Prognostic factor, mortality and survival of patients with tumors of III ventricle after combined treatment.

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Summary.

Tumors of the third ventricle are deep-located tumors and significantly impact on the surrounding vital structures of the brain. The widespread use of modern neuroimaging techniques has increased ability to diagnose these tumors, and also allowed the identification of topographic and anatomical features and the relationship with the structures of the brain. The analysis of the literature on various methods of surgical and combined treatment revealed the ambiguity of views on the radical removal tactics of this pathology, respectively histostructure and localization. Research of results of surgical treatment is necessary to optimize the treatment of tumors of III ventricle, which is a complex and urgent today. We has been studied and evaluated the results of surgical treatment (survival) in 285 patients treated at the Institute of Neurosurgery them. Acad. A P Romodanov NAMS of Ukraine from 1993 to 2009, with tumors of III ventricle.

Key words: III ventricle, tumors, surgical treatment, results of surgical treatment (survival), prognostic factor.

Introduction. Tumors of the third ventricular region are deep-located neoplasms; they impact on the surrounding vital brain structures. The main difficulty in surgical treatment of the third ventricle tumors lies in hard-to-reach of this brain region, in depth of their localization near the vital structures and in close links with important subcortical structures and brain stem regions, in variety of

topographic and anatomic variants and in specific features of neoplasms histology. The rates of lethality by such pathology are rather high and are connected with the abovementioned factors.

Such neoplasms are rear brain tumors and make 5-10 % of cases; they often appear at a young age [2, 8, 24].

The history of the third ventricle tumors dates back to the colloid cyst description of this localization made by Wallmann in 1858 [8]. The initial stage of the third ventricle surgery development lasted for the first two decades of the past century, up to the publication of a report on first implementation of bitemporal decompression in the patient with pineal gland tumor (Cushing 1904) [16].

The successful surgical treatment of the third ventricle tumors is connected with the name of Dandy. Since the first successful operation on colloid cyst excision made by Dandy in 1921, neurosurgeons from different countries have gained considerable experience in the third ventricle surgical treatment [8].

Due to the works dedicated to topography and microsurgical anatomy of the brain arteries and veins and detailed microsurgical anatomy of the third ventricle, A.Rhoton and co-authors contributed greatly to the substantiation of surgical approaches to different parts of the third ventricle [18, 23, 25, 26, 27, 28, 29, 30].

Surgical method is the main one in treatment of the third ventricular region tumors, but the radical excision of tumor is rather difficult because of its deep localization in the brain, rate of blood supply to the tumor and common blood supply to the tumor and different parts of brain, and also because of variety of tumor histological structures [1, 2, 4].

Histological structure of neoplasms of this brain region is represented by such forms as: craniopharyngioma; astrocytoma; colloid cyst; chiasmal glioma with invasion into the third ventricle; pituitary adenoma; Rathke's cleft cyst; tumors from pineal gland tissue (pineocytomas, pineoblastomas, pineal gland parenchyma tumor of intermediate differentiation); parietal tumors (gliomas, gangliocytomas, meningiomas, lipomas, epidermoid or dermoid cycts); tumors from embryonic

cells (germinomas, embryonic carcinomas, choriocarcinomas, teratomas, suprasellar brain tumors); glial cysts; plexus-papilloma [2, 8, 24].

Essential role in the enhancement of modern neurosurgery played the arrival of neuroimaging diagnostic techniques: computed tomography, magnetic resonance imaging, and angiography (investigation of brain and tumor vessels interrelations, and rate of blood supply). Both diagnostic techniques – CT and MRI are informative regarding localization determination, nature of process, rate of hydrocephalus intensity, but MRI appeared more informative regarding determination of tumor sizes, form of growth and relation to the surrounding brain structures [1, 2, 3, 4, 5, 6, 7, 10, 13, 15, 17, 19, 24].

On the basis of the tumors localization peculiarities and their interaction with the surrounding vital brain structures, which determine the choice of the most optimal and most sparing operational approaches, for convenience tumors are divided into three groups:

- tumors of the third ventricle anterior parts (which occupy its first part and spread to the imaginary line at the posterior border of interventricular foramina);
- tumors totally invading the third ventricle;
- tumors of the third ventricle posterior parts (which spread to the posterior border of interthalamic adhesion) [1].

The result and success of the surgical intervention in case of the third ventricular region tumors depend, to a considerable degree, on the right and adequate choice of surgical approach. When choosing an approach, topographic and anatomic features of tumor, correlation of tumor and surrounding brain structures, and rate of hydrocephalic intensity are of great significance. The requirement to the approach is presence of the nearest, the safest and the most rational approach to the third ventricle tumor. The surgical approaches to the third ventricle tumors are the following: transcortical-transventricular, subfrontal, transcallosal (anterior and posterior), pterional, occipital, transtentorial, infratentorial, supracerebral, and transsphenoidal approach [2, 8, 24].

