ORIGINAL STUDY

Role of Surgery in the Prognosis of Pediatric Thalamic Tumors

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Abstract

Objective: **This study aimed to present the authors' experience in managing 20 cases of pediatric thalamic brain tumors.**

Background: **Thalamic tumors constitute a small percentage (~0.84−5.2 %) of all brain tumors and are even rarer in the pediatric population, accounting for about 2−5% of pediatric brain tumors. These tumors present a significant challenge to neurosurgeons due to their intricate location within the brain and their proximity to crucial structures, especially in children. The management of these tumors necessitates careful consideration and expertise due to the potential risks associated with their critical position.**

Patients and methods: **In this retrospective study, the authors analyzed the cases of 20 pediatric patients with thalamic brain tumors who were admitted to Menoufia University Hospital and Children's Hospital of Cairo University between 2020 and 2022. The study focused on investigating the surgical interventions performed about different histopathological subtypes of the tumors, tumor size, patient age, and presenting symptoms.**

Conclusion: **Thalamic brain tumors in pediatric patients are mainly low-grade pilocytic astrocytoma's. Symptoms include increased intracranial pressure and contralateral weakness. Adjuvant therapy, such as chemotherapy and radiotherapy, has limited effectiveness in preventing disease progression but improves overall survival. Surgical excision benefits low-grade tumors, while stereotactic biopsy is preferred for diagnosis and guiding management decisions.**

Keywords: Brain, Children, Neurosurgery, Thalamic, Tumor

1. Introduction

Thalamic tumors are uncommon in pediatric patients, representing a small percentage, typically ranging from 0.84 % to 5.2 %, of all brain tumors as determined by pathological examination [1−4]. They account for ~2−5% of pediatric brain tumors [4,5]. In the past, surgical procedures carried significant risks of both mortality and morbidity, before the advancements in neuroimaging techniques such as tractography, microsurgery, neuronavigation, and improvements in postoperative care [6−9]. Although the complete removal of low-grade lesions (gross-total resection or subtotal resection) is supported by strong evidence, the benefits of this approach for high-grade lesions remain uncertain based on the available literature [2,7,9−14]. The role of chemotherapy and radiotherapy has evolved, serving as supplementary treatments in institutions where gross-total resection (GTR) is the primary approach for low-grade tumors. However, in certain institutions, chemotherapy and radiotherapy are still considered standard treatment regardless of specific histological findings [15−17]. The current literature lacks a clear differentiation between tumors originating in the thalamic region and those arising from other structures within the diencephalon and basal ganglia nuclei [9,10,12,13,18−20]. Therefore, the purpose of this study was to present our experience in managing 20 cases of thalamic brain tumors in pediatric patients with various histopathological types. Our management approach

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primarily relied on the histological grading of the tumor.

2. Patients and methods

We conducted a retrospective study between 2020 and 2022, enrolling 20 patients diagnosed with thalamic tumors. These patients received treatment at Menoufia University Hospital and Children's Hospital of Egypt, Cairo University. Informed consent was obtained from the patient's relatives before any procedures or treatment plans. Our study had specific eligibility criteria, categorized into inclusion, and exclusion criteria. The inclusion criteria encompassed patients below the age of 18 with tumors located in the thalamus, whether intrinsic or extrinsic. Conversely, the exclusion criteria included patients who had previously undergone surgical or nonsurgical treatments, as well as those with bilateral thalamic tumors, vascular lesions, inflammatory lesions, or poor general condition.

All patients underwent a comprehensive management approach, including detailed history taking, thorough physical examination, comprehensive investigations, and initial treatment. Patients with increased intracranial pressure due to hydrocephalus received ventriculoperitoneal shunt insertion. Those with small unilateral tumors underwent stereotactic biopsy, while patients with large tumors extensively infiltrating the surrounding tissues underwent direct surgical intervention.

Surgical procedures were performed using various techniques. Stereotactic biopsies were conducted using the frameless Brain Laboratory-guided navigation system for precise localization. An incision and burr hole were made based on the navigation system's guidance. When approaching thalamic tumors, transcortical approaches through the middle temporal gyrus or posterior parietal lobule were employed. The navigation system aided in determining the location of an inverted U-shaped incision with a wide base. The scalp flap was reflected as a single layer, followed by the creation of a free bone flap. The dura was then opened, cortisectomy was performed, and the tumor was removed. Hemostasis was achieved, and all layers were subsequently closed.

