African Journal of Urology (2016) **22**, 149–152

African Journal of Urology

Official journal of the Pan African Urological Surgeon's Association
web page of the journal

www.ees.elsevier.com/afju
www.sciencedirect.com

Uro-oncology
Original article

Clinical and pathological features of papillary renal cell carcinoma and prognostic value of its type-1 and type-2 subtypes

M.M. Gargouri*, Y. Ayari, M. Ben Chehida, Y. Ouanes, A. Sellami, S. Ben Rhouma, M. Chelif, Y. Nouira

Department of Urology, La Rabta University Hospital, Tunis, Tunisia

Received 13 June 2015; received in revised form 3 August 2015; accepted 15 August 2015
Available online 21 August 2016

KEYWORDS
Kidney;
Papillary carcinoma;
Pathology;
Surgery;
Prognosis

Abstract
Introduction and objectives: Papillary renal cell carcinoma (PRCC) accounts for 10–15% of renal tumors in adults. This type of tumor contains more than 75% of tubulo-papillary structures and is divided histologically into two subtypes. The distinction between these two subtypes is essential because of their prognostic value. The aim of this study was to compare the prognostic significance of the PRCC subtypes.
Patients and methods: This retrospective study included 34 patients operated for PRCC between January 2000 and December 2012. Clinical data including presenting symptoms, preoperative findings, pathological features, treatment and patient outcome were taken from the patients' medical records as well as from radiological analysis based on computed tomography (CT) findings. A second analysis of the histological slides was made in doubtful cases to clarify the histological subtype.
Results: PRCC was found in 12.7% of 267 patients operated for renal tumors during the study period. The patients' mean age was 62.4 years with a male predominance (sex ratio 3.6). All tumors were unilateral with a mean size of 6.9 cm. There was no clinical or radiological sign suggestive of this histological type, however, 80% of the tumors had an enhancement <40 HU. Treatment consisted of radical nephrectomy and nephron-sparing surgery in 74% and 26% of the cases, respectively. We found 20 type-1 tumors and 14 type-2 tumors. The 5-year overall and disease-free survival rates were 82% and 90% for type-1 and 42% and 54% for type-2 tumors, respectively.

* Corresponding author.
E-mail addresses: gargourimourad@yahoo.fr (M.M. Gargouri), yassinea89@gmail.com (Y. Ayari), dalibenchehida@yahoo.fr (M. Ben Chehida), yassineouanes@gmail.com (Y. Ouanes), sellamiahmed1@yahoo.fr (A. Sellami), sbenrhouma@yahoo.fr (S. Ben Rhouma), chlifmed@gmail.com (M. Chelif), nouirayassine@gmail.com (Y. Nouira).
Peer review under responsibility of Pan African Urological Surgeons' Association.

http://dx.doi.org/10.1016/j.afju.2015.08.003

Conclusion: PRCC represents the second most common histological type of renal cancer. It has no clinical or radiological predicting signs, although CT enhancement is usually <40 HU. Distinguishing between the two subtypes is essential because of their prognostic value.

Introduction

Papillary renal cell carcinoma (PRCC) accounts for 10–15% of renal tumors in adults. This type of tumor contains more than 75% of tubulo-papillary structures [1]. PRCC represents the second most common histological type after clear cell carcinoma (CCC). In 1997, Delahunt and Eble [2] described type-1 and type-2 subtypes of PRCC according to their cytological characteristics. This subdivision is important because of the prognostic value of each subtype [1–5].

In the present study covering a period of 13 years, we reviewed 34 cases of PRCC operated between January 2000 and December 2012 and performed a long-term survival analysis comparing type-1 and type-2 PRCC to validate this subclassification as a prognostic factor.

Patients and methods

During the study period, 34/267 patients (12.7%) operated for renal cancer at our institution were diagnosed with PRCC. Data were obtained from the patients' medical records. The presenting symptoms, preoperative findings, pathological features, treatment and patient outcome were analyzed, and a comparative study of type-1 and type-2 PRCC was carried out.

The tumor stage was determined according to the 2009 TNM classification. A second analysis of the histological slides was made in doubtful cases to clarify the histological subtype. The tumor was classified as type-1 PRCC when it showed papillae covered with a single or double layer of small cuboid cells with basophilic cytoplasm (Fig. 1). Type-2 PRCC contains papillae covered with large eosinophilic cells arranged in a pseudo stratified manner (Fig. 2).