As it was mentioned above, the third ventricular region tumors are represented by different histology: craniopharyngioma; astrocytoma; colloid cyst; chiasmal glioma with invasion into the third ventricle; pituitary adenoma; Rathke's cleft cyst; tumors from pineal gland tissue (pineocytomas, pineoblastomas, pineal gland parenchyma tumor of intermediate differentiation); parietal tumors (gliomas, gangliocytomas, meningiomas, lipomas, epidermoid or dermoid cycts); tumors from embryonic cells (germinomas, embryonic carcinomas, choriocarcinomas, teratomas, suprasellar brain tumors); glial cysts; plexus-papilloma [2, 8, 29].

Over the last decades the results of the third ventricle tumors surgical treatment became better due to the use of microsurgical techniques and possibilities of neuroanaesthesiology and intensive care [1, 2]. But in spite of the considerable success, the treatment, directed at conservation and improvement of patients' life quality, remains rather complicated and diverse till the present day.

All this requires studying of different approaches in treatment of neoplasms of this region that will allow providing tumor excision and enduring survival of patients.

Treatment mode, surgical approach, tumor volume excision, histological structure of the tumor may influence the survival rate after the surgical treatment of patients with the third ventricular region tumors.

Objective: studying of the treatment outcome (survival and lethality rates) of patients with the third ventricular tumors after neurosurgical interventions in order to optimize such pathology treatment and to determine the prognostic factor.

Materials and methods. The work is based on the analysis results of the complex examination and surgical treatment of 285 patients with the third ventricular region tumors, who underwent examination and treatment at the State Institution "Institute of Neurosurgery n.a. A.P. Romodanov, Academician of NAMS of Ukraine" in the period from 1993 to 2009. There were 148 patients of male sex (52 %) and 137 patients of female sex (48%) among them. Depending on the place of the initial growth and tumor localization towards the third ventricle walls, cases were divided into such groups: anterior parts tumors – 79 cases

(27,7%), cavity invading tumors – 70 cases (24 %) and posterior parts tumors – 136 cases (48,3 %). The patients underwent medical imaging procedures: 234 patients received brain CT before the operation, 132 patients underwent brain MRI before the operation. The operation was carried out in 285 cases (97,6 %).

There was estimated the approach to the third ventricular tumors and the volume of the excised tumor according to the histological form. For the excision of anterior parts tumors and the third ventricle cavity invading tumors transcortical-transventricular approach was more often used (49 % and 86 % of cases correspondingly); for the excision of posterior parts tumors of the third ventricular region suboccipital-transtentorial approach was mostly used (59 % of cases). There were **totally** excised: colloid cysts and plexus-papillomas in 100 % of cases, craniopharyngiomas (in 24 % of cases at the anterior parts of the third ventricle and in 20 % of cases invading the third ventricle cavity); astrocytomas (in 25 % of cases invading the third ventricle cavity and in 23% of cases at the posterior parts of the third ventricle); pineal gland parenchyma tumors (in 30 % of cases); germ cell tumors (in 38 % of cases). **Subtotally** were excised: craniopharyngiomas (in 35 % of cases invading the cavity and in 24 % of cases at the anterior parts of the third ventricle); astrocytomas (in 18 % of cases at the anterior parts, in 30 % of cases invading the cavity, and in 46 % at the posterior parts of the third ventricle cavity); pineal gland parenchyma tumors (in 40 % of cases); germ cell tumors (in 12 % of cases). **Partly** were excised: craniopharyngiomas in the anterior parts (in 32 % of cases); craniopharyngiomas invading the cavity (in 40 % of cases); astrocytomas in the anterior parts (in 76 % of cases); astrocytomas invading the cavity (in 40 % of cases); astrocytomas in the posterior parts (in 31 % of cases); pineal gland parenchyma tumors (in 30 % of cases); germ cell tumors (in 50 % of cases).

Cerebral shunts were placed in the patients with tumors of the third ventricle anterior parts – 8 cases, with tumors invading ventricle cavity – 6 cases; with tumors of the third ventricle posterior parts – 99 % of cases.

Radiotherapy was applied in 138 patients (49 % of cases), from which against the tumors of the anterior parts of the third ventricle – in 24 patients (18%), against the tumors invading the ventricle – in 22 patients (15 %), against the tumors of the posterior parts of the third ventricle – in 92 patients (67 %).

