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MORPHOLOGICAL CHARACTERISTICS OF THE LUNG AFTER CORRECTION WITH AN IMMUNOMODULATOR UNDER EXPERIMENTAL CHEMOTHERAPY

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Summary. Immunotherapy is an innovative method of cancer treatment. It is based on interference in the interaction of the patient's immune system and a malignant tumor. Immunotherapy goes well with classical methods of treatment [Ivanisova D.N., 2022]. The results of the analysis of literature data on the use of immunomodulators in the complex treatment of cancer patients with lung cancer during chemotherapy are presented.

Key words: morphometry, cancer, lungs, immunomodulator, chemotherapy.

МОРФОЛОГИЧЕСКИЯ ХАРАКТЕРИСТИКА ЛЕГКИХ ПОСЛЕ КОРРЕКЦИИ ИММУНОМОДУЛЯТОРОМ В УСЛОВИЯХ ЭКСПЕРИМЕНТАЛЬНОЙ ХИМИОТЕРАПИИ

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Аннотация. Иммунотерапия – это инновационный метод лечения онкологических заболеваний. В его основе лежит вмешательство во взаимодействие иммунной системы пациента и злокачественной опухоли. Иммунотерапия отлично сочетается с классическими методами лечения [Иванисова Д.Н., 2022]. Представлены результаты анализа литературных данных применения иммуномодуляторов в комплексном лечении при химиотерапии онкологических больных с раком легких.

Ключевые слова: морфометрия, рак, легкие, иммуномодулятор, химиотерапия.

EXPERIMENTAL KEMOTERAPİYADA IMMUNOMODULYATOR BILAN KORREKTSIYADAN KEYIN O'PKANING MORFOLOGIK XUSUSIYATLARI

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Buxoro davlat tibbiyot instituti

Annotatsiya. Immunoterapiya saraton kasalligini davolashning innovatsion usuli hisoblanadi. Bu bemorning immun tizimining o'zaro ta'siriga va yomon sifatli o'simtaga aylanishiga asoslangan. Immunoterapiya davolashning klassik usullari bilan qo'llaniladi [Ivanisova D.N., 2022]. Kimyoterapiya paytida o'pka saratoni bilan og'rigan saraton kasalliklarini kompleks davolashda immunomodulyatorlardan foydalanish bo'yicha adabiyotlarni tahlil qilish natijalari keltirilgan.

Kalit so'zlar: morfometriya, saraton, o'pka, immunomodulyator, kimyoterapiya.

Relevance. Lung cancer is one of the most common causes of death in cancer patients. Among the morphological forms, the most common is non-small cell lung cancer (NSCLC) of epithelial origin, represented mainly by adenocarcinoma and squamous cell carcinoma. Neuroendocrine tumors, in particular small cell lung cancer (SCLC), are much less common. In most cases, lung cancer is diagnosed in advanced stages. Until the 2000s, treatment decisions were based on differential diagnosis only between small cell and non-small cell lung cancer. Therefore, all diagnostic measures were aimed at obtaining a small sample of tumor tissue for subsequent simple histological examination, which, together with non-invasive techniques, made it possible to stage the tumor according to the TNM classification. The concept that NSCLC does not have histological variability (NOS), along with the predominant diagnosis already at advanced stages, determined the development of anticancer drugs until the 2000s, during which time platinum derivatives were included in the basis of medical palliative therapy at stage IV NSCLC [Schiller JH, Harrington D, Belani CP, Langer C, Sandler A, Krook J, et al., 2020]. The need to identify histological subtypes of NSCLC arose after the development of new chemotherapeutic drugs (pemetrexed) and monoclonal antibodies

(bevacizumab), which, depending on the morphological type of tumor, could both improve treatment results and initiate severe toxic reactions. [Scagliotti G.V., Parikh P., von Pavel J. et al., 2017]. Tumors previously considered undifferentiated should now be classified as squamous cell carcinoma or adenocarcinoma. These changes currently determine the requirements for diagnostic approaches, tools and their further development [Usachev V.S., Ragulin Yu.A., Silantyeva N.K., 2016]. In the last decade, the need for methods for adequate tissue sampling has increased, since modern drugs for the treatment of NSCLC require careful morphological and genomic diagnostics in order to individualize treatment. It is known that cancer is a heterogeneous group of malignant tumors from epithelial tissues, characterized by a tendency to infiltrative growth and metastasis, abnormal vascular growth, replicative immortality of cells, their resistance to cytostatics, impaired growth suppressors and immune surveillance, and a stable proliferative signal. A persistent signal of proliferative activity is usually caused by genetic mutations in certain oncogenes that encode the functioning of tyrosine kinases [Hanahan D, Weinberg RA., 2021].

Immunotherapy is an innovative method of cancer treatment. It is based on intervention in the interaction between the patient's immune system and the malignant tumor. Immunotherapy combines well with classical treatment methods [Ivanisova D.N., 2022].

Immunotherapy for lung cancer is gaining increasing popularity. One of its promising directions is the development of therapeutic monoclonal antibodies anti-PD-1 and anti-PD-L1, leading to the reactivation of a specific antitumor immune response. Assessment of the expression level of PDL1 molecules is considered as a potential biomarker for predicting the effectiveness and duration of treatment of malignant neoplasms, as well as a predictor of response to anti-PD1/PDL1 immunotherapy [14].

