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COMPLEX SURGICAL TREATMENT OF PATIENTS WITH HIGH-GRADE BRAIN TUMORS

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ABSTRACT

Currently, there are numerous complex methods of treatment of glial brain tumors, namely: chemotherapy, radiation therapy, stereotactic radiosurgery, surgical removal of the tumor. The surgical method of treatment can be considered one of the most effective, since removal of the focus eliminates the neoplasm as a source of volumetric impact and the cause of cerebral edema. The operation, significantly and rather quickly improves the general condition of the patient, leads to regression of cerebral and neurological symptoms, especially with large tumors.

The objective. To improve the results of surgical treatment of patients with malignant brain tumors (grade III-IV WHO) using complex treatment methods.

Materials and methods. During the period from 2009 to 2019 there are 2343 patients with glial brain tumors were examined and operated in the Republican specialized scientific practical medical center of neurosurgery. Patients underwent a comprehensive examination, including clinical and neurological examination of related specialists (fundus examination, neuro-ophthalmological examination, vestibulograms), instrumental research methods (CT, MRI of the brain, tractography of the pathways, if indicated, contrast examination and angiography of intracranial arteries), microsurgical removal of the tumor, histological verification of the biopsy and subsequent irradiation with a neutron capture therapy on the basis of the Institute of Nuclear Physics of the Academy of Sciences of the Republic of Uzbekistan.

Results. Compensated state 70 points and above - 1213 (51.7%) patients, subcompensated state 60-50 points - 1031 (44.0%) patients, decompensated state 40 points and below - 78 (3.3%) patients were noted. Analyzing operated patients with glial brain tumors, 1033 (44.1%) patients were discharged in good recovery, 729 (31.1%) patients were moderately disabled, 534 (22.8%) patients were severely disabled, mortality - 28 (1.7%) patients. Radiation therapy was received by 1169 (50.4%) patients. Relapses in glial brain tumors were found in 166 (7.2%) patients.

Conclusion. The maximal radical removal of the tumor and the use of radiation therapy in the treatment of malignant brain tumors allows to achieve good survival of patients and a long relapse-free period.

Key words: malignant neoplasms of the brain, surgical treatment, radiation therapy.

INTRODUCTION

Over the past decade, there has been a tendency for a steady increase in the incidence of malignant and multiple brain tumors in the world. Epidemiological studies have shown that the incidence of primary high-grade brain tumors currently in economically developed countries is 10.9 - 12.8% per 100 thousand population [2, 7]. The incidence of brain tumors has statistical differences depending on age, gender, geographic characteristics of the place of residence, social class and standard of living of the studied population group, and a number of other external factors. They occur equally often in men and women at any age, mainly on average 44% of cases occur between the ages of 26 and 45 years. Children (from 1 to 15 years old) account for 17%, and over 50 years old - 5.2% of cases. Mature and benign tumors are 3 times more common in women, and malignant tumors and cancer metastases are 3 times more common in men [3]. Among primary brain tumors, approximately 60% are malignant, 40% are benign [6, 14]. The reasons for the formation of primary brain tumors are still unknown. There is some evidence of the possible existence of a genetic etiological factor for some of them. Other potential oncogenic factors include exposure to certain chemicals, suppression of the immune system, and previous medical radiation to the head. The cause of secondary brain tumors, obviously, are always primary tumors that develop in some other part of the body. The increase in the incidence of primary brain tumors is associated with the deterioration of the environmental situation and the influence of negative environmental factors. A certain role in the objective growth of morbidity is played by such a positive social factor as an increase in the average life expectancy of the population in people of older age groups, the likelihood of occurrence increases. Basically, brain tumors are treated by methods of surgery, chemotherapy, radiotherapy, etc. [2, 6, 15]. It is mathematically calculated that an intracerebral tumor of an average size consists of 100 billion cells, respectively, when 99% of the tumor is removed, which is practically impossible, 1 billion cells remain in the human body, which actively multiply, contributing to the further development of the tumor process. Modern surgical technologies provide for high accuracy of instrumental manipulations, minimization of surgical trauma, maximum preservation of brain structures, and safety of operations [8, 11, 13]. Despite the fact that considerable progress has now been made in the surgery of brain tumors, surgical treatment almost never leads to the cure of patients, although the survival rate correlates with the radicality of tumor resection. Brain tumors cannot be completely cured, and the prognosis for such patients is extremely poor. Radiation therapy occupies an important place in the complex treatment of malignant tumors, as well as in incomplete removal and relapses of benign tumors. Most often, radiation therapy is used as part of a combination treatment after subtotal removal of brain tumors [1, 8]. Diagnosis of radiation injuries is based on the clinic, CT and MRI data, which usually reveal areas of reduced density, similar to cerebral edema. A crucial moment for a doctor supervising a patient operated on for a brain tumor is to assess his ability to work.

