



UDK 616.6;616-006.

**ANALYSIS OF MORPHOLOGICAL FEATURES AND PROGNOSTIC VALUE OF
INTRATUMORAL STROMAL MAST CELLS IN RENAL CELL CARCINOMA**

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**АНАЛИЗ МОРФОЛОГИЧЕСКИХ ОСОБЕННОСТЕЙ И ПРОГНОСТИЧЕСКОЙ
ЦЕННОСТИ ВНУТРИОПУХОЛЬНЫХ СТРОМАЛЬНЫХ КЛЕТОК ПРИ
ПОЧЕЧНО-КЛЕТОЧНОМ РАКЕ**

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**BUYRAK HUYAYRALI KARCINOMADA O'SMA ICHIDAGI STROMAL
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ABSTRACT

The prognostic relevance of intratumoral stromal mast cells (MCs) in renal cell carcinoma (RCC) remains insufficiently investigated and controversial. The present study aimed to evaluate the quantitative characteristics of stromal mast cells in RCC and to analyze their relationship with major clinical, anatomical, and histopathological prognostic factors. Surgical specimens obtained from 63 patients with renal cell carcinoma were examined using histological and immunohistochemical methods. Mast cells were identified by CD117 (c-Kit) expression and quantified in representative high-power fields. The analysis demonstrated a significant association between increased mast cell density and advanced tumor stage, aggressive histological variants, and the presence of metastatic disease. These findings suggest that stromal mast cell infiltration may serve as an additional prognostic indicator in renal cell carcinoma.

Аннотация: Исследовано прогностическое значение подсчета интратуморальных стромальных тучных клеток (ТК) при почечно-клеточном раке. Материалом для исследования послужил операционный материал 63 больных раком почки. Таким образом, результаты проведенного исследования показали, что число стромальных ТК в опухоли взаимосвязано с рядом важных прогностических клиничко-анатомических факторов ПКР, и поэтому данный параметр может быть использован в качестве дополнительного фактора прогноза.

Annotatsiya: Buyrak-hujayra saratoni paytida intratumoral stromal shishli hujayralarni (MH) hisoblashning prognostik ahamiyati tekshirildi. Tadqiqot uchun material buyrak saratoni bilan bog'langan 63 nafar bemorning operatsion materiali bo'ldi. Shu tariqa, o'tkazilgan tadqiqot natijalari ko'rsatishicha, o'simlikdagi stromal MH soni bir qator muhim klinik-anatomik omillar bilan bog'liq bo'lib, ushbu parametrlar qo'shimcha prognoz omili sifatida foydalanishi mumkin.

Key words: renal cell carcinoma, tumor microenvironment, stromal mast cells, prognosis.

Ключевые слова: Почечно-клеточный рак, стромально тучные клетки, опухоль.

Kalit so'zlar: Buyrak xujayrali rak, stromal shishli hujayralar, o'sma.

INTRODUCTION

Renal cell carcinoma (RCC) represents one of the most common malignant tumors of the genitourinary system and accounts for approximately 3% of all adult malignancies worldwide.



Despite advances in diagnostic imaging, RCC is frequently characterized by a prolonged asymptomatic course, resulting in late-stage detection in a substantial proportion of patients. At the time of diagnosis, nearly 40% of cases present with either locally advanced disease or distant metastases, while up to 30% of patients with initially localized tumors develop metastatic spread following surgical treatment.

The prognosis and therapeutic strategy for RCC largely depend on tumor histological subtype, stage, and biological behavior. Although targeted antiangiogenic therapies and immunotherapy have significantly improved outcomes in recent years, the clinical course of RCC remains highly heterogeneous. Tumors with similar histological features may demonstrate markedly different patterns of progression and response to treatment, highlighting the need for additional prognostic markers.

Increasing attention has been directed toward the tumor microenvironment as a key regulator of cancer progression. Among stromal components, mast cells are of particular interest due to their involvement in angiogenesis, extracellular matrix remodeling, and immune modulation. However, the prognostic significance of intratumoral mast cells in RCC has not been clearly established, and available data remain limited and contradictory.

MATERIALS AND METHODS

The study included surgical specimens from 63 patients diagnosed with renal cell carcinoma who underwent surgical treatment. The cohort consisted of 34 men (54%) and 29 women (46%), with a mean age of 58.2 ± 1.2 years. Tumors were classified according to the World Health Organization (WHO) 2004 classification system.

Histological examination revealed the following tumor subtypes: clear cell carcinoma (52 cases), papillary carcinoma (5 cases), chromophobe carcinoma (3 cases), and sarcomatoid (spindle cell) carcinoma (3 cases). Tumor staging was performed in accordance with the TNM classification of malignant tumors.

Tissue samples were fixed in 10% neutral buffered formalin and processed using standard histological techniques. Sections were stained with hematoxylin and eosin, as well as with colloidal iron for the detection of acidic mucopolysaccharides. Immunohistochemical identification of mast cells was performed using monoclonal antibodies against CD117 (c-Kit). Mast cell density was calculated as the average number of positively stained cells in three high-power fields ($\times 400$ magnification).

Statistical analysis was carried out using the Statistica 6.0 software package. Survival data were obtained from oncological registries and outpatient medical records.



RESULTS

According to TNM staging, 47 patients (74.6%) were classified as stage I, 3 patients (4.8%) as stage II, 8 patients (12.7%) as stage III, and 5 patients (7.9%) as stage IV. The mean tumor size was 7.1 ± 0.3 cm.