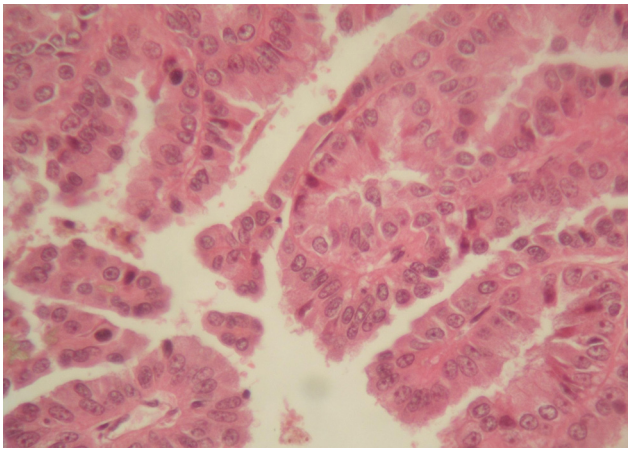

Figure 1 Type 1 PRCC tumors showing papillae covered with small cuboid cells with basophilic cytoplasm.

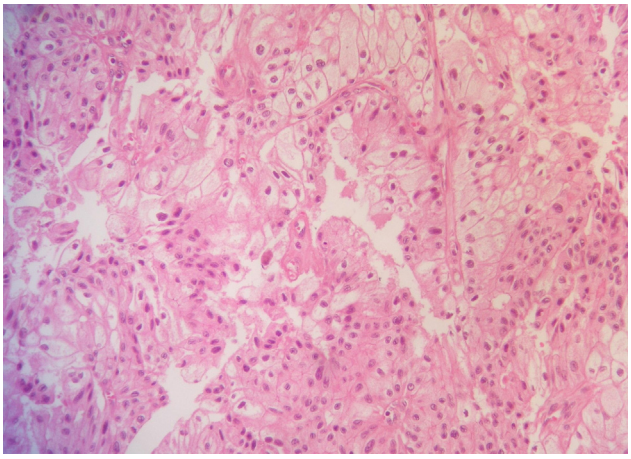

Figure 2 Type 2 PRCC tumors containing papillae covered with large eosinophilic cells arranged in a pseudo stratified manner.

The statistical tests used were the Chi-square test to compare the qualitative variables and student's *t*-test for continuous variables, while the survival curves were derived from Kaplan–Meier estimates. A log-rank test was used to compare the survival rates of both groups. A p value <0.05 was considered as statistically significant. The statistical analysis was carried out using the SPSS 10.0 program.

Results

PRCC was found in 34/267 patients (12.7%) that underwent surgery for renal cancer. It represented the second most common histological type after CCC (75%). The patient cohort consisted of 25 men (74%) and 7 women (26%) with a sex ratio of 3.6. The patients' mean age was 62.4 (range 24–86) years.

The main risk factors were hypertension and diabetes mellitus, noted in 32% and 18%, respectively. Hemodialysis for end-stage renal disease was found in one case (3%).

The main presenting symptoms were flank pain ($n = 22$) and hematuria ($n = 12$). The tumor was discovered incidentally in 9 patients (27%). Most incidental cases were diagnosed after the second half of the study period (8% before 2005 and 44% after that year).

The tumors were located in the right kidney in 52% and in the left kidney in 48% of the patients. All tumors were unilateral, and multifocality was noted in one case (3%). The median tumor size was 6.9 cm (range 1.9–24) cm.

Computer tomography (CT) did not show any specificity regarding this histological type, however, enhancement was low (less than 40 HU) in 80% of the cases.

Table 1 Comparison between Type 1 and Type 2 PRCC tumors.

	Type 1	Type 2	*P* value
Patients (*n*)	20	14	
Mean age (yr)	64.8	63.7	NS
Male/female	15/4	11/3	NS
Incidental diagnosis (%)	6/20 (30)	3/14 (21)	NS
Median tumor size (cm)	6.6	8.5	NS
Range	3–20	1.9–24	
Nephron sparing surgery (%)	6/20 (30)	3/14 (21)	NS
TNM classification (%)			
pT1 T2 N0 M0	17 (85)	6 (43)	<0.005
pT3 T4 N1 M0	3 (15)	8 (57)	
Fuhrman grade (%)			
Low (1.2)	15 (75)	4 (28)	<0.005
High (3.4)	5 (25)	10 (72)	

NS, not significant.

Radical nephrectomy was performed in 25 cases (74%), while 9 patients (26%) were subjected to partial nephrectomy. Only open partial nephrectomies with vascular clamping were performed at our institution. The mean warm ischemia time was 30 (range 20–45) min.

Immediate complications occurred in 5 patients (18%): urinary fistula in one, pulmonary embolism in one and wound infection in 3 patients. Internal drainage by ureteral stenting was needed for the treatment of urinary fistula. Blood loss was negligible in all but two cases that needed blood transfusion. Nephron-sparing surgery was noted to be associated with a higher morbidity. The mean hospital stay was 5 (range 3–30) days.

