Surgical treatment of thalamic tumors in children

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OBJECTIVE In the past, the outcome of surgical treatment for thalamic tumor was poor. These lesions were often considered inoperable. However, contemporary microsurgical techniques, together with improvements in neuroimaging that enable accurate presurgical planning, allow resection to be accomplished in a safer way.

METHODS The medical records, imaging studies, and operative and pathology reports obtained for pediatric patients who were treated for thalamic tumors at the authors' department were reviewed. Neuronavigation and intraoperative monitoring of motor and somatosensory evoked potentials were used. Preoperative tractography, which helped to identify internal capsule fibers, was very important in selecting the surgical strategy. Postoperatively, an MRI study performed within 24 hours was used to assess the extent of tumor resection as partial ($\leq 90\%$), subtotal ($> 90\%$), or gross total (no residual tumor).

RESULTS Since 2002, 27 children with thalamic tumors have been treated at the authors' department. There were 9 patients with unilateral thalamic tumors, 16 with thalamopeduncular tumors, and 2 with a bilateral tumor. These last 2 patients underwent endoscopic biopsy and implantation of a ventriculoperitoneal shunt. Thirty-nine tumor debulking procedures were performed in the remaining 25 patients. Different surgical approaches were chosen according to tumor location and displacement of the posterior limb of the internal capsule (as studied on axial T2-weighted MRI) and corticospinal tract (as studied on diffusion tensor imaging with tractography, after it became available). In 12 cases, multiple procedures were performed; in 7 cases, these were done as part of a planned multistage resection. In the remaining 5 cases, the second procedure was necessary because of late recurrence or regrowth of residual tumor.

At the end of the surgical phase, of 25 patients, 15 (60%) achieved a gross-total resection, 4 (16%) achieved a subtotal resection, and 6 (24%) achieved a partial resection. Eighteen patients harbored low-grade tumors in our series. In this group, the mean follow-up was 45 months (range 4–132 months). At the end of follow-up, 1 patient was dead, 12 patients were alive with no evidence of disease, 4 patients were alive with stable disease, and 1 was lost to follow-up. All patients were independent in their daily lives. The outcome of high-grade tumors in 9 patients was very poor: 2 patients died immediately after surgery, 6 died of progressive disease, and 1 was alive with residual disease at the time of this report.

CONCLUSIONS This institutional review seems to offer further evidence in favor of attempts at radical resection in pediatric patients harboring unilateral thalamic or thalamopeduncular tumors. In low-grade gliomas, radical resection in a single or staged procedure can be curative without complementary treatment. Recurrences or residual regrowth can be safely managed surgically. In high-grade tumors, the role of and opportunity for radical or partial resection remains a matter of debate.

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KEY WORDS thalamic tumor; glioma; transcallosal approach; subtemporal approach; transtentorial approach; choroidal approach; multimodality treatment; bleeding tumors; oncology

ABBREVIATIONS CST = corticospinal tract; DNT = dysembryoplastic neuroepithelial tumor; DTI = diffusion tensor imaging; GCS = Glasgow Coma Scale; GTR = gross-total resection; ICP = intracranial pressure; MTG = middle temporal gyrus; PLIC = posterior limb of the internal capsule; PR = partial resection; STR = subtotal resection; VP = ventriculoperitoneal.

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THALAMIC tumors are relatively uncommon: they account for approximately 1%–5% of all brain tumors in children,^{3,6,9,12,29,31,32,37} although differences in nomenclature and a limited number of exclusively pediatric series make it difficult to quantify. In the past, the outcome of surgical treatment for thalamic tumors was poor. These lesions were once considered inoperable because of the high risk of postoperative morbidity and mortality.^{3,4,6,8,9,11,13,20,22,36} However, contemporary microsurgical techniques, improvements in neuroimaging that enable accurate presurgical planning and image-guided surgery, and progress in intensive care allow safer and more extensive resection of these neoplasms.^{1,3,8,15,21,24,27,29,31,32,34}

In Toronto in 1984, Bernstein et al.⁶ were the first to perform 21 (35%) partial resections (PRs) in 60 patients, and finally concluded that the better choice was a resection, if deemed safe, followed by irradiation in selected cases. Beks et al.⁴ in 1987 and Franzini et al.¹⁷ in 1994 instead advocated a biopsy followed by irradiation as the first line of treatment. In the following years, Villarejo et al.³⁸ and Cuccia and Monges¹² reported surgical series of thalamic tumors in children, with low morbidity and mortality.

Ozek and Türe²⁹ in 2002 remarked on the progressive change in mentality in pediatric neurosurgeons regarding the first line of treatment of thalamic tumors and on their view that radical resection was the goal of treatment, especially in low-grade tumors. Albright,¹ analyzing his series in 2004 and reviewing the 4 major surgical series that had previously been reported, found that subtotal resection (STR) and gross-total resection (GTR) were achieved in 93% of the cases, with low mortality (3%) and acceptable morbidity (12.5%). However, he questioned the utility of aggressive resection in the case of high-grade tumors and discouraged attempts at GTR in the case of thalamopeduncular tumors. In 2002, Tomita and Cortes³⁵ instead reported on 5 patients who had peduncular low-grade astrocytomas with thalamic extension, in whom they achieved GTR and STR, with acceptable morbidity and no mortality. Subsequently, Puget et al.³¹ and Baroncini et al.³ described safe total and partial resection of thalamic tumors that had midbrain extension.

