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Heterogeneity of oligoastrocytoma: morphology, surgery, and survival in the series of 163 patients. Retrospective study

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Introduction. The current approach to oligoastrocytoma (OA) treatment includes surgery taking into account the anatomical and physiological accessibility using various radio- and chemotherapy protocols. Nevertheless, it should be recognized that influence of OA histological structure on the surgery of these tumors has not conclusively established.

Objective. To improve diagnostic and surgical tactics in oligoastrocytoma by comparing determined clinical-histological patterns.

Materials and methods. Retrospective clinical-morphological comparison and analysis of treatment results in 163 patients with OA were performed taking into account histological structure. OAII (WHO) was diagnosed in 32 patients (19.6 %), 131 patients (80.4 %) developed OAIII (WHO).

Results. In 52 OA cases (32 %) oligodendroglial component (oOA) prevailed, in 48 OA cases (29 %) astrocytic component (aOA) prevailed, in 63 OA cases (39 %) there was relatively equal cells distribution of both components (oaOA). The surgical treatment of 163 patients included the following: gross total removal, 60 patients (31.4 %); subtotal removal, 98 patients (60.2 %); and partial removal, 4 patients (2.4 %). A total of 106 (65.0 %) patients presented with Karnofsky Performance Status Scale (KPS) ≥ 80. One hundred and fifty-three patients (93.9 %) experienced postsurgery KPS ≥ 80. There was no perioperative death. All 163 patients received radiation therapy and 87 patients (53.4 %) received chemotherapy as well. A significant difference ($p < 0.05$) in overall survival (OS) was found between surgery results of OA histological groups. Clinical and MRI/CT findings significantly correlated with histological types of OA as well as results of treatment: the overall survival in patients with oOA was 100.5 ± 4.6 months, aOA — 48.2 ± 4.5 months, oaOA — 76.6 ± 4.9 months, averaging 49.9 ± 2.4 months.

Conclusions. Diagnosing, surgery, and survival of OA are determined by the uniqueness of the histological structure of these tumors, the interaction of their components, topography and expansion direction. The key to successful results is a differential approach to planning diagnostic tactics, method of removal and management in late post-op period.

Key words: *oligoastrocytoma; histology; surgery; survival*

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Неоднорідність олігоастроцитом: гістологія, хірургія та виживання у серії зі 163 пацієнтів. Ретроспективне дослідження

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Вступ. Сучасний підхід до лікування олігоастроцитом (ОА) передбачає хірургічне втручання з урахуванням анатомічної та фізіологічної доступності із застосуванням протоколів радіо- та хіміотерапії. Однак вплив гістологічної структури ОА на результати лікування цих пухлин не вивчено.

Мета: оптимізувати діагностичну та хірургічну тактику при ОА півкуль великого мозку за результатами вивчення клініко-гістологічних зіставлень.

Матеріали і методи. Клініко-гістологічне зіставлення та аналіз результатів лікування 163 хворих з ОА проведено ретроспективно з урахуванням гістологічної структури. Типову ОА діагностовано у 32 (19,6%) пацієнтів, анапластичну ОА – у 131 (80,4%).

Результати. В 52 (32%) ОА переважав олігодендрогліальний компонент (оОА), у 48 (29%) – астроцитарний (аОА), у 63 ОА (39%) випадках

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кількість клітин обох компонентів була приблизно однаковою (оаОА). У 98 (60,2%) пацієнтів проведено тотальне видалення, у 60 (31,4%) – субтотальне, у 4 (2,4%) – часткове. Індекс Карновського≥80 до операції відзначено у 106 (65,0%) пацієнтів, у післяопераційний період – у 153 (93,9%). Післяопераційна смертність – 0 %. Всім пацієнтам проведено променеву терапію, 87 (53,4%) – хіміотерапію. Клінічні та радіологічні дані корелювали з гістологічним типом ОА, а також з результатами лікування: загальне виживання у пацієнтів з оОА становило 100,5 ± 4,6 міс, з аОА – 48,2 ± 4,5 міс, з оаОА – 76,6 ± 4,9 міс, у середньому – 49,9 ± 2,4 міс.

Висновки. Особливості діагностики, хірургії та виживання хворих з ОА визначаються гістологічною структурою цих пухлин, взаємодією їх компонентів, топографією та напрямком поширення. Запорукою успішного лікування є застосування диференційного підходу до планування діагностичних побудов, способу видалення та ведення пацієнтів у післяопераційний період.

Ключові слова: *олігоастроцитома; гістологія; хірургія; виживання*

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Неоднородность олигоастроцитом: гистология, хирургия и выживание в серии из 163 пациентов. Ретроспективное исследование

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Вступление. Современный подход к лечению олигоастроцитом (ОА) предусматривает хирургическое вмешательство с учетом анатомической и физиологической доступности с применением протоколов радио- и химиотерапии. Однако влияние гистологической структуры ОА на результаты лечения этих опухолей не изучено.

Цель: оптимизировать диагностическую и хирургическую тактику при ОА полушарий большого мозга по результатам изучения клинико-гистологических сопоставлений.

