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MORPHO-FUNCTIONAL FACTORS OF STOMACH CANCER PROGNOSIS

Resume: Gastric cancer (RV) is a heterogeneous group of carcinomas with a high malignant potential and an unfavorable prognosis. Obviously, there are a number of issues in the study of RS that require further in-depth research. There is no comprehensive data on the effect of the regularities of cell renewal of carcinoma and the functional immunophenotype of tumor cells on the malignant potential of RV. The prognostic significance of the expression of intercellular and cell-matrix adhesion molecules (E-cadherin (E-SUB), type 4 collagen (CO4)), extracellular matrix proteins and proteases (ECM) remains debatable; tenascin-C (TC-C), matrix metalloproteinases of type 2 and 3 (MMR2 and MMRZ)), as well as the regulatory protein galectin-3 (VAZ), including in various IFT variants of RV. A generally accepted algorithm for the individual prognosis of carcinomas of this localization has not been developed, taking into account the key molecular biological factors of the malignant potential of the tumor.

Key words: stomach cancer, morphofunctional and morphobiological characteristics.

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МОРФО-ФУНКЦИОНАЛЬНЫЕ ФАКТОРЫ ПРОГНОЗА РАКА ЖЕЛУДКА

Резюме: Рак желудка (РЖ) представляет собой гетерогенную группу карцином с высоким злокачественным потенциалом и неблагоприятным прогнозом. Очевидно, что в изучении РЖ имеется ряд вопросов, требующих дальнейшего углубленного исследования. Отсутствуют

комплексные данные о влиянии закономерностей клеточного обновления карциномы и функционального иммунофенотипа опухолевых клеток на злокачественный потенциал РЖ. Остается дискутабельной прогностическая значимость показателей экспрессии молекул межклеточной и клеточно-матриксной адгезии (Е-кадхерина (Е-САБ), коллагена 4 типа (СОЬ4)), протеинов и протеаз внеклеточного матрикса (ВКМ; тенасцина-С (ТК-С), матриксных металлопротеиназ 2 и 3 типа (ММР2 и ММР3)), а также регуляторного белка галектина-3 (вАЬЗ), в том числе при различных ИФТ вариантах РЖ. Не разработан общепринятый алгоритм индивидуального прогноза карцином этой локализации, учитывающий ключевые молекулярно-биологические факторы злокачественного потенциала опухоли.

Ключевые слова: рак желудка, морфофункциональная и морфобиологическая характеристика.

Relevance. Worldwide, stomach cancer (RV) remains one of the leading causes of death from malignant neoplasms (ZNO), is characterized by diagnosis in the late stages of the disease due to the late appearance of clinical symptoms, which significantly limits the effectiveness of the treatment [2,3,5].

The pathogenesis of RV is characterized as a multi-stage and heterogeneous process with a wide range of genetic changes – gene (functional single-nucleotide polymorphisms that determine genetic predisposition to the disease), genomic (change in the number of chromosomes, or aneuploidy) and chromosomal mutations (change in the structure of chromosomes), as well as epigenomic remodeling of chromosomes (DNA methylation, histone modification, microRNA profile change), leading to a violation of the regulation of the most important signaling pathways of the cell, a change in the body's response to environmental factors, which determines cellular disorders cycle, cell differentiation, processes of DNA repair and apoptosis and leads to the development of RV [1,3,4].

The purpose of the study. The purpose of this study was to improve the morphological diagnosis of RV with a comprehensive assessment of the malignant potential of the neoplasm and the development of additional prognosis criteria.

Materials and methods of research. The object of the study was the current surgical material of the removed stomachs of 55 patients operated for cancer. Carcinomas with glandular differentiation, histological stage T1-TK (according to the system "SHM, 2011), removed within healthy tissues, were selected. There were 30 men (55%), 25 women (45%), sex ratio - 1.2:1, age 27-71 years (average -57.3±7.6 years), median - 58.0.

The results of the study. According to the immunohistochemical expression of mucins M11C1, MiS2, MiS5AS, MiSb, as well as SOY glycoprotein, which are produced by gastric epithelial cells in various combinations and serve as immunophenotypic markers of functional heterogeneity of the glandular epithelium of the gastric mucosa in normal and pathological conditions, gastric carcinomas can be divided into gastric, intestinal and mixed immunophenotypic variants, while the functional immunophenotype of cancer it does not depend on the localization in the stomach, as well as the histological type and histological stage of the tumor process.

