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Efficacy and prognosis of selected therapies for cancers of the central nervous system – meningiomas, astrocytomas and ependymomas

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Abstract:

Introduction and purpose: There has been a global increase in the prevalence of adults diagnosed with primary brain tumors. Meningiomas are the most common primary brain tumors, the majority are benign. For asymptomatic, slow-growing tumors, observation with imaging studies may be considered. Surgical resection is the main form of treatment. Other options are radiotherapy and chemotherapy. Astrocytomas are biologically and morphologically diverse group of brain tumors divided into two classes - low-grade and highly malignant. IDH-wild-type tumors are classified as grade IV astrocytomas. They are widespread malignant brain tumors in adults. Despite aggressive therapy consisting of surgical resection, radiotherapy and temozolomide as many as 90% of grade IV gliomas will have a local recurrence. Ependymoma is a primary tumor. The most proper method of treatment is GTR, in addition radiotherapy is considered helpful.

Material and Methods: Bibliographic research was limited to papers published between 2014 and 2024. We have analyzed articles with free and paid access. The articles were identified using the PubMed and Google Scholar search, using key terms.

Results: The paper focuses on efficacy and prognosis of selected therapies for cancers of the central nervous system with varying degrees of malignancy. This study
reviews the prevalence, current diagnostic tools and evidence-based methods.

Conclusions: Brain tumor treatment depends on the type of tumor and the patient's condition. Meningiomas can be treated from observation to surgical removal, and if the tumor cannot be

completely removed, radiotherapy is used. Low-grade gliomas are treated surgically, while high-grade gliomas require additional chemotherapy and radiotherapy. Modern surgical techniques and stereotactic radiosurgery (SRS) improve treatment results. Ependymoma, a rare CNS tumor, requires complete removal in the case of benign changes, and radiotherapy in the case of higher-grade tumors.
Key words: meningiomas, astrocytomas, IDH-wild-type tumors, ependymomas, oncological treatment.

INTRODUCTION:

Brain cancer is identified as one of the most formidable forms of cancer due to several hurdles posed by anatomy and physiology on therapeutic strategies. [1] There has been an increase in the prevalence of adults diagnosed with and treated for primary brain tumors. Proven risk factors for these tumors include certain genetic syndromes and exposure to high-dose ionizing radiation. [2] The classification is complicated, the fifth edition of the WHO classification of central nervous system tumors was published in 2021. [3] Treatment options are generally based on surgical resection as extensive as is safely possible is the cornerstone of treatment in most tumors and is now also recommended early in the treatment of patients with radiological evidence of histologically low-grade tumors. Some patients should receive combination of surgical treatment, radiotherapy, immunotherapy and chemotherapy. [4]Treatment decisions are individualized by a multidisciplinary team based on tumor type and location, malignancy potential, and the patient's age and physical condition. [2]

The paper focuses on efficacy and prognosis of selected therapies for cancers of the central nervous system – meningiomas, astrocytomas, IDH-wild-type tumors and ependymomas. Due to the increasing prevalence of brain tumors these types of cancers have been chosen for further analysis. Our goal was to select CNS cancers with varying degrees of malignancy.

Bibliographic research was limited to papers published between 2014 and 2024. We have analyzed articles with free and paid access. The articles were identified using the PubMed and Google Scholar search, using key terms related to oncological treatment of brain cancers: meningiomas, astrocytomas, IDH-wild-type tumors, ependymomas, oncological treatment, radiotherapy, surgical treatment, chemotherapy. 95 articles were included for further analysis.

To avoid excluding essential studies, the research was not restricted by type of publication or study design.

1. MENINGIOMAS

In the adult patient population, meningiomas are the most common primary brain tumors. [5] Histologically, meningiomas can be divided according to the World Health Organization 2016 classification into Grade I- Benign, Grade II- Atypical and Grade III- Anaplastic/Malignant. [6] The WHO 2021 classification introduced one type of meningioma with 15 subtypes. [7] The vast majority are benign tumors. Malignant, or WHO Grade III meningiomas account for about 1%. [8] The incidence of meningiomas is more common in people over 70 and those exposed to radiation. Also, genetic syndromes: Neurofibromatosis 2 (NF2) and Schwannomatosis are associated with a higher incidence of meningiomas. [5] The 5-year survival rate for anaplastic meningioma is 50%, overall survival is estimated at 2-3 years. [8] There are various forms of therapy. For asymptomatic, slow-growing tumors, observation with routine imaging studies may be considered. [9,10] MRI is the gold standard for imaging meningiomas.[9]