THE OBJECTIVE OF STUDY.

To improve the results of surgical treatment of patients with malignant brain tumors (grade III-IV WHO) using complex treatment methods.

MATERIALS AND METHODS.

For the period from 2009 to 2019. in the Republican specialized scientific practical medical center of neurosurgery 2343 patients with glial brain tumors were examined and operated on. Patients underwent a comprehensive examination, including clinical and neurological examination, examination of related specialists (eye fundus examination, neuro-ophthalmological examination, vestibulograms), instrumental research methods (CT, MRI of the brain, tractography of the pathways, if indicated, contrast examination and angiography of intracranial arteries), microsurgical removal of the tumor, histological verification of the biopsy and subsequent irradiation with boron neutrone capture therapy on the basis of the Institute of Nuclear Physics of the Academy of Sciences of the Republic of Uzbekistan.

RESULTS.

Depending on the malignancy of the brain tumor, patients are divided into different histological structures: anaplastic astrocytoma - 718 (30,7%), oligoastrocytoma - 47 (2%), fibrillar - protoplasmic astrocytoma - 166 (7,1%), medulloblastoma - 251 (10.7%), glioblastoma - 248 (10,6%), astrocytic glioblastoma - 112 (4.7%), polymorphocellular glioblastoma - 55 (2.3%), oligodendroglioma - 159 (6.8%)), anaplastic oligoastrocytoma - 11 (0.4%), anaplastic oligodendroglioma - 43 (1.8%), fibrillar astrocytoma - 172 (7.3%), diffuse astrocytoma - 6 (0.2%), pilocytic astrocytoma - 21 (0.8%) patients. Also, depending on their benignity, meningiomas of the brain are divided into several histological variants: typical - 218 (44.7%) patients, angiomatous - 27 (5.5%), psammomatous - 22 (4.5%), fibroblastic - 84 (17.2%), meningothelial - 49 (10.0%), indifferentiated - 52 (10.6%), anaplastic - 6 (1.2%), sarcomatous – 29 (5.9%) patients (Fig. 1, Table1).

