Comparison of Immunohistochemical Profiles of Papillary Renal Cell Carcinoma Subtypes

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ABSTRACT

Background: Papillary renal cell carcinoma (PRCC) is characterized morphologically by the presence of fibrovascular cores, lined by papillae of malignant epithelial cells. It is further sub-classified into 2 types based on cell type. Type 2 tumors are generally believed to have a poorer prognosis than Type 1 tumors. This prognostic difference has led some to believe that some of the Type 2 tumors may actually represent a separate entity from PRCC. This study was designed to compare the immunohistochemical profiles in both subtypes of PRCC.

Design: A tissue microarray block with 124 cases of PRCC was constructed. The tumors were stained with the following diagnostic antibodies: CK7, EMA, CD10, CAIX, vimentin, CK903, C-kit, racemase, PAX-8, PAX-2 and CEA. A stain was deemed to be positive if it demonstrated at least weak intensity in at least 10% of the tumor cells. Intensity was scored as 1+, 2+ and 3+ for weak, moderate and strong intensity, respectively. A score of 0 was given for negative staining.

Results: Results of the immunohistochemical stains are listed in **Table 1.** The best immunohistochemical profile for both subtypes is: CK7: positive, EMA: positive, racemase: positive, PAX-8: positive, CD10: variable, PAX-2: variable, CAIX: negative, vimentin: negative and CK903: negative. There was no correlation between the staining pattern and tumor characteristics such as tumor type, location, nuclear grade, and presence of desmoplasia.

Conclusions: The immunohistochemical profiles of both Types 1 and 2 PRCC are essentially the same. There is no prognostic significance to any of the immunostains. The similar immunohistochemical profile confirms that PRCC is one entity with divergent histologic features. The 2 subtypes can only be differentiated based purely on morphologic features.

BACKGROUND

Papillary renal cell carcinoma (PRCC) has been subclassified into 2 major subtypes. To date the distinction between Type 1 and Type 2 PRCC has been based solely on morphologic criteria. Type 1 tumors have papillae covered by a single or double layer of small cuboidal cells with scant pale cytoplasm and small ovoid nuclei with inconspicuous nucleoli (**Figure 1A**). Type 2 tumors have large spherical nuclei, prominent nucleoli and nuclear pseudostratification with voluminous, granular, eosinophilic cytoplasm (**Figure 2A**). In terms of prognosis, it has been reported that Type 2 tumors have a poorer prognosis. In several studies, univariate analysis indicated a longer mean survival in patients with Type 1 PRCC. These findings were corroborated by the results of multivariate analyses, taking into account tumor stage and grade. This has led some to believe that Type 2 tumors represent a separate type of RCC distinct from PRCC. This study was designed to compare the immunohistochemical profiles in both subtypes of PRCC and to determine if there was any prognostic significance to any of the immunochemical stains.

DESIGN

The archives of the Department of Pathology at Yale University were searched for all cases of nephrectomy and kidney tumor biopsy between 1985 and 2011. Cases with the final diagnosis of PRCC were selected. The slides were reviewed and cases were classified as either Type 1, Type 2 or mixed type.

For these cases, a tissue microarray block and histologic slides were produced in order to evaluate for immunohistochemical staining by the following diagnostic antibodies: CK7, EMA, CD10, CAIX, CK903, PAX-8, PAX-2, CEA, Racemase, and Vimentin.

Staining intensity was scored as 0, 1+, 2+, and 3+ corresponding to no staining, weak, moderate or strong staining intensity, respectively. A stain was considered positive if at least 10% of the cells showed at least 1+ intensity.

The data was collected for each stain and then analyzed based on the tumor subtype. The immuno-histochemical profile produced by our quantifiable results secondary to analysis of the microarray and H&E slides is provided.