Surgical resection of the tumor is the main form of treatment for meningiomas, used as first-line treatment for all stages in both adult and pediatric populations. [5,6,11] The extent of resection is assessed using the Simpson Scale. It includes grades ranging from 1, which corresponds to the most extensive resection, to grade5. The risk of recurrence is higher with incomplete resection, and also increases with time after surgery(after 15 years, up to 60%). [5] Also, factors such as female gender, The World Health Organization histopathological grade and old age increase the likelihood of recurrence. [5,12] Recurrence rates are up to 23% for WHO stage I, up to 55% for stage II and up to 78% for stage III. [13] For anaplastic meningioma, Simpson grade 1 resection offers the best results, although it is not feasible in every case and the full clinical picture should always be viewed. [8] Surgical treatment, despite its significant efficacy, can be associated with neurological, functional and neurocognitive complications.[13]

Another form of therapy used for meningiomas is radiation therapy. It can be used as the main form of treatment or as adjuvant therapy. [14,15] It is used for tumors that are incompletely resected, without surgical access or recurrent. [5] As first-line treatment, it is used, for example, in skull base lesions containing neurovascular structures such as the optic nerve sheath or cavernous sinus. [6] Forms of radiation therapy used are Fractionated radiation therapy for larger tumors and Stereotactic radiosurgery (SRS) for small lesions. [5] The 5-

year local control rate for WHO stage I meningiomas treated with SRS at a dose of 12-18 Gy was shown to be 86-100%. [16] adjuvant radiotherapy has significant benefits even for large resections. [6] It is used in stage I for incomplete resection, in stage II its use is historically uncertain, although new studies support the use of RTH in some cases, while in stage III it is recommended in all cases. [8,17] In malignant meningiomas, radiotherapy as adjuvant treatment also has positive results. External beam therapy (EBRT) and focal radiotherapy are used.[4]EBRT in stage III meningiomas is associated with a 5-year progression-free survival benefit in follow-up treatment of 15-80% . [13] For aggressive, recurrent meningiomas after surgical treatment and EBRT, interstitial brachytherapy can be considered as adjuvant treatment, also in combination with laser interstitial thermal therapy as salvage therapy. [18,19]However, radiotherapy may contribute to malignant transformation of the tumor.[6]

Systemic treatment of meningiomas is reserved for cases in which surgical treatment or radiation therapy cannot be used, and in the absence of efficacy of these therapies.[9]Classic chemotherapy regimens using doxorubicin, temozolomide, ifosfamideirinotecan are described as ineffective for both benign and malignant forms. [6,8]The treatment of meningiomas is not recommended. Hormonal treatment with tamoxifen or mifepristone did not affect the progression and overall survival of patients. [6] Various forms of targeted therapies are being further developed with promising trial results.[20,21]Prominent are anti-angiogenic molecules such as tyrosine kinase inhibitors targeting VEGFR-sunitinib and vatalanib, or monoclonal antibody- bevacizumab, as meningiomas exhibit increased VEGF activity and are highly vascularized. [13,20] It should be noted that studies have shown a significant increase in VEGF content in atypical and malignant tumors relative to benign ones. [22] Immunotherapy with immune checkpoint inhibitors and new therapeutic perspectives, for example newly researched Meningioma-exclusive antigens for HLA class I and II. [23] Molecular identification of target mutations: FAK-inhibitors for NF2 mutations, which are present in up to 60% of meningiomas, and vismodegib for SMO mutations. Newly researched not-NF2 mutations, for examplePIK3CA, TRAF7, AKT1, KLF4 and POLR2A are also promising in newforms of systemic treatment.[6,24]

In summary, various forms of therapy are used in the treatment of meningiomas, ranging from observation to surgical removal. When choosing the best form, it is important to look at the patient's entire clinical picture. It should be remembered that different forms are fraught with different side effects and varying efficacy. Still, the first-line treatment in most cases remains radical excision. Radiation therapy is also frequently used. Systemic treatment is used the least, which, however, is under intensive research.

2. ASTROCYTOMAS

Astrocytomas are a biologically and morphologically diverse group of brain tumors. They arise from a stellate glial cell called an astrocyte. Its role is crucial in supporting the function of the central nervous system, including regulating ion concentrations and water quantity, stimulating the immune response, developing and maintaining the blood-brain barrier (BBB) or affecting synaptogenesis.[25] These tumors are customarily divided into two classes - low-grade and highly malignant staphylomas. The first class includes grade I and II tumors, which are usually slow-growing, well-differentiated tumors. Their location is most often the cerebellum, and treatment usually consists of surgical resection only. The second class is high-grade tumors, or grade III and IV tumors. Their differentiation is relatively poor and growth is rapid. In their case, surgical treatment seems to be ineffective or insufficient, and a significant role seems to be assigned to chemotherapy and radiation therapy.[26]

The pathogenesis of the cancer includes genetic alterations that have been linked to some syndromes such as Lynch, Cowden, Li-Fraumeni and NF1 (neurofibromatosis type 1). Despite a number of noticeable mutations that appear to affect the cancer itself or be the target of treatment, the function of the gene encoding O6-methylguanine-DNA methyltransferase (MGMT) is cited as an important factor in the response to the primary chemotherapeutic agent temozolomide. In addition to this drug, bevacizumab is also used as a relapse therapy.[25]

Surgical resection can provide a complete cure for low-grade malignancy, while for high-grade it is part of palliative therapy [27–29]. Two terms have been defined - GTR (gross total resection) and STR (subtotal resection) meaning, respectively, resection of the entire lesion mapped with T1 enhancement on MRI [30] and partial obliteration of the lesion with sparing of T1 enhancement margins. A meta-analysis showed that GTR results in a clinically and statistically significant reduction in the relative risk of death and progression at 2, 5 and 10 years compared to STR.[31] From this, it can be concluded that GTR, compared with STR, can improve the morbidity and mortality of patients with low-grade medulloblastomas. Other studies have also shown similar benefits of GTR in treating spinal medulloblastomas, despite the rare use of this method due to the delicate nature of the region.[32,33] Some studies have even focused on extending the ablation zone farther than the boundaries of the GTR.[34] Such a zone is most often mapped using T2 FLAIR sequences instead of T1 [30,35]. Many studies have indicated an ideal FLAIR resection range of 20-53% [[36–39]], but a more recent study

suggests that the ideal volume varies and ranges from 10-29% for limited tumors, 10-59% for moderately disseminated tumors, and 30-90% for highly disseminated tumors. [40] While many studies confirm improved overall survival and progression-free time with resection in a zone wider than GTR versus GTR boundaries [30,35,41–43] , advanced techniques and equipment are needed to avoid functional damage during wide zone resection. One of the techniques used today is neurological navigation. It takes place intraoperatively and involves mapping pathways based on preoperative images. It uses electromagnetic or optical sensors to locate surgical instruments during surgery (in real time) relative to the patient's brain, which, previously mapped, becomes a three-dimensional reference point [44,45] . However, the benefits of this method are limited. If swelling occurs intraoperatively, the brain will be displaced and will not be adequate to the map created from the preoperative image. Likewise, a reduction in tumor mass can cause all structures to shift. [44,45]. Intraoperative imaging was introduced to prevent such complications. It has many benefits, while performing magnetic resonance imaging intraoperatively (iMRI) significantly increases the time of the entire operation [46] , which can increase the risk of other postoperative complications. An alternative method to MRI for monitoring brain structure during surgery is motor evoked potential (MEP) testing. In this study, the primary motor cortex is stimulated with appropriate electrical impulses and the effect is observed in the form of an action potential in the muscles. [26] This method avoids key brain regions by first checking their function. [46] Another technique that facilitates visualization of the brain is fluorescence. This uses appropriate tracers that accumulate in tumor cells. One of them, 5-aminolevulinic acid, is even metabolized by stellate cells into a colored substance, protoporphyrin IX, which is visible under violet light at 370-440 nm [47,48]. One study showed that the use of this tracer in the resection of highly malignant gliomas was associated with a 26% increase in GTR. [49] Another tracer, sodium fluorescein, works by binding to blood proteins that accumulate at the tumor-damaged blood-brain barrier. [48] The tracer itself has fluorescent capabilities and is visible under light of 465-490 nm [48,50] . A recent meta-analysis suggested that sodium fluorescein increases the number of GTRs by 29.5%. [48] In contrast, some see some benefit from the simultaneous use of both of these fluorophores, so this may be an object of future research. [51] Undoubtedly, it can be said that the first effective non-surgical method used in the treatment of staphyloma (especially with high malignancy) is radiotherapy. It uses two methods - stereotactic radiosurgery (SRS) and whole brain radiotherapy (WBRT). The former is characterized by greater precision and less radiation toxicity (and therefore less risk of

radiation necrosis). On the other hand, it has questionable implications in increasing survival compared to whole brain radiotherapy.[25]

While radiation therapy is only one component of combination treatment with chemotherapy and surgical resection, it is radiation therapy that has played a key role over the past 50 years. [52] Initial clinical trials in patients with malignant gliomas have shown a significant benefit in the treatment of combined whole-brain radiotherapy with surgical resection relative to treatment with resection alone. [25] Another study tested the correlation of increasing the titration dose of WBRT with median survival. The results indicate that patients receiving doses of 5000-6000 rad have significantly longer median survival relative to non-irradiated patients. [25] Over time, stereotactic radiosurgery has been added to whole-brain radiotherapy in stellate cancer treatment recommendations. It has introduced many changes in the approach to therapy. Its main difference and advantage over WBRT is its very high level of precision - this method targets the tumor lesion and spares healthy tissue to a much greater extent than WBRT. Stereotactic radiosurgery uses gamma radiation emitted from the decay of the radioactive isotope 60Co or linear accelerator-based photon therapy (LINAC). [53] One study compared the treatment effects of whole-brain radiotherapy in combination with temozolomide versus stereotactic radiosurgery in combination with temozolomide. An analysis of the results concludes that the two methods have comparable efficacy due to similar overall survival. At the same time, it was observed that therapy with SRS has significantly less toxicity than classic WBRT. [54] The lack of increased efficacy of stereotactic radiosurgery is similar to other focal treatments [55] while it is possible to use it in other situations such as to support systemic immunotherapy and as a salvage therapy for recurrent staphyloma. In addition to SRS, partial brain radiotherapy is also effectively introduced. It has been shown that its use does not reduce survival compared to whole brain radiotherapy. [56] On this basis, the American Society for Radiation Therapy Oncology (ASTRO) issued guidelines for the treatment of high-grade staphyloma. It included as a “strong recommendation” partial radiotherapy targeting areas of the brain with the highest risk of recurrence, i.e. within 2 cm of the primary tumor site. [56] Similar guidelines were also issued by the European Neuro-oncology Association (EANO). According to them, depending on prognostic factors, focused radiotherapy with a margin of 1-2.5 cm is used. The same guidelines also cite stereotactic radiotherapy as a suggested option for treating recurrence, which improves treatment efficacy and spares healthy structures. [57] For the treatment of low-grade staphyloma, guidelines have been issued by the Spanish Society of Medical Oncology. They concern the timing and dosage of therapy and were based on studies

conducted by this organization.[58] According to these studies, early radiotherapy results in a significant increase in PFS, while it does not affect overall survival. It has also been shown that low doses of radiation are equivalent to high doses, while they result in a reduced risk of radiation necrosis and other toxic effects of radiation therapy. [58] Chemotherapeutic chemotherapeutics for the treatment of staphylococcus have taken on a very significant role in recent years. Today, a frequently used chemotherapeutic agent is the alkylating drug, temozolomide, which is a derivative of dacarbazine. It is used in combination with or as an adjunctive treatment after radiation therapy. One study evaluated the efficacy of temozolomide in the treatment of patients with low-grade staphyloma, among others. In this group, median overall survival time was not reached and no significant differences in PFS (progression-free time) were observed between patients treated with radiotherapy alone and those treated with temozolomide alone. [59] However, the efficacy of TMZ is correlated with the presence of mutations in the gene encoding O6-methylguanine-DNA methyltransferase (MGMT). One publication shows that median survival from combination therapy (radiotherapy with temozolomide) in those with the MGMT mutation is 34.4 months, while it was only 12.7 months, or 63% less, in those without the mutation.[25] They also tested how combination therapy (radiotherapy with temozolomide) would be affected by the addition of another substance - lomustine - which is also an alkylating drug. It has been shown that the group receiving two chemotherapeutics - lomustine and temozolomide - achieves an increase in overall survival of up to 16.7 months relative to patients receiving temozolomide alone.[60] In addition, TMZ shows better tolerability relative to other drugs such as carmustine or three-drug combination therapy (procarbazine, lomustine, vincristine).[25]

The American Society of Clinical Oncology (ASCO) and the Society for Neurooncology (SNO) have issued research-based guidelines for the treatment of stage II to IV staphyloma with radiotherapy with adjuvant chemotherapy using TMZ. [61] Another drug used in the treatment of staphyloma is a monoclonal antibody called bevacizumab. Its mechanism is believed to involve binding to vascular endothelial growth factor (VEGF), inhibiting its binding to Flt-1 (VEGFR-1) and KDR (VEGFR-2) receptors on the surface of endothelial cells. Despite the approval of this drug in adult patients diagnosed with cancer recurrence, a double-blind placebo-controlled study showed no increase in survival in these patients after bevacizumab was administered with radiotherapy and temozolomide relative to patients who received radiotherapy alone combined with temozolomide. [62] Despite the prolongation of PFS in patients, a coincident increase in adverse effects such as neutropenia, thromboembolic complications, increased symptom severity or decreased quality of life was noted. [62]

Another randomized, double-blind, placebo-controlled phase III study reached similar conclusions.[63]

2.1 IDH-wild-type tumors (grade IV astrocytoma)

Astrocytomas are classified into four grades based on the degree of malignancy and severity of clinical symptoms. IDH-wild-type tumors are classified as grade IV astrocytomas and are characterized by poorly differentiated neoplastic astrocytes with cellular polymorphism, nuclear atypia, high mitotic activity, necrosis, vascular proliferation, and thrombosis. [64] IDH-wild-type is the most common malignant brain tumor in adults [65–71] ,accounting for 52% of all brain tumors. [72] Despite aggressive therapy consisting of surgical resection followed by radiotherapy in combination with temozolomide [65,69,70,73] and then chemotherapy with temozolomide [65,69,74], as many as 90% of grade IV gliomas will have a local recurrence within 2 years. The 2-year survival rate is 26.5%, and the median survival time is 14.6 months. [65] The 5-year survival rate is even lower and is only 10% [75] , and according to some studies even 6.8%.[76] The reasons for the poor prognosis in patients with IDH-wild type are mainly the highly infiltrative nature of glioma into the surrounding normal brain tissues, a high degree of migration from the tumor core and the ability to produce secondary microsatellite tumors in normal brain parenchyma [77] , as well as the difficult to access location (mainly the blood-brain barrier), resistance to many drugs and frequent relapses and rapid growth.[76] Age is the most common prognostic factor for IDH-wild type - the higher the patient's age, the worse the prognosis [71,74]. Studies conducted by Morgan et al. showed a significantly worse prognosis in older patients. Survival in the group under 65 years of age was 11.2 months, while in the group over 65 years of age it was 7.2 months.[74] Other risk factors associated with lower survival include partial tumor resection, low preoperative functional status (Karnofsky performance status < 70), no postoperative radiotherapy and chemotherapy or less than 4 courses of postoperative radiotherapy with temozolomide (TMZ). [71] Good prognostic factors in multivariate analysis include immunotherapy, proton therapy and complete tumor removal. [78] The standard of care is maximal surgical resection followed by chemoradiation. The primary goal of surgery is to obtain a tissue sample for pathological diagnosis and eliminate as much of the tumor as possible without damaging the surrounding healthy tissue. Lacroix et al analyzed the relationship between the extent of surgery and survival and showed that survival significantly increases with the extent of surgery of 98% or more. The median survival with resection of 98% or more was 13 months, while with resection of less than 98% the survival was only 4.2

months. [76] Patients with IDH-wild type that is inoperable and treated with radiotherapy/chemotherapy alone have a median survival of less than 9 months. Laser interstitial thermal therapy is an alternative cytoreductive technique for patients with inoperable glioblastoma.[79] This technology uses a laser-tip probe, inserted into the centroid of a brain lesion, to produce a controlled thermal injury by heating surrounding tissue. Real-time magnetic resonance imaging (MRI) thermometry allows for continuous monitoring of the ablation zone, and ablation can be stopped at any time.[80]

The primary goal of radiotherapy is to eliminate the remaining cancer cells that have invaded the surrounding non-cancerous tissue despite surgery. The study found that patients who received radiotherapy had a median survival of 29.1 weeks. In comparison, patients who were not irradiated had a median survival of 16.9 weeks. [76] The most common form of chemotherapy used to treat wild-type IDH is temozolomide, but about half of patients develop resistance to the drug and ultimately all patients fail treatment.[81] Temozolomide is an orally administered alkylating agent that causes base mismatches and subsequent double-strand breaks in DNA, ultimately leading to cell death. In a study by Witthayanuwat et al, the median survival time of patients who were treated surgically and then received postoperative temozolomide concurrently with radiotherapy (with or without adjuvant temozolomide) was shown to be longer than that of patients who were treated surgically and then received postoperative radiotherapy alone.[82] In other studies, the addition of temozolomide extended median survival by 2.5 months and increased 2-year survival from 10.4% to 26.5% compared with postoperative radiotherapy alone. In addition, high doses of corticosteroids are required to reduce intracranial pressure and minimize the side effects of inflammation caused by radiotherapy. [69] Due to aggressive cancer treatment, lymphopenia may occur, which may worsen the outcome of cancer treatment.[69]

Human cytomegalovirus (CMV) nucleic acids and proteins are present in 90% to 100% of glioblastomas. A study was conducted to examine whether antiviral therapy affects treatment outcome and found that patients with newly diagnosed glioblastoma had longer 2-year survival and median survival when they received valganciclovir in addition to standard therapy than in control groups who received only standard therapy. [83]Molecularly targeted therapy or immunotherapy is also available for the treatment of wild-type IDH, but most are in clinical trials. [84] The immunotherapies include monoclonal antibodies, checkpoint inhibitors, vaccines, and oncolytic viruses. [85] Apart from bevacizumab, which prolongs progression-free survival, none of these therapies have been shown to improve patient

survival. [84] There was no significant difference in overall survival for newly diagnosed IDH-wild-type patients using molecularly targeted drugs, but progression-free survival was improved with molecularly targeted drugs. There have also been more adverse events observed with molecularly targeted drugs than with standard treatment.[86]

One of the theories of cancer development is the stem cell (SC) theory of cancer, which assumes that cancers arise from cancer stem cells (CSCs) present in the tissue and accumulate all the mutations necessary to initiate tumorigenesis. Currently, there are 5 methods of eradicating cancer stem cells: immunotherapy, gene therapy to limit CSC proliferation, use of differentiation factor(s) to stimulate CSCs to differentiate into normal cells, increasing the sensitivity of CSCs to radiotherapy and chemotherapy by using a reactive factor(s), targeting new molecular protein signal pathway(s) of CSCs with new targeting therapeutic agent(s). Stem cell therapy is emerging as a potentially revolutionary and new strategy in the treatment of wild-type IDH. Due to their intrinsic tropism to the tumor, stem cells are particularly suited to deliver anticancer agents to the tumor site. Due to the short half-life of conventional drug delivery systems, stem cells or extracellular vesicles released by stem cells have been used to deliver antitumor payloads. [77] Most wild-type IDH recurs at or near the original site of origin.[65,68] The median time to recurrence of wild-type IDH is 6 months.[77] There are no established standards of care for patients with recurrent wild-type IDH[65,70]. In such cases, surgical retreatment, re-irradiation, systemic therapy, and supportive care may be considered.[65]

3. EPENDYMOMAS

Ependymoma, derived from glial cells, is a primary CNS tumor. These tumors can be located intracranial or around the spinal cord. It is a relatively rare tumor, which is why reported studies and reviews are statistically low. In 2021, WHO introduced a new classification for CNS tumors, according to which ependymomas were divided into 10 categories.[87] Due to the recentness of this division in scientific works, these tumors are still commonly divided into three stages according to the WHO classification. Stage one refers to benign tumors, including subependymomas and MPE. Stage II ependymomas presenting with high cellularity and papillary structures. The highest stage - III, is anaplastic ependymomas. [88]

For benign tumors (subependymoma, MPE) the therapy of choice is [89] and at the same time often considered preferred by scientists is GTR [88,90–92] radiotherapy is considered helpful

in some cases. [89–92] , however its use in spinal ependymal tumors still seems to be controversial, further research on this topic is necessary. [91,92]

Also in the case of higher grade tumors the most commonly used method of surgical treatment is GTR. It is a relatively safe and effective method of treatment. Its use is effective for both intracranial ependymomas [89,93–95] and spinal ependymal neoplasms. GTR for spinal ependymal tumors had a more positive prognosis for the occurrence of potential recurrences and patient survival compared to STR [89,92] or surgery followed by radiotherapy. [91] Patients who underwent GTR have a high survival rate [89,91–93] and we should strive to perform it in treatment, but it is only possible in 41% to 72% of cases.[89]

The independent predictor of GTR, which should be taken into account, was the size of the tumor [91,92]. Therefore, the earliest possible diagnosis of the tumor and rapid performance of the procedure are important, especially since the postoperative improvement in the follow-up was mainly observed in patients without significant neurological deficits before treatment.[91]

In the case of an anaplastic tumor (WHO grade III), the effectiveness of performing GTR despite surgical success significantly decreases. [88,89,93] In connection with these data, it is not enough to perform surgery alone, but it is necessary to subject the patient to radiotherapy after the procedure. And in the case of relapse, reoperation with radiotherapy should be considered.[89] The use of chemotherapy in the case of surgical excision and radiotherapy did not bring results seems pointless, does not contribute to prolonging the life of patients and should not be used [88,89,93]

Low ki-67 index could be considered a significant predictor of PFS in patients with spinal ependynoma. [91] The correlation of a given factor has yet to be thoroughly established, we also have data in which the ki-67 index correlation is small regarding PFS [92], however, we can wonder here about the small sample size. Another important predictive factor influencing patient survival and their permanent deterioration in functioning in studies is the age of patients and histological grade of tumor. [88,89] MPE (grade I) is characterized by a high rate of survival. The 1-year, 2-year, and 10-year survival rate was 100%, 100%, 95.8% respectively. [92] 10-year survival was also strongly correlated with the age of patients, ranging from 70–89%. [89] The correlation between patient survival and grade 2 and 3 according to the WHO classification is still uncertain. In the literature, we can find both works claiming that grade 3 tumors have a worse prognosis [88,93] and those that contradict it. [89] However, it is important that worldwide neurooncology experts have reached a consensus that

the decision regarding the choice of treatment cannot be dictated by the WHO histological division.

Neurological decline after surgery is a common complication, and may result from irritation resulting from surgical procedures. The percentage of patients who improve varies depending on the studies. [91,95] One of the most serious adverse effects may be complete paralysis.[92] Performing a surgical procedure within the spinal cord may require intermittent catheterisation. Additionally, during follow-ups, patients from this group had post-operative urinary tract disorders. [90,92] The predictive factor for the durability of postoperative neurological damage may be the increasing age of the patients, as well as the cervical location of the tumor. [91]

Complications resulting from the removal of ependymoma within the intracranial area include viligance, ataxia and shunt dependency. [95] Complications related to procedures on 4th ventricle tumors that should be taken into account include cranial nerve deficits. These problems may result from direct damage to the nerve or its nucleus due to their close anatomical proximity to the tumor.[95]

CONCLUSIONS:

Various forms of therapy are used in the treatment of brain tumors. Treatment options of meningiomas range from observation to surgical removal. When choosing the most suitable form, it is crucial to analyze the patient's entire clinical state. Treatment involves surgical resection, the effectiveness of which depends on the extent of tumor removal. Radiotherapy is applied for tumors that cannot be completely removed. Systemic treatment is not very effective, but targeted therapies and immunotherapy are being studied. Low-grade astrocytomas are typically treated with surgery, while high-grade tumors require surgery followed by chemotherapy and radiation. Genetic mutations impact treatment response, particularly to temozolomide. Advances in surgery include techniques like fluorescence and intraoperative imaging. Stereotactic radiosurgery (SRS) plays a key role for high-grade tumors. Temozolomide is used, however resistance may develop. IDH-wild-type astrocytomas are treated by options sucha as surgery, radiotherapy, temozolomide, immunotherapy and stem cell-based treatments. Despite aggressive treatment, recurrence is common. Ependymoma is a rare primary CNS tumor that originates from glial cells and can be found in the brain or spinal cord. The preferred treatment for benign tumors is GTR, with radiotherapy considered helpful in some cases. For higher-grade tumors, GTR is still common

surgical approach, offering better outcomes compared to subtotal resection. Early diagnosis is crucial for a successful outcome. For anaplastic tumors, GTR alone is insufficient, and radiotherapy is recommended. Chemotherapy is not effective in these cases. Due to the increasing number of CNS tumors cases it is crucial to develop increasingly effective therapies and to reduce the side effects of treatment.

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