Материалы и методы. Клинико-гистологическое сопоставление и анализ результатов лечения 163 больных с ОА проведены ретроспективно с учетом гистологической структуры. Типичную ОА диагностировали у 32 (19,6%) пациентов, анапластическую – у 131 (80,4%).

Результаты. В 52 (32%) ОА преобладал олигодендроглиальный компонент (оОА), в 48 (29%) – астроцитарный (аОА), в 63 (39%) случаях количество клеток обоих компонентов было примерно одинаковым (оаОА). У 98 (60,2%) пациентов проведено тотальное удаление, у 60 (31,4%) – субтотальное, у 4 (2,4%) – частичное. Индекс Карновского ≥80 отмечен до операции у 106 (65,0%) пациентов, в послеоперационный период – у 153 (93,9%). Послеоперационная смертность – 0 %. Всем пациентам проведена лучевая терапия, 87 (53,4%) – химиотерапия. Клинические и радиологические данные коррелировали с гистологическим типом ОА, а также с результатами лечения: общая выживаемость у пациентов с оОА составила 100,5 ± 4,6 мес, с аОА – 48,2 ± 4,5 мес, с оаОА – 76,6 ± 4,9 мес, в среднем – 49,9 ± 2,4 мес.

Выводы. Особенности диагностики, хирургии и выживание больных с ОА определяются гистологической структурой этих опухолей, взаимодействием их компонентов, топографией и направлением распространения. Залогом успешного лечения является применение дифференцированного подхода к планированию диагностических построений, способа удаления и ведения пациентов в послеоперационный период.

Ключевые слова: *олигоастроцитома; гистология; хирургия; выживание*

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Introduction

Oligoastrocytoma (OA) is a subset of brain tumors that present with an appearance of mixed astrocytic and oligodendroglioma glial cell [1]. About 2.3–23 % of all reported gliomas are diagnosed as oligoastrocytoma, the OA incidence rate is 0.16–1.47 cases per 100,000 population per year [2–4].

Despite the fact that the first reports of OA date back to the beginning of the last century, for a long time OAs were considered as a type of oligodendrogliomas. It could be explained by the lack of clear histological criteria for this tumor. Only in 1993 OA was included into the WHO classification of brain tumors [3,5]. No purposeful histological studies of OA on significant material have

This article contains some figures that are displayed in color online but in black and white in the print edition

been conducted. There is no ratio and interaction analysis of oligodendroglioma and astrocytoma components in OA in the literature. There are no clear morphological criteria for anaplasia of these neoplasms. At the present, OA as an independent tumor type is confirmed by the achievements of immunohistochemistry and genetics [6–8]. However, even the results of these studies cannot explain OA origin and its histological features [4,6,9].

The long-term neurosurgical experience has shown that OA treatment remains one of still unclarified problems in oncology [10,11]. It is known that the deep expansion of OA, especially in the central brain structures, in combination with the histological features and infiltrative nature of the tumor, adversely impact the treatment results [12]. Insufficient knowledge of OAs topography limits the surgical treatment potential or leads to unreasoned total resection with damage of eloquent cortical areas and central brain structures [9,12,13]. This fact can cause neurological deficiency and irreversible disorders, which significantly affect the results of OAs treatment in general, worsening the early results and quality of life and life expectancy [13,14]. All this necessitates the development and implementation of advanced methods to remove OA.

Objective. To improve diagnostic and surgical tactics in OA by comparing determined clinical-histological patterns.

Material and methods

Patients

All patients with supratentorial mixed oligoastrocytoma operated within the 10-year period from 2005 to 2015 were identified using the data of the Intracerebral Tumors Department, the State Institution Romodanov Neurosurgery Institute of the National Academy of Medical Sciences of Ukraine. Patient charts, as well as histological sections, were reviewed and all pertinent clinical data were entered into an electronic database. Some follow-up information was retrieved by contacting patients, their family or their physicians directly. Patients under 18 yrs and cases with inadequate pathological material or pure oligodendroglioma as well as astrocytoma were excluded. One hundred and sixty-three patients were considered eligible for the study.

Clinical data

The diagnostic method that determined the surgical tactic included the results of a complex neurological examination and CT, MRI, SPECT findings in routine modes as well as advanced (fMRI, DWI, PWI). All patients were examined by a therapist, an ophthalmologist, and an anesthetist. The general condition of patients in the pre- and postoperative period was evaluated using Karnofsky Performance Status Scale, and the degree of neurological deficiency was determined at all stages of treatment.

Pathological findings

The analysis of the material applied the international classification of CNS tumors, adopted by the WHO in 2007, taking into account WHO 2016 [5]. The microscopic examination was carried out after biopsy sample staining with hematoxylin at 200-, 400- and 800-fold magnification.