Histological studies showed a tubulo-papillary aspect in 63% of the cases, while a pure papillary aspect was seen in 37%. The presence of sarcomatoid cells was noted in one case.

We found 20 cases of type-1 (59%) and 14 cases of type-2 PRCC (41%). Immunohistochemical study was necessary in one case to confirm the histologic diagnosis. It showed cells positive for cytokeratin 7.

The median follow-up after surgery was 42 (range 6–100) months. The 5-year overall survival and disease-free survival rates were 73.3% and 92%, respectively. Recurrence occurred in 3 cases two years after surgery; none of them had had partial nephrectomy as initial treatment.

The tumor characteristics according to the pathologic subtype are summarized in Table 1. Type-2 tumors were associated with a more advanced TNM stage, a high Fuhrman grade (grades 3 and 4) and a worse prognosis. The overall and disease-free survival rates were 82% and 90% for patients with type-1 tumors and 42% and 54% for those with type-2 tumors, respectively. The Kaplan–Meier overall survival is presented in Fig. 3.

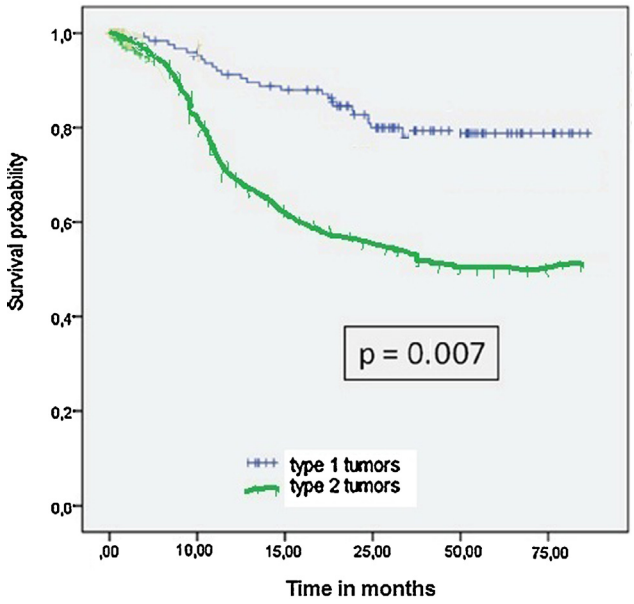

Figure 3 The Kaplan–Meier overall survival curves according to tumor subtype.

Discussion

PRCC derives from cells of the distal tubule of the nephron [1]. This type of tumor represents the second most common histological type of renal cancer after CCC, accounting for 10–5% of the cases. It is usually diagnosed between the age of 50 and 60 [6] and occurs more frequently in men with a sex ratio of 1.6–5.

The most common risk factors for renal cancer are hypertension, diabetes mellitus, obesity and smoking [7,8]. End-stage renal failure is a well-known risk factor of PRCC [9,10], but this was not found in our study. The male predominance (3/4 of our patients with PRCC) noted in this study confirms the results of previous studies [1].

According to the literature, renal cancer is diagnosed incidentally in 60–70% of cases [7]; however in our study, incidental diagnosis was not common (29%) because we lack ultrasonography in rural hospitals.

Multifocality is another known feature of PRCC, with a reported incidence of 20% to 41% [2], however, this high percentage is usually found in hereditary cases [11]. Cytogenetic studies suggest that many mutations in different locations of the same kidney explain multifocality in hereditary PRCC [12]. In sporadic cases, multifocality of PRCC has been reported to account for around 7% [1,5]. In our study, we did not find any association between multifocality and PRCC as all cases were sporadic.

CT scan is the gold standard for exploring renal tumors. PRCC is usually more homogenous than CCC, especially in tumors <3 cm with less enhancement [13,14]. These findings are usually correlated to low-stage tumors [4]. There are no radiological signs that can distinguish between the two PRCC subtypes. In this study we found that 80% of the tumors had an enhancement < 40 HU.

The histological pattern shows that PRCC is characterized by a predominance (more than 50–70%) of papillary or tubulo-papillary structures in the absence of clear cells [9]. In doubtful cases we can use immunohistochemical studies to search for a positive reaction to cytokeratin 7. Delahunt and Eble [2] were the first to describe the existence of two PRCC subtypes. This subclassification was added to the WHO classification of 2004 [15]. Tumors are classified as type-1 PRCC when they show papillae covered with small cuboid cells with basophilic cytoplasm, whereas type-2 tumors contain papillae covered with large eosinophilic cells. The latter are

usually associated with a high TNM grade and a worse prognosis. This prognostic value was confirmed by other studies, where a disease-free survival rate of 92% was reported for type-1 compared to 44% for type-2 PRCC tumors [1,16].