Continuous monitoring of patients included regular neurological examinations, assessments of visual acuity, and fundus examinations to evaluate neurological outcomes, and identify any new neurological deficits, seizures, behavioral changes, or complications. Additionally, A Magnetic Resonance Imaging (MRI) of the brain with contrast was conducted immediately after surgery and repeated every 3–6 months for each patient. These MRI scans aimed to detect changes in tumor size, progression or regression, and potential complications.

Informed consent was taken from all patients regarding information on the procedures and their possible complication. Approval was obtained from the ethical committee of scientific research of the faculty of medicine, at Menoufia University under code no. (9/2021NEUR35).

2.1. Statistical analysis

The collected data were coded, tabulated, and statistically analyzed using IBM SPSS Statistics (Statistical Package for Social Sciences) version 28 (IBM Corp., Armonk, NY, USA). Quantitative data was tested for normality using the Shapiro-Wilk test, then described as mean ± SD (standard deviation) as well as minimum and maximum of the range, and compared using the ANOVA test. Qualitative data is described as numbers and percentage and compared using the χ^2 test and Fisher's exact test for variables with small expected numbers. Bonferroni test was used for post hoc comparisons. The level of significance was taken at *P*-value less than 0.050 was significant, otherwise was nonsignificant.

3. Results

We included a total of 20 patients with thalamic brain tumors in our study. Out of these patients, 7 were female, accounting for 35 % of the cases, while the remaining 13 were male, representing 65 % of the cases. The age of the patients at the time of presentation ranged from 2.7 to 16.2 years, with a mean age of 10.25 ± 3.41 years and an average 8.6 years old (Table 1).

Among the cases, 17 (85 %) patients exhibited symptoms indicative of increased intracranial pressure, including headache, vomiting, and blurred of vision. Contra-lateral weakness was observed in 16 (60 %) patients, while squint was reported in two (10 %) patients. Involuntary movements, specifically tremors, were experienced by one (5 %) patient, and facial palsy was observed in another patient. (Fig. 1) (Table 1).

All patients who presented to us with symptoms of increased intracranial tension underwent a ventriculo-peritoneal shunt on the affected side of the thalamic lesion, except in a few exceptional cases. The purpose of this procedure was to alleviate the symptoms and reduce the mid-line shift. In 70 % of the cases, the initial treatment approach involved the placement of a Ventriculoperitoneal shunt. In 60 % of the patients, stereotactic biopsy was

Table 1. Demographic data, Clinical picture, Pathological grading and complications of surgical outcome for Thalamic Tumors in pediatric patients.

Demographic	Number (N) = 20	Percent (100 %)
Male	13	65 %
Female	7	35 %
Clinical Picture ($n = 20$)		
Increased intracranial tension	17	85 %
Contralateral weakness	16	60 %
Squint	2	10 %
Tremors	1	5 %
Facial palsy	1	5 %
Pathological grading ($n = 20$)		
Pilocytic Astrocytoma G1	8	40 %
Gannglioglioma Grade 2	2	10 %
Ana Ganglioglioma Grade 3	4	20 %
Glioblastoma	2	10 %
Pxa	1	5 %
High Grade Glioma	3	15 %
Complication ($n = 20$)		
No complication	7	35 %
Progressive weakness	5	25 %
Cns infection	5	25 %
Intratumoral hge	2	10 %
Subdural hygroma	1	5 %

performed as the first step for diagnostic purposes. Transcortical excision with an external ventricular drain was undertaken in 25 % of the cases as the primary treatment, while the endoscopic biopsy was performed in one patient, constituting 5 % of the total.

Ventriculoperitoneal shunt served as the secondary treatment option in only 15 % of the cases, and transcortical excision was performed in 5 % of the cases after the alleviation of intracranial tension. Additionally, subtotal resection or debulking procedures were performed in 4 cases, while gross total resection or near-total resection was achieved in 2 cases. Out of the total patient population, 30 % of the individuals had tumors located in the right thalamus, while the remaining 70 % had tumors in the left thalamus.