Puget et al. proposed a surgical classification of thalamic tumors and placed those with predominant and symmetrical midbrain extension in a group called thalamopeduncular. However, the main contribution of these investigators was the analysis of the largest series of thalamic tumors, which included 69 children (54 with unilateral thalamic presentation) in whom the authors observed that short duration of symptoms, large tumors, incomplete resection, and high-grade histology were independent poor prognostic factors with statistical significance. Broadway et al.⁸ presented their experience with exclusive thalamopeduncular tumors in children, remarking on the utility of diffusion tensor imaging (DTI) in presurgical MRI for planning the safest approach and obtain low levels of morbidity, and even improvement of presurgical motor deficits in some cases. When considering only the lesions with high-grade histological findings, Kramm et al.²³ showed, in a large retrospective multiinstitutional series of 99 thalamic high-grade gliomas in pediatric patients, that ag-

gressive surgical debulking, achieving either STR (> 90% removal) or PR ($\leq$ 90% removal), was associated with better event-free and overall survival than simple biopsy or straightforward radiotherapy without histological assessment. Finally, Bilginer et al.,⁷ reporting their experience with 45 thalamic tumors in pediatric patients, concluded that resective surgery for unilateral thalamic tumors is associated with low surgery-related morbidity and mortality.

These data from the literature suggest that an aggressive resection is associated with improved survival, especially in patients with low-grade tumors. There is no consensus, however, about the management of children with high-grade tumors in this region. Chemotherapy and radiotherapy are still considered to be the gold standard of treatment in many centers, regardless of histological findings, with a variable success rate.^{16,18,19,23,28,33} We performed a retrospective review of pediatric patients treated at our department for thalamic tumors in the last 14 years. We report our experience with resective surgery in the context of a multimodality treatment of these tumors.

Methods

Patient Population

Since 2002, 27 children with thalamic tumors have been treated at the Department of Pediatric Neurosurgery of Santobono-Pausilipon Children's Hospital of Naples, which is the only referral center for pediatric neurosurgery for a population area of 3 million. Medical records, imaging studies, and operative and pathological reports were retrospectively analyzed.

Clinical and Neuroimaging Data

Clinical and radiological characteristics of the patients, including clinical presentation, previous treatment, immediate postoperative outcome, and final outcome, were reviewed. All patients were studied using contrast-enhanced MRI. Since 2009, diffusion tensor echo planar images with tractography have also been acquired and analyzed before surgery. All radiological studies, both pre- and postoperative, were retrospectively reviewed by a neuro-radiologist (D.C.) who was blinded to histological findings and clinical conditions, to assess at presentation the tumor volume (in cm³), tumor site and extension, radiological features, displacement of the corticospinal tract (CST) on T2-weighted and FLAIR MR images, pyramidal tract displacement or infiltration on DTI when available, and presence of hydrocephalus.¹⁰ On preoperative imaging studies, tumors were classified as unilateral, bilateral, or thalamopeduncular according to the surgical classification suggested by Puget et al.³¹ The presence of hydrocephalus, heterogeneity and cystic nature of the lesions, and presence of calcification, edema, and necrosis were noted as features on T1- and T2-weighted MRI.

All immediate postoperative MRI studies, performed within 24 hours in all cases, were evaluated to assess the extent of resection and the existence of postoperative surgery-related complications. All follow-up MRI studies performed at 3 months postsurgery, then every 6 months for 3 years, and then every year for the following 3 years were retrospectively reviewed to assess the presence and

timing of recurrence or regrowth of postoperative residual tumor. The timing of follow-up MRI was of course adapted to possible modifications of clinical conditions.

Surgical Approach

All patients, except the ones harboring a bilateral tumor, underwent surgical treatment with an attempt to achieve radical tumor resection by using a microsurgical technique. Neuronavigation and intraoperative monitoring of motor and somatosensory evoked potentials were systematically used. Since April 2011, intraoperative CT scanning has been available and has also been used. The goal of each operation was the resection of the entire contrast-enhancing mass, defined mainly on MRI sequences and checked before closing with the support of intraoperative CT, after it became available. In cases with associated hydrocephalus, this was always treated before tumor resection (see *Results* section). The surgical approach was chosen based on the location of the lesion in the thalamus and the tumor's relationship with surrounding structures that it had displaced.

As a general rule, the approach was planned to traverse nonessential brain tissue, avoiding the posterior limb of the internal capsule (PLIC) identified on the axial T2-weighted MRI or the CST identified on the DTI (when this was obtained), and maximally preserving displaced or compressed normal thalamic structures. Although MRI was extremely helpful in determining the position of the CST on multiplanar 2D imaging, the 3D reconstruction of the CST obtained with DTI offers the surgeon a view of the relationship between the tumor, the CST, and the planned trajectory, increasing the understanding of the anatomical deformations and displacements induced by the tumor and enhancing the surgeon's awareness regarding possible pitfalls encountered due to the surgical trajectory and during tumor debulking. Although impossible to quantify in a retrospective series and for each individual case, careful analysis and dynamic manipulation of the 3D DTI model of CST with the neuroradiologist (Videos 1–4) was always key to the choice of the approach, offering visual and anatomical information that takes longer and is less precise to reconstruct on the basis of multiplanar 2D MR images alone.

VIDEO 1. This video clip shows the removal of a right thalamopuncular tumor (low-grade astrocytoma) in a 3-year-old boy through 2 surgical procedures, via a transtemporal approach. Copyright Giuseppe Cinalli. Published with permission. [Click here to view.](#)

VIDEO 2. This video clip shows the surgical removal of a right thalamic tumor (grade IV glioma) via an interhemispheric transcallosal approach in a 13-year-old girl. Copyright Giuseppe Cinalli. Published with permission. [Click here to view.](#)

VIDEO 3. This video clip shows the surgical removal of a left thalamopuncular tumor (low-grade glioma) in a 9-year-old boy through 2 surgical procedures, via an interhemispheric transcallosal transchoroidal approach. Copyright Giuseppe Cinalli. Published with permission. [Click here to view.](#)

VIDEO 4. This video shows the surgical removal of a right posterior thalamic tumor (low-grade glioma) in a 12-year-old boy via a posterior interhemispheric transtentorial approach. Copyright Giuseppe Cinalli. Published with permission. [Click here to view.](#)

Finally, various surgical approaches (middle temporal gyrus [MTG], anterior interhemispheric transcallosal, anterior interhemispheric transcallosal transchoroidal, posterior interhemispheric parasplenial, posterior interhemispheric transtentorial, and subtemporal) were used.

Postoperatively, on postcontrast MRI performed within 24 hours, the extent of tumor resection was defined as PR ($\leq 90\%$), STR ($> 90\%$), or GTR (no residual tumor), based on the imaging findings.

Follow-Up and Adjuvant Therapy

In accordance with histological findings, clinical status, and postoperative imaging, the best treatment was chosen by a multidisciplinary team consisting of neurosurgeons, oncologists, and radiotherapists. For low-grade tumors, MRI follow-up at 3 months without adjuvant treatment was chosen in most cases. For high-grade tumors, radiotherapy was used with different protocols of chemotherapy in accordance with the histological findings. A tumor was defined as recurring if the patient experienced the appearance of previously nonexistent contrast-enhancing tissue in the surgical cavity, or in the case of increased volume of a known postoperative tumor residue. Patients who were still alive were categorized according to the status of the tumor and their grade of dependence at the last follow-up visit.

Results

From 2002 to 2016, 27 children with thalamic tumors underwent operation in our center. There were 10 girls (37%) and 17 boys (63%), with a female/male ratio of 1:1.85. The mean age at the time of tumor resection was 9.53 years (range 3–17 years). Five of these children were referred after previous surgical procedures and/or other treatment modalities. The mean follow-up was 46 months for low-grade tumors and 15 months for high-grade tumors. Nine patients died during follow-up, 11 are alive in complete remission, and 7 are alive with stable disease (Tables 1 and 2).

Clinical and Radiological Features

Sixteen tumors were right-sided (59.2%), 9 were left-sided, and 2 were bilateral. All patients were symptomatic at the time of treatment except 1, whose tumor was discovered following a CT scan for head trauma. Motor deficits were the most common form of presentation (14 cases, 51.8%), with symptoms of increased intracranial pressure (ICP) (14 cases, 51.8%) related to hydrocephalus (12 cases) or to the volume of tumor itself (2 cases). Two patients were admitted in emergency status with a Glasgow Coma Scale (GCS) score of 3 and fixed dilated pupils, due to an intratumoral hemorrhage and acute hydrocephalus. One patient never awakened from anesthesia and died in intensive care a few days after surgery (case 19), and the other recovered well, but died 2 years later because of progressive disease (case 22) (Table 2). Less frequent symptoms were visual problems (14.8%), tremor (7.4%), epilepsy (7.4%), third cranial nerve palsy (7.4%), and visual field defect (7.4%). Interestingly, there were no patients with sensory deficits in our series.

