Papillary renal cell carcinoma: pictorial review

Poster No.: C-1772
Congress: ECR 2011
Type: Educational Exhibit
Authors: H. S. Rodrigues Duarte¹, P. F. R. Oliveira da Silva², C. Fernandes¹, A. Rodrigues¹, M. F. Ribeiro¹, A. T. Aguiar¹; ¹Porto/PT, ²Braga/PT
Keywords: Neoplasia, MR, CT, Oncology, Kidney
DOI: 10.1594/ecr2011/C-1772

Any information contained in this pdf file is automatically generated from digital material submitted to EPOS by third parties in the form of scientific presentations. References to any names, marks, products, or services of third parties or hypertext links to third-party sites or information are provided solely as a convenience to you and do not in any way constitute or imply ECR’s endorsement, sponsorship or recommendation of the third party, information, product or service. ECR is not responsible for the content of these pages and does not make any representations regarding the content or accuracy of material in this file.

As per copyright regulations, any unauthorised use of the material or parts thereof as well as commercial reproduction or multiple distribution by any traditional or electronically based reproduction/publication method ist strictly prohibited.

You agree to defend, indemnify, and hold ECR harmless from and against any and all claims, damages, costs, and expenses, including attorneys’ fees, arising from or related to your use of these pages.

Please note: Links to movies, ppt slideshows and any other multimedia files are not available in the pdf version of presentations.

www.myESR.org
Learning objectives

To describe imaging findings in histological proven papillary renal cell carcinomas (pRCCs) cases from our hospital.
Background

RENAL CELL CARCINOMAS (RCCs)

Renal cell carcinomas (RCCs) are the most common primary tumor arising in the kidney, accounting for approximately 80 to 85 percent of such tumors. Transitional cell carcinomas of the renal pelvis are the next most common (approximately 8 percent). Other parenchymal epithelial tumors, such as oncocytesomas, collecting duct tumors, and renal sarcomas occur infrequently. Nephroblastoma or Wilms’ tumor is common in children (5 to 6 percent of all primary renal tumors), while renal medullary carcinoma is a rare form of RCC, seen in sickle cell disease.

EPIDEMIOLOGY

The incidence of RCC varies widely from region to region with the highest rates observed in Scandinavia and North America. Although the incidence is lower in Africa, whites and blacks appear to be equally affected in the United States.

The incidence of RCC is gradually increasing, partly due to increased number of asymptomatic tumors detected as a result of widespread use of noninvasive abdominal imaging modalities.

In older studies, RCC was at least twice as frequent in men as women. However, more recent data suggest that this gap has slightly narrowed.

RCC occurs predominantly in the sixth to eighth decade of life with median age at diagnosis around 64 years of age. It is unusual in patients under 40 years of age and rare in children.

The five-year survival rate of patients with kidney cancer has doubled over the last fifty years, from 34 percent in 1954 to 69 percent in 2002. This improved survival and case-fatality rate is mostly due to earlier diagnosis and potential earlier surgical treatment.

A number of environmental and clinical factors have been implicated in the etiology of RCC. These include smoking, hypertension, occupational exposure to toxic compounds, obesity, acquired cystic disease of the kidney (typically associated with dialysis), analgesic abuse nephropathy, and genetic predisposition.
PATHOLOGY

Previously, RCCs were classified by cell type and growth pattern. This classification has recently changed to more accurately reflect the morphology, growth pattern, cell of origin, histochemical, and molecular basis of the different types of carcinomas. Several distinct subtypes of RCC have been identified, including:

- Clear cell (75 to 85 percent of tumors)
- Papillary (chromophilic) (10 to 15 percent)
- Chromophobic (5 to 10 percent)
- Oncocytic (uncommon)
- Collecting duct (Bellini’s duct) (very rare)

Less than 5 percent of RCCs are considered unclassified.

Histologic grade is an independent factor correlating with survival. Multiple systems are used to grade RCC, of which the Fuhrman’s grade is the most widely used. Fuhrman’s grade is on a scale of I-IV, where grade I carries the best prognosis and grade IV the worst.