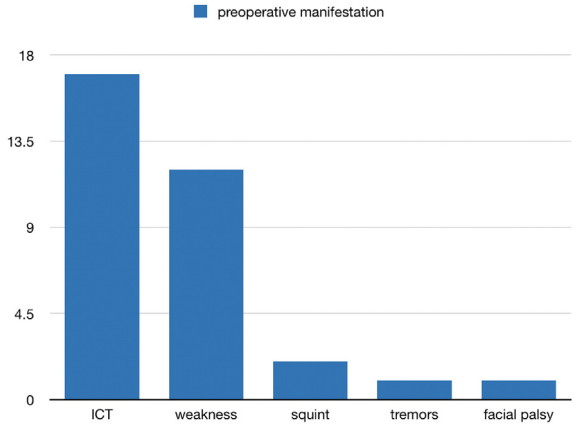

Fig. 1. Preoperative manifestation of thalamic tumors patients.

All patients underwent magnetic resonance imaging (MRI) upon admission as a baseline assessment. Subsequent imaging was performed at various intervals throughout the treatment and follow-up period to compare with the initial baseline scan. For patients presenting with symptoms of increased intracranial pressure (ICP), computed tomography (CT) scans were conducted both before and after the ventriculoperitoneal (VP) shunt procedure. The initial tumor volume, determined by MR imaging, ranged from 12.9 to 110.9 ml, with an average volume of 68.4 ml.

The examination of gross pathology revealed that among the cases studied, 10 cases were identified as high-grade glioma (HGG), while another 10 cases were classified as low-grade glioma (LGG). The histopathological analysis of the obtained samples provided further insights into the specific types and grades of the tumors. From the available data, it was determined that 40 % of the patients (8 cases) were diagnosed with pilocytic astrocytoma grade 1, while 20 % (4 cases) were identified as having anaplastic ganglioglioma grade 3, and 15 % (2 cases) were diagnosed as ganglioglioma grade 2. A single patient (5 %) exhibited anaplastic piloxanthoastrocytoma, and glioblastoma was observed in 10 % of the cases (2 cases). Furthermore, 15 % of the patients (3 cases) were diagnosed with high-grade glioma. These findings are illustrated in Fig. 2. (Table 1).

Among the 20 cases, complications were reported. Conversely, 7 (35 %) cases had no complications. Progressive weakness was observed in (25 %) 5 cases, while (25 %) 5 cases experienced fever accompanied by signs of infection. In (10 %) 2 cases, there was intratumoral hemorrhage following biopsy, and (5 %) 1 case developed a subdural hygroma (Table 1).

Chemotherapy was administered in 15 cases, while radiotherapy was utilized in 11 cases. The size of the tumor has a significant impact on the overall survival rate, as indicated by the results of the univariate linear regression analysis. The adjusted R-square value of 0.352 suggests that 35.2 % of the variation in survival can be attributed to the tumor volume. This relationship is statistically significant, as evidenced by the low *P*-value of 0.003. The unstandardized B coefficient of −0.541 indicates that for every unit increase in tumor volume, there is a corresponding decrease in survival. The 95 % confidence interval for the coefficient ranges from −0.879 to −0.204, further supporting the significance of this relationship.

