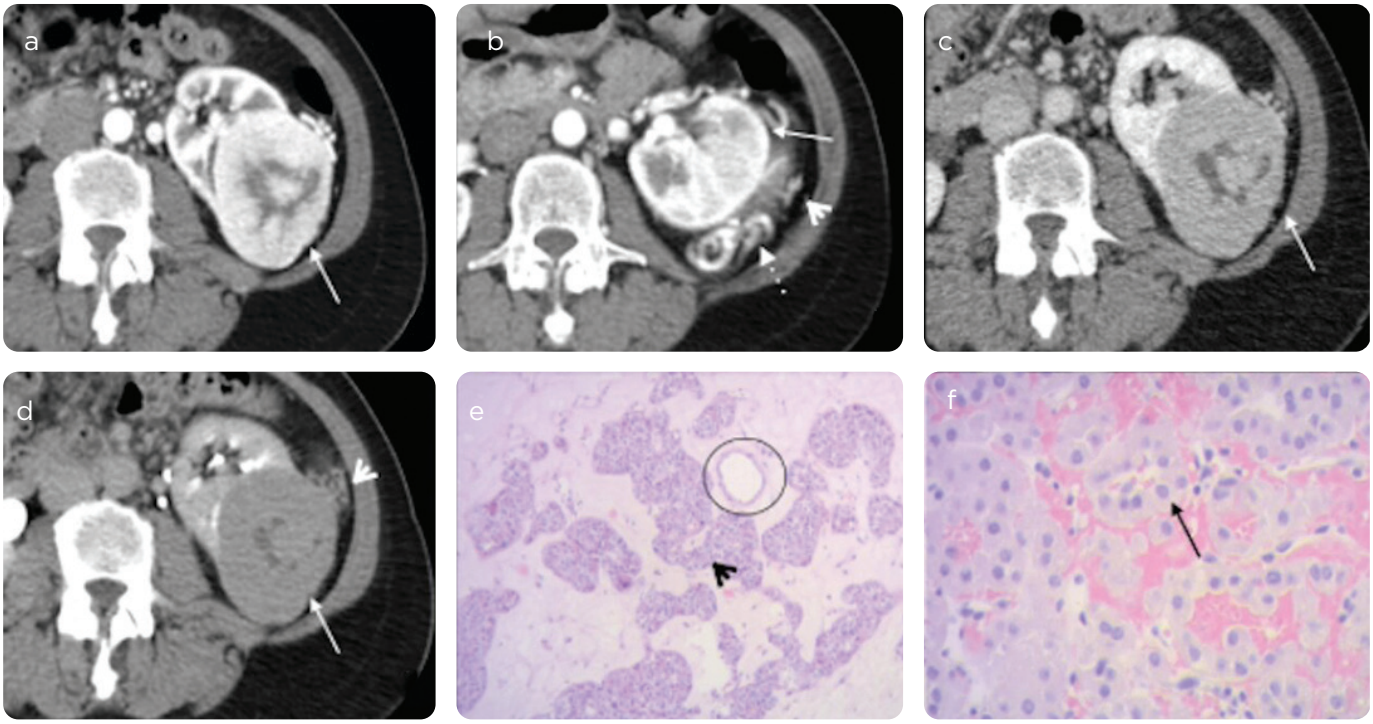

Figure 5. Oncocytoma with central scar. CT scan, a and b) corticomedullary phase, c) nephrographic and d) excretory. Solid formation (arrow), with two segments, one of high peripheral density and another of low central density in corticomedullary phase. Perirenal neovascularization (dotted arrow). Increase in density of adjacent fat planes (arrowhead). The behavior of the central zone visible in this case does not allow differentiating it from necrosis or ischemia. e) Histology with hematoxylin and eosin 100x and f) 400x where edematous areas with cell nests (black arrow head) with delicate vessels (circle) and oncocytic cells with rounded nuclei and eosinophilic cytoplasm (black arrow) are evidenced.