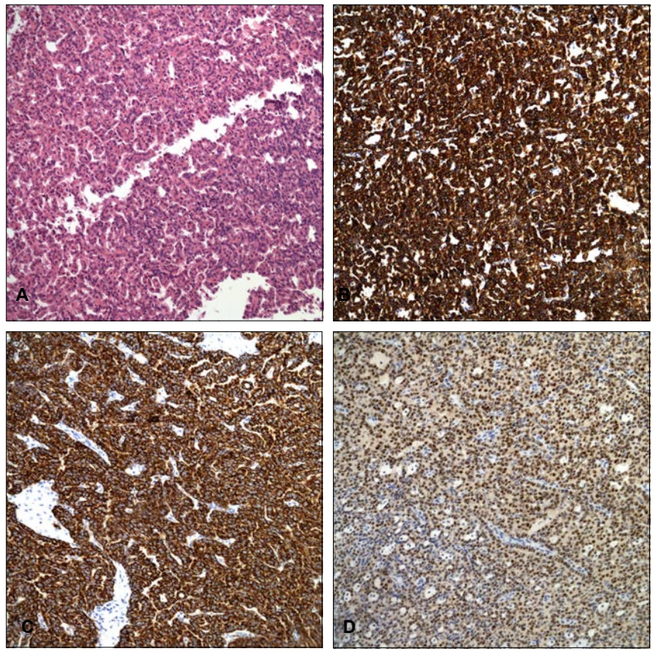

Figure 1. Type 1 Papillary renal cell carcinoma. **(A)** H&E, **(B)** CK7, **(C)** Racemase, **(D)** PAX-8

RESULTS

- A total of 124 cases had material for immunohistochemical analysis (66 Type 1, 44 Type 2, and 14 mixed type).
- None of the immunohistochemical stains showed a statistically significant difference between tumor subtypes.
- Both subtypes of PRCC are generally positive for CK7, EMA, Racemase and PAX-8 (**Figures 1** and **2**).
- Both subtypes are generally negative for CAIX, Vimentin, and CK903.
- CD10 and PAX-2 show variable staining in both subtypes.
- **Table 1** summarizes the results of the staining in both subtypes.
- **Table 2** summarizes the immunohistochemical profiles of both tumor subtypes.

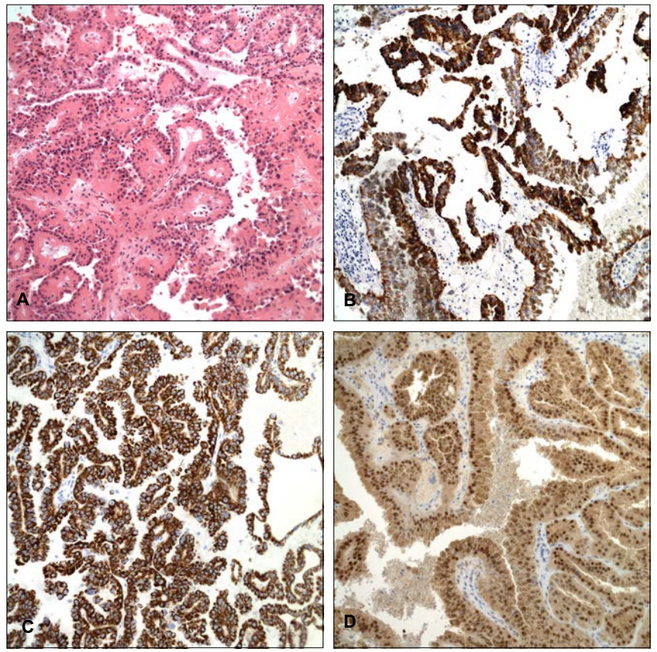

Figure 2. Type 2 Papillary renal cell carcinoma. **(A)** H&E, **(B)** CK7, **(C)** Racemase, **(D)** PAX-8

Table 1. The proportion of cases of each subtype showing positive staining for each of the listed markers

	Type 1	Type 2	Mixed
CK7	62/66	34/44	14/14
CD10	33/63	33/44	9/14
EMA	55/62	30/43	14/14
CAIX	6/56	7/43	4/14
Vimentin	8/62	2/43	1/14
CK903	16/57	9/43	3/14
C-kit	1/59	0/44	0/14
Racemase	60/61	35/42	14/14
PAX-8	48/57	38/42	11/13
PAX-2	27/61	22/41	8/13
CEA	4/57	3/43	1/14

Table 2. Immunohistochemical Profile

Type 1 PRCC	CK7, EMA, Racemase, PAX-8 positive; PAX-2 variable; CAIX, Vimentin, CK903 negative
Type 2 PRCC	CK7, EMA, Racemase, PAX-8 positive; PAX-2 variable; CAIX, Vimentin, CK903 negative

CONCLUSIONS

- PRCC is a distinct pathological entity with divergent histological features.
- The immunohistochemical profiles of the 2 subtypes of PRCC are very similar, hence immunohistochemical analysis does not help to ascertain the subtype of these tumors.
- Subtyping PRCC according to the morphological criteria on H&E slides remains the best tool to differentiate between both subtypes of PRCC.
- No prognostic significance of any of the immunohisto-chemical stains used in this study was identified (results not shown).

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