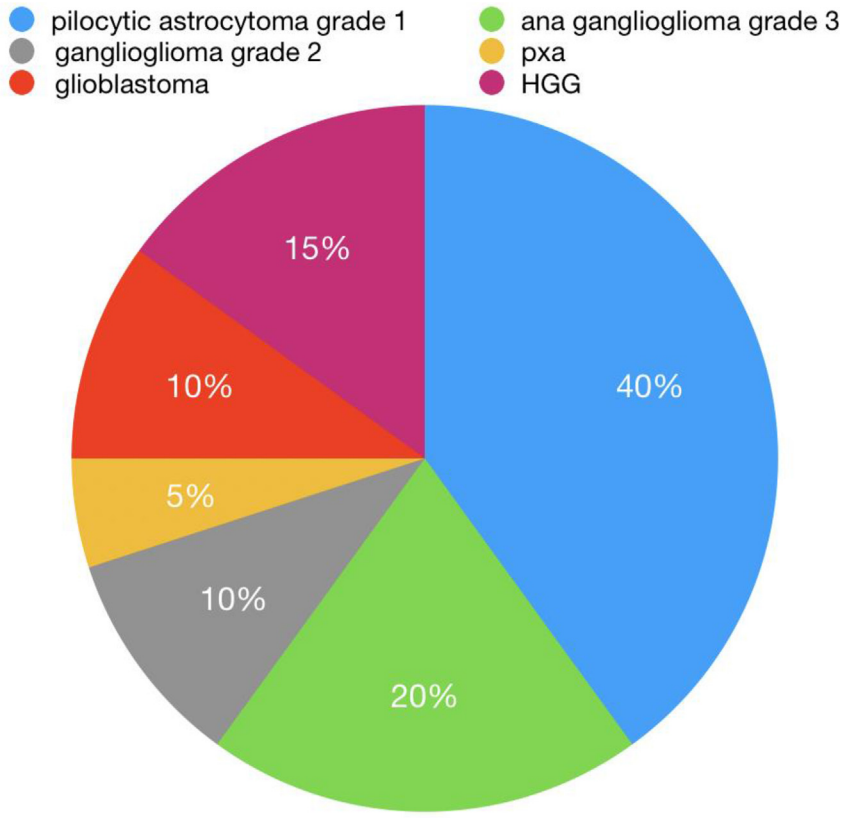

Fig. 2. Different histopathological types of thalamic tumors.

The findings suggest that patients who underwent biopsy had a higher progression-free survival (PFS) rate of 60.609 % compared with those who underwent debulking surgery, with a PFS rate of 22.350 %. The 95 % confidence interval for the biopsy group ranged from 33.258 % to 87.96 %, indicating a relatively wide range of possible PFS rates. Similarly, the confidence interval for the debulking group ranged from 3.496 % to 41.204 %.

However, when comparing the two groups using the log-rank test, the resulting *P*-value of 0.604 indicates that the observed difference in PFS rates between the biopsy and debulking groups is not statistically significant. (Fig. 3).

The PFS rate for patients diagnosed with LGG was found to be 102.413 %, with a 95 % confidence interval ranging from 83.368 % to 121.457 %. On the other hand, for patients diagnosed with HGG, the PFS rate was significantly lower at 8.489 %, with a 95 % confidence interval ranging from 4.658 % to 12.320 %.

The comparison of PFS rates between LGG and HGG groups using the log-rank test yielded a *P*-value of 0.000, indicating statistical significance. (Fig. 4).

The overall survival rate for patients who underwent biopsy was determined to be 74.062 %, with a 95 % confidence interval ranging from 46.989 % to 101.135 %. However, for patients who underwent debulking surgery, the overall survival rate was found to be 42.400 %, with a 95 % confidence interval ranging from 9.553 % to 23.676 %.

The *P*-value associated with the comparison of these two groups using the log-rank test was 0.611, indicating that the difference in overall survival between the biopsy and debulking groups is not statistically significant (Fig. 5).

4. Discussion

Approximately half of all brain tumors in children are located in the supratentorial region. Among these, the most common type of tumor is glioma, which originates from astrocytes [1,2,21]. According to various reports, the prevalence of thalamic tumors ranges from 0.84 % to 5.2 % [1,2,10–13,22]. The difficulty in distinguishing between primary tumors originating from the thalamus and secondary tumors arising from nearby structures contributes to the variation in estimated incidence rates