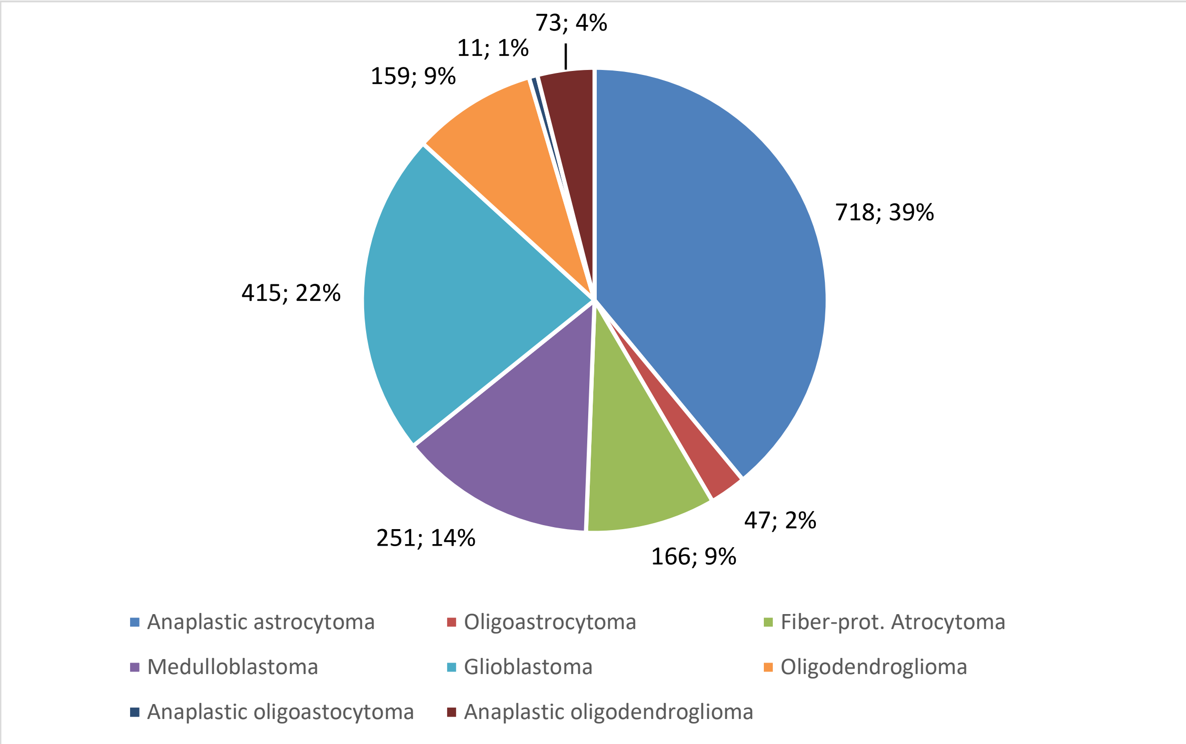

Figure 1. Distribution of patients with glial brain tumors according to the histological pattern

Table 1

Histology	**abs**	**%**	**Histology**	**Abs**	**%**
Anaplastic astrocytoma	718	30,7%	Subependymal astrocytoma	6	0,2%
Oligoastrocytoma	47	2,0%	Subependymoma	14	0,5%
Fibrillar-protoplasmic astrocytoma	166	7,1%	Paraventricular ependymoma	7	0,2%
Medulloblastoma	251	10,7%	Myxomatous ependymoma	3	0,1%
Glioblastoma	248	10,6%	Malignant ependymoma	99	4,2%
Glioblastoma of astrocytic origin	112	4,7%	Anaplastic ependymoma	34	1,4%
Glioblastoma polymorphic cell	55	2,3%	Giant cell glioblastoma	4	0,1%
Oligodendroglioma	159	6,8%	Protoplasmic astrocytoma	40	1,7%
Anaplastic oligoastrocytoma	11	0,4%	Diffuse astrocytoma	5	0,2%

Anaplastic oligodendroglioma	43	1,8%	Indifferentiated oligoastrocytoma	14	0,5%
Fibrillar astrocytoma	172	7,3%	Indifferentiated astrocytoma	88	3,7%
Diffuse astrocytoma	6	0,2%	Anaplastic fibrillar astrocytoma	13	0,5%
Pilocetic astrocytoma	21	0,8%	Pineoblastoma	2	0,08%

When analyzing 2338 operated patients, depending on localization, glial neoplasms of the brain were most often found in the frontal lobe - 305 (13.0%) patients, frontotemporal - 178 (7.6%), fronto-parietal - 172 (7.3%), frontal - parietal - temporal - 99 (4.2%), temporal - 232 (9.9%), temporo-occipital - 109 (4.6%), parietal - 185 (7.9%) , parieto-temporal - 148 (6.3%), parieto-occipital - 127 (5.4%), occipital - 98 (4.1%), lateral ventricle - 105 (4.4%), cerebellum - 133 (5.6%), the pons - cerebellar angle - 51 (2.1%), the cavity of the 4th ventricle - 293 (12.5%). The least of all the tumor was noted in the third ventricle - 34 (1.4%) patients, sellar region - 18 (0.7%), pineal region - 19 (0.8%), corpus callosum - 17 (0.7%), thalamus - 9 (0.3%), brainstem - 6 (0.2%). As can be seen from the table, malignant neoplasms of the brain are mainly found in the left hemisphere than in the right. Depending on the radicality in malignant brain tumors, total removal was performed - 977 (41.7%) patients, subtotal - 1127 (48.2%), partial - 234 (10.0%) (Table 2).

DISCUSSION

One of the main features of brain tumors is that they develop in a tightly limited space of the cranial cavity and, therefore, sooner or later lead to damage to both adjacent to the tumor and distant parts of the brain. Direct compression or destruction due to tumor infiltration of brain tissue causes the appearance of local symptoms. If a brain tumor is suspected, the necessary information can be obtained from a number of diagnostic studies. Thorough neurological, ophthalmological and otoneurological examinations. CT and MRI are the most informative modern diagnostic methods in neurosurgery. The resulting image makes it possible to judge with a fairly high degree of reliability about the localization of the tumor, its relation to adjacent structures, blood supply, histological structure, etc.

