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PRACA ORYGINALNA
ORIGINAL PAPER

Histopathological analysis of brain lesion samples acquired from stereotactic and navigated brain biopsy: A single cohort study

Histopatologiczna analiza próbek zmian w mózgu uzyskanych poprzez stereotaktyczną i nawigowaną biopsję mózgu – badanie kohortowe

Igor Andjelić[1], Maciej Laskowski[1], Małgorzata Gola[1], Marcin Ciekalski[1], Agnieszka Koperczak[1], Bartłomiej Błaszczyk[2], Anna Zioła-Paździora[3], Piotr Paździora[2], Adam Rudnik[2]

[1]Students' Scientific Club, Department of Neurosurgery, Faculty of Medical Sciences in Katowice, Medical University of Silesia, Katowice, Poland

[2]Department of Neurosurgery, Faculty of Medical Sciences in Katowice, Medical University of Silesia, Katowice, Poland

[3]Department of Pediatric Surgery, Upper Silesian Children's Health Center named after St. John Paul II, Independent Public Clinical Hospital No. 6, Medical University of Silesia, Katowice, Poland

ABSTRACT

INTRODUCTION: Brain tumors are a complex group of neoplasms originating from various cell types within the central nervous system. Their classification, based on histopathological and molecular characteristics, guides therapeutic strategies and prognosis. Advances in neuroimaging and biopsy techniques have enhanced diagnostic accuracy, allowing for tailored and more effective treatment approaches. Brain biopsy (BB) is an indispensable neurosurgical procedure for the histological diagnosis of neoplastic brain lesions, playing a pivotal role in patient management. The aim of this study is to evaluate the histological outcomes of BBs and to identify the age groups, gender distribution, topography, and different histological types of brain tumors.

MATERIAL AND METHODS: We conducted a retrospective cohort study at a single academic medical center, analyzing 112 patients who underwent BB between January 2017 and August 2023. The study focused on the histological results and molecular markers obtained from stereotactic and neuronavigated brain biopsies, examining the success rate in achieving diagnostic samples and the application of the brain tumor classification system developed by the World Health Organization (WHO). We also studied correlations between histological result and complications.

RESULTS: Histological examination confirmed the diagnostic accuracy of BB, with a similar distribution of success between stereotactic and neuronavigated methods. The WHO classification of brain tumors was applied to categorize the lesions, which facilitated standardized treatment planning. The study observed a low rate of complications, demonstrating the procedure's safety.

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Address for correspondence: lek. Igor Andjelić, Klinika Neurochirurgii, Uniwersyteckie Centrum Kliniczne im. prof. K. Gibińskiego ŚUM, ul. Medyków 14, 40-752 Katowice, tel. +48 32 789 45 01, e-mail: igor.andjelic.med@gmail.com

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CONCLUSIONS: The findings of this study indicate that the spectrum of brain tumor diagnoses in our cohort closely parallels global epidemiological trends. The WHO classification framework enabled enhanced diagnostic precision and facilitated standardized therapeutic decision-making.

KEYWORDS

brain tumors, neuro-oncology, epidemiology, histopathology, WHO

STRESZCZENIE

WSTĘP: Guzy mózgu stanowią złożoną grupę nowotworów wywodzących się z różnych typów komórek ośrodkowego układu nerwowego. Ich klasyfikacja, oparta na cechach histopatologicznych i molekularnych, determinuje strategie terapeutyczne oraz rokowanie. Postępy w neuroobrazowaniu i technikach biopsji zwiększyły precyzję diagnostyczną, umożliwiając bardziej spersonalizowane i skuteczne metody leczenia. Biopsja mózgu (*brain biopsy* – BB) jest nieodzownym zabiegiem neurochirurgicznym, służącym do histologicznej diagnostyki nowotworowych zmian mózgu, odgrywającym kluczową rolę w postępowaniu z pacjentem. Celem badania jest ocena wyników histologicznych BB oraz identyfikacja grup wiekowych, rozkładu płci, topografii i różnych histologicznych typów guzów mózgu.
MATERIAŁ I METODY: Przeprowadzono retrospektywne badanie kohortowe w jednym z akademickich ośrodków medycznych, analizując 112 pacjentów poddanych BB w okresie od stycznia 2017 r. do sierpnia 2023 r. Badanie koncentrowało się na wynikach histologicznych oraz markerach molekularnych uzyskanych z biopsji stereotaktycznych i z użyciem neuronawigacji, oceniając skuteczność w uzyskiwaniu próbek diagnostycznych oraz zastosowanie systemu klasyfikacji nowotworów mózgu opracowanego przez Światową Organizację Zdrowia (World Health Organization – WHO). Analizowano również korelacje pomiędzy wynikami histologicznymi a powikłaniami.
WYNIKI: Badanie histologiczne potwierdziło wysoką skuteczność diagnostyczną BB, przy zbliżonej skuteczności metod stereotaktycznych i z zastosowaniem neuronawigacji. Do kategoryzacji zmian zastosowano klasyfikację nowotworów WHO, co również pozwoliło na zaplanowanie dalszego leczenia onkologicznego. Zaobserwowano niski odsetek powikłań, co potwierdza bezpieczeństwo procedury.
WNIOSKI: Wyniki wskazują, że spektrum rozpoznań nowotworów mózgu u badanych pacjentów jest zbieżne z globalnymi trendami epidemiologicznymi. Zastosowanie klasyfikacji WHO umożliwiło zwiększenie precyzji diagnostycznej oraz ułatwiło standaryzację decyzji terapeutycznych.

SŁOWA KLUCZOWE

guzy mózgu, neuroonkologia, epidemiologia, histopatologia, WHO

INTRODUCTION

Brain and other central nervous system (CNS) tumors account for a significant percentage of mortality and morbidity for people of all ages [1]. They consist of a broad range of malignant cancers that originate in the brain and its surrounding structures. In recent decades, brain tumors have been classified largely based on histogenesis concepts. An international standard for the classification of brain and spinal cord tumors is the World Health Organization's (WHO) Classification of Central Nervous System Tumors. The WHO published its initial classification of CNS tumors in 1979, with updates coming in 1993, 2000, 2007, and most recently in 2021 [2]. The story of the WHO classification of CNS tumors spans over half a century, marked by continual revisions and refinements. Early efforts to categorize brain tumors were met with limited success until the WHO undertook the task, influenced by previous work such as the AFIP Fascicle. Throughout the development of the WHO's CNS tumor classification, profound debates ensued among international experts, which often centered around the concept and utility of tumor grading. The contention largely stemmed from differing viewpoints on the significance of grading for therapeutic and prognostic purposes versus the challenges posed by its imprecision. This was further complicated by the variability in tumor behavior, the impact of tissue sampling, and the dynamic nature of tumor progression. The WHO grading system evolved to incorporate both clinical malignancy – reflecting the tumor's growth properties and potential for lethality – and histologic malignancy, based on cellular and tissue characteristics. Despite these challenges, the WHO's classification system has strived to create a balanced, pragmatic approach to categorizing CNS tumors, aiming to provide a useful framework for clinical and research applications. This has included the consideration of survival times, risk of recurrence, and the integration of both clinical and histological data to inform grading. The result has been a series of classifications that have not only informed clinical practice, but have also evolved in response to advances in tumor biology and diagnostic technology [2].

The 2016 WHO classification represented a significant improvement over the previous one in that it was the first to define many tumor entities using molecular criteria in addition to histology. This made it possible to classify CNS tumors more precisely and accurately. Historically diffuse gliomas, which are the most

common brain tumors in adults, include WHO grade II and III astrocytomas, grade IV glioblastomas, and grade II and III oligodendrogliomas [3].

The WHO Classification of Central Nervous System Tumors of 2021 considers the microscopic image as well as the profile of the tumor molecule. Molecular characteristics of tumors are prognostic and determine the possibilities of adjuvant oncological treatment. This classification includes diffuse gliomas, medulloblastomas, and embryonal tumors and it incorporates new entities that are defined by both histological and molecular features, including IDH--wildtype glioblastoma and IDH-mutant glioblastoma; H3 K27M-mutant diffuse midline glioma; ZFTA fusion-positive supratentorial ependymoma; WNT--activated medulloblastoma and SHH-activated medulloblastoma; and embryonal tumor with multilayered rosettes, C19MC-altered [4].

Gliomas can be treated with a variety of therapies, which are customized to the individual patient and may include surgery, radiation therapy, chemotherapy, targeted therapy, immunotherapy, or observation. However, most glioma patients need a surgical approach as the first line of treatment [5]. Non-surgical treatment options are usually selected when resection is not an option due to the tumor's diffuse, infiltrative nature or its proximity to critical structures. Preparation for surgical treatment begins with neuroimaging, where the possibility of performing a safe radical surgery is assessed and the surgical access is planned. In most cases, brain tumors are removed by craniotomy using an operating microscope and the patient is given aminolevulinic acid (5-ALA) before the surgery to allow for better visualization. In cases of extensive tumors or tumors located within deep structures, when safe surgical removal of the lesion may not be possible, a tumor biopsy is performed for histopathological verification [6,7]. High-grade gliomas are typically treated with additional radiotherapy immediately after surgery, whereas for grade 2 gliomas it can either be administered right away or after the onset of new symptoms or the progression of the tumor [8].

Chemotherapy is often used in combination with radiation therapy. The most common in the treatment of gliomas is temozolomide (Temodar); it has several effects on the immune system that are dependent on the dosing strategy [9]. It has been proven that temozolomide sensitizes tumors to radiation, making it more effective. After radiation treatment is finished, patients with high-grade gliomas often require a second round of temozolomide, which is typically administered for at least 6 months [10]. Temozolomide has been noted to cause DNA double-strand breaks, similar to the effect of ionizing radiation. This suggests that while it acts as a radiation sensitizer, it also has independent antitumor activities by inducing apoptosis, cellular senescence, and autophagy. This dual role implies that temozolomide can be effective both in conjunction with radiation therapy and as a standalone treatment in certain contexts [11]. However, it is worth noting that half of treated patients have temozolomide resistance and all patients eventually fail therapy. Bevacizumab, also marketed as Avastin, is an antibody therapy that specifically targets vascular endothelial growth factor (VEGF), a critical molecule involved in the formation of new blood vessels, a process known as angiogenesis. This is particularly important in the context of glioblastomas, where VEGF stimulates the growth of blood vessels that feed the tumor cells, aiding in their growth and survival [12,13].

Brain biopsies have been integral in providing vital histopathological data for diagnosing new intracranial lesions. They are particularly crucial in the management of neoplastic brain diseases where the diagnostic yield is high, significantly impacting clinical decision-making. However, in cases of non-neoplastic brain disease – especially when conventional investigations return negative – the decision to proceed with a biopsy is more complex due to the inherent risks and lower diagnostic yields [14].

Stereotactic brain biopsy (SBB) has a rich history dating back to the early 1900s; it was pioneered by Horsley and Clarke. This method utilizes a coordinate--based system to accurately pinpoint and extract tissue from targeted brain regions. SBB is precise enough to isolate samples with minimal error, typically ranging from 1 to 3 millimeters, thereby preserving adjacent healthy tissue. The technique is recognized for its low complication rates and is exceptionally beneficial for biopsying lesions situated in hard-to-reach or functionally critical areas of the brain [15,16]. Neuronavigational brain biopsy (NBB) is a relatively new development that incorporates modern imaging technologies like MRI and CT scans into the surgical process. These neuronavigation systems produce a live 3D map of the patient's brain to assist the surgeon throughout the biopsy. This approach is known to improve the safety and accuracy of brain biopsies by visualizing the biopsy needle's path in relation to the patient's brain structure, helping to avoid vital areas and lessen the risk of complications. Research has shown that NBBs can increase the rate of accurate diagnoses from brain biopsies while maintaining a low rate of postoperative complications, establishing it as an important instrument in contemporary neurosurgery [17,18,19].

MATERIAL AND METHODS

Ethics

This project complies with the ethical principles for medical research stipulated in the World Medical Association Declaration of Helsinki.

Study design and data collection

This is a single-institution retrospective study that includes all patients who underwent a brain biopsy for suspected primary CNS malignancy between January 2017 and August 2023. Clinical information about the patients was registered and documented. The study data was obtained from the electronic medical records. We excluded all patients without complete data or follow-up information. The following variables were registered: demographic information, clinical presentation and symptoms, length of hospital stay, whether the biopsy was successful, location of biopsy, type of biopsy, comorbidities, details of the surgical procedure, post-operative complications within the first 30 days, biopsy results, and molecular markers. The final study group consisted of 112 patients, at an average age of 58 years, of whom 48.2% were female and 51.8% were male.

Histological and molecular classification

We gathered the histological diagnoses and molecular markers of our patients. While we were unable to categorize all brain lesions using the latest 2021 classification due to our pathomorphologist applying an earlier system, we endeavored to align our cases with the WHO classification criteria, as outlined in Table I. Additionally, we introduced categories for cases which did not display malignant features, for multiple sclerosis (MS), for inflammatory processes, and for non-neoplastic glial tissue affected by hemorrhages and gliosis.

Table I. Groups we created to classify all the histopathological diagnoses

1	no malignant features
2	glioblastoma
3	diffuse glioma WHO II
4	diffuse glioma WHO III
5	diffuse astrocytoma WHO II
6	diffuse astrocytoma WHO III
7	pleomorphic xanthoastrocytoma WHO II
8	anaplastic astrocytoma WHO III
9	oligodendroglioma WHO II
10	oligodendroglioma WHO III
11	anaplastic oligodendroglioma WHO III
12	diffuse large B-cell lymphoma
13	schwannoma WHO I
14	ganglioma WHO I
15	metastasis
16	MS
17	inflammation
18	no unreliable/glial tissue with hemorrhages and gliosis
19	astrocytoma WHO II

WHO – World Health Organization; MS – multiple sclerosis.

Molecular markers

Biopsy location

We created 10 groups according to the location of lesions that were biopsied: frontal lobe, cortex lobe, parietal lobe, occipital lobe, brainstem, cerebellum, cerebral hemisphere, corpus callosum, great commissure, frontotemporal lobe, insula/thalamus, and lateral ventricle. We also assessed which side the biopsied lesions were located on.

Symptoms and risk factors

The patients' symptoms were divided into groups: seizures, headaches, behavioral disturbances, altered levels of consciousness, memory impairments or cognitive dysfunctions, speech disturbances, aphasia, dizziness, muscle weakness, partial paralysis, sensory, visual disturbances, and ataxia. We collected data about risk factors, such as hypertension, type 2 diabetes, atherosclerosis, hyperlipidemia, venous thrombosis, cancer other than CNS, and hypo- and hyperthyroidism.

Statistics

Statistical analysis of the collected data was conducted using the software program Statistica 13.0 (StatSoft, Krakow, Poland). Categorical variables were described using numbers and percentages, while quantitative variables were described using the mean and its standard deviation. The normality of the distribution of the results was assessed using the Shapiro–Wilk test.

RESULTS

There were 112 successive cases of brain tumors, with 58 (51.8%) of the patients being male and 54 (48.2%) female, resulting in an almost equal ratio between men and women. The patients ranged from 18 to 82 years old, averaging 57.96 years (SD 14.76). The primary affected age group was 60 to 69 years old (30.69%; Figure 1).

The thalamus and subcortical nucleus were the most frequently affected sites (24.1%), followed by the frontal (21.4%), temporal (16.1%), and parietal (11.6%) lobes (Figure 2). The brain stem (2.7%) and cerebellum (2.7%) were the least affected. Table II presents the quantity, percentage, average age with standard deviation, and gender distribution among our brain tumor patients.

Glioblastomas displayed a slight male predominance, with a median affected age of 59.46 (SD 11.72). The primary affected sites were the temporal lobe (20%)

and the thalamus and subcortical nucleus (20%). Diffuse large B-cell lymphomas (DLBCLs) were more common among the women, who had a mean age of 69.88 (8.36%), and were mainly located in the frontal lobe (36.84%). Diffuse astrocytoma WHO II occurred almost equally in both genders, with a male-to-female ratio of 5:4. The mean age of male patients with diffuse astrocytoma WHO II was 61.00 (SD 7.18), and among female patients, it was 47.00 (SD 8.98). The most common locations were the frontal, temporal, and parietal lobes, each contributing 22.22% of the cases. Other less frequent brain tumors seen in our series were diffuse astrocytoma WHO III and anaplastic oligodendroglioma WHO III, which each represented 3.57% of the total cases.

Among biopsies that did not result in a malignancy diagnosis, 14 (12.5%) revealed no signs of pathology, another 5 (4.46%) were deemed unreliable due to gliosis with hemorrhages, 5 (4.46%) indicated inflammation, and 1 (0.89%) biopsy showed an MS lesion.

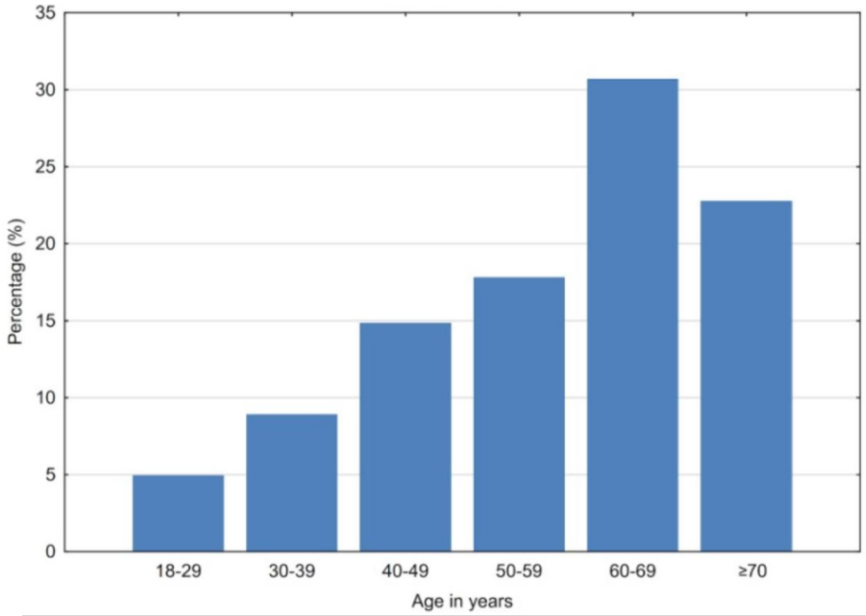

Fig. 1. Distribution of central nervous system tumor cases by age group

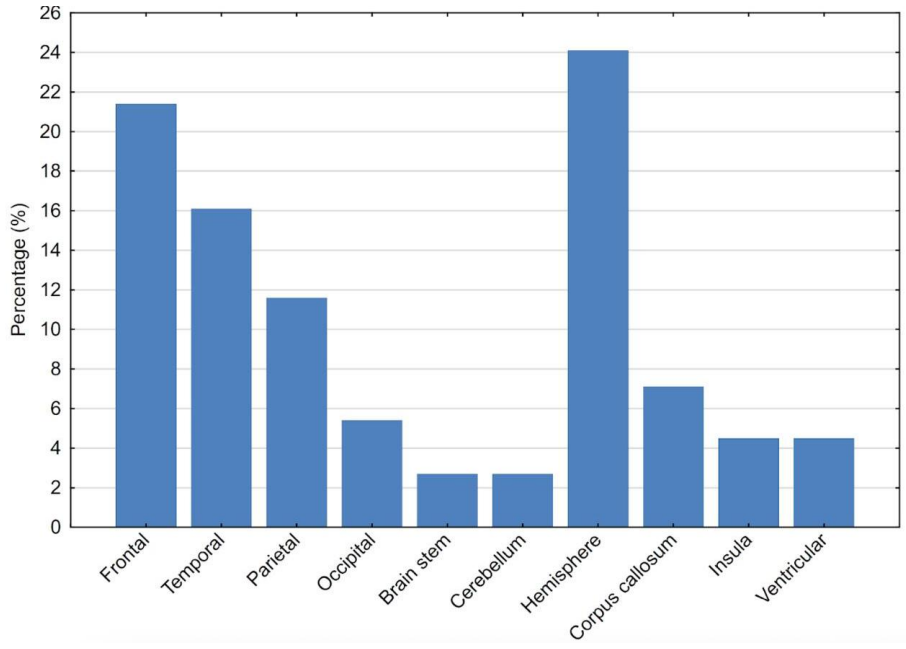

Fig. 2. Distribution of central nervous system tumor cases by location

Table II. Histopathological distribution of central nervous system (CNS) tumors concerning gender variations

Diagnosis	Sex								Total			
	Male				Female							
	N	%	Mean age	SD	N	%	Mean age	SD	N	%	Mean age	SD
No malignant features	7	12.07	65.29	4.39	7	12.96	51.00	19.19	14	12.50	58.69	14.77
Glioblastoma	17	29.31	59.46	11.72	13	24.07	66.00	11.04	30	26.79	62.46	11.65
Diffuse glioma WHO II	1	1.72	39.00	–	2	3.70	57.50	27.58	3	2.68	51.33	22.23
Diffuse glioma WHO III	2	3.45	72.50	0.71	0	0	–	–	2	1.79	72.50	0.71
Diffuse astrocytoma WHO II	5	8.62	61.00	7.18	4	7.41	47.00	8.98	9	8.04	54.78	10.51
Diffuse astrocytoma WHO III	2	3.45	56.00	15.56	2	3.70	48.50	14.85	4	3.57	52.25	13.15
Pleomorphic xanthoastrocytoma WHO II	1	1.72	67.00	–	0	0	–	–	1	0.89	67.00	–
Anaplastic astrocytoma WHO III	1	1.72	71.00	–	2	3.70	48.50	0.71	3	2.68	56.00	13.00
Oligodendroglioma WHO II	1	1.72	35.00	–	2	3.70	31.00	15.56	3	2.68	32.33	11.24
Oligodendroglioma WHO III	1	1.72	67.00	–	0	0	–	–	1	0.89	67.00	–
Anaplastic oligodendroglioma WHO III	3	5.17	51.00	15.87	1	1.85	65.00	–	4	3.57	54.50	14.73
Diffuse large B-cell lymphoma	8	13.79	54.86	10.40	11	20.37	69.88	8.36	19	16.96	62.87	11.89
Schwannoma WHO I	0	0	–	–	1	1.85	79.00	–	1	0.89	79.00	–
Ganglioma WHO I	1	1.72	46.00	–	0	0	–	–	1	0.89	46.00	–
Metastasis	2	3.45	71.50	12.02	1	1.85	53.00	–	3	2.68	65.33	13.65
MS	0	0	–	–	1	1.85	24.00	–	1	0.89	24.00	–
Inflammation	3	5.17	53.00	10.82	2	3.70	62.00	4.24	5	4.46	56.60	9.34
No unreliable/glial tissue with hemorrhages and gliosis	1	1.72	55.00	–	4	7.41	57.50	17.25	5	4.46	57.00	14.98
Astrocytoma WHO II	0	0	–	–	1	1.85	18.00	–	1	0.89	18.00	–
No data	2	1.79	50	36.77	0	0	–	–	2	1.79	50	36.77
Total	58	100	58.70	12.48	54	100	57.15	17.03	112	100	57.96	14.76

WHO – World Health Organization; MS – multiple sclerosis.