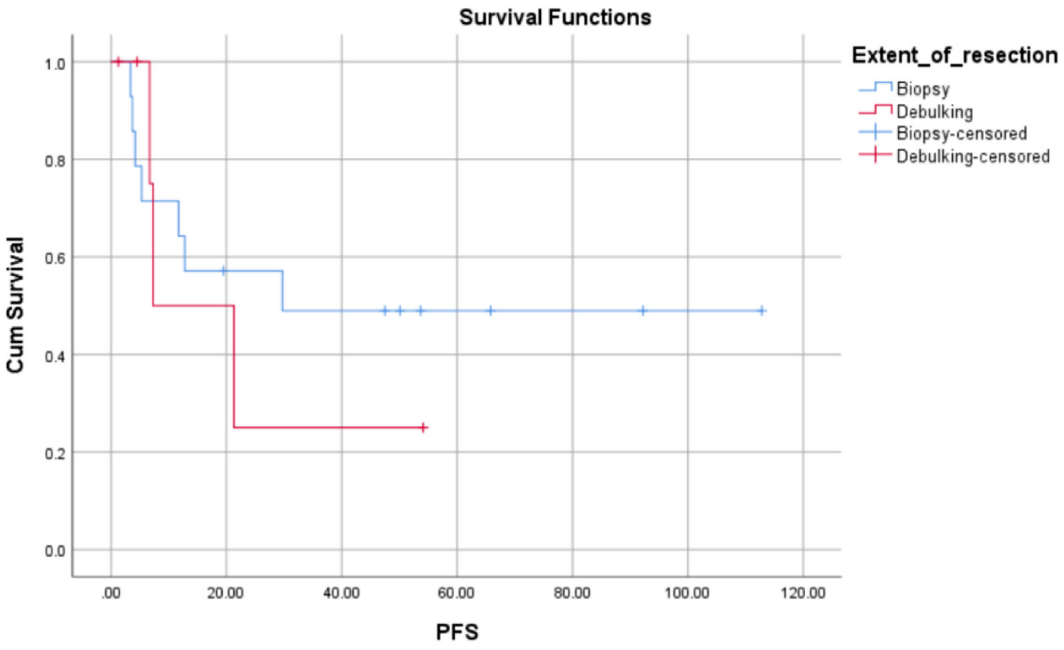

Fig. 3. Progression free survival for both biopsy and debulking group.

[8,14,17,20,23–25]. The age at which thalamic tumors are diagnosed shows a considerable range, spanning from 2.7 to 16.2 years according to our study findings. In our series, the average age at diagnosis was 8.6 years, which aligns with the results reported in other studies [6,15,16,26,27].

Common manifestations of thalamic tumors often encompass sensory and motor impairments, movement abnormalities, increased pressure within the skull, obstructive hydrocephalus, and seizures. Typically, the diagnosis is promptly established shortly after the onset of symptoms [2,5,9,10,12–14,20,24].

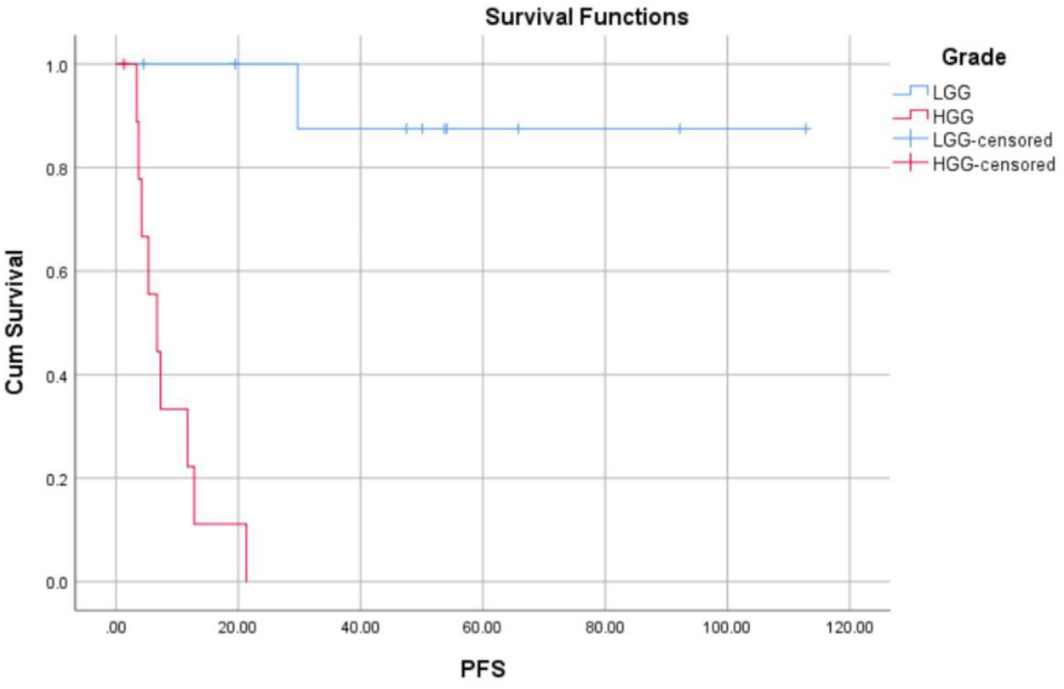

Fig. 4. Progression free survival for both low-grade glioma and high-grade glioma group.

