Original Article

# Tumor Resection in Stages as a Strategy for Approaching Giant Intracranial Tumors in Childhood

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**Abstract**

**Background:** Giant pediatric intracranial tumors (GPIT) are associated with high morbidity and mortality and pose a challenge for treatment. This study evaluated the morbimortality-related outcomes of staged resection of GPIT. An observational study was undertaken. **Materials and Methods:** Twenty children with GPIT were retrospectively evaluated for demographics, clinical presentation, histopathology, weight at first intervention, hemotransfusion rate, weight gain between stages, complications, and survival factors. Non-parametric tests were performed owing to the sample size. The significance level adopted was 5% with a 95% confidence interval. **Results:** The average age was 3 years and 11 months. Fourteen (70%) patients had tumors in the supratentorial compartment. Thirty-seven interventions were performed with an average weight gain of 1.7 kg between the stages. The most frequent histological types were choroid plexus carcinomas (3), medulloblastomas (3), atypical rhabdoid teratoid tumor (2), and ganglioglioma (2). The mean blood transfusion rate was 28.4 mg/kg. The mean follow-up duration was 19.8 months (range: 1–68 months). **Conclusion:** The treatment strategy of resecting GPIT in stages proved to be effective in minimizing bleeding, obtaining maximum safe resection, and enabling the patient to recover between procedures. Notably, the degree of malignancy remains the most limiting factor in the survival of these patients.

**Keywords:** *Giant intracranial tumors, outcome, pediatric neurosurgery, resection*

## Introduction

The treatment of giant pediatric intracranial tumors (GPIT), defined as those with at least 5 cm diameter in size, is challenging for pediatric neurosurgeons who need to balance between maximum tumor resection and the high risk of morbidity and mortality owing to the expected intraoperative bleeding, especially in young children.[1-8]

Notably, there is a paucity of reports in the literature regarding the management of these tumors because of the less frequency and different surgical strategies considered, such as block resection of giant supratentorial tumors and preoperative embolization of tumors with high bleeding potential.[2,9] However, most of these strategies are not always feasible owing to the major risk of bleeding and impossibility of gross total resection. Other strategies aim to remove giant tumors in stages to preserve the patient's stability, minimizing excessive blood transfusions, and morbidity and mortality.[1,2,7,9-13] In addition, the impossibility of performing radiotherapy in children less than 3 years of age contributes to the worst prognosis.[3,6,14-19]

Nevertheless, we surmised that resecting these tumors in stages, which means resecting the tumor through

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multiple procedures, in patients with unfavorable condition, such as lower age and weight, combined with huge intracranial tumor, could decrease the mortality risk and improve the management of GPIT.

In this study, we present our experience of managing GPIT by adopting the strategy of resecting in stages in most patients based on the intraoperative risk evaluation by pediatric neurosurgeon and the effect on morbimortality.

## Subjects and Methods

### Patients and eligibility criteria

After the approval by the ethics committee of Vila da Serra Hospital and Faculty of Medical Sciences of Minas Gerais (Protocol: CAAE:32805120.5.0000.5134), an observational study was conducted and the medical records of all patients admitted for neurosurgical intervention at Vila da Serra hospital, Nova Lima, Minas Gerais, were obtained between January 2006 and December 2016. Patients aged less than 18 years and with a confirmed diagnosis of an intracranial tumor of at least 5 cm in one of the three dimensions were evaluated [Figure 1]. No written consent was requested by our institutional ethics board.

Children diagnosed with giant tumors, which were defined based on the size of higher than 5 cm in the largest diameter on magnetic resonance imaging, in the upper or infratentorial compartments were selected. Those without sufficient data for analysis or whose tumors did not meet the minimum size criterion were excluded.

### Data collection

The study considered variables like demographics, clinical presentation, weight immediately before neurosurgical intervention, weight gain between surgeries, hemotransfusion rate in mL/kg, tumor localization, histopathology, and gradation (benign or malignant).

The degrees of resection were defined as follows: a biopsy when less than 25% of the tumor was removed, partial if about half of the tumor was resected, subtotal resection when almost the entire tumor was resected, and complete removal of tumor. All patients underwent magnetic resonance imaging preoperatively.