STAGING

The Tumor Node Metastasis (TNM) staging system on page 7 is used for staging all histologic variants of renal carcinoma. This system was revised in 2010, and is supported by both the American Joint Committee on Cancer (AJCC) and the International Union for Cancer Control (UICC). These TNM criteria define the anatomic extent of disease and stage and have been shown to correlate with prognosis, providing important information for patient management.

PROGNOSIS

Prognosis is determined by the extent of disease, histopathology, and clinical factors.

The anatomic extent of disease is the most consistent factor that determines prognosis in patients with RCC. The tumor node metastasis (TNM) staging system is used to assess the anatomic extent of disease.
Patients with stage I (T1N0) RCC have a five-year survival rate over 90 percent. The median survival for patients with stage IV disease (T4 primary tumor, N2 involvement, or distant metastases) is only 16 to 20 months, and the five-year survival rate is less than 10 percent for patients with distant metastases.

In addition to the anatomic extent of disease, clinical factors can influence survival. Negative prognostic signs include a poor performance status, the presence of symptoms and/or paraneoplastic syndromes (eg, anemia, hypercalcemia, hepatopathy, thrombocytosis, fever, weight loss), and obesity.

TREATMENT

Surgery is curative in the majority of patients without metastatic RCC and is therefore the preferred treatment for patients with stages I, II, and III disease. Surgery can involve either a radical nephrectomy or a variety of renal-sparing approaches in carefully selected patients, depending upon the extent of disease. Surgery may be carried out through a conventional approach or by laparoscopy.

**Radical nephrectomy** has been the most widely used approach and remains the preferred procedure when there is evidence of invasion into the adrenal, renal vein, or perinephric fat.

Partial nephrectomy (either open or laparoscopic) is an alternative for smaller tumors and is particularly valuable in patients with bilateral or multiple lesions, those with inherited syndromes in whom there is an increased risk of an additional primary tumor, and those with impaired renal function.

For elderly patients and those with significant comorbid disease that increases the risks of surgery, **ablative techniques** (cryoablation, radiofrequency ablation) are an alternative.

PAPILLARY RCC (pRCC)

Papillary RCC is the second most frequent RCC subtype, accounting for approximately 10-15% of all known RCC lesions.

Although most pRCC are unilateral, pRCC is the most common multifocal or bilateral renal tumor. pRCCs commonly present as small, early stage tumors.
Patients usually present in the third to eighth decades of life. The male-to-female ratio ranges from 2:1 to 3.9:1.

As with clear cell cancers, pRCCs originate from the proximal tubule, but they are morphologically and genetically distinct malignancies. Multiple genetic abnormalities have been described. While inherited papillary RCCs have been associated with mutations in the c-met oncogene, such mutations have not been routinely detected in sporadic cases.

Papillary carcinomas have been subdivided into two subtypes, based upon histologic criteria and distinctive gene expression profiles. Type 1 tumors tend to be low-grade and have a better prognosis, while type 2 lesions generally are high-grade and have a poorer prognosis. Patients with type 1 pRCC have an excellent survival in contrast to patients with type 2 pRCC, which are high grade tumors with dysregulation of the G2-M checkpoint gene.
Fig. 0: Tumor Node Metastasis (TNM) staging system for RCC

*Fig. 0:* Percent five-year survival in RCC by TNM stage in several contemporary cohorts

COMPUTED TOMOGRAPHY

At nonenhanced CT, calcification on page 11 is seen slightly more often in pRCC than in clear cell RCC (cRCC), however this is not of value in making this differentiation.

pRCC typically enhances to a lesser degree than cRCC in all phases of postcontrast imaging. The difference in the degree of enhancement between pRCC and cRCC is due to differences in the intratumoral vascularity, measured in terms of microvessel density.

Differences in enhancement peak in the corticomedullary phase, being less marked in the excretory phase.