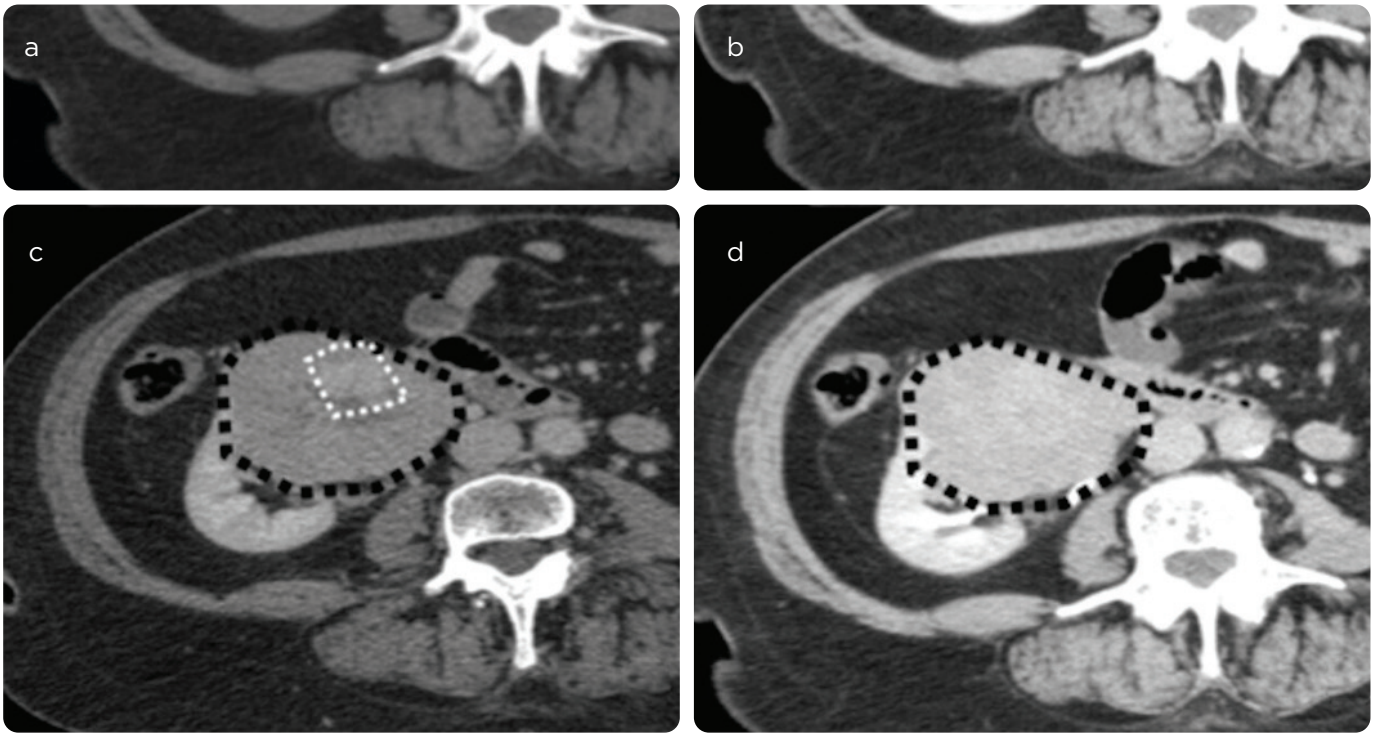

Figure 6. Segmental enhancement investment. CT, a) phase without contrast, b) corticomedullary, c) nephrographic and d) excretory. c) shows tumor enhancement (black dotted line), except for the central region (white dotted line). d) shows segmental enhancement inversion of the mass. The central segment in this phase is of high density with respect to the periphery, contrary to what is observed in the corticomedullary phase. In the excretory phase, the differences between the two tumor components are lost.