Treatment

The neuronavigation and laser techniques were used during surgical interventions. The navigational support was carried out using the Medtronic StealthStation TREON Plus (Medtronic, USA). The following was used as a source of laser radiation: Semiconductor Lika-Chirurg (wave length $\lambda = 0.808$ and 1.47 μm, 30 W and 7 W). The volume of OA removal was evaluated according to CT/MRI findings, performed within 24 hours after surgery. Assessing tumor volume to be removed the following classification was used [15]: total (tumor removal more than 95 %), subtotal (tumor removal 80–94 %), partial (tumor removal 50–79 %), and the biopsy (tumor removal less than 50 %). Radiotherapy (60 Gy) was recommended for all patients at the time of discharge from the department; chemotherapy (PCV) was additionally recommended for patients with high-grade OA (***Table 1***).

Statistical analysis

All statistical analyses were performed using SPSS 23.0 software (SPSS, Chicago, IL, USA). Descriptive statistics was performed. A probability value less than 0.05 was deemed significant. Standard procedures (Fisher exact test, chi-square test, Student's t-test, ANOVA) were used for univariate analyses as indicated. Survival endpoints were analyzed with Kaplan–Meier estimates using the log-rank test for comparisons. To assess the association of survival with multiple characteristics of a patient, tumor, and treatment, backward step-wise procedures were used for generating proportional hazards general linear models, as proposed by Cox.

Results

Patient demographics and treatment

The study group of 163 patients consisted of 91 male patients (55.8 %) and 72 female patients (44.2 %), ranging in age from 18 to 71 years (median, 37.4 ± 11.4 yrs). A total of 106 (65.0 %) patients presented with KPS ≥80 %. A postoperative KPS ≥ 80 % was determined in 87.7 % of patients. New neurological deficits or increased neurological deficits were observed in 3.2 % of cases.

The surgical treatment of 163 patients included the following: gross total removal, 60 patients (31.4 %); subtotal removal, 98 patients (60.2 %); and partial removal, 4 patients (2.4 %). There was no postsurgery death.

All 163 (100 %) patients received radiation therapy, and 87 (53.4 %) received chemotherapy. Detailed demographical data, tumor characteristics, and treatment options can be found in ***Table 2***.

Table 1. Components of PCV chemotherapy

Drug	Schedule and dosage	Frequency of delivery
Procarbazine	Days 8–21: 60 mg/m^2/day, orally	
CCNU (Lomustine)	Day 1: 110 mg/m^2, orally	Every 8th week
Vincristine	Days 8 and 29: 1.4 mg/m^2, IV	Every 6th week

***Table* 2.** Comparison of OA histological types

Parameter	Total, N = 163	oOA, N = 56	oaOA, N = 50	aOA, N = 57
Sex (male)	91	31	28	32
Age	37.4 ± 11.4	35.1 ± 6.4	38.1 ± 11.9	39.4 ± 9.1
Median duration of symptoms	1.1 ± 0.7	2.5 ± 0.9	1.9 ± 0.8	0.5 ± 0.3
Histopathology				
OA II	32	10	14	8
OA III	131	46	36	49
Tumor size				
< 3 cm	23	4	6	13
3–5 cm	106	35	33	39
> 5 cm	34	17	11	5
Eloquent tumor location	54	18	16	20
Presurgery neurological deficit	103	33	29	41
Neurological deficit at discharge	34	11	10	13
Pre-surgery seizures	135	67	43	25
Seizures at discharge	22	8	7	7
Contrast enhancement (MRI)	81	26	25	30
Calcification (CT)	84	42	30	12
Paraventricular location	81	44	30	7
Cysts	35	17	13	5
Preoperative KPS ≥ 80 %	106	37	31	38
KPS ≥ 80 % at discharge	153	54	46	53
Extent of resection				
Total	61	25	22	14
Subtotal	98	31	28	39
Partial	4	0	0	4
Neuronavigation	163	56	50	57
Laser	34	11	10	13
Adjuvant therapy				
Radiotherapy	163	56	50	57
Chemotherapy	87	30	26	31

Clinical manifestations and neuroimaging

The OA signs were represented with seizures, headache, mental status changes, vertigo or nausea, visual complaints, and weakness, which are similar in general to other intracerebral tumors. However, the tumor place, the expansion direction and histological type determined the dynamics of clinical course in OA patients. So, these tumors are characterized by relatively long period of the disease from the first complaints occurrence to hospitalization: it was the longest in OA of the parietal compartment, with the dominant oligodendroglioma component ($p = 0.041$), and the shortest in the localization of OA with dominant astrocytic component in the eloquent brain compartment ($p = 0.035$).

The onset and the progress of the disease also depended on the OA histological characteristics and topography. Thus, OAs with dominant oligodendroglioma component in structure were more often characterized by periventricular growth ($p = 0.021$); therefore, a headache was the determining factor in the disease. First of all, it concerned with the following topographic groups of OAs: frontal-basal, temporal-parietal, frontal-parietal. A focal sign that occurred in patients with histological variant of OA mentioned above was characterized by seizures that after a long time gave way to lose symptoms. In patients with a prevalence of astrocytoma component, the tumor affected more superficial parts of the cerebral hemispheres ($p = 0.041$); therefore, focal deficit exacerbated patient's condition and hypertension syndrome at the time of hospitalization was slightly expressed. The focal symptoms in these cases were characterized by a rapid change in clinical manifestations — from symptoms of irritation to loss symptoms that often occurred in the frontoparietal, frontotemporal and front-temporal-parietal localization of OA.