In practice, if a heterogenous mass enhances to a degree similar to that manifested by the renal cortex, it is likely to be a cRCC. A mass that enhances to a lesser degree is likely to represent a pRCC or a chromophobe RCC. Herts et al (2002) have shown that the likelihood of papillary RCC is close to 50% when the tumor-to-aorta or tumor-to-kidney enhancement ratio is less than 0.25.

pRCC can be classified on the basis of their CT appearance as solid or cystic masses. Solid tumors can appear homogeneous and uniform or heterogeneous with areas of necrosis. At CT, pRCC is more likely to be homogeneous in comparison with cRCC, particularly in cases of smaller tumors (<3cm in diameter). pRCC larger than 3cm may be heterogeneous with areas of necrosis and hemorrhage (chromophobe RCCs tend to be homogeneous even when large).

Small tumors (<3cm in diameter) are better identified on nephrographic phase images than on corticomedullary phase images.

The imaging features of type 1 and type 2 pRCC are very similar. Type 2 pRCCs tend to be of a more advanced stage.

The relative hypovascularity of pRCC can cause it to be mistaken for a simple renal cyst. Simple cysts do not enhance by more than 10 HU from precontrast to postcontrast imaging. Enhancement of 10-20 HU is considered suspicious. In the absence of
precontrast images, the presence of de-enhancement or contrast material washout at delayed phase imaging, is equally useful information and an indicator of vascularity.

pRCCs can occasionally manifest as cystic masses. Their cystic nature may be due to their inherent architecture or secondary to cystic degeneration and extensive necrosis.

**MR IMAGING**

At MR imaging, pRCC frequently shows a pseudocapsule with homogenous low signal intensity on both T1- and T2-weighted images, whereas cRCC has higher signal intensity on T2-weighted images. Oliva *et al* (2009) suggested that T2 hypointense feature of pRCCs correlated only with presence of a fibrovascular stalk, the hallmark of a papillary architecture on page 11, not with the presence of hemosiderin or other iron-containing materials.

pRCC shows homogeneous low-level enhancement on page 14 after intravenous contrast material administration, less intense than in cRCC. The ability to subtract post- and precontrast images can help detect subtle enhancement.

Necrosis and hemorrhage on page 19 may be present in low-grade type 1 tumors and, when present, result in a more heterogeneous appearance. Type 2 (eosinophilic) pRCCs consist of large eosinophilic cells with pleomorphic nuclei. At MR imaging, they usually have more complex appearance than do low-grade papillary tumors, with hemorrhage and necrosis.

Cystic pRCCs demonstrate enhancing soft-tissue mural nodules on page 23 (papillary projections) at the periphery of a cystic hemorrhagic mass and can be better depicted on subtraction images.

Although extremely rare, the presence of macroscopic fat (corresponding histologically to cholesterol-laden macrophages) is also a helpful feature.
Fig. 0: Case 1 - Female, 87 years old. pRCC type 2, Fuhrman III. Contrast enhanced CT scans (axial - a; coronal - b). Heterogeneous pRCC mass in the right kidney. Enhancing intramural nodules (yellow arrows). Calcification (white arrow).

© Radiologia, IPO Porto, Instituto Português de Oncologia do Porto - Porto/PT
Fig. 0: Case 1 - Photomicrograph (H-E stain - 100x). Cells have abundant eosinophilic cytoplasm, with prominent nucleoli, and aggregates of foamy macrophages within the papillary cores.

© Radiologia, IPO Porto, Instituto Português de Oncologia do Porto - Porto/PT
Fig. 0: Case 2 - Male, 69 years old. pRCC type 2, Fuhrman III. Axial T2-weighted MR imaging (a) shows a left renal round hypointense tumor.

© Radiologia, IPO Porto, Instituto Português de Oncologia do Porto - Porto/PT
Fig. 0: Case 2 - Axial unenhanced (b) and gadolinium-enhanced (c) fat-saturated T1-weighted images. Homogeneous low-level enhancement of the left renal tumor.