Immunotherapy is a fundamentally new method of treating malignant tumors, which has already proven its effectiveness in various solid tumors. Immune checkpoint inhibitors are approved for use in kidney cancer, bladder cancer, melanoma, colon cancer (in the presence of microsatellite instability), hepatocellular cancer, non-small cell lung cancer, etc. Therefore, it was extremely interesting to study the effectiveness of this type of therapy in SCLC, an extremely malignant tumor for which no effective inhibitor has been found in the era of targeted therapy. Over the past 20 years, not a single new drug has been registered for the treatment

of SCLC. SCLC has always been considered a tumor with high immunogenic potential due to its characteristic paraneoplastic syndromes, in particular Lambert-Eaton syndrome, which manifests itself as an increase in myasthenia gravis as a result of an immune response to antigens expressed by both SCLC and the neural tissue. For this reason, SCLC patients with paraneoplastic syndromes have a better prognosis due to the activation of the immune system against the tumor. The prognosis of patients with SCLC is also influenced by the composition of the population of tumor-infiltrating lymphocytes. Thus, it is known that patients with localized SCLC have significantly more effector CD4+ T lymphocytes compared to common ones, including those that produce interleukin-17, which, in turn, recruits effector T lymphocytes, activates dendritic cells and has a direct antiproliferative effect . and the ability to induce apoptosis [Young M.R., 2016]. SCLC is a tumor with one of the highest levels of somatic mutations, including mutations in the DNA repair system [Gazdar A.F., Bunn P.A., Minna J.D., 2017]. The more somatic mutations in the tumor, the more neoantigens are associated with the tumor, which can ultimately trigger an adaptive immune response [Sabari J.K., Lok B.H., Laird J.H., Poirier J.T., Rudin C.M., 2017] and increase the effectiveness of immunotherapy [Efremova M., Finotello F., Rieder D., Trajanoski Z., 2017]. It has also been shown for various tumors that mutational load predicts the effectiveness of immunotherapy [Goodman A.M., Kato S., Bazhenova L., Patel S.P., Frampton G.M., Miller V. et al., 2017]. Despite the high level of mutational load, SCLC is characterized by a pronounced immunosuppressive phenotype. SCLC, including cell lines, is characterized by a low level of expression of class 1 antigens of the major histocompatibility complex - HL-A, B, C and β2-microglobulins. And class 2 antigens of the major histocompatibility complex are not detected at all in the tumor (SCLC) and tumor-infiltrating lymphocytes [He Y., Rozeboom L., Rivard C.J., Ellison K., Dziadziuszko R., Yu H. et al., 2017]. Loss of histocompatibility antigens allows SCLC cells to evade the immune response and promotes resistance to immune checkpoint inhibitors. Despite the high level of mutational load, SCLC is characterized by a low content of tumor-infiltrating lymphocytes and a clearly low CD8/CD3 ratio [Schalper K.A., Carvajal-Hausdorf D.E., McLaughlin J.F., Altan M., Chiang A.C., Velcheti V. et al., 2016]. Thus, the immune characteristics of SCLC did not allow us to reliably assert the high effectiveness of immunotherapy,

and only clinical studies could provide a convincing answer [A.E. Kuzminov et al., 2019].

"The goal of cancer immunotherapy is to make the patient's immune system work in such a way that it can independently counteract the growth of a malignant tumor." As for chemotherapy, in most cases its combination with immunotherapeutic drugs is most effective. For example, dendritic cell vaccination may occur between chemotherapy cycles, or chemotherapy may precede CAR T cell therapy. Certain chemotherapy regimens can enhance the immune response against tumors, which allows patients to quickly achieve cancer remission [Zhilyuk D.V., 2022]. Chemoradiation therapy can be used in a number of nosologies not for the purpose of actively affecting the tumor, but as a conditioning regimen to create favorable conditions for the activity of the administered specific autologous CTL, with which immunotherapy should begin in these cases [6].

At the moment, it is time to think about changing the treatment paradigm for some types of cancer from chemotherapy to immunotherapy as relatively low-toxic, which allows for a personalized approach to the patient, has a broad base for development, provides a good quality of life for patients and has shown its effectiveness in a number of studies. This requires the formation of treatment protocols based specifically on the principles of immunotherapy and excluding chemoradiotherapy where it has not demonstrated its effectiveness. There is no doubt that the implementation of immunotherapeutic programs requires a clinical base with modern laboratories and specialists in the field of cell cultivation, immunology, molecular genetics and can only be implemented in specialized centers with high scientific potential [I.S. Dolgopolov, G.Z. Chkadua, 2018].

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СОВРЕМЕННЫЕ ПОДХОДЫ К ВЕДЕНИЮ ПАЦИЕНТОК С МИОМОЙ МАТКИ

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Резюме: В данном научном исследовании изучалась эффективность консервативного лечения с использованием препарата Гинестрил (мифепристон) у пациенток в перименопаузе с миомой