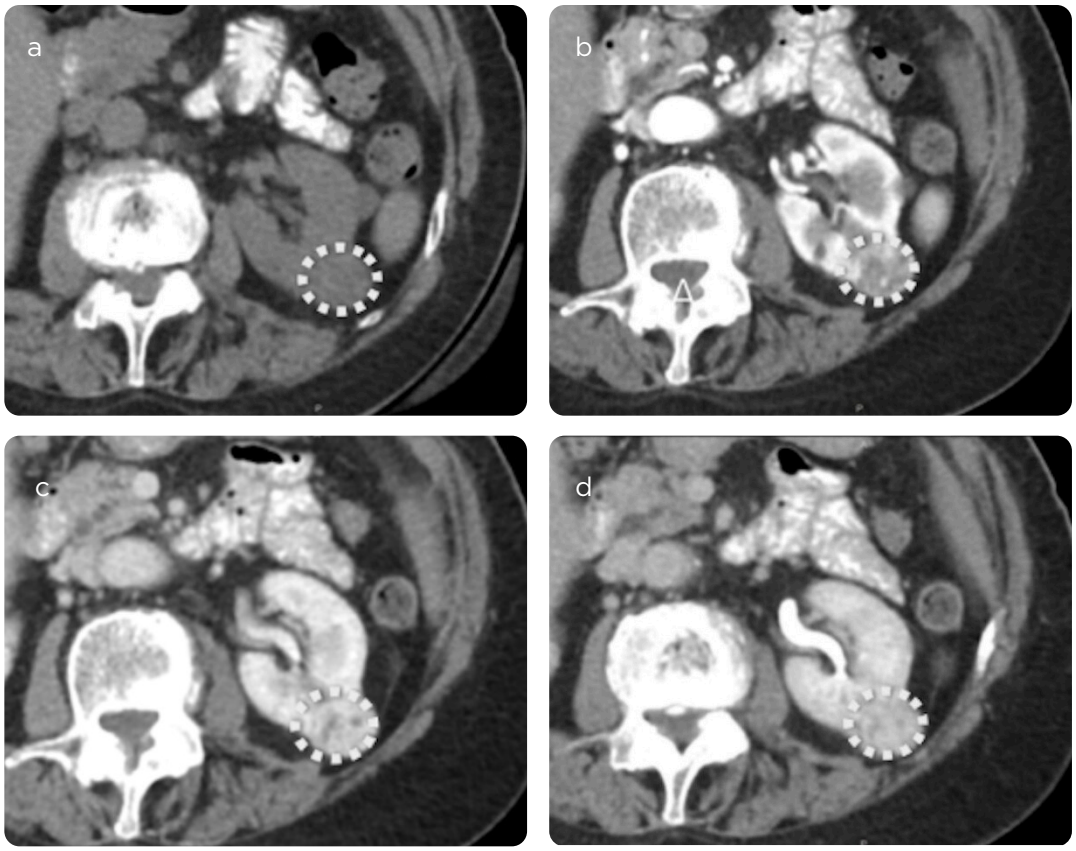

Figure 7. Solid oncocytoma, small, with heterogeneous enhancement. CT scan, a) phase without contrast medium, b) corticomedullary, c) nephrographic and d) excretory. Tumor less than 4 cms (dotted line). The corticomedullary phase (b) shows a central focal area of low density in the lesion. The nephrographic phase shows a low density focal area in the same region.

Kim and collaborators (13) described a segmental pattern with inversion in the corticomedullary and nephrographic phases in small oncocytomas. The oncocytoma has two components, evidenced after the administration of the contrast medium, in the corticomedullary phase, one of high and the other of low attenuation, but in the nephrographic phase the patterns are inverted.

However, some studies found that this pattern of enhancement is controversial for oncocytomas (14-16). In this series of cases, only one case with enhancement inversion was presented. One reason for the discrepancy in the prevalence of this finding is attributable to the differences in the CT protocols used (1). Although in this study a standardized protocol was used and those patients who had not been studied in four CT phases were excluded, it should be taken into account that this finding appears in 6% of the oncocytomas and in those oncocytomas smaller than 4 cms (14). Another possible explanation is that the histoarchitecture of oncocytomas is more variable than one might think.

The subjective tumor heterogeneity, after the administration of the intravenous contrast medium, is an important parameter in tumor characterization (3, 12, 16). Oncocytomas tend to be more homogeneous than RCC (17).

The central scar corresponds to a central zone of connective tissue, with fibrotic bands projected towards the periphery of the lesion. It has been reported in 33% of cases, and is more frequently found in lesions larger than 25 mm (1). However, it is not a pathognomonic sign and it is indistinguishable from the central necrosis that RCCs usually present (18). In this sample, this sign was seen in 15 tumors (31.25%) and all of them were lesions larger than 4 cms.

Differentiating a benign mass from a malignant one represents the main objective in the characterization of renal lesions, which contributes to reduce the incidence of unnecessary procedures (7), although it is difficult to differentiate oncocytomas from malignant lesions such as chromophobic RCC (19).

Considering the difficulties that imaging often presents in the accurate differentiation of a benign lesion from a malignant one, small renal mass biopsy may be useful when considering major surgery (20) or minimally invasive procedures such as radiofrequency ablation or cryoablation (21).

Radiomics is defined as the conversion of images to quantitative data, and the subsequent extraction of these data for better decision support (22). Quantitative image characteristics based on intensity, shape, size or volume, and texture, provide information about the tumor phenotype and the microenvironment (or habitat), are different from what is provided by the results of laboratory tests and genomic and proteomic analyses or conventional imaging reports (22). The analysis of these imaging biomarkers could help in the characterization of oncocytomas, without the need to subject the patient to unnecessary surgery (22).

The retrospective nature of this work represents a weakness. In this first stage of analysis, a descriptive study of the variables mentioned was carried out, so that the frequency of their appearance was assessed. The comparison with other populations is not part of this presentation, and constitutes an analysis still in progress for future comparisons.

In all the cases studied in this group, there was anatomopathological surgical confirmation and there are few works with this number

of sample population, even less in Spanish speaking (according to the bibliographic search, there are two articles). Finally, all the tumors were studied with the same protocol, in order to eliminate the variability of the technique.

Heterogeneous enhancement with a peak in the nephrographic phase was the finding that best characterized in this study oncocytomas, both larger and smaller than 4 cms.

In the case of those less than 4 cms, this finding combined with the inversion of segmental enhancement were the most frequently found, and those that combined help to identify these lesions.

As for those larger than 4 cms, the heterogeneous enhancement in nephrographic phase together with the presence of a low density central scar were the most frequent combined findings.

Conclusion

The finding of a solid mass with more intense enhancement than the surrounding parenchyma during the nephrographic phase forces to consider the oncocytoma among the differential diagnoses. In the case of lesions smaller than 4 cms, segmental inversion reinforces this possibility.

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