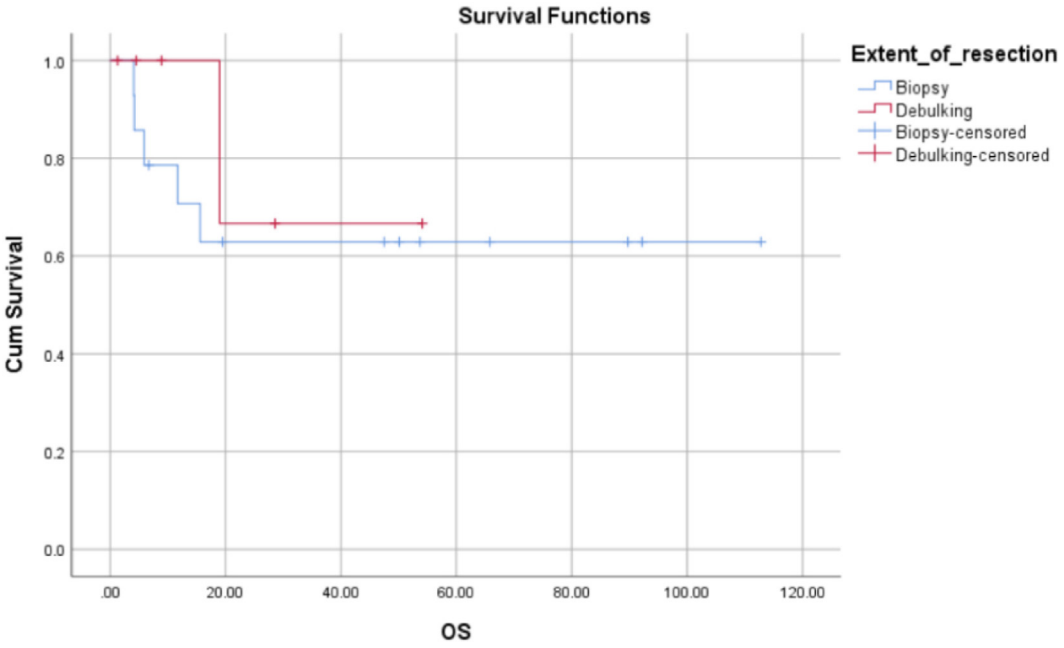

Fig. 5. Overall survival rate for both biopsy and debulking group.

Thalamocytuncular tumors, which emerge at the junction between the thalamus and cerebral peduncles, form a distinct subgroup among unilateral tumors. These tumors commonly exert pressure and compression on the descending pyramidal tract fibers located within the cerebral peduncles, resulting in contralateral weakness. Additionally, the majority of tumors in this subgroup were observed to extend into neighboring structures such as the basal nuclei, third ventricle, optic chiasma, and midbrain [4,6,7,14,17,28–30].

It should be emphasized that not all thalamic lesions are associated with tumors, particularly in the case of bilateral thalamic lesions. These lesions can also be caused by non-neoplastic conditions such as encephalitis or metabolic diseases. Therefore, it is crucial to accurately determine the neoplastic nature of these thalamic lesions before considering any potentially harmful adjuvant therapies. This confirmation is typically achieved through the use of magnetic resonance spectroscopy. If the lesions are confirmed to be neoplastic, a stereotactic biopsy is performed to establish a definitive diagnosis and identify the specific pathology involved [4–8,15,16,26,27,30].

In the majority of cases, stereotactic biopsy involving twelve biopsy samples was employed as the primary diagnostic procedure. However, direct debulking surgeries were performed in exceptional cases where patients experienced rapid deterioration of consciousness and significant midline shifts observed on neuroimaging. Stereotactic biopsy is considered a safe procedure with minimal associated morbidities and an extremely low mortality rate. Furthermore, it has shown a high diagnostic yield, providing accurate results for the identification of the tumor [6,14,26,27].