Catamneses of 253 patients were studied (89 % of cases observed) and varied from 2 to 171 months (the median made 41 months).

Lethality in the early postoperative period occurred in 31 cases (17 cases with tumors invading the third ventricle cavity, 7 cases with tumors of posterior parts and 7 cases with tumors anterior parts), lethality in the distant period occurred in 10 cases (tumors of the posterior parts in the third ventricle – 6 cases, tumors invading the cavity – 2 cases, and tumors in the posterior parts – 2 cases).

The general condition of a patient at the time of primary examination, at the discharge and in the remote period was estimated on the Karnofsky scale (in points) for adults and on the Lansky scale for children.

In order to explore adverse factors there were studied: age, location of tumor in the third ventricle, kind of operation, degree of radical excision, and histological structure of the tumor. Adverse prognostic factors were estimated on the Karnofsky scale within the points from 0 to 70. The importance of factors was determined by means of χ^2 nonparametric method and corresponding level of statistical significance (p), when comparing two samples.

The investigation was carried out to make samples of patients with favorable outcome in the remote period within two time spans: 2-5 years (early remote period) and 6-10 years (late remote period) inclusive.

Statistical data processing was conducted using a software package “Statistica”, vers.6.0. Calculation of survival rate was made with help of Kaplan-Meier method [9].

Main results and their consideration.

The aim of surgical treatment of patients is to save life, to enhance the quality of life of patients and to minimize risks of recurrent tumors. The main criteria to

estimate the effectiveness of the surgical treatment of the third ventricle tumors are quality of life, survival rate and life span of patients after the operation.

The curve of survival rate for the whole sample is represented in figure No 1:

Fig. 1. Survival rate after combined therapy of patients with the third ventricular region tumors

As it is shown in the picture, for all the tumors of the third ventricle the survival rate after combined therapy was 7,5 years in 85 % of cases, and 10-year survival rate was with 83 % of cases.

Comparative characteristics of lethality in the postoperative and remote periods depending on the localization of the process in the third ventricle are represented in the diagram (fig. No 2):

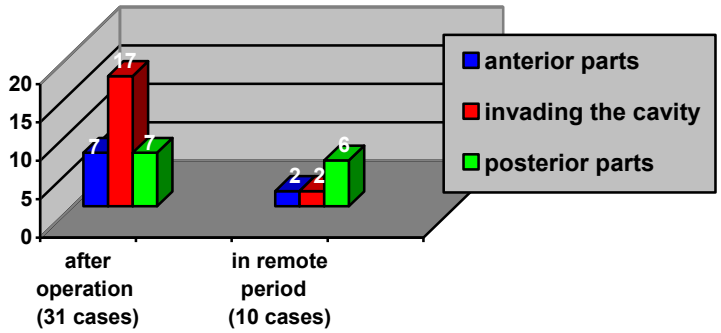

Fig. 2. Lethality rate after surgical treatment of patients with the third ventricular tumors

In the early postoperative period 17 patients died after excision of tumors invading the third ventricle. In the remote period most patients died after excision of tumors in the third ventricle posterior parts (6 of 10 lethal cases).

The lethality of patients depending on the degree of radical excision of the third ventricle tumor is represented in the diagram (fig. No 3):

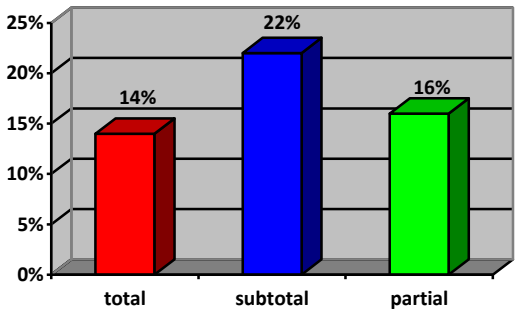

Fig. 3. Lethality of patients depending on the degree of radical excision of the third ventricular region tumor

As it is shown in the diagram low mortality was observed after the total excision of tumor.

After analyzing the catamnesis data it was stated that survival rate of patients after the operation depends on the extensivity rate of tumor excision, on histology of the third ventricle tumor and on radiation therapy employment.