The postoperative 4-year adjusted relapse-free survival of patients with gastric cancer of the histological stage T2-TK is statistically significantly associated with the functional immunophenotype of the tumor and is 26% in patients with gastric immunophenotype, 12% with mixed immunophenotype.

Quantitative indicators of immunohistochemical expression of galectin-3 and matrix metalloproteinases of type 2 and 3 in gastric carcinomas are statistically significantly associated with the histological variant and functional immunophenotype of the tumor.

Quantitative indicators of immunohistochemical expression of the adhesive molecule E-cadherin, galectin-3, and matrix metalloproteinases of types 2 and 3

are statistically significantly associated with postoperative survival of patients with gastric cancer. Signs of an unfavorable prognosis are: <50% of tumor cells immunopositive to E-cadherin and galectin-3, >40% - immunopositive to matrix metalloproteinase type 2 and >50% - to matrix metalloproteinase type 3.

Indicators of cell proliferation (mitotic index, K167 index), as well as cell death by type of apoptosis (apoptotic index) in gastric carcinomas are statistically significantly associated with the histological variant and functional immunophenotype of the tumor.

For diagnostic purposes, the proliferative potential of gastric cancer can be assessed by a conditional quantitative indicator - the "coefficient of cellular renewal" (KKO), equal to the ratio of mitotic and apoptotic indices. The value of KCO > 0.7 is a reliable sign of an unfavorable prognosis of stomach cancer. Mitotic and apoptotic indices have less prognostic significance, however, an unfavorable prognosis is likely with a mitotic index >30%o and an apoptotic index <40%o.

Thus, the functional immunophenotype of carcinoma according to a set of immunohistochemically expressed mucins and SOY, the "coefficient of cell renewal", mitotic and apoptotic indices, as well as quantitative indicators of immunohistochemical expression of E-cadherin, galectin-3 and matrix metalloproteinases of type 2 and 3 are independent factors for the prognosis of gastric cancer. Immunohistochemical expression of collagen 4 of the basement membranes, tenascin-C of the extracellular matrix, membrane expression of E-cadherin, as well as the K167 index in gastric carcinomas have no prognostic significance.

The extent of the tumor infiltrate obtained during the preoperative diagnosis of "proximal" gastric cancer of the histological stage T2-TK by magnetic resonance imaging significantly exceeds the true size of the tumor and needs correction with a correction factor equal to 0.4.

It has been shown that the malignant potential of RV is due not only to the histological variant and indicators of proliferative activity of tumor cells, but also to other important regulatory mechanisms: the intensity of cell death by type of apoptosis, morpho-functional differentiation of tumor cells and the level of expression of proteins and proteinases involved in intercellular and cell-matrix interactions. A comprehensive analysis of the results made it possible to develop additional objective quantitative criteria for individual prognosis in RV, available for use in everyday practice.

Conclusion. The study confirmed the assumption about the possibility of the influence of functional IFT of tumor cells on the malignant potential of RV. A certain contribution has been made to the study of the parameters of cell renewal, as well as the IHC expression by tumor cells of a number of molecular biological markers associated with tumor growth in carcinomas of this localization.

LIST OF LITERATURE:

1. Alekseev V.V. Improving the method of hyperthermic chemoperfusion in the system of complex treatment of patients with peritoneal carcinomatosis: dis. ... candidate of medical Sciences. Saint Petersburg, 2015. 113 p.

2. Kaprin A.D., Starinsky V.V., Petrova G.V. The state of oncological care for the population of Russia in 2016. Moscow: RIIS FIAN, 2017. 236 p.

3. Chikina A.S., Alexandrova A.Yu. Metastasis: cellular mechanisms and their regulation // Molecular Biology. 2014. No. 2. pp.195-213.

4. Shen L., Zhang X., Chen L.T., Shan Y.S., Hu H.M., Yang Y.H., Price T.J., Sirohi B., Yeh K.H., Sano T., Yang H.K., Park S.R., Kang Y.K., Fujii M. Management of gastric cancer in Asia: resource-stratified guidelines. Lancet Oncol. 2013. no 14. P.535-547.

5. Kanda M., Kodera Y., Sakamoto J. Updated evidence on adjuvant treatments for gastric cancer. Expert Rev. Gastroenterol. Hepatol. 2015. no 9. P.1549-1560.