TABLE 1. Low-grade tumors in 18 patients

Case No.	Age (yrs)	Histology	Previous Tx*	Grade of Resection†	Staged Surgery	Complementary Txs	FU (mos)	Recurrence & Tx	Present Status
Thalamic tumors									
1	5	Ganglioglioma	No	GTR	No	No	132	Yes (7 yrs, GTR)	ANED
2	15	Diffuse astro	No	GTR	Yes	No	16	No	ANED
3	13	Pilocytic astro	Chemo, RT	STR	No	No	108	Yes (8 yrs, GTR)	ANED
4	13	Pilocytic astro	Biopsy + chemo + RT	STR	Yes	No	12	No	ANED
5	12	DNT	No	GTR	No	No	4	No	ANED
6	12	Ganglioglioma	No	STR	No	No	12	No	ASD
Thalamopeduncular tumors									
7	17	Ganglioglioma	PR + chemo + RT	STR	No	Chemo	30	No	ASD
8	5	Ganglioglioma	No	PR	No	No	88	Yes (6 yrs, progression to HGG, PR)	DOD
9	3	Pilocytic astro	No	GTR	Yes	Chemo	36	No	ANED
10‡	4	Pilocytic astro	No	PR	No	Chemo	41	No	ASD
11§	12	Pilocytic astro	PR	GTR	No	RT	27	Yes	LTF
12	3	Pilocytic astro	No	GTR	No	No	29	No	ANED
13	7	Pilocytic astro	No	GTR	No	No	60	Yes	ANED
14	3	Pilocytic astro	No	GTR	No	No	60	Yes	ANED
15	11	Pilocytic astro	PR + chemo	GTR	No	No	12	No	ANED
16	9	Pilocytic astro	No	GTR	Yes	No	8	No	ANED
17	9	Pilocytic astro	No	GTR	No	No	19	Yes	ANED
18	13	Pilocytic astro	No	PR	No	No	5	No	ASD

ANED = alive, no evidence of disease; ASD = alive, stable disease; astro = astrocytoma; chemo = chemotherapy; DOD = dead of disease; FU = follow-up; HGG = high-grade glioma; LTF = lost to follow-up; RT = radiotherapy; Tx = treatment.

* Treatments performed at other centers before referral to our hospital.

† As judged on postoperative MRI at the end of the surgical phase (i.e., following staged surgeries, if required).

‡ Patient with involvement of hypothalamus and visual pathways.

§ Patient referred to another hospital at the time of recurrence.

All patients underwent CT and MRI studies. The radiographic appearance of the tumor was classified according to the surgical classification of Puget et al.³¹—9 patients presented with unilateral thalamic tumors (33.3%), 16 patients with thalamopeduncular tumors (59.2%), and 2 patients with a bilateral thalamic tumor (7.4%). The lesions

demonstrated a heterogeneous contrast enhancement in 21 patients (77.8%); 10 lesions were multicystic (37%), 10 had central necrosis (37%), and 3 had intralesional hemorrhage (11.1%). Surrounding edema was found in 8 lesions (29.6%); in 10 cases there was associated obstructive triventricular hydrocephalus (37%), and 2 cases with bilater-

TABLE 2. High-grade tumors in 9 patients

Case No.	Age (yrs)	Histology	Type of Tumor	Grade of Resection	Staged Surgery	Complementary Txs	FU (mos)	Present Status
19*	7	GBM	Thalamopeduncular	STR	No		0	POD
20	13	GBM	Thalamopeduncular	GTR	No	Chemo + RT	16	DOD
21	16	Anaplastic astro	Thalamopeduncular	GTR	Yes	Chemo + RT	15	DOD
22	12	Germ cell tumor	Thalamic	GTR	Yes	Chemo + RT	12	DOD
23	14	Gliomatosis cerebri	Bilat	Biopsy	No	Chemo + RT	24	DOD
24	15	GBM	Thalamopeduncular	PR	No	Chemo + RT	7	DOD
25	14	GBM	Thalamopeduncular	PR	No		0	POD
26	8	GBM	Bilat	Biopsy	No	Chemo + RT	9	DOD
27	3	GBM	Thalamopeduncular	PR	No	Chemo + RT	7	ASD

GBM = glioblastoma; POD = postoperative death.

* Patient with a GCS score of 3 and fixed and dilated pupils who underwent emergency operation; died 10 days later in intensive care.

al involvement had obstructive biventricular hydrocephalus (7.4%). Tumor volume calculated on MRI sequences varied from 2.8 to 156 cm³, with a mean value of 46 cm³.

Management of Hydrocephalus

Of the 12 hydrocephalic patients, only 1 had mild symptoms, which were completely resolved after tumor removal. In the other 11 patients, in comparison, acute hydrocephalus required an external ventricular drain in 3 patients, an endoscopic third ventriculostomy in 6 patients, and an endoscopic septostomy followed by endoscope-guided placement of a ventriculoperitoneal (VP) shunt in 2 cases with bilateral tumor. Postoperatively, external ventricular drains were removed in 1 case and transformed to a VP shunt in 1 case. Three of these patients developed a subdural collection, which required temporary subdural-peritoneal shunting. Only 1 patient, who had a high-grade glioma, developed hydrocephalus during follow-up, with loculation of the surgical cavity, and required a VP shunt with endoscopically controlled placement of the proximal catheter. If hydrocephalus was not present, an external lumbar drain was implanted preoperatively in all cases requiring the subtemporal or posterior interhemispheric transtentorial approach, to facilitate lobe retraction during the earliest phases of the approach. The drain was always removed immediately after surgery.