Histological grading based on the Fuhrman system showed grade G1 in 31 cases (49.2%), G2 in 14 cases (22.2%), G3 in 13 cases (20.6%), and G4 in 5 cases (8%). Metastatic disease was identified in 11 patients (17.5%), while 52 patients (82.5%) had localized tumors.

Quantitative analysis revealed a progressive increase in mast cell density with advancing tumor stage. The mean number of mast cells was 1.85 ± 0.15 in stage I, 2.7 ± 0.4 in stage II, 4.3 ± 0.4 in stage III, and 6.3 ± 0.6 in stage IV tumors. A statistically significant difference was observed between early-stage and advanced-stage disease.

When analyzed by histological subtype, the highest mast cell density was observed in sarcomatoid carcinoma (6.3 ± 0.6), while the lowest values were noted in papillary carcinoma (1.05 ± 0.4). Clear cell and chromophobe carcinomas demonstrated intermediate mast cell counts.

Patients without regional or distant metastases exhibited a significantly lower mast cell density (2.0 ± 1.2) compared to those with metastatic disease (4.7 ± 0.4).

DISCUSSION

The obtained results indicate a clear association between intratumoral stromal mast cell accumulation and aggressive clinicopathological features of renal cell carcinoma. Increased mast cell density correlated with advanced tumor stage, high-grade histological variants, and metastatic spread.

These findings support the hypothesis that mast cells actively participate in tumor progression, possibly through stimulation of angiogenesis, promotion of tumor invasion, and modulation of the immune microenvironment. The particularly high mast cell content observed in sarcomatoid carcinoma may reflect the aggressive biological behavior of this subtype.

Despite the growing interest in tumor microenvironment research, morphometric studies focusing on stromal cellular components in RCC remain scarce. The use of quantitative immunohistochemical analysis allows for reproducible assessment and may enhance the objectivity of prognostic evaluation.

CONCLUSION



The study demonstrates that an increased number of intratumoral stromal mast cells is significantly associated with unfavorable prognostic factors in renal cell carcinoma. Mast cell density correlates with tumor stage, histological aggressiveness, and metastatic potential. Therefore, assessment of stromal mast cell infiltration may be considered an additional prognostic criterion in patients with renal cell carcinoma and may contribute to improved risk stratification.

REFERENCES.

1. Aleksandrov N. S. et al. Use of Raman fluorescence spectroscopy for the diagnosis of clear cell renal cell carcinoma //Clinical and Experimental Morphology. – 2017. – No. 4. – Pp. 59-65.
2. Aleksandrov Nikolai Sergeevich Comparative Immunomorphological and Spectroscopic Characteristics of Kidney Tumors: Author's abstract. Dissertation... Candidate of Medical Sciences. Moscow, 2019. 24 pp.
3. Alyaev Yu. G. et al. Features of the diagnosis of kidney neoplasms up to 4 cm //Medical imaging. – 2003. – No. 2. – P. 33-38.
4. Alyasova A. V. et al. Matrix RNAs of the fcgr3a and fcgr3b genes as monitoring markers for the course of clear cell renal cell carcinoma (pilot study) //Modern technologies in medicine. – 2022. – Vol. 14. – No. 3. – P. 22-27.
5. Anikanova E. V. et al. IGG4-associated ureteral disease //Experimental and Clinical Urology. – 2021. – No. 4. – P. 56-62.
6. Anoyko E. A., Guzeeva E. A. The significance of morphological and immunohistochemical studies in the diagnosis of kidney tumors //Bulletin of Medical Internet Conferences. – Science and Innovation Limited Liability Company, 2013. – Vol. 3. – No. 2. – P. 263-264.
7. Apolikh O. I. et al. Cryoablation of localized renal cancer in a group of patients at high surgical risk //Experimental and Clinical Urology. – 2014. – No. 3. – P. 32-35.
8. Atkins MB, Tannir NM. Current and emerging therapies for first-line treatment of metastatic clear cell renal cell carcinoma. //Cancer Treat Rev. 2018;70:127–137.
9. Baek J, Jang NR, Shim YR, Gu MJ. ATRX protein is a potential prognostic marker in clear cell renal cell carcinoma.// Indian J Pathol Microbiol. 2022 Jul-Sep;65(3):598-603



10. Barata P.C., Rini B.I. Treatment of renal cell carcinoma: current status and future directions. //CA Cancer J Clin 2017; 67(6): 507-524.
11. Bazzocchi MV, Zilioli C, Gallone VI, Commisso C, Bertolotti L, Pagnini F, Ziglioli F, Maestroni U, Aliprandi A, Buti S, Procopio G, Ascenti G, Martini C, De Filippo M. The Role of CT Imaging in Characterization of Small Renal Masses. //Diagnostics (Basel). 2023 Jan 17;13(3):334.
12. Bhatnagar N., Ahmad F., Hong H.S., Eberhard J., Lu I.N., Ballmaier M., Schmidt R.E., Jacobs R., Meyer-Olson D. FcyRNI (CD16)-mediated ADCC by NK cells is regulated by monocytes and FcyRII (CD32). //Eur J Immunol 2014; 44(11): 3368-3379.
13. Capitanio U, Bensalah K, Bex A, et al. Epidemiology of renal cell carcinoma. //Eur Urol. 2019;75(1):74–84.
14. Chen T, Peng Y, Lei T, Wu C, Wang H, Shi Y. Low-grade oncocytic tumour (LOT) of the kidney is characterised by GATA3 positivity, FOXI1 negativity and mTOR pathway mutations. //Pathol Oncol Res.- 2023 Feb 1;29: