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ORIGINAL ARTICLE

Thalamic tumors in children: case series from our institution and literature review

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Abstract

Purpose To describe a case series of children with thalamic tumors treated at our institution in a 5-year period.

Method A retrospective and observational study was performed. The records of 15 patients between 2013 and 2018 were analyzed.

Results From 2013 to 2018, 15 patients were treated at our institution. The male to female index was 1.5, and the median age was 8.9 (IQR 4.75–13). Seven (46%) tumors were left-sided, seven (46%) were right-sided, and one (6%) was bilateral. All patients were symptomatic at the time of treatment. Motor deficit was the most common form of presentation (73%). Gross-total resection was performed in two (13.3%) patients, subtotal resection was performed in two other patients (13.3%), and for the rest of the patients (73.3%), the chosen surgical approach was a stereotactic-guided biopsy. The average of procedures was 3.4, mostly related to the treatment for hydrocephalus. Twelve patients (80%) received treatment for hydrocephalus. Nine patients (75%) were treated with ventriculoperitoneal shunts, and four patients (33%) underwent endoscopic third ventriculostomy. High-grade tumors predominated. Grade IV tumors were diagnosed in six patients (40%), followed by grade III in four patients (26.6%), grade II in three (20%) patients, and grade I in two (13.3%) patients. Chemotherapy was given in 93% of the cases, being temozolomide, the most used drug.

Conclusion The clinical and surgical approaches for thalamic tumors in children have changed over time. At our institution, the lesser invasive surgical procedures are now being used more frequently.

Keywords Thalamic tumors · Stereotactic biopsy · High-grade glioma · Low-grade glioma · Case series

Introduction

Thalamic tumors in children are rare, representing 0.84–5.2% of brain tumor pathology [1–4]. Before the advent of neuroimaging technologies such as tractography, microsurgery, neuronavigation, and improvements in postoperative care, surgery for this pathology was associated with high morbidity and mortality. Even though several published series such as Cinalli et al. and Bilginer et al. show evidence in favor of gross-total resection (GTR) for low-grade lesions, the benefits of this approach for high-grade lesions are still not clear [5, 6].

The role of chemotherapy and radiotherapy has changed throughout time, being very important as an adjuvant treatment in centers where GTR is the first treatment option for

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low-grade tumors, and remaining as the gold standard in some institutions, regardless of the histological findings.

Methods

We conducted a 5-year retrospective and observational study of patients with thalamic tumors treated in the Department of Pediatric Neurosurgery at the Hospital "Juan P. Garrahan" in Buenos Aires, Argentina. We excluded patients with tumors arising from adjacent structures that invaded the thalamus.

Patient population

From 2013 to 2018, 15 patients have been treated in our institution. Medical records, image studies, and operative and pathological reports were retrospectively analyzed.

Clinical and neuroimaging data

Age, gender, clinical presentation, previous treatments, surgical approach, histological findings, number of surgical interventions, presence and treatment for hydrocephalus, chemotherapy and radiotherapy scheme applied, immediate postoperative outcome, and final outcome were reviewed.

On preoperative imaging studies, tumors were classified as unilateral, bilateral, or thalamopeduncular according to the surgical classification suggested by Puget et al.

We defined GTR as the absence of macroscopic lesion after surgery, subtotal resection as the resection of 90% or more of the lesion, and partial resection as anything less than that.

Analysis

Continuous variables were expressed as mean ± standard deviation and categorical variables as counts (percentage). For descriptive purposes, survival analysis was performed by fitting Kaplan-Meier curves censoring patients that were lost to follow-up. All analyses were performed using Python scientific library, and survival curves were done using the lifelines package.

Results

From 2013 to 2018, 15 patients were treated in our institution. There were 9 boys (60%) and 6 girls (40%) with a male to female ratio of 1.5. The mean age was 8.9 (IQR 4.75–13) (Table 1).

Clinical and radiological features

Eleven (73%) patients presented with a motor deficit, which was the most common form of presentation and was associated with intracranial hypertension in 54% (6) of the cases. Four patients (26%) presented with altered sensorium in the majority due to hydrocephalus, and only in one patient, this was due to intratumoral bleeding with ventricular hemorrhage.

Seven (46%) tumors were left-sided, seven (46%) were right-sided, and one (6%) was bilateral (Fig. 1). All patients were symptomatic at the time of treatment.

According to Puget's categorization of thalamic tumors in children, nine (60%) were unilateral thalamic, five (33%) were thalamopeduncular, and one (6%) was bilateral.

Nine (60%) of our patients presented with a solid non-enhancing mass, followed up by an equal distribution between solid enhancing (13.3%), cystic non-enhancing (13.3%), and cystic enhancing (13.3%) lesions.

Surgical approach/treatment

In two (13.3%) patients, GTR was performed through a transparietal approach to the lateral ventricles. In two other patients (13.3%), subtotal resection was achieved through a transparietal and interhemispheric approach. For the rest of the patients (73.3%), the chosen surgical procedure was a stereotactic-guided biopsy.

The average of procedures per patient was 3.4; most of them related to the treatment for hydrocephalus.

Management of hydrocephalus

Twelve patients (80%) received treatment for hydrocephalus. Nine patients (75%) were treated with ventriculoperitoneal shunts (VP shunts); five of these patients underwent septostomy. Four patients (33%) underwent endoscopic third ventriculostomy (ETV), and three of them underwent septostomy at the same time. Subsequently, two of them (50%) later required the placement of a VP shunt.

Histological findings

High-grade tumors predominated. Grade IV tumors were diagnosed in six patients (40%), followed by grade III in four patients (26%), grade II in three patients (20%), and grade I in two patients (13%).Among grade IV tumors, five (33%) corresponded to glioblastomas and one to an atypical rhabdoid teratoid tumor. Among grade III tumors, three (75%) corresponded to anaplastic astrocytomas and one (25%) to an anaplastic tumor with glial and neuronal components. All grade II lesions were diffuse infiltrating gliomas. And finally, grade I tumors consisted of pilocytic astrocytoma and a ganglioglioma (Table 2).

Table 1 Summary of thalamic tumors in the 15 patients

Case	Sex	Age (years)	Location	Histology	Approach	Treatment for hydrocephalus	Chemotherapy
1	F	4	Left/thalamopeduncular	Glioblastoma	Stereotactic biopsy	First ETV then VP shunt	Temozolomide
2	M	0.8	Left/thalamopeduncular	Anaplastic tumor with glial and neuronal components.	Transparietal approach to the lateral ventricles	VP shunt	Temozolomide
3	M	13	Left/thalamopeduncular	Glioblastoma	Stereotactic biopsy	VP shunt	Temozolomide + bevacizumab
4	M	13	Right/thalamic	Glioblastoma	Transparietal approach to the lateral ventricles	VP shunt	Temozolomide
5	F	7	Bilateral/thalamic	Anaplastic astrocytoma	Stereotactic biopsy	VP shunt	Temozolomide
6	M	11	Right/thalamic	Pilocytic astrocytoma	Stereotactic biopsy	VP shunt + septostomy	Vincristine and carboplatin
7	F	10	Right/thalamic	Glioblastoma	Stereotactic biopsy	ETV + septostomy	Temozolomide + bevacizumab
8	M	8	Right/thalamopeduncular	Diffuse astrocytoma	Stereotactic biopsy	VP shunt + septostomy	Vincristine and carboplatin
9	F	15	Left/thalamic	Diffuse astrocytoma	Stereotactic biopsy	ETV then ventriculoperiton-eal shunt	Temozolomide + bevacizumab
10	F	10	Left/thalamopeduncular	Diffuse astrocytoma	Stereotactic biopsy	VP shunt + septostomy	Temozolomide + bevacizumab
11	M	2	Left/thalamic	Atypical teratoid rhabdoid tumor	Transparietal approach to the lateral ventricles	No	Doxorubicin, topotecan, etoposide, carboplatin, and ifosfamide.
12	M	15	Right/thalamic	Ganglioglioma	Interhemispheric	No	No
13	F	15	Right/thalamic	Anaplastic astrocytoma	Endoscopic biopsy	VP shunt + septostomy	Temozolomide
14	M	7	Right/thalamic	Anaplastic astrocytoma	Transparietal approach to the lateral ventricles	First ETV + septostomy then VP shunt	Temozolomide
15	F	3	Left/thalamic	Glioblastoma	Stereotactic biopsy	No	Temozolomide

Chemotherapy and radiotherapy

Fourteen (93%) patients received chemotherapy treatment. Eleven (78%) of them were treated with temozolomide, and three received bevacizumab posteriorly. Two (14%) patients received combined treatments that included vincristine and carboplatin (SIOP protocol). Only one (8%) patient received therapy with doxorubicin, topotecan, etoposide, carboplatin, and ifosfamide.

Whole-brain radiotherapy was indicated in eleven patients (73%).

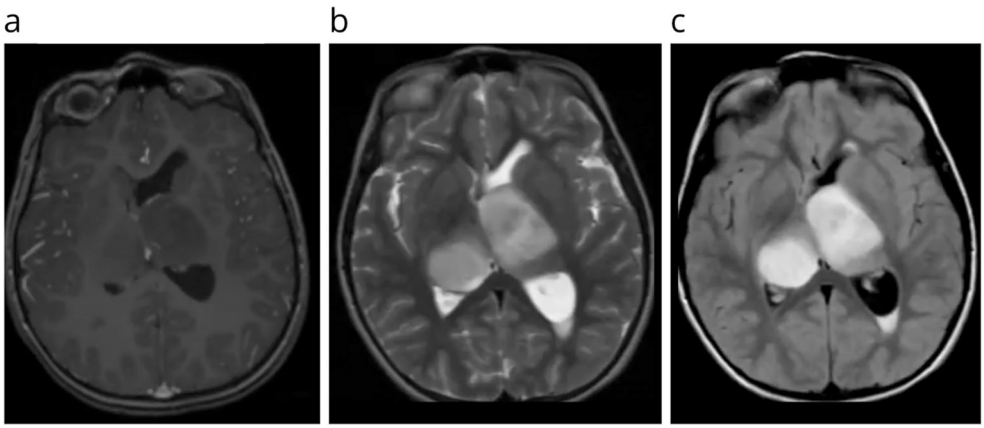

Fig. 1 A 7-year-old girl with a history of hemiparesis. MRI showed a bilateral thalamic tumor. A stereotactic biopsy was performed. Histological findings revealed an anaplastic astrocytoma. **a** T1-gadolinium postcontrast sequence. **b** T2-weighted image (T2WI). **c** Fluid-attenuated inversion recovery (FLAIR) sequence

Table 2 Summary of histological diagnosis in the 15 patients

Tumor type	WHO grade	No. of patients
Low grade		
Diffuse astrocytoma	II	3
Ganglioglioma	I	1
Pilocytic astrocytoma	I	1
High grade		
Anaplastic tumor with glial and neuronal component	III	3
Anaplastic astrocytoma	IV	5
Atypical teratoid rhabdoid tumor	IV	1
Glioblastoma	III	1

Outcome

Figure 2 shows the Kaplan-Meier survival curves for all patients and stratified by histology and location.

Among the 4 patients who died during follow-up, the median survival time was 13 months (range 11–48). All of them had high-grade lesions. Among the rest, the median follow-up was 22 months (range 12–84), including 4 that were lost to follow-up and 7 that continue to receive care at our institution.

Dissemination was seen in 3 (20%) patients. Two of them presented leptomeningeal dissemination (LMD), and one of them also had optic tract involvement. The last patient presented intramedullary disease (Fig. 3).

Discussion

Supratentorial lesions represent about 50% of intracranial neoplasms in children. Among these, the most frequent tumors are gliomas arising from astrocytes [1]. Thalamic tumors represent between 0.84 and 5.2% according to different reports [1–4]. The challenge in identifying tumors that arise from the thalamus (primary tumors) from those originating from adjacent structures (secondary tumors) is one of the reasons for the inconsistency in incidence estimations [7]. The mean age of diagnosis varies from 7.7 to 11.6 [9]. In our series, the mean age was 8.9 (IQR 4.75–13).

Symptoms usually include sensory and motor deficits, movement disorders, intracranial hypertension, obstructive hydrocephalus, and seizures. Typically, the diagnosis takes a short time since the beginning of the symptoms [8, 9]. Generally, in bilateral lesions, the duration of the symptoms is shorter compared with unilateral lesions (2.5 versus 8.7 months) [10].

Neuroimaging findings showed a prevalence of unilateral thalamic lesions, and the most frequent pattern was that of a solid non-enhancing lesion in 9 of our patients. Postcontrast enhancement was only evident in 26% of the patients.

As the opposite, as seen in our case series, most reports on thalamic tumors show a prevalence of low-grade lesions followed up in frequency by high-grade gliomas [7]. It is worth mentioning that one of the patients in our series presented an embryonal tumor, which is relatively rare and has not been extensively described in the literature [9, 11].

Hydrocephalus is a significant cause of morbidity in these patients since lesions tend to obliterate the posterior third ventricle and the foramina of Monro generating an obstruction to CSF flow. In these cases, endoscopic septostomy and ventriculostomy might be the treatment of choice, similarly as the placement of a VP shunt. Other causes of hydrocephalus might be associated with hemorrhage, craniotomy, infection, and tumor dissemination.

Thalamic lesions are not easily accessible, and surgery may lead to severe morbidity. Nevertheless, low-grade thalamic tumors present better survival rates when more than 90% of the tumor is resected, according to Puget et al. [3]. Gross-total resection confirmed with postoperative imaging is becoming the target in these tumors.

For high-grade lesions, the survival rate reported usually does not exceed the year since the diagnosis. Some authors suggest the lack of invasion of the pyramidal tract and brainstem as a criterion for surgical resection [12]. However, for these lesions, the role of the surgery and the efficacy of a cytoreductive procedure are controversial since no evidence suggests that overall survival improves even with GTR [5, 8]. As we found in our series, recurrence and dissemination, even after successful resection, have been reported for these tumors [12]. Further studies must be performed to create better evidence on aggressive resective surgery for high-grade tumors.

The role of chemotherapy and radiation therapy in the treatment of these tumors depends on the type of tumor and the patient's age. Chemotherapy is accepted as a primary treatment for non-surgical patients with low-grade glioma (LGG) of all ages since it is useful for postponement or omission of radiotherapy, which has proven a slightly better tumor control but with higher toxicity. It is also used in patients with LGGs that underwent incomplete resections or with evidence of progression. Children with high-grade tumors are usually treated with radiation therapy independently of the extent of resection, and chemotherapeutic agents have also been used, with mixed results. In small children and infants with low-grade gliomas, it is used after surgical resection to delay or replace radiation therapy. This reduces or eliminates the long-term effects of radiation [13–16].

In our case series, 73.3% of the patients underwent a partial resection (biopsy). GTR and subtotal resections were only achieved in 26.6% of the patients. Ninety-three percent (93%) of the patients received chemotherapy, and 73% radiotherapy. We were not able to determine surgical morbidity due