Tumor Resection

During the period of investigation, 37 microsurgical procedures of tumor debulking were performed in 25 patients, with the aim of achieving as large a tumor resection as possible (preserving function). In 11 cases, multiple procedures were performed; in 6 of them, the second procedure was necessary because of late recurrence or regrowth of residual tumor. In the remaining 5, the second surgery was part of a planned multistage resection, which was eventually accompanied by adjuvant chemotherapy according to histological findings. One patient underwent operation 3 times. The effect of chemotherapy in the 3 cases in which it was performed was not very favorable: in 2 patients the lesion progressed, and in the third patient the residual tumor remained stable. In the 2 cases with bilateral involvement with an infiltrative pattern, the tumor was only biopsied, under endoscopic guidance.

The surgical approach was planned based on MRI findings. Axial T2-weighted images were the sequence of choice to determine the location of the PLIC in relation to the tumors. In 16 recent cases, DTI with tractography was performed preoperatively to localize the CST. The PLIC was displaced anterolaterally in 18 (66.7%) cases, laterally in 3 (11.1%), and medially in 2 (7.4%), and it was infiltrated by tumor in 4 (14.8%) cases. We found just 1 case with discordant information, in which the PLIC was interpreted as displaced anterolaterally on T2-weighted MRI, whereas tractography showed the CST infiltrated by the tumor. In cases in which the CST was infiltrated by the tumor, resection was stopped in a safe area, according to neuronavigation findings and intraoperative monitoring, to reduce the risks of postoperative neurological deficits. The following approaches were used.

FIG. 1. Case 9. A 3-year-old boy presenting with rapidly progressive hemiparesis. Preoperative MRI shows a large right thalamopeduncular tumor (A). The DTI shows posterior displacement of the pyramidal tract (B). Tumor is partially resected via a transtemporal MTG approach (C). The tumor was completely resected 4 months later for regrowth of the residual lesion in spite of chemotherapy. The 4-year follow-up MRI study shows no evidence of disease (D). Figure is available in color online only.

Transtemporal Approach

In 9 patients (33%) tumors were mainly resected via an MTG approach (Fig. 1 and Video 1). Very important factors for a decision to choose the MTG approach were the significant size (> 5 cm), usually associated with more marked lateral expansion of the tumor, often in proximity to the temporal horn (Fig. 1A), and the presence of significant tumor cyst with lateral extension. In giant tumors (> 6 cm) without tumor cyst, entering the temporal horn should be considered a necessary preliminary step to achieve the largest possible exposure of the tumor volume (Fig. 1). In fact, failure to open the temporal horn adequately in 1 patient (case 9; Fig. 1A, C, and D) resulted in a too-narrow surgical corridor that led to inadequate exposure of the upper and lower poles of the tumor, which were left as residual tissue (Fig. 1C). This obliged us to perform a second surgical procedure combining the existing corridor with a subtemporal approach to achieve complete removal (Fig. 1D). When tumor cysts were present, usually the surgical corridor was dictated by the location of the cyst that contributed to significant displacement of the CST. These cysts were key in obtaining a large surgical corridor, minimizing the need for retraction that occurs if using the transparenchymal route. Another transcortical approach, which was used in only 1 case, was via the middle parietal gyrus for a giant thalamopeduncular tumor.

Interhemispheric Transcallosal Approach

An interhemispheric transcallosal approach was per-

FIG. 2. Case 20. A 13-year-old girl presenting with headache, vomiting, diplopia, and left hemiparesis. Preoperative MRI shows right thalamopeduncular tumor with hydrocephalus (A). The DTI in 3D reconstruction shows anterolateral displacement of the pyramidal tract (B). After surgery via a transcallosal approach, complete removal was achieved (C). Figure is available in color online only.

formed in 9 patients (33.3%) (Fig. 2 and Video 2), and was preferentially chosen for all paramedian tumors with a significant intraventricular component or located immediately below the ependyma in proximity to the choroid plexus attachment. These tumors usually induced significant anterolateral (Fig. 2B) or posterolateral displacement of the CST, and the transcallosal route allowed for excellent visualization of the major tumor axis without crossing or interfering with the CST trajectory, allowing for its safe preservation.

Interhemispheric Transcallosal Transchoroidal Approach

An interhemispheric transcallosal transchoroidal approach was used in 1 case (Fig. 3 and Video 3). It was chosen because the tumor was of small dimensions (diameter < 3 cm) and localized in a paramedian region of the posterior thalamus, bulging into the third ventricle and separated from the ependyma of the lateral ventricle by a thick region of normal basal ganglia tissue. Access to the tumor was completely blocked from lateral approaches by the CST (Fig. 3B), whereas access from the contralateral ventricle and contralateral choroid fissure made it possible to expose the whole volume of the tumor, allowing complete removal (Fig. 3C) without traversing brain parenchyma, except for the callosotomy.

Subtemporal Approach

A subtemporal approach was performed as a single approach in 2 patients. Candidates for this approach were considered to be patients with a significant peduncular component, with the equatorial diameter of the tumor bulging superficially at the level of the tentorial edge and inducing anterior or posterior displacement of the CST. The subtemporal approach was combined with an MTG approach during the second procedure in case 9 (see above and Video 1).

Posterior Interhemispheric Transtentorial Approach

A posterior interhemispheric transtentorial approach was used in 4 patients (Fig. 4 and Video 4); it was chosen for lesions mainly affecting the pulvinar region or with prevalent midline localization with predominant third ventricular invasion and upward displacement of the internal cerebral veins complex (Fig. 4A and B). Staged resection allowed for fine dissection and preservation of both internal cerebral veins, even in the presence of very dense adhesion following previous surgeries and radiotherapy performed in other centers (Fig. 4E and F). This approach was always preferred over the supracerebellar infratentorial approach by the senior author (G.C.), who considers the dissection of

FIG. 3. Case 16. A 9-year-old boy presenting with severe papilledema and visual loss. Preoperative MRI shows left thalamopeduncular tumor with obstructive hydrocephalus (A). The DTI in 3D reconstruction shows anterolateral displacement of the pyramidal tract (B). Staged 2-step procedure via a transcallosal-transchoroidal approach allowed complete removal without neurological deficits (C). Figure is available in color online only.

FIG. 4. Case 4. A 13-year-old girl referred from another center following biopsy for a thalamic pilocytic astrocytoma that was resistant to chemo- and radiotherapy. Preoperative MRI shows a large midline tumor invading the third ventricle (**A and B**), with upward displacement of both internal cerebral veins. The posterior interhemispheric transtentorial approach allowed partial removal of the lesion (**C and D**), which was completely resected via the same approach 2 months later (**E and F**).

the vein of Galen and of the internal cerebral veins complex from the tumor to be easier through the transtentorial route. In 1 patient (case 7), the procedure was started as a posterior transcallosal splenic approach, but this was rapidly converted to a transtentorial approach because the tumor exposure was considered inadequate and manipulation of the internal cerebral veins complex too risky from above. Subtotal removal was achieved.

Endoscopic Septostomy Plus Biopsy With VP Shunt Placement

In the 2 cases of thalamic tumor with bilateral involvement, an endoscopic septostomy plus a biopsy and an endoscope-guided placement of a VP shunt was performed. Bithalamic gliomas usually present with a highly infiltrative and diffuse pattern, inducing global swelling of both thalami without contrast-enhancing masses. These lesions are usually considered electively nonsurgical and are referred to oncologists after endoscopic biopsy for complementary treatment.

Intraoperative Imaging

Intraoperative CT was used in 23 procedures (15 first procedures, 8 reoperations) out of 37. In 13 cases, intraoperative imaging confirmed the surgeon's impression of GTR; in 7 cases, it confirmed the impression of PR, but induced the surgeon to stop the operation in agreement

with a preplanned staged resection strategy; and in 3 cases, CT showed a larger than expected residual tumor volume, inducing the surgeon to continue debulking, and obtaining GTR in 2 cases and further but still partial removal in the third case.

From the initial 25 procedures performed with the intent to resect, GTR was achieved in 8 (32%), STR in 9 (36%), and PR in 8 (32%). Eight patients who underwent an initial STR or PR achieved a GTR (in 7) and an STR (in 1) in a subsequent surgery, as part of a planned multimodal treatment. Accordingly, at the end of the surgical phase in 25 patients, 15 (60%) achieved a GTR, 5 (20%) achieved an STR, and 5 (20%) achieved a PR.

Postoperative Complications

Postoperative complications and adverse events were classified as transient or permanent, and are summarized in Tables 3–5 in relation to the localization of the tumor and the approach used. Two postoperative deaths occurred: The first patient underwent operation with a GCS score of 3 and bilateral fixed pupils, and died during the immediate postoperative period. The second, harboring the largest tumor of this series (145 cm³), with complete encasement of both internal cerebral veins, presented with bilateral fixed pupils 12 hours after STR because of diffuse brain edema. The tumor was diagnosed as WHO grade IV glioma.

TABLE 3. Histological diagnosis of thalamic tumors in 27 patients

Tumor Type	WHO Grade	No. of Patients
Low-grade tumors		18 (67%)
Pilocytic astro	I	12
DNT	I	1
Diffuse astro	II	1
Ganglioglioma	II	4
High-grade tumors		9 (33%)
Gliomatosis cerebri	III	1
Anaplastic astro	III	1
Germ cell tumor	IV	1
Glioblastoma	IV	6

Histological Findings

The histological results in our 27 patients showed 18 low-grade and 9 high-grade tumors. Tumors with low-grade histologies were as follows: 12 pilocytic astrocytomas (44.4%), 4 gangliogliomas (14.8%), 1 diffuse astrocytoma (3.7%), and 1 dysembryoplastic neuroepithelial tumor (DNT) (3.7%). Tumors with high-grade histologies were as follows: 6 glioblastomas (22.2%), 1 gliomatosis cerebri, 1 anaplastic astrocytoma, and 1 mixed germ cell tumor with a hemorrhagic presentation (3.7% each). High-grade tumors account for 33.3% of lesions in our series. One case of partially resected ganglioglioma progressed to glioblastoma after 6 years.

Outcome in Patients With Low-Grade Tumors

Low-grade tumors account for 66.7% of lesions in our series (Table 1). There were 12 thalamopeduncular tumors and 6 thalamic tumors. A GTR was achieved in 7 cases at first operation. Five cases underwent repeat operation following histological investigation, obtaining a GTR. In 66.7%, a GTR was achieved at the end of the surgical phase; a GTR was achieved in 8 of 12 thalamopeduncular tumors and in 4 of 6 thalamic tumors.

