

Immunohistochemical Profile of Renal Cell Carcinoma in Patients Younger than 45 Years of Age: Analysis of 87 Cases of Different Tumor Subtypes



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ABSTRACT

Background: Renal cell carcinoma (RCC) is distinctly rare in children and young adults. Because of the rarity of the tumor in this age group, the immunohistochemical profile has not been fully described. The goal of this study is to define the immunohistochemical profile of the various subtypes of RCC in patients aged 45 years and younger.

Design: A tissue microarray block with 87 cases of RCC (49 clear cell [CRCC], 23 papillary [PRCC], 10 chromophobe [ChRCC] and 5 translocation-associated [TxRCC]) was constructed. The tumors were stained with following diagnostic antibodies: cytokeratin (CK) AE1/AE3, CK7, CK903, TFE3, TFEB, CD10, AMACR, C-KIT, vimentin, EMA, CAIX; and with the following prognostic antibodies: PAX-8, survivin and VHL. The slides were reviewed and a stain was deemed to be positive if it demonstrated moderate to strong intensity in more than 5% of the tumor cells.

Results: Results of the immunohistochemical stains are listed in Table 1. The overall profiles of the different tumor types are listed in Table 2.

Conclusion: There is a significant overlap between the immunoprofile of RCC subtypes in patients aged 45 years and younger and that in RCC subtypes of older patients. PAX-8 is expressed by a significant proportion of PRCC and variable proportions of the other subtypes, with a distinctive nuclear staining pattern. Survivin is expressed in a significant proportion of all RCC subtypes while VHL is highly expressed in ChRCC and variably expressed in all other subtypes. The significance of this finding is uncertain, as further work needs to be done to determine the prognostic significance of these markers on the various subtypes of RCC.

BACKGROUND

Renal cell carcinoma (RCC) is a distinctly uncommon entity in children and young adults, with the vast majority of cases occurring between the fifth and seventh decades. Histologic subclassification of RCC has been demonstrated to have prognostic significance, and different subtypes have disparate responses to various types of clinical therapy. This is particularly important due to the potentially different clinicopathologic disease course in younger patients. Immunohistochemistry is being used with increasing frequency to make these important distinctions. This is amplified in situations in which the clinical findings and basic histolopathologic features are non-specific, which can occur in a significant number of cases. The aim of this study was to evaluate the significance of various diagnostic and prognostic immunohistochemical markers for RCC, to further define the immunohistochemical profiles in various pathologic subtypes of RCC and to compare these findings to the standard profiles found in RCCs in older patients.

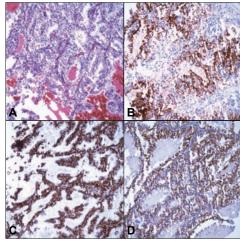
DESIGN

We retrospectively analyzed 87 cases of RCC in patients aged 45 years or younger from our institutional file database. For these cases, a tissue microarray block and histologic slides were produced in order to evaluate for immunohistochemical staining by the following (1) diagnostic antibodies: cytokeratin (CK) AE1/AE3, CK7, CK903, TFE3, TFEB, CD10, AMACR, C-KIT, Vimentin, EMA, CAIX; and (2) prognostic antibodies: PAX-8, survivin and VHL. A stain was deemed to be positive if it demonstrated moderate to strong intensity in more than 5% of the tumor cells.

The immunohistochemical stains were quantified by RCC tumor subtype (clear cell, papillary, chromophobe and translocation-associated), and were analyzed in comparison with the standard immunohistochemical profile for each tumor subtype generalized for tumors in patients of all ages. The immunohistochemical profile produced by our quantifiable results secondary to analysis of the microarray and H&E slides is provided.

RESULTS

Figure 1. Clear cell renal cell carcinoma. (A) H&E, (B) CD10, (C) Vimentin, (D) CAIX



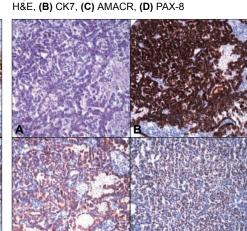


Figure 2. Papillary renal cell carcinoma. (A)

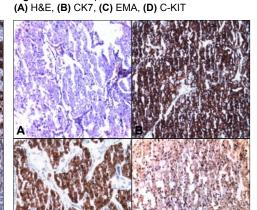


Figure 3. Chromophobe renal cell carcinoma.