### Outcome

All patients were treated by the senior neurosurgeon (J.A.C.V.F) during hospitalization and were evaluated monthly after discharge. The Glasgow Outcome Scale (GOS) was divided into GOS 1 (death), 2 (neurovegetative state, when the patient is not responsive), 3 (moderate disability, when patients carry on with daily activities independently), and 5 (excellent recovery without disabilities). The GOS was applied retrospectively based on the clinical condition of patients during follow up.

### The technique of resection in stages

Staged resection is a tumor resection planned to be performed by the neurosurgeon through multiple surgeries, with the aim of causing less injury to patients, minimizing the volume of hemotransfusion, promoting cytoreduction in a safe way, and ensuring the best possible patient recovery between surgeries, without causing major disabilities, and minimizing postoperative infections, which are worsened by patients' immobility. In addition, staged resection involves adoption of a set of measures to reduce blood loss during surgical access.

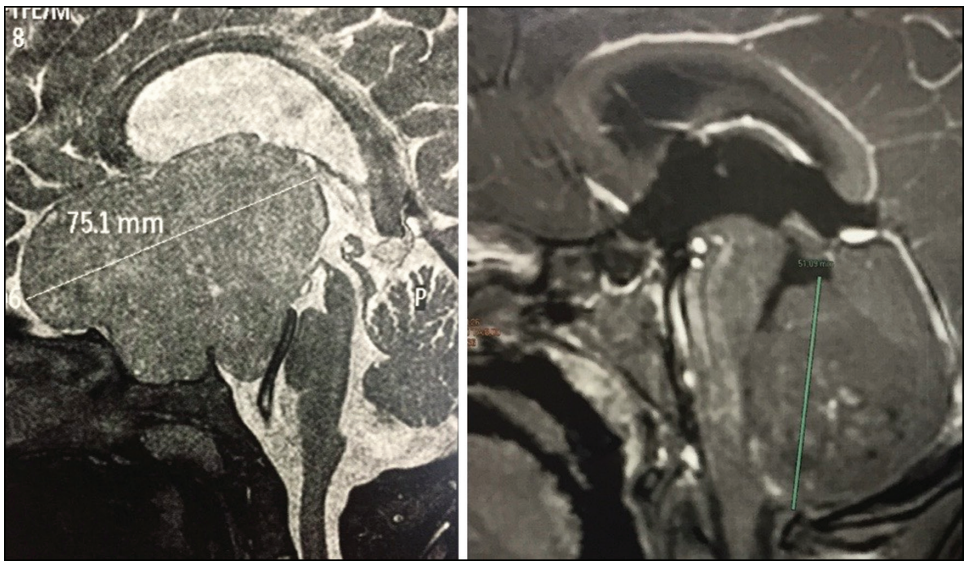


**Figure 1:** Giant intracranial tumors in childhood. Left: giant suprasellar tumor (patient 20). Right: giant medulloblastoma of the fourth ventricle (patient 5). Both demonstrated more than 50 mm of extension

### Infratentorial approach

Under general anesthesia and intraoperative neuromonitoring, patients were positioned prone with their heads fixed on a three-pin support if older than 3 years or on a horseshoe support if younger. The skin was incised using electrocautery with a colored tip and the occipital bone was exposed. The craniotomy was performed extending from the upper nuchal line, including the posterior edge of the foramen magnum and the posterior arch of C1, with the lower extension of the tumor relative to the foramen magnum. After a Y-shaped durotomy, the tumor was resected under microscopic vision. The decision to interrupt the procedure was based on the pediatric neurosurgeon's decision, in agreement with the anesthesiologist and neurophysiologist, in case of minimal signs of hemodynamic instability or reduction of potentials. The bone flap was replaced with plates and absorbable screws [Figure 2].

### Supratentorial approach

In supratentorial approaches, in addition to the steps similar to the infratentorial approach related to cutaneous incision and positioning, the pericranium was left *in situ* to avoid unnecessary bone hemorrhages.

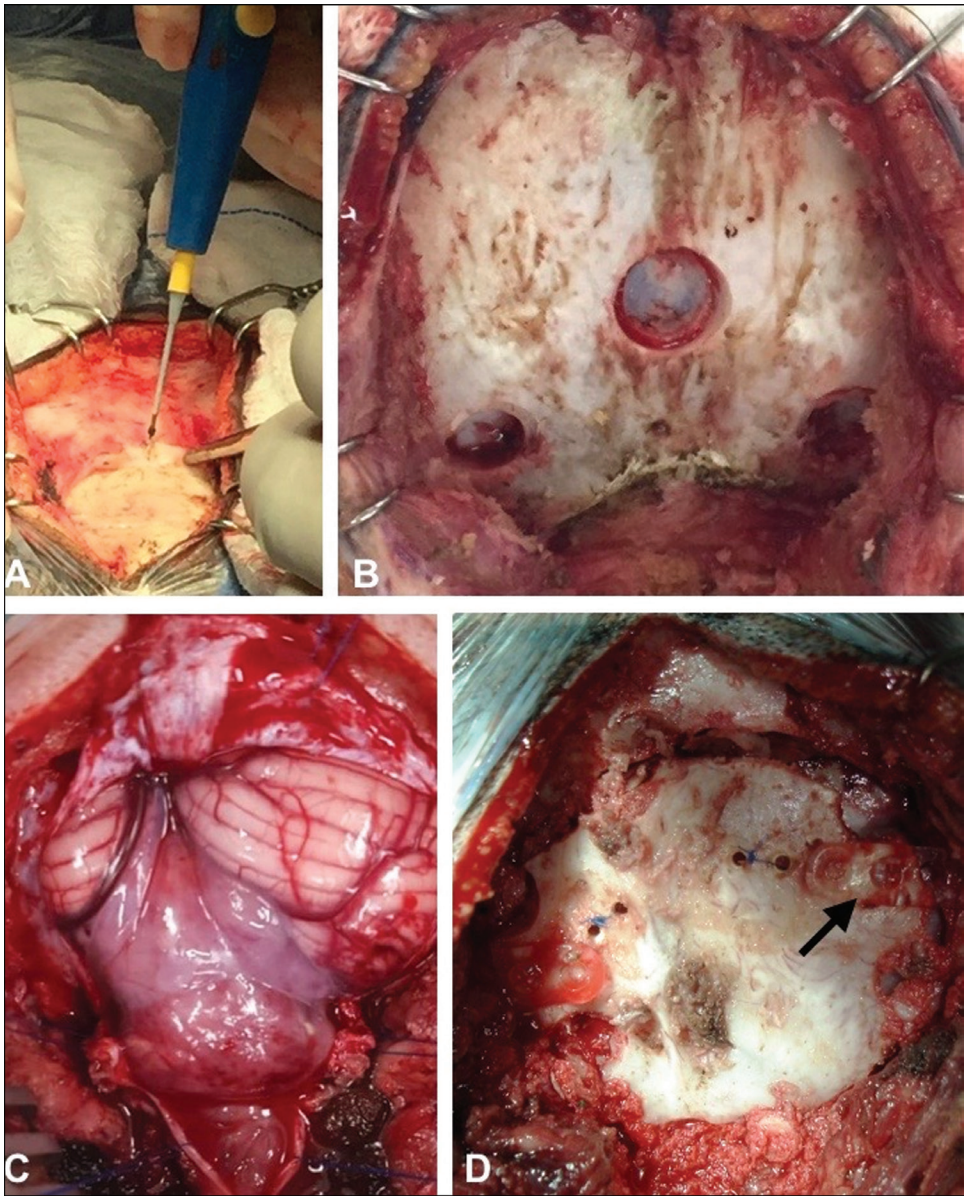


**Figure 2:** Stages in the microsurgical approach of infratentorial giant tumors. (A) Suboccipital access with electrocautery and Colorado tip. (B) Usual points of brocage being the inion and occipital bone with dissection of the foramen magnum. (C) After craniotomy and durotomy the magna cistern occupied by the tumor is visible. (D) Cranial reconstruction with occipital flap fixation with absorbable plates (black arrow). Moreover, thin bone fragments are relocated to facilitate bone integration

In both the approaches, mannitol was used during access to make durotomy less traumatic with lower risk of cerebral herniation from dural opening and bleeding.