The curve of survival rate of patients with the third ventricular tumor depending on degree of radical surgery is represented in figure No 4:

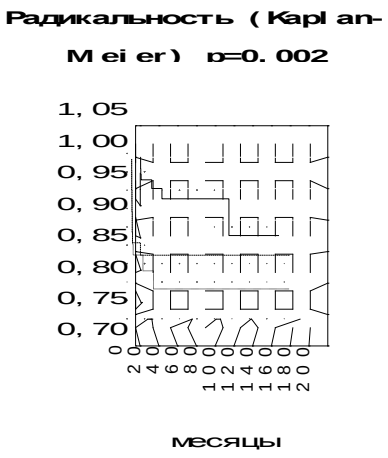

Fig. 4. Survival rate of patients with the third ventricular tumor depending on degree of radical surgery

As it is shown in the given graphs, the majority of patients with survival rate of more than 10 years were found in the group of patients who underwent the total tumor excision (83 % of cases), comparing to patients who underwent subtotal and partial tumor excision, where the 10-year survival rate made 74 % of cases and 77% of cases correspondingly (p=0.002). After employing cerebral shunts, 5-year survival rate made 94 %, and 7-year and longer survival rate was observed in 87 % of cases. Such high survival rate may be explained by the fact that the condition gravity of patients was caused by occlusal hydrocephaly which was eliminated after employing ventricular peritoneotomy.

Histological structure of the tumor may also influence the survival rate of patients after the operation.

The survival rate of patients depending on histological structure of the third ventricle tumor is represented in the graph (fig. No 5):

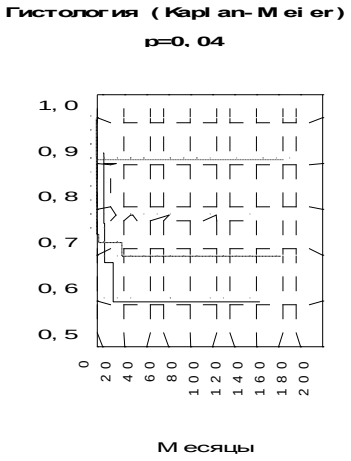

Fig. 5. Survival rate of patients with the third ventricle tumor depending on histological structure

Comparing the curves of survival rate as per histology, one must conclude that after astrocytoma excision, not depending on the localization, the survival rate made more than 10 years almost in 90 % of cases, which is much more (p=0.04),

in comparison with the survival rate after craniopharyngioma excision (up to 2 years – 72 % of cases, 5 years and longer – about 62 % of cases), after pineal gland parenchyma tumor excision (5 years and longer – in 60 % of cases), after germ cell tumor excision (5-yaer survival rate – in 78 % of cases).

After total excision of colloid cysts there were no lethal cases registered.

Radiation therapy was employed mostly in patients after excision of tumor in the third ventricle posterior parts (67 % of cases). When analyzing eradiation of tumor and employment of radiation therapy, it was stated that the most patients received radiation therapy after the partial excision of tumors of the third ventricle anterior parts (46 % of cases) and of tumors invading the third ventricle cavity (45 % of cases), and also after cerebral shunts placement in the patients with tumors of the third ventricle posterior parts (75 % of cases). Depending on the histological structure, mostly patients with astrocytomas received radiotherapy: 62 % of cases in the group of patients with tumors of the third ventricle anterior parts, 74 % of cases – with tumors invading the third ventricle cavity, and 39 % of cases in the group of patients with tumors of the third ventricle posterior parts.

The survival rate of patients after surgical treatment and radiotherapy is represented in the graph (Fig. 6):

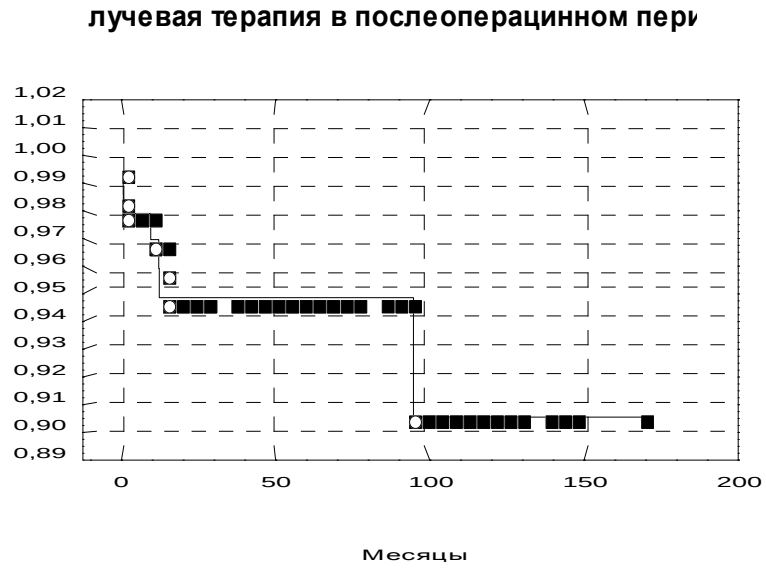

Fig. 6. Survival rate after radiotherapy in the postoperative period

Seven-year survival rate made practically 94 % of cases, and 10-year and longer survival rate was observed in almost 90 % of cases. Lethality after surgical treatment and radiotherapy employment occurred in 6 cases: 2 patients – after the partial excision of pinealoma and germinoma, 1 patient – after the total excision of pinealoma, and 3 patients – after cerebral shunt placement.

