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TUMOR GROWTH AND DEVELOPMENT UNDER THE INFLUENCE OF DRUGS

Ibragimova Mahliekhon Sayidalikhon Kizi
Assistant Professor, Department of Oncology
Andijan State Medical Institute Andizhan city , Uzbekistan

Relevance of the topic. Malignant neoplasms are one of the main causes of death in most countries of the world; in the overall mortality structure, it is up to 15-20%. According to WHO, the incidence of various tumors ranges from 150 to 400 cases per 100 thousand people. However, despite the importance of this problem, the treatment of malignant neoplasms is still insufficiently developed. Indeed, even complex (chemotherapeutic, surgical, X-ray and radiological, etc.) treatment of tumors often turns out to be ineffective, especially in the terminal stages. Based on this, the search for new drugs for the therapy of tumor disease is a very urgent problem.

At present, significant progress has been made in the chemotherapeutic treatment of tumors. However, the use of synthetic drugs often leads to life-threatening side effects, sharply disrupts metabolism, and causes intoxication of the body [4, 5, 6]. In this regard, herbal drugs have very important advantages. They have a wide spectrum of action, are practically non-toxic, are well tolerated by patients, have a positive psychotropic effect, generally have no side effects, are more accessible, etc. The diversity of clinical manifestations in oncological diseases, caused by the biological properties of the tumor, complicates the choice of optimal treatment methods. At present, the treatment of patients with malignant neoplasms, although considered complex (surgical, radiation, chemotherapeutic, etc.), is aimed mainly at the main focus - the tumor and its metastases. Such therapy is largely palliative in nature. At the same time, the problem of the effect of drugs not only on the growth and development of the tumor, but also the host organism, has not been sufficiently developed. Meanwhile, there is no doubt that there is a direct connection between the occurrence and development of a tumor and the corresponding " blastomogenic " induced changes in all tissues, systems and organs. In this regard, of particular

interest are drugs that not only change the metabolism in the tumor cell, but also normalize the metabolism in the whole organism [2].

Thus, based on the tumor's ability to intensively consume glucose, a method of its selective sensitization to damaging effects using high hyperglycemia was developed [6]. As is known, minor hyperglycemia, as a rule, stimulates tumor growth, primarily, apparently, due to a good supply of its cells with energy material [7]. Indeed [2], there is a certain relationship between the proliferative activity of tumor cells and the degree of their utilization of substrates that serve as precursors of macroergic compounds. At the same time, with very high hyperglycemia and due to sharply stimulated glycolysis, excess lactate is formed in tumor cells , which reduces the pH of the environment, disrupts microcirculation and promotes blastoma necrosis. These data were obtained in studies conducted both in both in vitro and in vivo [7, 9] . In particular, R.E. Kavetsky et al . [7] established that intravenous administration of a 20% glucose solution to rats with Guerin's carcinoma reduces the pH in the tumor tissue from 6.82 to 5.69 by the 3rd hour. Similar data are also presented by other authors . Moreover, healthy tissues do not exhibit a similar reaction to excess glucose, and hyperlactacidemia is quickly neutralized by the buffer systems of the blood and tissues. S.N. Osinsky et al., having analyzed the kinetics of the activity of some glycolytic enzymes in transplanted Guerin's carcinoma with different doses of glucose administration, established that LDH activity completely disappeared already at a pH of 6.9. Hexokinase activity in tumor tissue at a pH of 6.0 dropped by 20-30 times, and at a pH of 5.5 it was zero; with a decrease in pH from 7.6 to 5.5, the activity of glucose-6-phosphatase decreased by 13.5-36.2 times. Undoubtedly, the indicated changes in enzymes discoordinate metabolic processes in the tumor cell, which leads to inhibition of its growth and development.

The mechanism of most antitumor drugs is based on their ability to suppress DNA synthesis in malignant cells. In addition, these drugs can affect carbohydrate and protein metabolism in tumor tissues, significantly disrupting it. Thus, it was found that when rats with brain tumors were given sarcosinamide chloroethylnitrosourea , a reliable decrease in tumor size directly correlated with a decrease in glucose utilization by tumor tissue [192, 216]. The drug dinalin in experiments in vitro

inhibited amino acid transport and disrupted protein metabolism in colon cancer cells [211].

As an example of enzyme therapy for malignant neoplasms, asparaginase should be mentioned . This enzyme in immobilized form is capable of destroying asparagine, which is vital for the growth and development of some leukemic cells [91, 110]. Japanese scientists have found that subcutaneous injection of superoxide dismutase to rats after implantation of KMT-17 fibrosarcoma leads to suppression of tumor growth, and a single injection of this enzyme before implantation leads to an increase in the life expectancy of the experimental animals [209].

Antimetabolites, substances that are similar in their chemical structure to metabolic products but inhibit their transformations and physiological activity, are of particular interest in the treatment of tumors. Of great practical interest at present are methotrexate , a folic acid antagonist; mercaptopurine and 6-thioguanine, purine antagonists; fluorouracil (fluorofur and cytarabine), pyrimidine analogues. In general, the cytostatic effect of all these drugs is associated with disruption of nucleic acid synthesis. Thus, methotrexate inhibits phosphate reductase activity. As a result, tetrahydrofolic acid, which participates in the biosynthesis of nucleic acids, is not formed .

Conclusion

All this determines the need to search for new means for tumor therapy that would not only have a clearly expressed antitumor effect, but also correct impaired functions and metabolic processes, increase the overall resistance of the body to the development of neoplasm. Medicinal plants are of undoubted interest in this regard.

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