In the preoperative period, neuroimaging findings demonstrated the location of the lesion, size, relation to brain tissue and vessels, determined the expansion, involvement of eloquent brain areas. Obtained data permitted to suppose the OA histological structure. Despite the differential diagnosis of OA is quite difficult, it should consider specific features such as localization, the presence of calcifications, heterogeneity of tumor node structure and contrast enhancement. The presence of calcifications (on CT), predominant localization in frontal and fronto-parietal areas, and growth nearby the lateral ventricles are common for OAs and oligodendrogliomas [13]. However, in OA calcifications are less common — in 60 % of cases (under 90 % in OG), intensive thinning of the cortex and the average size of the tumor node are larger (due to more rapid growth). Structure heterogeneity, the severity of perifocal edema, fuzzy boundaries make OA similar to astrocytoma, but the presence of oligodendroglioma signs, lower ability to contrast enhancement allow to differentiate these tumors.

Pathological features

The WHO grade of OA II was diagnosed in 32 patients. The microscopic architectonics of the oligodendroglioma component in the WHO grade OAII in most cases corresponded to the typical histological structure of oligodendrogliomas with a characteristic isomorphic cellular composition. The tumor cell nuclei were predominantly spherical, compact, fine-grained chromatin and well-defined nucleolus, and around a nucleus, a narrow optically-

devastated zone was identified, which is a typical feature of the so-called "comb-like" structure of oligodendrogliomas. Due to the close location of tumor cells in such areas, intercellular membranes — contours of the cytoplasmic bodies are well observed. Cell-dense oligodendroglioma complexes, surrounded by thin fibers of astrocytoma glia were partially determined on the background. In contrast to the oligodendroglioma regions, the rarefied location of tumor cells with the formation of glial reticulum is typical in dominant astrocytoma component of this OA. Oligodendroglioma component predominated in 10 OAII cases, astrocytoma component prevailed in 8 OAII cases. Approximately equal cell distribution of both components was determined in 14 OAII cases (***Fig. 1***).

The WHO grade OAIII was diagnosed in 131 patients. The morphological signs of anaplasia — cellular polymorphism, cellular densification, pathological mitoses, vascular pathologies, necrosis and violations of typical microarchitectonics were determined in OA grade III. The severity of anaplasia signs may differ in the oligodendroglioma and astrocytic components of the same tumor. Like OAs grade II, anaplastic OAs also contained the areas of oligodendroglioma and astrocytoma tumors in different proportions. In 46 observations areas of oligodendroglioma predominated in OA tissue. More common areas of astrocytoma were found in 49 observations. In 36 OAs, the prevalence of both components was approximately the same.