### Statistical analysis

In this study, the software programs SPSS V20, Minitab 16, and Excel office 2010 were used. Non-parametric tests were performed owing to the sample size. The significance level adopted was 5% with a 95% confidence interval.

The equality test of its proportions was used in the analysis of the relative frequency of qualitative variables.

## Results

The present study evaluated 20 patients diagnosed with giant intracranial tumors in childhood who underwent a neurosurgical approach. During the same period, our neurosurgical service had operated 250 intracranial tumors in pediatric patients. The study patients comprised 13 (65%) girls and 7 (35%) boys ($P = 0.058$), with the mean age of 3 years and 11 months (median: 2 years; variation: 7 days to 15 years) [Table 1].

Regarding the anatomical distribution, 14 patients had tumors in the supratentorial compartment (four intraventricular, seven intraparenchymal, and three suprasellar) and 6 (30%) in the infratentorial region (fourth ventricle). The initial clinical presentations varied with the most frequent being headache, vomiting, and motor regression [Table 1].

All patients were subjected to an anatomopathological study, and in 12 of them the tumor was graded malignant. Among the tumors considered to be benign, pilomyxoid astrocytoma, hemangiopericytoma, ganglioglioma, choroid plexus papilloma, giant cell subependymal astrocytoma, craniopharyngioma, and prolactinoma were observed. Notably, the patient who presented with prolactinoma was first considered for surgery and debulking because of the severity of optic chiasma compression, and with no expected decrease in tumor size after treatment with cabergoline, gross total resection was adopted as the second-line treatment.

Surgical resection over more than one operative period was performed in 14 patients, resulting in total resection in nine and subtotal resection in five [Figures 3 and 4]. The number of surgeries was 2–4 per patient, totaling 31 surgical interventions in this group. In six patients, the neurosurgical approach was performed at a single surgical time point because of extreme severity of the case, excellent response to adjuvant treatment, or unexpected tumor regression [Table 2]. Subtotal resection was performed in a patient with medulloblastoma, one with craniopharyngioma, and another with fronto-orbitary hemangiosarcoma. Partial resection was performed in a child with insular rhabdoid teratoid tumor and a carcinoma of the choroid plexus of the fourth ventricle. A biopsy was performed in a newborn girl aged 7 days diagnosed with fronto-orbitary hemangiopericytoma. This case

**Table 1: Demographic characteristics of 20 children with giant intracranial tumors**

| Case | Gender | Age | Weight (kg) | Location | Histopathology | Clinical presentation |
|---|---|---|---|---|---|---|
| 1 | F | 5y 3m | 19 | VL | ASCG | Headache and vomiting |
| 2 | F | 1y 4m | 12 | VL | PPC | Motor delay |
| 3 | F | 2y 4m | 15 | VL | Ganglioglioma | Motor delay and headache |
| 4 | F | 3y 9m | 20 | Temporoparietal | EA | Headache |
| 5 | M | 1y | 11.8 | Fourth ventricle | Medulloblastoma | Motor regression |
| 6 | F | 15y | 25 | Suprasellar | Craniopharyngioma | Hypopituitarism |
| 7 | M | 15y | 45.3 | Suprasellar | Prolactinoma | Hemianopsia |
| 8 | M | 8m | 7.0 | Fourth ventricle | Medulloblastoma | Vomiting and opstotone |
| 9 | M | 6y | 20 | Fourth ventricle | Ganglioglioma | Convulsive crisis and slimming |
| 10 | F | 12y | 27 | Fourth ventricle | Medulloblastoma | Ataxia |
| 11 | F | 1y 1m | 7.5 | Insular | TTR | Motor regression |
| 12 | M | 4y 6m | 15 | Fourth ventricle | EA | Headache and ataxia |
| 13 | F | 1y 10m | 13 | Frontal | Ependymoblastoma | Strabismus and coma |
| 14 | F | 3y | 9.8 | Fronto-orbital | Hemangiosarcoma | Proptosis |
| 15 | F | 7d | 3.5 | Fronto-orbital | Hemangiopericytoma | Proptosis |
| 16 | M | 1y 8m | 9.0 | Frontoparietal | TTRA | Strabismus |
| 17 | F | 2m | 5.5 | VL | CPC | Bulging fontanel |
| 18 | M | 2m | 4.0 | Fourth ventricle | CPC | Horizontal nystagmus |
| 19 | F | 3y | 16 | Parietal | CPC | Convulsive crisis |
| 20 | F | 1y 11m | 12 | Suprasellar | Pilomyxoid astrocytoma | Nystagmus and vomiting |

VL = lateral ventricle, EA = anaplastic astrocytoma, ASCG = subependymal giant cell astrocytoma, PPC = papilloma of the choroid plexus, TTRA = atypical teratoid rhabdoid tumor, CPC = carcinoma of the choroid plexus, GOS = Glasgow outcome scale

evolved unexpectedly into spontaneous regression of the lesion without comorbidities.

The mean weight of children before the first surgical approach was 14.9 kg (median: 12.5 kg; variation: 3.5–45.3 kg; standard deviation: 9.7 kg). Moreover, a mean weight gain of 1.7 kg was observed (median: 0.5 kg; variation: 0–10 kg; standard deviation: 2.5 kg) among patients undergoing more than one surgery. The mean volume transfused during the 37 surgeries performed was 28.4 mL/kg (median: 10.2 mL/kg, variation: 0–183.3 mL/kg; standard deviation: 46 mL/kg).

The following postoperative complications were noted in 11 patients: liquoric fistula (1); focal neurological deficit, hemiparesia or hemiplegia (3); salt-losing brain syndrome (1); pneumonia (1); deep vein thrombosis (1); dysphagia (1); dysphonia (1); sepsis (1); and hemodynamic instability (1).

Furthermore, as an adjunctive treatment, 30% of patients received chemotherapy, 5% radiotherapy, and another 5% cabergoline along with stereotactic radiosurgery.

The mean follow-up was 19.8 months (median: 8; variation: 0.1–68; standard deviation: 22.6). After applying the GOS, the following distribution was obtained: GOS 1 in 8 patients (40%), GOS 3 in 1 (5%), GOS 4 in 2 (10%), and GOS 5 in 9 (45%).

Moreover, of the eight deaths observed during the follow-up period, three occurred within 30 days postoperatively. One patient died because of pulmonary complications after medulloblastoma resection, another patient with insular rhabdoid teratoid tumor because of rapid tumor progression, and an infant with fourth ventricular choroid plexus carcinoma because of sepsis. In addition, the five remaining deaths observed in the group of patients subjected to more than one surgery were because of cancer progression after at least 3 months of follow up [Table 2].

## Discussion

The early diagnosis of pediatric intracranial tumors could be challenging owing to the difficulty in