The curve of survival rate after combined therapy depending on degree of radical surgery and tumor histological structure is represented in the figures No 7 and No 8:

Fig. 7. Survival rate after radiotherapy employment depending on type of surgical invasion

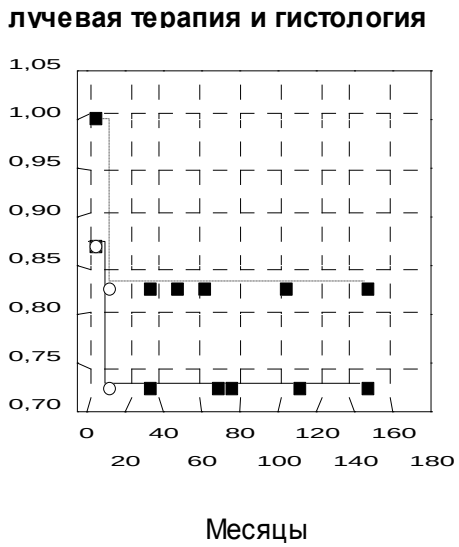

Fig. 8. Survival rate after radiotherapy employment depending on histology

The survival rate of patients up to one year, after operation and radiotherapy depending on degree of radical surgery, made 100 % of cases after the total excision, 98 % of cases after cerebral shunt placement, 96 % of cases after the partial excision; 10-year survival rate occurred in 91 % of cases after the partial excision, and in 89% of cases after the total excision and cerebral shunt placement ($p>0.05$).

Depending on histology, 10-year survival rate of patients was registered mostly (84 % of cases) after combined therapy of patients with pineal gland parenchyma tumors, comparing to the patients with germ cell tumor treatment, who made the rate of 73 % of cases ($p>0.05$).

The great role in studying of the third ventricle tumors and their combined therapy plays determination of favorable and adverse prognostic factors.

Favorable prognostic factor for treatment of patients with the third ventricle tumors are the following: quality of life on the Karnofsky scale more than 70 points and the total tumor excision.

Adverse prognostic factors that influence the result of surgical treatment of the third ventricle tumors for the early remote period (2-5 years) are the following:

- age range from 20 to 30 years ($p<0.01$);
- cerebral shunt placement without tumor excision ($p<0.05$);

In the late remote period (6-10 years), adverse prognostic factors that influence the result of surgical treatment after the third ventricle tumor excision are the following:

- patients' age;
- tumor localization;
- degree of radical surgery;
- histological structure of the tumor.

The most adverse influence on the result of treatment, depending on patients' age, was registered in the range from 1 to 10 years ($p<0.05$). Depending on tumor location, the adverse prognostic factor was determined in the group of patients with

tumors invading the third ventricle ($p<0.01$). Comparing the degree of radical surgery, the most adverse influence on the result of treatment was made by the partial tumor excision ($p<0.01$). Depending on histological form, it was statistically-valid established that craniopharyngioma had an adverse prognostic effect ($p<0.001$).

Summary:

1. Survival rate of patients with the third ventricular region tumors depend on tumor location, degree of radical surgery, radiotherapy employment and histological structure of the tumor.

2. The highest survival rate of patients (ten-year long) was achieved after the "total" excision of the third ventricular region tumor (83 % of cases), comparing to "subtotal" (74 % of cases) and "partial" (77 % of cases) excisions ($p=0.002$).

3. The survival rate of patients after colloid cyst and astrocytoma excision is higher in comparison to the survival rate after craniopharyngioma tumor, pineal gland parenchyma tumor and germ cell tumor excision: 100 % survival rate after the total colloid cyst excision and 10-year survival rate after astrocytoma excision (90 % of cases); 5-year survival rate after craniopharyngioma excision – 62 % of cases, after pineal gland parenchyma tumor excision – 60 % of cases, and after germ cell tumor excision – 78 % of cases ($p<0.05$).

5. Favorable prognostic factors for treatment of patients with the third ventricular region tumors are: quality of life on the Karnofsky scale more than 70 points and the total tumor excision. Adverse prognostic factors in the remote period are: age of patients from 1 to 10 years ($p<0.05$), tumors invading the third ventricle cavity ($p<0.01$), partial tumor excision ($p<0.01$), and craniopharyngioma ($p<001$).

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