The treatment approach for these tumors involves a combination of chemotherapy and radiation therapy, which is determined based on the tumor type and the age of the patient. Chemotherapy is considered a primary treatment option for patients who are not suitable for surgery and have LGG, regardless of their age. It serves the purpose of delaying or avoiding the need for radiation therapy, which offers slightly better tumor control but comes with increased toxicity. Additionally, chemotherapy is utilized in cases where incomplete resections have occurred or when there is evidence of tumor progression in patients with LGGs. For children diagnosed with high-grade tumors, radiation therapy is typically administered regardless of the extent of surgical resection. In some cases, chemotherapeutic agents are also employed, although the outcomes have been mixed. In the case of small children and infants with low-grade gliomas, chemotherapy is employed after surgical removal to delay or substitute the need for radiation therapy. This approach aims to reduce or eliminate the potential long-term effects associated with radiation treatment [7,12,14,16,22,24,25,27,30].

Our study showed that tumor size has a significant effect on overall survival. The results of the linear regression analysis indicate that 35.2 % of the variation in survival can be attributed to tumor volume. The negative coefficient (−0.541) suggests

that as tumor volume increases, survival decreases. This relationship is statistically significant [15,16,26,27].

Previous findings indicate that surgical excision alone does not prevent disease progression in patients with high-grade tumors, but it can certainly extend their overall survival. The impact of surgical excision on outcomes differs between high-grade and low-grade tumors, where it significantly influences the outcome in cases of low-grade tumors. Furthermore, the results strongly indicate that adjuvant therapy, encompassing both chemotherapy and radiotherapy, does not provide any advantages in impeding the progression of high-grade tumors. The analysis highlighted the influence of tumor grade on PFS and overall survival. Patients diagnosed with LGG had a significantly higher PFS rate 102.413 % compared with those diagnosed with HGG 8.489 %. The log-rank test confirms the statistical significance of this difference (P-value = 0.000). These results emphasize the importance of tumor grade in predicting the prognosis of pediatric thalamic brain tumor patients [5–7,15,16,26,27].

There are few data in the literature on the clinical outcome of patients undergoing resective surgery for thalamic tumors after resective surgery because these tumors are uncommon and are rarely operated on. For that reason, all series are retrospective, with a variety of different histopathological diagnoses [5–7,14,15,26–28].

The approach to thalamic tumors needs to be planned according to the location of critical neural structures. Gross Total Resection (GTR) or Subtotal Resection (STR) of thalamic tumors in children bears acceptable morbidity and may even improve preoperative deficits. Surgery alone can be curative in low-grade tumors; in high-grade or infiltrating tumors, GTR is only part of the overall. Finally, the study evaluates the overall survival rates between the biopsy and debulking groups [4,8,9,11,14–16,22,23,27]. Our analysis shows that there is no statistically significant difference in overall survival between these two groups (P-value = 0.611). This suggests that the choice of surgical approach (biopsy or debulking) does not significantly impact the overall survival outcomes for patients in this study.

4.1. Conclusion

Thalamic brain tumors commonly observed in the pediatric age group are predominantly low-grade pilocytic astrocytomas. Typically, these tumors manifest through symptoms related to increased intracranial pressure and/or contralateral weakness. Patients with high-grade tumors, whether treated with stereotactic biopsy or debulking surgery, received adjuvant therapy, including chemotherapy alone or a combination of chemotherapy and radiotherapy. Although this adjuvant therapy did not exhibit significant effectiveness in preventing disease progression, it generally contributed to extended overall survival. The outcome of patients was influenced by two factors: the histological grading of the tumor and the extent of surgical intervention. While surgical excision did not have a substantial impact on the outcome of high-grade tumors, it played a significant role in improving the outcome of low-grade tumors. Stereotactic biopsy emerged as the preferred diagnostic technique for determining the histopathological types of thalamic tumors, guiding their management, and facilitating decisions regarding surgical debulking or adjuvant therapy.

Funds

No funds

Conflicts of interest

No conflict of interests.

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