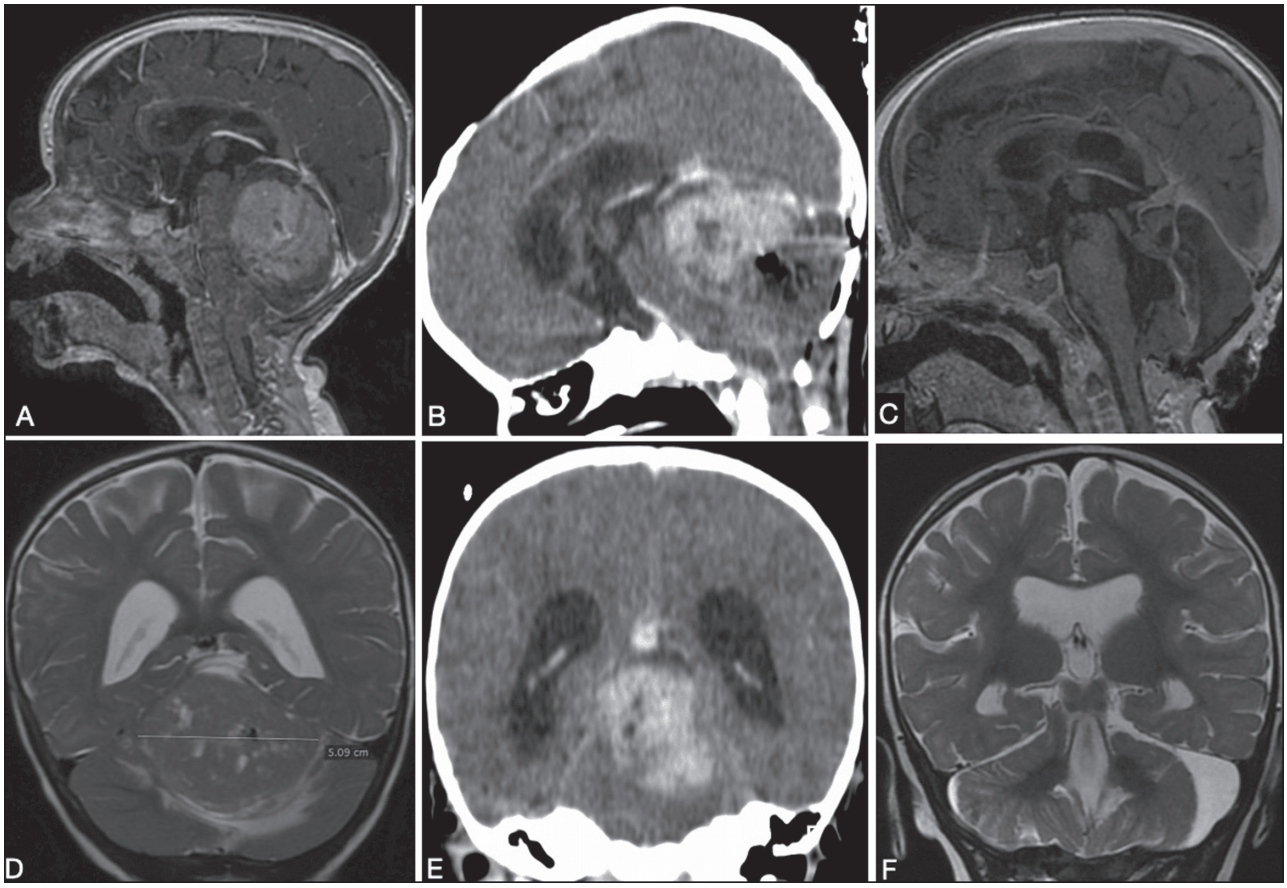


**Figure 3:** Complete resection of a giant medulloblastoma (patient 8) in two stages. (A) Magnetic resonance imaging sagittal weighted T1 with gadolinium and (D) MRI coronal weighted T2 depicted a giant posterior fossa tumor. After 4 days of a third ventriculostomy, the tumor was partially resected through a suboccipital craniotomy because of increased bleeding as revealed on the computerized tomography with contrast (B and E) after 30 days and initial adjuvant therapy, the second step was performed with complete resection of the tumor and the patient exhibited a favorable outcome, as revealed on MRI weighted T1 sagittal with gadolinium (C), MRI T2 coronal (F)