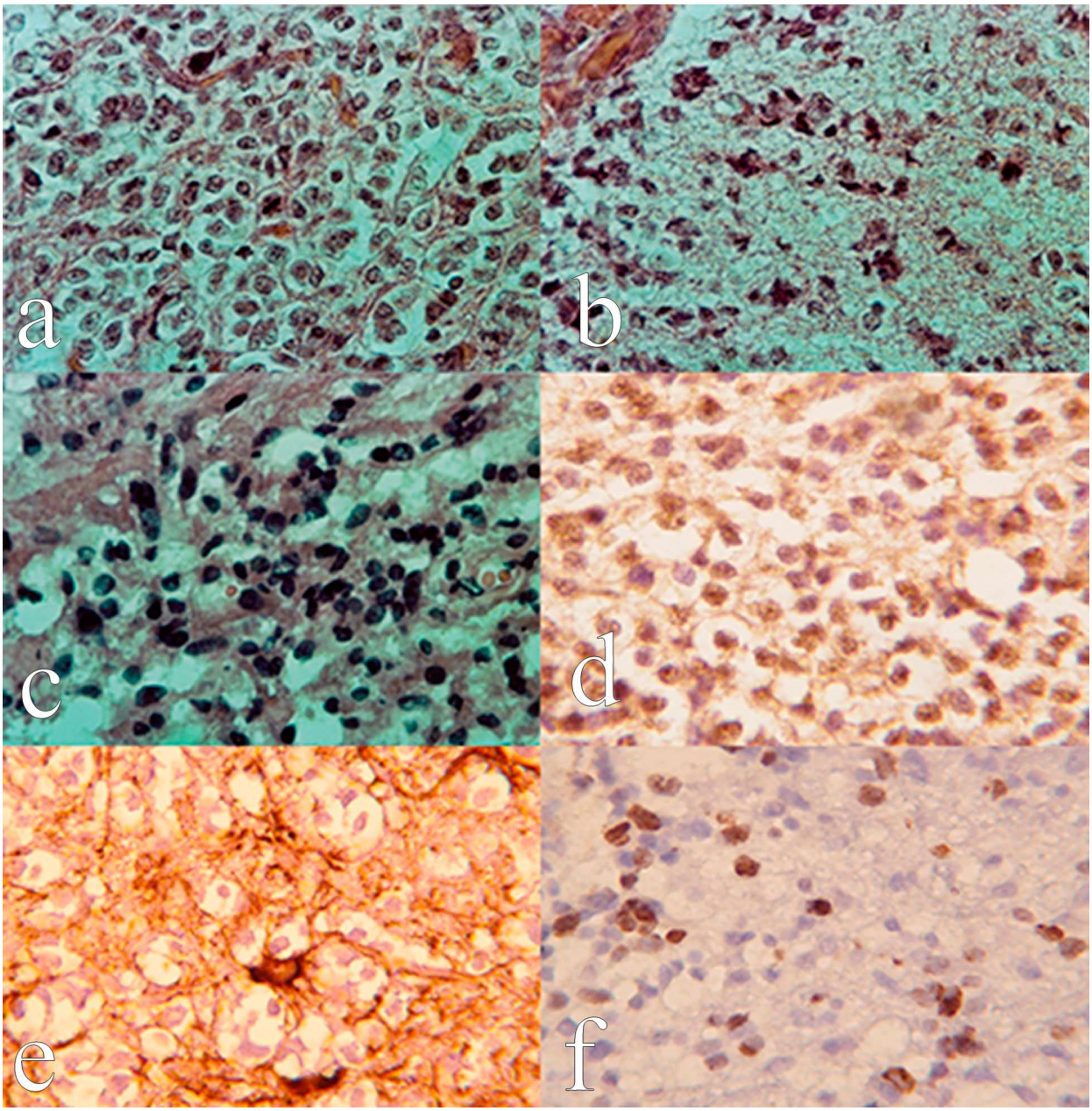

Fig. 1. a. The predominance of oligodendroglioma component in OA. Hematoxylin, x800. **b.** The predominance of an astrocytic component in OA. Hematoxylin, x 800. **c.** The accumulation of tumor oligodendrocytes among astrocytic cells is a conditionally uniform distribution of OA components. Hematoxylin, x800. **d.** Expression of MBP antibodies & Mayer Hematoxylin, x800. **e.** Expression of GFAP antibodies & Mayer Hematoxylin, x800. **f.** Expression of Ki-67 antibodies & Mayer Hematoxylin, x800

Surgery

In 54 (33 %) patients OA affected eloquent brain areas. Surgery in these cases had some tricks, which, first of all, concerned with access and removal techniques. In case of tumor localization in the eloquent brain area, we performed an encephalotomy using no direct approaches to OA. Thus, to access the tumor of the precentral gyrus, encephalotomy was performed in the premotor area, and in tumors of the post-central gyrus, encephalotomy was performed in the upper-parietal brain area. Those parts of tumors located directly inferior the precentral gyrus were removed subcortically by aspiration, but then in the direction from the center to the edge (as far as possible, until the tissue of the unaffected brain appears).

In 81 (49 %) patients the OA affected the median structures or placed in immediate proximity to the brain ventricles. Encephalotomy in OAs associated with the anterior horn of lateral ventricle was performed through the middle frontal gyrus. In case of the temporal-basal OAs, the encephalotomy was performed in the dominant hemisphere within the inferior temporal gyrus, in the non-dominant — within the inferior and middle temporal gyri. Access to OAs of the lateral ventricle triangle was performed through the inferior parietal lobe. Careful inspection of ventricular cavity found OA to invade its wall but was separated from its cavity by ependyma.

The use of multimodal neuronavigation systems for OA removal allowed determine safe resection volume considering the tumor characteristics, the degree of anatomical and functional permissibility. Due to detailed neuronavigation 3D-planning and intraoperative neuronavigation support of surgical intervention, the optimal surgical path was chosen in every single point of surgical instrument position that determined radicality of surgical treatment and minimized injury to surrounding neural structures.

Methods of laser-surgical removal of OA include laser vaporization, thermodestruction and coagulating laser radiation mode with changing parameters, depending on the planned effect of laser influence at the stages of intervention and in accordance with the structural and histological features of the tumor. When planning the laser stage, the results of CT/MRI/SPECT allowed optimizing the choice of laser radiation parameters (wave length, power) and an effective method for laser tumor removal. So, in low-grade OAs, which vascularity is not contrasted during the CT examination, and the enhancement of the radioisotope is not observed during SPECT examination, the tumor removal was planned using the laser vaporization method. For this purpose, laser radiation with wave length $\lambda = 1.47$ μm and power of 7 W was used. The intensive vascularity, typical for anaplastic OAs, required the application of semiconductor laser radiation with wave length $\lambda = 0.808$ μm and power of 30 W, which has good coagulating properties. Tumor expansion to eloquent areas and to the medial central structures (according to CT and MRI findings), were mainly subject to laser destruction. The laser destruction allowed fragmentarily destroy the tumor, avoiding injury to adjacent brain structures.

Univariate and multivariate survival analyses

There were 12 feasible prognostic factors for which adequate data were available to permit uni- and multivariate analyses of patient survival: three patient factors: age (< 44 vs > 45), sex (male vs female), and KPS before resection (< 80 vs > 81); five tumor factors: tumor site (frontal vs temporal vs other), size (< 5 cm vs > 6 cm), tumor crossing midline (present vs absent), ventricles involved (present vs absent), calcification (present vs absent), and MRI enhancement (present vs absent); two pathological factors: tumor grade (the WHO: low vs high) and dominant cellular component (oOA vs aOA vs oaOA) and two treatment factors: extent of surgical resection (gross total or subtotal vs partial), chemotherapy (none [i.e., surgery with radiotherapy] vs < PCV).

In the univariate analyses, low WHO grade ($p = 0.001$), dominant cellular component ($p = 0.001$), KPS ($p = 0.045$), tumor none crossing midline ($p = 0.0481$), intact ventricles ($p = 0.036$), gross total resection ($p = 0.001$), and chemotherapy ($p = 0.001$) were associated with improved survival. In the multivariate analyses, low WHO grade ($p = 0.001$), dominant cellular component ($p = 0.001$), gross total resection ($p = 0.001$) and chemotherapy ($p = 0.008$) were associated with improved survival (***Table 3***). Age, sex, tumor site, size, calcification, MRI enhancement were not significantly associated with survival.

***Table* 3.** Median survival and hazard ratio in patients with OA: multivariate model construction

Parameter	O/N	Survival (mm)	95% CI		HR	95% CI		P
			Lower	Upper		Lower	Upper	
WHO grade								
II	32	107.1 ± 5.9	95.4	118.9	0.229	0.122	0.428	0.001
III	131	67.6 ± 3.4	60.9	74.2	1			
Dominant component								
oOA	56	100.5 ± 4.6	91.5	109.6	0.324	0.191	0.550	0.001
aOA	57	48.2 ± 4.5	39.4	57.0	2.046	1.339	3.128	0.001
oaOA	50	76.6 ± 4.9	66.9	86.4	1			
Tumor volume removal								
Subtotal/ partial	102	52.9 ± 3.3	46.5	59.4	2.117	1.415	3.166	0.001
Total	61	111.4 ± 2.9	105.6	117.2	1			
Chemotherapy								
None	76	67.1 ± 5.6	56.1	78.1	2.340	1.435	3.816	0.008
Yes	87	82.1 ± 3.4	75.4	88.7	1			