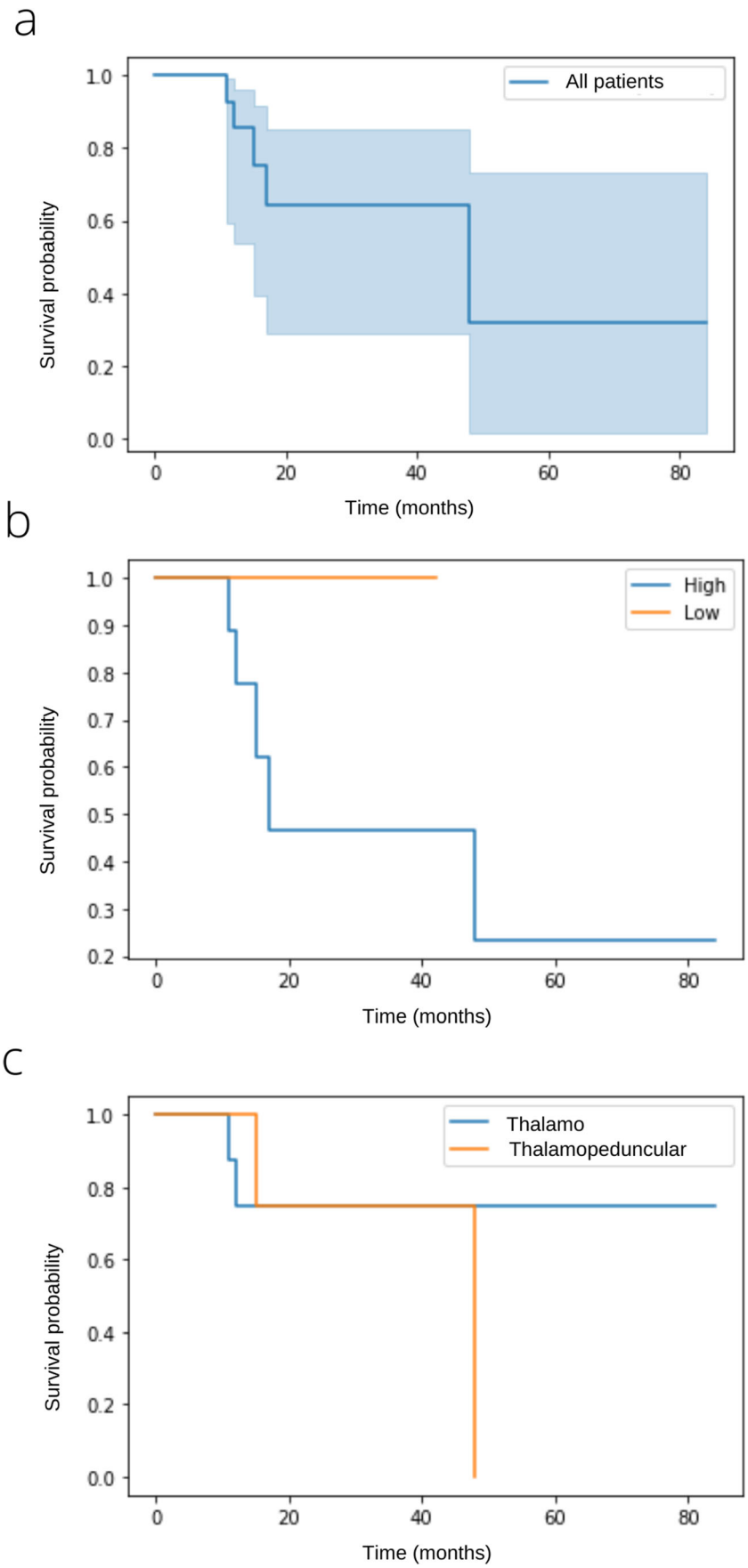

Fig. 2 Kaplan-Meier survival curves. **a** For all patients. **b** For high and low-grade lesions. **c** According to the localization (thalamic or thalamopeduncular)

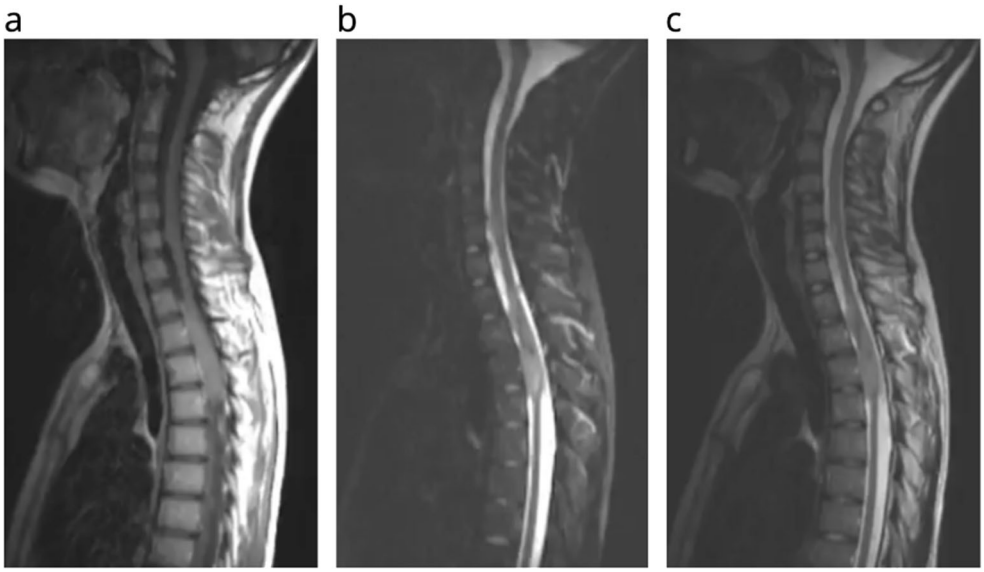

Fig. 3 MRI showing intramedullary dissemination in a 13-year-old boy with diagnosis of left thalamic glioblastoma after treatment with temozolomide and bevacizumab, and whole-brain radiation therapy. **a** T1 sequence. **b** Short-TI inversion recovery sequence (STIR). **c** T2-weighted image (T2WI)

to the lack of evaluation with a validated and standardized clinical score.

The surgical approach for each case was decided in multidisciplinary meetings, and it was tailored for each patient according to the lesion's characteristics, surgeon's experience, resources available at the time of the procedure, or clinical limitations regarding the patient's status, without having a unified criterion for the selection of the surgical approach. Despite this, we can observe that, in our series, the general trend was towards less invasive procedures.

At our institution, in the past, the first surgical approach was gross-total resection. Although poorly documented, limited data from previous years (unpublished) show that outcomes observed in most patients were poor, and because of this, we believe that functional preservation was preferred over more radical procedures in the last few years.

Strengths and limitations

This study has some limitations. This is a retrospective study with only a descriptive analysis. Although the number of patients that were treated at this institution in 5 years is higher than the incidence reported in other series, the sample size is still modest. However, we consider this series worth reporting due to the currently limited amount of pediatric thalamic tumor case series described in the literature.

Conclusion

The clinical and surgical approach for thalamic tumors in children has changed over time. At our institution, high-grade lesions predominated, and the lesser invasive surgical approaches were the main chosen option for treatment.

Compliance with ethical standards

Conflict of interest The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Ethics approval All procedures performed in the studies involving human participants followed the ethical standards of the institutional and national research committee and the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Consent to participate Not applicable.

Consent for publication Not applicable.

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