CORRECTIONS WITH IMMUNOMODULATORS IN EXPERIMENTAL CHEMOTHERAPY

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The relevance of research. Every year, more than 600 thousand people are diagnosed with malignant tumors of the large intestine. Moreover, in 60-70% of patients, late stages of the disease are detected. Colorectal cancer is more commonly found in patients older than 50 years of age. The gender ratio is 1:1.5 (men get sick more often). Colorectal cancer is formed as a result of malignant transformation of intestinal epithelial cells. Most often, the tumor occurs in the descending colon. The mechanism of neoplasia has not been studied. Presumably, the development of the disease is promoted by chronic inflammatory processes, contacts with carcinogens, and the presence of polyps in the intestine [Makarov O.G., 2022]. 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 goal of cancer immunotherapy is to get the patient's immune system to work in such a way that it can counteract the growth of a malignant tumor on its own." As for chemotherapy, in most cases it is most effective in combination with immunotherapy drugs. For example, vaccination with dendritic cells may occur between cycles of chemotherapy, or chemotherapy may precede CAR T cell therapy. Certain chemotherapy regimens can enhance the immune response against tumors, which allows patients to achieve cancer remission faster [Zhilyuk D.V., 2022]. The obtained studies have shown that the growth of most malignant neoplasms is accompanied by changes in the parameters of various parts of the immune response. To determine the nature and intensity of

damage to the immune system, a panel of monoclonal antibodies (MCA) to differentiation antigens of immunocompetent cells and a number of tests that determine their functional activity are currently used. For quite a long time, the main changes that were given priority were considered to be disturbances in the ratio of immunoregulatory subpopulations of T-lymphocytes, a decrease in the number and decrease in the functional activity of natural killers [Kadagidze Z.G., 2022]. Chemoradiation therapy can be used in a number of nosologies not for the purpose of actively influencing the tumor, but as a conditioning regimen to create favorable conditions for the activity of administered specific autologous CTLs, with which immunotherapy should be started in these cases. In this case, various methods of CTL administration should be envisaged, depending on the location of the tumor and the expected degree of its accessibility to CTL (intravenously, intrathecally). The transition to dendritic cell vaccines seems appropriate only after the restoration of the ability of the immune system to generate a response to antigenic stimulation - 1.5–2 months after the end of chemotherapy. An example of the consistent use of chemoradiotherapy and immunotherapy is the work of S. Rosenberg et al. [Cercek A, Lumish MA, Sinopoli JC, et al., 2022], where 3- and 5-year survival in 93 patients with metastatic melanoma who received immunotherapy with autologous tumor-infiltrating lymphocytes was 36 and 29%, which is at least comparable to with indicators achieved with the use of programs with chemotherapy. In 20 patients who achieved a complete response, the survival rates in the above terms were 100%. The toxicity was not due to the cellular immunotherapy itself, but to an interleukin 2 preparation that was administered to patients at high doses. According to other studies, chemoradiation preparation of patients is not mandatory for effective CTL immunotherapy. In a study by J. Wolchok et al. [Verschoor YL, van den Berg J, Beets G, et al., 2022], which included patients with stage III–IV melanoma treated with antibodies to CTLA-4 and PD-1 receptors, more than 50% of cases achieved long-term positive clinical response with significant reduction in visible tumor. However, only in 9% of cases, therapy was interrupted due to the development of acute toxicity. There were no

deaths due to treatment. Encouraging results in the absence of toxicity were shown by the tactics of immunotherapy using dendritic cell vaccines and in the treatment of patients with recurrent and chemotherapy-resistant glioblastoma multiforme. In patients, not only stabilization and shrinkage of the tumor were noted, but also a significant (3 times) increase in the non-progressive interval compared with the control group, and in some cases chemoradiotherapy-resistant gliomas and complete long-term (more than 5–7 years) remission [Cohen R, Taieb J, Fiskum J, et al., 2021].

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