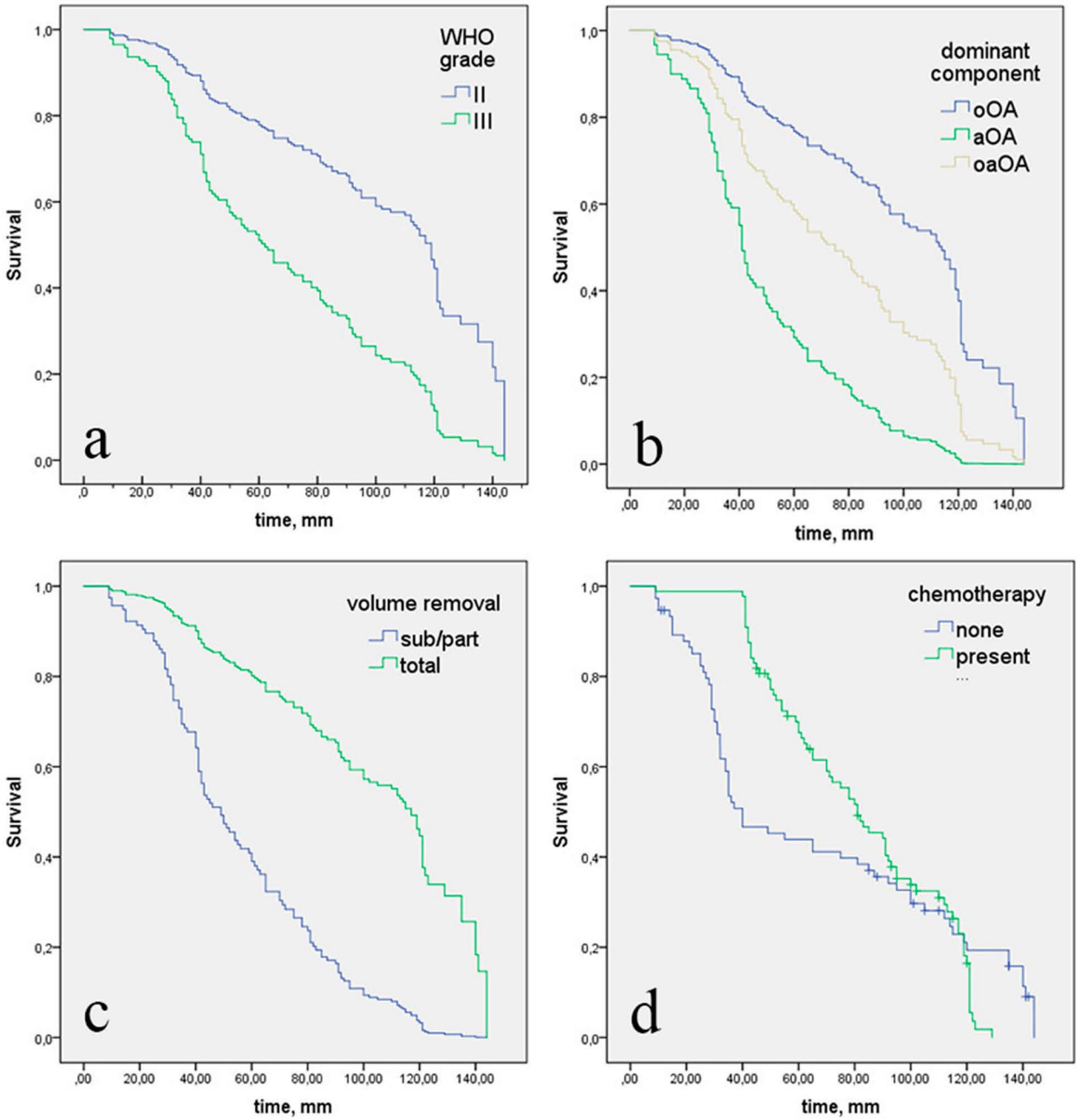

Fig. 2. Graphs shows survival of patients with OA: a — by WHO grade, b — by the dominant component, c — by the extent of surgical resection, d — by chemotherapy

Figure 2a shows the association of WHO grades with survival. The median survival was 8.9 years, and the 5- and 10-year survival rates of 32 patients with grade II tumors were 78 % and 42 %, respectively, compared with 5.6 years, 51 %, and 15 % for the 131 patients with grades III tumors (P = 0.001).

Figure 2b demonstrates the correlation of survival and dominant cellular component (oOA, aOA, or oaOA). For 56 patients with oOA, the median survival and 5- and 10- year survival rates were 8.3 years, 78 % and 35 %, respectively, compared with 4.0 years, 25 % and 8 %, respectively, for 49 patients with aOA and 6.3 years, 52 % and 20 %, respectively, for 50 patients with oaOA (P = 0.001).

Figure 2c shows the survival curves for the patients who did or did not undergo gross total resection. Sixty-one patients who had undergone gross total resection had a median survival of 9.3 years and 5- and 10-year survival rates of 82 % and 46 %, respectively, compared with 4.2 years, 32 % and 7 %, respectively, for 102 patients undergone subtotal resection (P = 0.001).

Figure 2d demonstrates the association of postoperative chemotherapy with survival. The median survival of the patients with OA undergone surgery + radiotherapy (n = 76) or chemotherapy (n = 87) was 5.6 years, with 5- and 10-year survival rates of 41 % and 19 %, respectively, compared with 6.8 years, 68 % and 35 %, respectively, for the patients receiving postoperative PCV.

Discussion

The specificity of neurosurgical treatment in patients with OAs is determined by the uniqueness of the histological structure of these tumors, the heterogeneity of their morphology, the interaction of the constituent components and the features of growth. A detailed study of the OAs morphological properties explains the clinical manifestations, the neuroimaging examination, and surgical treatment results. In our opinion, the key to successful neurosurgical treatment of OAs is a differentiated approach to planning diagnostic, surgical strategy and management of a patient in the late postoperative period.

We divided OAs cases into 3 groups by histology specificity: dominant astrocytic component — 35.6 %, dominant oligodendroglioma component — 33.7 %, with approximately similar representation of astrocytic and oligodendroglioma components — 30.7 %. E.G. Shaw in his studies paid much attention to the heterogeneity of OAs histological structure [13]. The point of view of different scientists regarding the contribution of the astrocytic component in OAs is still ambiguous. Most authors do not focus on any particular minimum percentage of tumorous astrocytes in OA and simply state the astrocytoma fraction, which can usually range from 1 to 50 % [16]. D. Naugle [17] gives to the astrocytic component a portion of 30 %. According to other researchers, the portion of astrocytic component may be at least 20 % [6,7]. We believe that this approach of researchers is not quite true because the diagnosis of OA is often determined by subjective evaluation made by histologist, who also investigated not the entire volume of the removed tumor, but only a certain slice. Overall, we believe that tumor must be diagnosed as OA when the oligodendroglioma cells are mixed with tumor astrocytes from glial fibers formed by them, or when the same tumor combines oligodendroglioma and astrocytoma areas.

The results of many molecular genetic studies also demonstrate the heterogeneity of OAs [8,12,18]. It would seem that since OA is a mixed tumor, it must combine the properties of astrocytoma and oligodendroglioma, but the biological, therapeutic and prognostic significance of genetic changes in OA remains unclear. It is known that 30–70 % of OAs are characterized by LOH 1p and LOH 19q mutations, i.e. genetic features of oligodendroglioma [7,9]. At the same time, 30 % of OAs are associated with gene TP 53 or LOH 17p mutations — signs of astrocytoma [4,19]. That is, there is heterogeneity of OA, not a simple banal combination of astrocytoma and oligodendroglioma properties. Analysis of genetic factors for OAs development may play an important role in determining the tactics of their treatment [13,17,19].