Conclusions

PRCC represents the second most common histological type of renal cancer. It has no clinical or radiological predicting signs, although CT enhancement is usually less than 40 HU. Distinguishing between its two subtypes is essential because of their prognostic value.

Authors contribution

Gargouri Mohamed Mourad: Writing article and correction

Ayari Yassine: Data collection and writing article

Ben Chehida Mohamed Ali: Data collection

Ouanes Yassine: Data analysis

Sellami Ahmed: Data analysis

Ben Rhouma Sami: Article correction

Chelif Mohamed: Article overview and verifiying references

Nouira Yassine: Article overview and corrections

Ethical committee approval

Ethical committee approved.

Conflict of interest

The authors have no conflict of interest to declare.

Funding

None.

References

[1] Pignot G, Elie C, Conquy S, Vieillefond A, Flam T, Zerbib M, et al. Survival analysis of 130 patients with papillary renal cell carcinoma: prognostic utility of type 1 and type 2 subclassification. Urology 2007;69(2):230–5.

[2] Delahunt B, Eble JN. Papillary renal cell carcinoma: a clinicopathologic and immunohistochemical study of 105 tumors. Mod Pathol 1997;10:537–44.

[3] Allory Y, Ouazana D, Boucher E, Thiounn N, Vieillefond A. Papillary renal cell carcinoma: prognostic value of morphological subtypes in a clinicopathologic study of 43 cases. Virchows Arch 2003;442:336–42.

[4] Combes F, Saidi A, Delaporte V, Lechevallier E, André M, Daniel L, et al. Les tumeurs tubulo-papillaires du rein: intérêt pronostique de la distinction type 1/type 2: à propos de 58 cas. Prog Urol 2005;15:1062–9.

[5] Sukov WR, Lohse CM, Leibovich BC, Houston Thompson R, Cheville JC. Clinical and pathological features associated with prognosis in patients with papillary renal cell carcinoma. J Urol 2012;187:54–9.

[6] Rao Q, Chen JY, Wang JD, Ma HH, Zhou HB, Lu ZF, et al. Renal cell carcinoma in children and young adults: clinicopathological, immunohistochemical, and VHL gene analysis of 46 cases with follow-up. Int J Surg Pathol 2011;19(2):170–9.

[7] Cohen HT, McGovern FJ. Renal-cell carcinoma. N Engl J Med 2005;353:2477–90.

[8] Méjean A, André M, Doublet JD, Fendler JP, de Fromont M, Hélénon O, et al. Tumeurs du rein. Prog Urol 2004;14:997–1035.

[9] Amin MB, Corless CL, Renshaw AA, Tickoo SK, Kubus J, Schultz DS, et al. Papillary (chromophil) renal cell carcinoma: histomorphologic characteristics and evaluation of conventional pathologic prognostic parameters in 62 cases. Am J Surg Pathol 1997;21:621–35.

[10] Ishikawa I, Kovac J. High incidence of papillary renal cell tumours in patients on chronic haemodialysis. Histopathology 1993;22(2):135–40.

[11] Wadt KA, Gerdes AM, Hansen TV, Toft BG, Friis-Hansen L, Andersen MK. Novel germline c-MET mutation in a family with hereditary papillary renal carcinoma. Fam Cancer 2012;11:189–94.

[12] Jones TD, Eble JN, Wang M, MacLennan GT, Delahunt B, Brunelli M, et al. Molecular genetic evidence for the independent origin of multifocal papillary tumors in patients with papillary renal cell carcinomas. Clin Cancer Res J 2005;11:7226–33.

[13] Vikram R, Ng CS, Tamboli P, Tannir NM, Jonasch E, Matin SF, et al. Papillary renal cell carcinoma: radiologic–pathologic correlation and spectrum of disease. Radiographics 2009;29(3):741–54.

[14] Yamada T, Endo M, Tsuboi M, Matsuhashi T, Takase K, Higano S, et al. Differentiation of pathologic subtypes of papillary renal cell carcinoma on CT. Am J Roentgenol 2008;191:1559–63.

[15] Lopez-Beltran A, Scarpelli M, Montironi R, Kirkali Z. 2004 WHO classification of the renal tumors of the adults. Eur Urol 2006;49(5):798–805.

[16] Combes F, Saidi A, Delaporte V, Lechevallier E, André M, Daniel L, et al. Les tumeurs tubulo-papillaires du rein: intérêt pronostique de la distinction type 1/type 2. A propos de 58 cas. Prog Urol 2005;15:1062–9.