The mean follow-up was 45 months (range 4–132 months). One patient was lost to follow-up at 27 months; at that time, he had a recurrence and was referred to another hospital for operation because he was an adult and could not be treated in our department. During the follow-up, 5

patients underwent complementary treatment: chemotherapy in 3 patients with PR, and radiotherapy in 1 patient each with PR and GTR.

The tumor recurred or progressed in 10 patients: in 4 patients following GTR and in 6 patients following PR. All underwent reoperation. One patient underwent operation at another center and was lost to follow-up. All the reoperations in our center were performed via the same surgical approach as the first operation. In 1 patient, a ganglioglioma that had been partially resected progressed to glioblastoma at the second operation, which was performed 6 years later. The patient finally died 1 year later of tumor progression, despite radio- and chemotherapy. In the other 4 cases, GTR was obtained in 3 and STR in 1.

At the end of follow-up (in 18 patients), 1 patient was dead, 10 were alive with no evidence of disease, and 7 were alive with stable disease. All patients are independent in their daily lives.

Outcome in Patients With High-Grade Tumors

Nine patients presented with high-grade tumors in our series (Table 2). The outcome was very poor: 2 patients presenting in critical condition died immediately after surgery (see *Postoperative Complications*). All the other patients died of progressive disease, despite aggressive surgical treatment (GTR was achieved in 3 cases) and chemo- and/or radiotherapy. Only 1 patient survived, with a follow-up of 9 months following PR, chemotherapy, and radiotherapy, and at the time of this report had presented with a slowly progressive disease.

Discussion

Our patients presented mainly with contralateral motor deficits and symptoms of increased ICP, similarly to other reported series.^{1–3,25,29,31} Specifically, 2 patients in our series developed a sudden increase of ICP due to intratumoral bleeding, with a rapid deterioration in the level of consciousness to a GCS score of 3, mydriatic pupils, and the need for urgent surgery. This onset modality was previously described by Baroncini et al.³ In that series, 25% of 16 patients underwent operation on an emergency basis, although it was not specified whether the emergency procedure was a CSF-diverting or a resective procedure. The surgical results were good, with no perioperative deaths.

Our institutional review seems to offer further evidence

TABLE 4. Surgical approaches to thalamic tumors

Surgical Approaches	No. of Tumors			Total
	Thalamic	Thalamopeduncular	Bilat Thalamic	
MTG	3	6		9
Anterior interhemispheric transcallosal	3	6		9
Posterior interhemispheric transtentorial	3			3
Subtemporal		2		2
Anterior interhemispheric transcallosal transchoroidal		1		1
Posterior parasplenial transcallosal + posterior interhemispheric transtentorial		1		1
Endoscopic biopsy + VP shunt			2	2

TABLE 5. Complications related to location and surgical approach in thalamic tumors

Surgical Approaches	Complications	
	Thalamic Tumors	Thalamopeduncular Tumors
MTG	1 worsened motor deficit (T); 1 subdural hygroma	3 worsened motor deficits (T)
Anterior interhemispheric transcallosal	1 Parinaud syndrome (T) + subdural hygroma	2 worsened motor deficits (T); 1 worsened motor deficit (T) + subdural hygroma; 1 hemiparesis/aphasia (P); 1 hemiplegic aphasic (P) + hydrocephalus; 2 deaths
Posterior interhemispheric transtentorial	1 worsened motor deficit (T) + hemianopia (T)	NA
Subtemporal	NA	CN IV palsy (T)
Anterior interhemispheric transcallosal transchoroidal	NA	NA
Posterior parasplenial transcallosal + posterior interhemispheric transtentorial	NA	1 diplopia (T)
Endoscopic biopsy + VP shunt	NA	NA

CN = cranial nerve; NA = not applicable; P = permanent; T = temporary.

in favor of attempts at radical resection in pediatric patients harboring unilateral thalamic or thalamopeduncular tumors. Maximum grades of resection, with minimum morbidity and no deaths related to the surgery, were possible in all patients harboring low-grade tumors, even in cases in which part of the CST was included in the tumor. In low-grade histological types, purely surgical management allowed excellent results, with 17 of 18 patients disease free or with stable disease (94.4%).

Staged resection can be useful in very large tumors. Usually the first surgery allows for very safe resection of the largest tumor volume (> 70%–80%), leaving the deepest and more dangerous part of the lesion for a second procedure. The personal experience of the senior author is that tumor tissue and cleavage plane, which can be more difficult to recognize at the end of the first procedure after a long time dedicated to debulking, can be identified very easily during the second procedure in the depth of the previous surgical cavity, making the final dissection and complete removal safer and easier. For these reasons, although all patients are approached with the deliberate intent to achieve a GTR in a single procedure, the surgeon should reserve the option to abort the procedure depending on the tumor texture and anatomical definition in relation to normal tissue. This possibility should be explained to the parents before surgery.

Intraoperative imaging techniques, including ultrasound and intraoperative CT scans, are important to avoid underestimation of the amount of tumor volume removed. Intraoperative MRI is not available at our facility and would have certainly been extremely helpful in obtaining higher-definition images of possible tumor residues with volumetric sequences, offering the possibility of re-navigating during surgery and performing intraoperative tractography to further enhance the possibilities of function preservation. Presurgical planning and careful choice of the best approach are of utmost importance to obtain the best results. They should be used only to choose the best surgical route, not to decide between surgery and palliative treatment.

Postoperative deficits are possible, but they tend to improve rapidly and significantly during the follow-up pe-

riod. Sometimes these patients are referred after completion of different treatment protocols (mainly palliative) in other centers. This is not a reason to exclude them from an attempt at GTR, especially in the case of low-grade tumors in which radical removal remains the best treatment modality. For these reasons, surgery should be considered in thalamic tumors both at presentation and at recurrences in all cases of low-grade tumors, considering the use of adjuvant therapy based on histological types in cases of recurrence.

In high-grade tumors with a wide extension, even if the prognosis remains poor, PR of the tumor in a first step can be recommended and is feasible. Cytoreductive surgery with careful attention to neurological functions reduces the target volume of radiotherapy, and can help in the management of hydrocephalus and throughout the administration of radiation therapy and chemotherapeutic treatment. The possible impact of surgical debulking on the length of survival remains difficult to determine in small series like the present one, because of the lack of a historical institutional cohort for comparison, and the impossibility of organizing a randomized trial due to the rarity of the disease. However, there are eloquent data in the literature that suggest surgical debulking as a preferable option over biopsy and radiotherapy to prolong survival.²³

For the choice of the surgical approach, we considered the relationship of the tumor with the internal capsule and CST to be the most important. In fact, the improvement in neuroradiology in recent years, with 3-T MRI and development of DTI and tractography, allowed more accurate localization of PLIC (with MRI) or CST (with DTI), emphasizing the accuracy and utility of DTI as a valuable tool for the preoperative planning of approaches to thalamic and thalamopeduncular tumors.^{5,8,26,30} In our series, the PLIC or CST was mostly displaced anterolaterally; accordingly, the surgical routes more frequently chosen were the MTG approach and the interhemispheric transcallosal approach in cases with an important intraventricular component. In all of our patients, it was possible to define a surgical corridor not crossing the PLIC or CST or other

eloquent areas, and in no case was the anatomical situation considered a contraindication to surgery, at least for a generous debulking. Only the 2 patients with a bithalamic lesion of a diffuse, infiltrative, nonenhancing type were treated with endoscopic biopsy and septostomy to facilitate the CSF diversion, followed by complementary treatment. In these 2 patients, an attempt at surgical debulking was never considered to be a reasonable option.¹⁴

With respect to morbidity, independently of localization or extension of the tumor and extent of resection, we achieved stabilization, and in many cases improvement, of the motor impairment of our patients after surgery, as well as improvement in other neurological deficits. We attribute this to the release of the mass effect exerted on the thalamus and surrounding structures, as was suggested by Moshel et al.²⁷ and by Ozek and Türe,²⁹ without damage to functional structures. For this reason, we suggest consideration of an attempt at radical surgery in cases in which tractography shows fascicles of CST included in tumor, as in 3 of our patients—the beneficial effect of removing the mass may exceed the risk of cutting the previously damaged fascicles enclosed in the tumor.

Conclusions

Either GTR or STR of low-grade thalamic or thalamopeduncular tumors of any size with unilateral extension was always possible in this consecutive series of pediatric patients, allowing for long-term control of the disease in 94.4% of the cases, with minimal neurological consequences and an acceptable rate of complications. Surgical management of high-grade tumors was more difficult, especially in cases with very large lesions or very acute presentation. Although surgical debulking was technically possible in the majority of high-grade lesions, its real impact on the survival and quality of life of the patients could not be estimated in the present series.

Patients presenting with dramatic clinical conditions due to intratumoral hemorrhage or extremely large tumor volume should be considered to be at high surgical risk. Surgical debulking can still be considered as a life-saving option, but parents should be informed of the high risk of perioperative mortality.

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Disclosures

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

Author Contributions

Conception and design: Cinalli. Acquisition of data: Cinalli, Aguirre, Ruggiero, Aliberti, Nastro, Spennato. Analysis and interpretation of data: Cinalli, Cascone, Quaglietta, Buonocore, Nastro, Spennato. Drafting the article: Cinalli, Aguirre, Ruggiero, Spennato. Critically revising the article: Cinalli, Mirone, de' Santi, Spennato. Reviewed submitted version of manuscript: Cinalli, Spennato. Approved the final version of the manuscript on behalf of all authors: Cinalli. Administrative/technical/material support: Cinalli, Aguirre, Mirone, Spennato. Study supervision: Cinalli.

Supplemental Information

Videos

Video 1. <https://vimeo.com/234306297>.

Video 2. <https://vimeo.com/234306483>.

Video 3. <https://vimeo.com/234306567>.

Video 4. <https://vimeo.com/234306630>.

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