

Determination of Malignant Gliomas Radicality Surgical Removal by in Vitro Method

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Abstract: The paper presents the laboratory method of determine surgical removal radicality of malignant gliomas. The method is based on the definition of blood cell aggregation indices using the biosensor "Plasmon" constructed with the use of the physical phenomenon of surface plasmon resonance. The theoretical basis of the method was the peculiarities of blocking calcium channels in blood cells by the NMDA-dependent calcium blocker – verapamil. In tumor-associated inflammation, glutamate activates NMDA-dependent calcium channels at significantly lower concentrations than with conventional non-tumor origin inflammation, hence the concentration of calcium channel blockers will also be significantly lower. This allows differentiate the tumor-associated inflammation and, in its absence, conclude the successful removal of malignant gliomas in patients.

Keywords: Gliomas; radicality of surgical removal; verapamil-hydrochlorid; surface Plasmon resonance; tumor-associated inflammation; blood cells aggregation.

INTRODUCTION

Radical removal of intracerebral tumors, such as malignant gliomas, is often a difficult task [1] because of the localization of the tumor in close contact with vital intracerebral centers. With the development of edema in the early postoperative period, it is not always possible to determine the presence or absence of tumor tissue residues by modern visualizing methods.

From the completeness of tumor removal depending the tactics of the patients treatment in the postoperative period. Information on changes in tumor size is also important in the patients, who were treatment with modern antitumor agents. Considering the presence of tumor-associated inflammation (TAI) accompanying the growth and progression of malignant gliomas, by the definition of an inflammatory process in the body one can argue the presence of residual tumor tissue in the brain in the postoperative period [2].

To develop a laboratory method for determining the radicality of surgical removal of tumor tissue, the parameter of blood cells aggregation (BCA), characterizing the II stage of inflammation, was taken as a basis. Widely used in the clinical methods of determining BCA in gliomas due to the presence of a blood-brain barrier are insensitive. The biosensor

"Plasmon" was used in the work on the basis of the biophysical phenomenon of surface plasmon resonance (SPR), which allows to investigated minimal changes in the level of BCA [3]. To distinguish TAI from an inflammatory process that was not associated with tumor growth, a modification of the ion channels of blood cells was performed with different concentrations of the calcium channel blocker - 0.25% solution of verapamil- hydrochloride ("Farmak"), which changes the BCA level depending on the drug concentration at different degrees of it dilutions.

The aim of the research was the development of an auxiliary laboratory method for analyzing the radical surgical removal of cerebral malignant gliomas in the postoperative period.

MATERIALS AND METHODS

In the study of 78 patients with glioblastomas were examined before and on the 7th day after the operation, as well as 25 healthy individuals. Verapamil - hydrochloride (0.25% dilution) was added to the blood taken from a patient at various concentrations in the dilution interval with water (without ions) from 10^{-1} to 10^{-6} times before *in vitro* studies.

RESULTS

In the group of healthy individuals, used dilution of verapamil from 10^{-1} to 10^{-6} times showed that the drug did not significantly affect the level of aggregation of blood cells at all dilutions *in vitro*.

In the group of patients with glioblastoma verapamil at a dilution of 10,000 times contributed to an increase in the level of ABC (decrease in the parameters of SPR) with a more complete removal of tumor tissue and, conversely, led to a decrease in the level of ABC (increase in SPR) with incomplete removal of the tumor.

When verapamil is added to the blood 100 times diluted, changes in aggregation of blood cells are noted with the development of aseptic inflammation associated with the operating wound. This result can be interpreted as a different activity of calcium channels in inflammation associated with or unrelated to the growth of gliomas and, consequently, the need to use different concentrations of verapamil to differentiate them. To confirm this conclusion, the data obtained in [4] are used: in the inflammatory process of

the non-tumoral nature, ionotropic NMDA receptors are activated by the millimolar concentrations of glutamate, while inflammation associated with tumor growth is sufficient to activate the receptors of micromolar concentrations of glutamate. Therefore, with a higher glutamate concentration, the receptor activity will be greater and, accordingly, the concentration of the blocker will also be greater. And, conversely, with tumor-associated inflammation, the receptor activity will be less, respectively, the concentration of the blocker will also be significantly less. By the difference in the concentrations of blockers,

a conclusion is drawn about various types of inflammatory process in the postoperative period, which makes it possible for the absence of TAI (Fig. 1).

CONCLUSIONS

A new auxiliary laboratory method has been developed to determine the radicality of surgical removal of brain malignant gliomas. The theoretical basis of the method was the peculiarities of blocking calcium channels in blood cells with different concentrations of verapamil – calcium channels blocker.

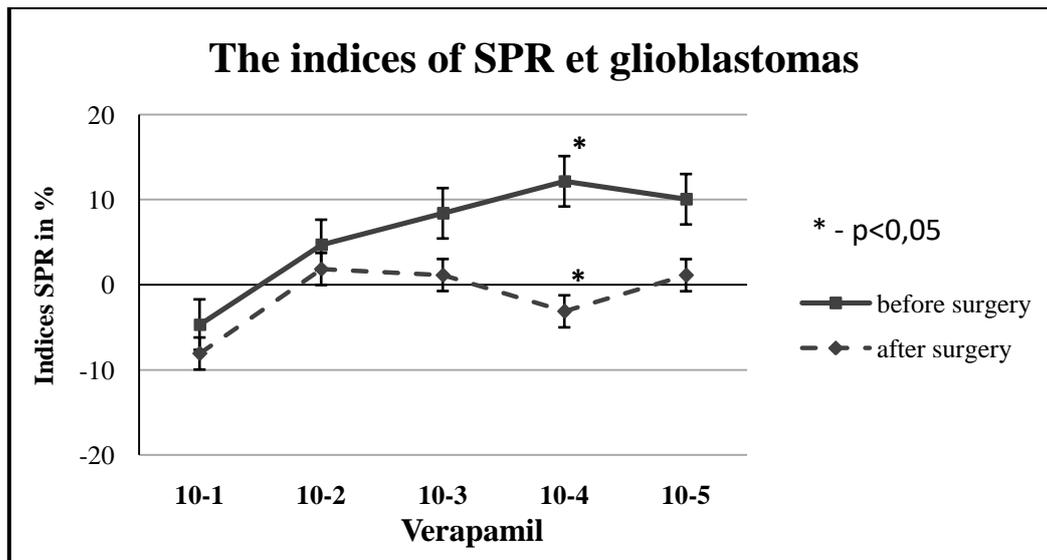


Fig. 1. The ratio of blood cells aggregation indices (SPR) by the action of verapamil dilutions in the patients with glioma of IV grade of malignancy before surgery and on the 7th day after surgery.

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