DISCUSSION

The analysis of the data in our hospital-based study indicated a consistent distribution of CNS tumors over this period, with no significant fluctuations observed. The age range aligned with the age range most commonly affected by lesions in similar studies conducted globally.

In our study, the average age for patients with gliomas of different grades was 60 years. However, some studies reported an average age of diagnosis for low--grade gliomas to be approximately 33.32 years, whereas for high-grade gliomas, the average age was higher (50.35). This finding is consistent with other research indicating that the grade of brain gliomas tends to increase with the patient's age: patients with grade IV gliomas show a higher average age than those with lower-grade tumors [20]. Also, the average age of patients with B-cell lymphoma in our study group was 62, while in another study the median age for patients diagnosed with DLBCL was reported as 59.5 years [21]. Another study focusing on DLBCL, a common type of B-cell lymphoma, indicated a median age at diagnosis of 70 years, with a significant portion of diagnoses occurring in patients over 75 years old, a demographic that is growing rapidly [22].

DLBCL was the most common diagnosis in our study; it occurred mostly in women. In the literature, the average age of diagnosis for DLBCL, which can also present in the brain, is generally 60–65 years. However, it is important to note that DLBCL can occur in individuals of any age, including children. The incidence of DLBCL increases with age, with most patients being over 60 years old at the time of diagnosis [23]. In terms of gender distribution, DLBCL is slightly more common in men than in women. For men, the risk of developing DLBCL increases from 0.13% before the age of 39 to 1.77% after the age of 70. Similarly, for women, the risk increases from 0.09% before the age of 39 to 1.4% after the age of 70 [24].

For grade III oligodendrogliomas, we only had 1 patient, who was 67 years of age, which puts him closer to the expected median age, as another study reported a median age at diagnosis ranging from 45 to 50 years.

Anaplastic WHO grade III oligodendroglioma is a rare malignant tumor; it presents with features of

oligodendroglial origin and the highest incidence occurs between 45 and 50 years of age. A single case of grade II oligodendroglioma was observed in our patients (67 years of age). On average, the median age is approximately 7 to 8 years older than for grade II oligodendroglioma [25]. The peak incidence for oligodendrogliomas of WHO grade II is between the ages of 30 and 40 years, which was reflected in our data on 3 patients, whose mean age was 32.33 [26].

Low-grade astrocytomas are predominant in individuals aged 30 to 40; for the 9 patients in our study with diffuse astrocytoma WHO II, we found a median age of 54.78. While for grade III astrocytoma, the mean age for our 3 patients with anaplastic astrocytoma WHO III was 56 years – and among the 4 patients with diffuse astrocytoma WHO III it was 52.25 years – the mean age at diagnosis according to Kapoor et al. [27] is approximately 40 years for astrocytoma WHO grade III. A small outlier which appeared among our data was a single patient with pleomorphic xanthoastrocytoma WHO II at the age of 67, which is much later than the mean age of 26 reported in a study on 71 patients [28].

CONCLUSIONS

The findings of this study indicate that the spectrum of brain tumor diagnoses in our cohort closely parallels global epidemiological trends. Implementing the WHO classification framework enabled the systematic categorization of lesions, thereby enhancing diagnostic precision and facilitating standardized therapeutic decision-making. Brain biopsy, whether performed via stereotactic or neuronavigated techniques, demonstrated consistently high diagnostic yields, confirming its reliability for histopathological evaluation. The low complication rate further attests to the safety and clinical utility of these methods in contemporary neurosurgical practice.

Authors' contribution

Study design – I. Andjelić, P. Paździora

Data collection – M. Gola, A. Koperczak, M. Laskowski

Data interpretation – P. Paździora, B. Błaszczyk, A. Rudnik, A. Zioła-Paździora

Statistical analysis – M. Ciekalski, M. Laskowski, A. Zioła-Paździora

Manuscript preparation – I. Andjelić, M. Laskowski

Literature research – I. Andjelić, M. Laskowski

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