Taking into account the results of the clinical and morphological comparison, arguably, a detailed study of the patient's neurological status, as well as anamnesis, gives to neurosurgeon valuable information about the topography, nature, expansion of OA. Our investigation demonstrates a great variety of clinical manifestations, which is largely due to the variability of OA structure and should be taken into account by the surgeon before planning further diagnostic strategy.

It is necessary to note that the possibilities of modern neuroimaging diagnostic methods are limited due to the properties of OA. First of all, this relates to early diagnosis and control of the tumor volume removal. Thus, oligodendroglioma component is characterized by slow growth, dense cellularity, and preserved blood-brain barrier. This means that the contrast reaches the tumor through the blood and is accumulated in the tumor in a very small amount, which, in turn, causes a low rate of detection of patients with the tumor at the early stages and with a small tumor size. Astrocytic component is characterized by faster growth, but relatively poor vascularity. The restrictions in performing radiological examinations caused by this component are associated with insufficient osmolality of a small number of cells (which are located between normal CNS cells), especially in the postoperative brain, to form postoperative edema, which allows the surgeon to talk about total removal based on MRI and CT findings. In addition, despite the presence of some specific diagnostic signs obtained by neuroimaging, diagnosing OA is extremely difficult without histological examination.

Currently, surgery continues to be the mainstay in treatment for most OA patients [14,20,21]. Obtaining tissue sample is still essential for establishing an accurate diagnosis, and tumor resection can be used to reduce mass effect causing symptoms and neurologic deficits [13,20]. The features of surgical intervention for OA appear at all stages of the surgery. So, given the relatively slow rate of OA growth, at the time of hospitalization the size of the tumor is already quite significant and therefore requires a relatively large trepanation window. A high incidence of dominant cystic component in the structure of OA also impacts the tactics of the neurosurgeon in the planning of access, since aspiration of the liquid content at the initial stage of tumor removal creates an additional and rapid factor for intracranial decompression. The presence of two components in OA and their various ratios predetermine the heterogeneity of the tumor topography within the cerebral hemispheres, and hence the peculiarity of the surgical approach to the tumor. Thus, OA with dominant astrocytic component is often located more superficially, often with invasion into cortex, therefore in such cases removal of the tumor should be started with a circular resection of the affected area of the cortex. In OA with dominant oligodendroglioma component, the tumor is mostly located deep, and access to it should be through encephalotomy. Features of each of the components of OA also determine the method of removing these neoplasms. Oligodendroglioma variant of OA has dense consistency with the inclusion of calcium salts and insignificant peritumoral edema, and is often removed by a single complex in the perifocal zone after encephalotomy. The astrocytoma variant of OA has a milder, gelatinous consistency, significant perifocal edema, and therefore these tumors are usually removed using wedge-shaped resection. The histogenesis of OAs mostly appears in the periventricular compartments of the cerebral hemispheres; therefore, in order to remove the entire volume of the tumor, the surgery is often complicated with porencephalia development. The last one, in addition, provides an additional factor for intracranial decompression.

The results of the performed surgical interventions using laser radiation and neuronavigation demonstrated their high efficiency, which finds expression in positive

postoperative CT, MRI findings, in the uncomplicated course of the postoperative period and patient's high quality of life. Thus, the number of patients with preoperative KPS of 60 points and below decreased from 57 (35.0 %) to 10 (6.1 %). At the same time, the number of patients with preoperative KPS of 80 points increased from 106 (65.0 %) to 153 (93.9 %).

This study did not pay attention to the role of adjuvant therapy, especially chemotherapy in the endpoint treatment results of patients with OAs. We have not distributed patients by groups according to the type of chemotherapy, the number of courses, and the therapeutic pathomorphosis. These issues will be the subject of our further researches. We believe that in the near future, the progress in the treatment of patients with OAs will be determined by successful molecular genetic studies of this tumor, which would shed light on its origin, reveal processes determining the further tumor progression, and will find new effective mechanisms of sensitivity to chemotherapeutic agents.

Conclusions

The histological structure of OAs has similar evidence with oligodendroglioma and astrocytoma as well as distinctive. According to the histological features, there are three types OAs: with dominant astrocytic component, dominant oligodendroglioma component, and with the equal representation of the astrocytic and oligodendroglioma components that coexist in the complex interaction. Diagnostic, surgery, and survival in OA are determined by the uniqueness of the histological structure of these tumors, the interaction of their components, topography and direction of expansion. The key to successful results is a differential approach to the planning of diagnostics, method of removal and management of a patient in the late postsurgery period.

Disclosure

Conflict of interest

The authors declare no conflict of interest concerning any drugs, materials, devices or methods used in this study or the findings specified in this paper.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

The written informed consent was obtained from each patient or appropriate family member before the surgery.

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