Table 2

Region of localization		**abs**	**%**	**Region of localization**		**abs**	**%**
Frontal	on right	147	6,2%	Lateral ventricle	on right	48	2,0%
	on left	158	6,7%		on left	57	2,4%
Fronto-temporal	on right	84	3,5%	Cerebellar hemisphere	on right	61	2,6%
	on left	94	4,0%		on left	72	3,0%

Frontal-parietal	on right	93	3,9%	Cerebellopontine angle	on right	27	1,1%
	on left	79	3,3%		on left	24	1,0%
Fronto-parietal-temporal	on right	51	2,1%	IV ventricle cavity		293	12,5%
	on left	48	2,0%				
Temporal	on right	112	4,7%	Brain stem		6	0,2%
	on left	120	5,1%				
Tempo-occipital	on right	41	1,7%	Thalamus		9	0,3%
	on left	68	2,9%				
Parietal	on right	89	3,8%	Sellar area		18	0,7%
	on left	96	4,1%				
Parieto-temporal	on right	82	3,5%	III ventricle		34	1,4%
	on left	66	2,8%				
Parieto-occipital	on right	62	2,6%	Corpus callosum		17	0,7%
	on left	65	2,7%				
Occipital	on right	40	1,7%	Pineal area		19	0,8%
	on left	58	2,4%				

Currently, an in vitro study is underway regarding the introduction of the neutron capture therapy (NRT) method into clinical neurooncology based on the neutron generator of the Institute of Nuclear Physics of the Academy of Sciences of the Republic of Uzbekistan. NRT is a selectively energetically destructive method for tumor cells. To date, neutron capture therapy has shown encouraging results in the treatment of malignant human brain tumors. The development and application of neutron therapy can prove to be a valuable addition to the spectrum of practical radiation therapy tools for our Republic. The technology of gadolinium neutron capture therapy (GdNCT) of malignant human brain tumors for clinical practice is being developed. Introduced into practice for the treatment of malignant neoplasms of the brain in the RSSPMCN MoH RUz together with INP AS RUz. A study was carried out from 2018 to 2020, including 56 patients with malignant neoplasms of the brain. Depending on the malignancy of the tumor, the patients were divided into different histological structures: anaplastic astrocytoma - 15 (26.7%) patients, oligoastrocytoma - 5 (8.9%), fibrillar - protoplasmic astrocytoma - 1 (1.7%) patient, glioblastoma - 7 (12.5%), glioblastoma of astrocytic origin - 2 (3.5%), polymorphic cell glioblastoma - 1 (1.7%) patient, oligodendroglioma - 2 (3.5%), anaplastic oligodendroglioma - 1 (1, 7%), fibrillar astrocytoma - 3 (5.3%), anaplastic ependymoma - 1 (1.7%), pilocetic astrocytoma - 1 (1.7%), giant cell glioblastoma - 1 (1.7%), metaplastic meningioma - 1 (1.7%), chromophobic pituitary adenoma - 2 (3.5%), neurolemoma - 3 (5.3%), transient meningioma - 5 (8.9%), meningotheliomatous meningioma - 1 (1.7 %), fibrous meningioma - 1 (1.7%), psammomatous meningioma - 1 (1.7%), hemangiopericytic meningioma - 1 (1.7%). Experiments carried out on the samples showed that after 6 hours of incubation after irradiation, histological analysis did not reveal significant changes.

After 17 hours of incubation of the samples after irradiation, necrosis was detected. Tumor tissue samples used in the experiment are tumors of various types, including tumors with necrotic areas. In accordance with the experimental design, samples are taken during the operation; there is no histological analysis data at this stage. Therefore, in order to detect necrosis that developed in the tumor before the operation, an additional control was introduced into the experiment. After the operation, part of the removed tumor was immediately fixed in formalin for control. This control makes it possible to detect the degree of necrosis present before surgery and subtract it from the degree of necrosis after irradiation and incubation of the samples.

CONCLUSION

The most valuable informative methods for diagnosing malignant brain tumors are X-ray research methods (MRI and / or MRI with contrast enhancement), which can reveal the presence of tumors and their recurrence and the possibility of surgical interventions. The disadvantages of the surgical method are the risks associated with open intervention - bleeding, circulatory disorders, the development of neurological disorders, infections. The incidence of complications is higher in tumors of the base of the skull, in addition, radical removal of the tumor of this localization is impossible and the remnants not removed are a source of continued tumor growth. The most radical removal of the tumor and the use of radiation therapy in the treatment of malignant brain tumors can achieve high patient survival and a long relapse-free period. The histological types of malignant brain tumors have been established, which is an important factor in determining the biological behavior of the tumor and a decisive factor in the choice of additional methods of complex treatment.

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