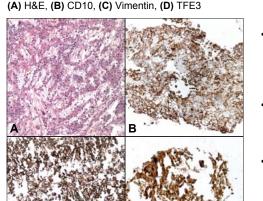


Figure 4. Translocation-associated renal cell carcinoma.

<u>AMACR</u>: Positive in all of PRCC cases, whereas the majority of the cases for the other three subtypes were found to be negative.

<u>C-KIT</u>: Positive in 80% of ChRCC cases, with exceedingly rare positive results in all other subtypes.

- <u>CAIX</u>: Positive staining was present in a significant proportion of CRCC cases (69.4%), while staining was minimal in PRCC cases (17.4%) and negative in ChRCC and TxRCC cases.
- <u>CK7</u>: Positive in the majority of PRCC (78.3%) and ChRCC (90%) cases. CRCC cases were predominantly negative (32.7% positive) and TxRCC cases were universally negative.
- PAX-8: PAX-8 demonstrates the most significant findings in our PRCC cases, with 73.9% exhibiting positive staining. Additionally, 16/17 positive cases demonstrated at least moderate quantitative intensity (2+ or 3+). These results are contrasted by the findings in the other subtypes in which the majority of cases are negative, and those that are positive are predominantly mild in intensity (1+).

Table 1: Results of Immunohistochemical Stains

	CRCC	PRCC	ChRCC	TxRCC
AE1/AE3	45/49	23/23	6/10	1/5
TFE3	0/49	0/23	0/10	5/5
TFEB	0/49	0/23	0/10	0/5
CD10	38/49	10/23	7/10	4/5
AMACR	17/49	23/23	1/10	2/5
C-KIT	1/49	1/23	8/10	0/5
CK903	4/49	9/23	0/10	0/5
Vimentin	49/49	23/23	2/10	5/5
CK7	16/49	18/23	9/10	0/5
EMA	31/49	18/23	10/10	1/5
CAIX	34/49	4/23	0/10	0/5
PAX-8 (Qualitative)	21/49	17/23	2/10	2/5
PAX-8 (Quantitative)				
0	28/49	6/23	8/10	3/5
1+	11/49	1/23	1/10	2/5
2+	7/49	5/23	0/10	0/5
3+	3/49	11/23	1/10	0/5
Survivin	39/49	18/23	9/10	2/5
VHL	17/49	4/23	10/10	2/5

Table 2: Immunohistochemical Profile

CRCC	AE1/AE3, Vimentin, CD10, EMA, CAIX positive; PAX-8 variable; C-KIT, CK903 negative
PRCC	AE1/AE3, AMACR, Vimentin, CK7, EMA, PAX-8 positive; C-KIT, CAIX negative
ChRCC	AE1/AE3, CD10, C-KIT, CK7, EMA positive; AMACR, Vimentin, CK903, CAIX, PAX-8 negative
TxRCC	TFE3, CD10, Vimentin positive; AE1/AE3, C-KIT, CK903, CK7, CAIX negative

 ${\sf CRCC-Clear\ Cell\ RCC; PRCC-Papillary\ RCC; ChRCC-Chromophobe\ RCC; TxRCC-Translocation-associated\ RCC.}$

- The immunohistochemical profile of the different tumor subtypes is highlighted in **Table 1** and **Table 2**.
- Cytokeratin AE1/AE3: Predominantly positive in CRCC (91.8%), PRCC (100%) and ChRCC (60%) cases, whereas only one out of five TxRCC cases was positive.
- TFE3: Universally positive in TxRCC cases and universally negative in all other subtypes.

CONCLUSIONS

There is a significant overlap between the

immunoprofile of RCC subtypes in patients aged 45 years and younger and that in RCC subtypes of older patients. CAIX is the most important immunohistochemical stain that distinguish between CRCC and other subtypes. PAX-8 is expressed by a significant proportion of PRCC and variable proportions of the other subtypes with a distinctive nuclear staining pattern Survivin is expressed in a significant proportion of all RCC subtypes while VHL is highly expressed in ChRCC and variably expressed in all other subtypes. The significance of this finding is uncertain, but it appears that VHL is expressed more in the RCC subtypes with better prognosis. Further work needs to be done to determine the prognostic significance of these markers on the various subtypes of RCC.

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