© Radiologia, IPO Porto, Instituto Português de Oncologia do Porto - Porto/PT
**Fig. 0:** Case 2 - Axial fat-saturated T1-weighted image (d). Postcontrast subtraction images (e, f, g). Low-level enhancement of the nodule.

© Radiologia, IPO Porto, Instituto Português de Oncologia do Porto - Porto/PT
Fig. 0: Case 2 - Photomicrograph (H-E stain 100x) shows papillae with eosinophilic cytoplasm and aggregates of foamy macrophages within the papillary cores.

© Radiologia, IPO Porto, Instituto Português de Oncologia do Porto - Porto/PT
**Fig. 0:** Case 3 - Female, 60 years old. pRCC, type 1, Fuhrman II. Axial T1- (a) and T2-weighted (b) images. Homogenous low signal intensity on both T1 and T2 images.

© Radiologia, IPO Porto, Instituto Português de Oncologia do Porto - Porto/PT
**Fig. 0**: Case 3 - Coronal T2-weighted image. Homogeneous low signal intensity pRCC tumor (white arrow). Note the renal cyst (blue arrow).

© Radiologia, IPO Porto, Instituto Português de Oncologia do Porto - Porto/PT
**Fig. 0:** Case 3 - Axial unenhanced (d) and gadolinium-enhanced (e) fat-saturated T1-weighted images. Homogeneous low-level enhancement of the tumor.

© Radiologia, IPO Porto, Instituto Português de Oncologia do Porto - Porto/PT
**Fig. 0**: Case 4 - Male, 65 years old. Left multifocal pRCC, Fuhrman III. Axial T1-weighted images in (a) and out (b) phase and T2-weighted image (c). Large pRCC mass in the left kidney. T1 hyperintense component is consistent with blood products. The peripheral nodules of the mass (arrows) are clearly T1 hypointense relative to the hemorrhagic component with low signal in T2-weighted images, consistent with solid component.

© Radiologia, IPO Porto, Instituto Português de Oncologia do Porto - Porto/PT
**Fig. 0:** Case 4 - Coronal T2-weighted image (d). Large heterogeneous mass in the left kidney.

© Radiologia, IPO Porto, Instituto Português de Oncologia do Porto - Porto/PT
**Fig. 0**: Case 4 - Axial (e) and coronal (f) T2-weighted images showing low-signal intensity nodule (white arrow) in the same kidney consistent with multifocal pRCC. Note the presence of a renal cyst (blue arrow).

© Radiologia, IPO Porto, Instituto Português de Oncologia do Porto - Porto/PT
Fig. 0: Case 4 - Axial unenhanced (g, i) and gadolinium-enhanced (h, j) fat-saturated T1-weighted images. Multifocal pRCC: low-level enhancement of the peripheral nodules in the heterogeneous mass (h); similar low-level enhancement of the other nodule in the same kidney (j).

© Radiologia, IPO Porto, Instituto Português de Oncologia do Porto - Porto/PT
**Fig. 0:** Case 4 - Axial fat-saturated T1-weighted image (k). Postcontrast subtraction images (l, m, n). Low-level enhancement of the peripheral nodules in the mass (arrow).

© Radiologia, IPO Porto, Instituto Português de Oncologia do Porto - Porto/PT
Conclusion

pRCC demonstrate different patterns of enhancement both on CT and MR imaging, allowing its distinction with high sensitivity and specificity.

The application of this knowledge offers an alternative to invasive methods of subtyping while providing a comprehensive pretreatment imaging evaluation.
Personal Information

Hálio Rodrigues Duarte

Instituto Português de Oncologia (IPO) do Porto Francisco Gentil
Departamento de Imagem
Rua Dr. António Bernardino de Almeida, 4200-072 PORTO, PORTUGAL

e-mail: halioduarte@gmail.com
References


Oliva MR, Glickman JN, Zou KH, et al. Renal cell carcinoma: T1 and T2 signal intensity characteristics of papillary and clear cell types correlated with pathology. AJR 2009; 192:1524-1530.