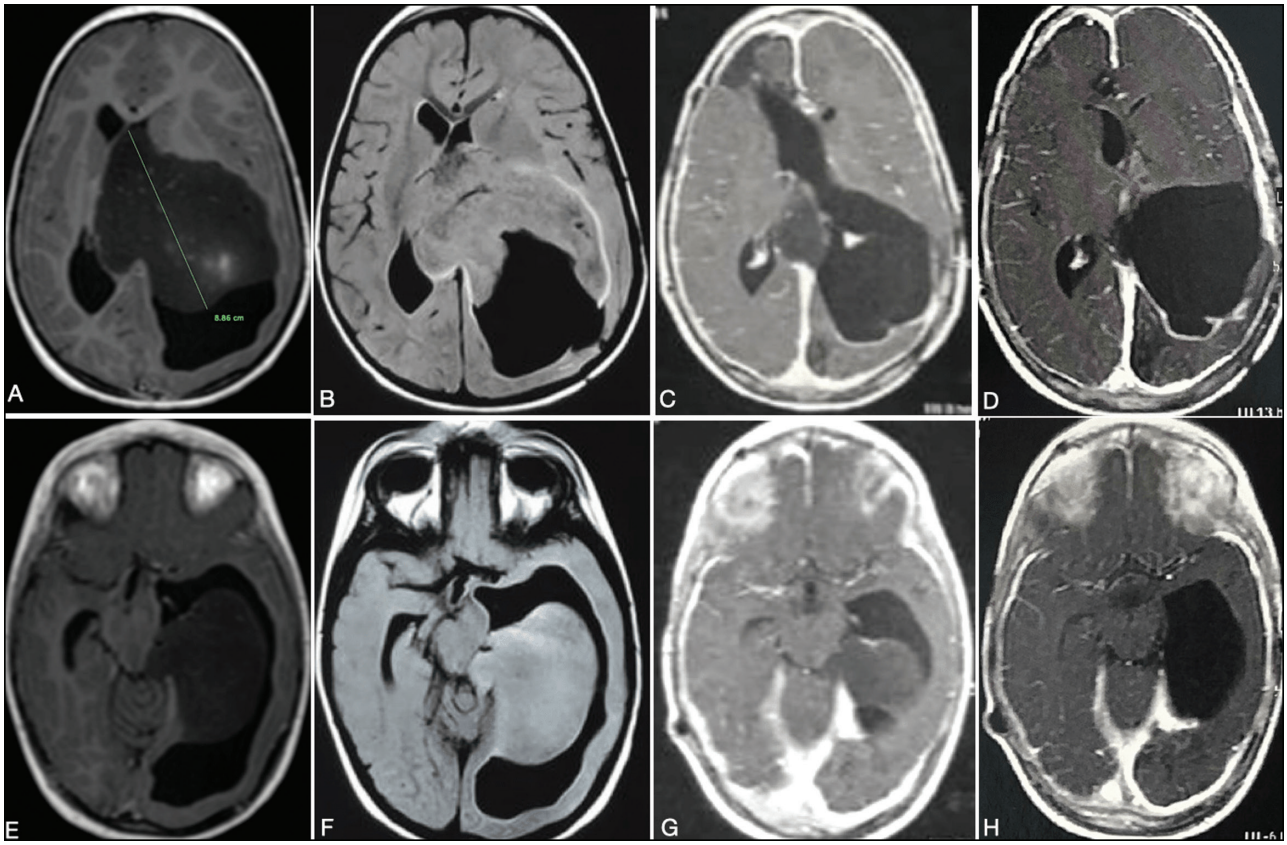


**Figure 4:** Staged resection of a giant ganglioglioma of lateral ventricles (patient 3). MRI weighted in T1 axial revealed a giant intraventricular tumor (A and E) first resection through a left parietal approach (B and F). (C) and (G) reveal MRI weighted T1 with gadolinium after the second and third steps, with a right frontal approach and resection of the tumor off the body of both lateral ventricles. (D) and (H) depict the MRI weighted T1 with contrast after the fourth step in a left temporal approach and a complete resection

recognizing some nonspecific symptoms, such as weight loss, vomiting, and headache, to be associated with central nervous system compromise, leading to a delay in the diagnosis and causing tumor growth. This fact was corroborated by some studies based on the rise in GPIT and the increased severity of cases.[3,16,20-26] Conversely, in our study, we observed the nonspecific symptoms in only few cases, and a low weight and low age were associated with more malignant tumors and dismal prognosis.

Nevertheless, the primary goal of intracranial tumor management is maximum and safe resection of tumor, with the intention of providing best cytoreduction and preserving the patient's stability. Notably, GPIT has the following four main situations: (1) huge malignant tumor in a child with low weight; (2) huge malignant tumor in a child with normal or high weight; (3) huge benign tumor in a child with low weight; and (4) huge benign tumor in a child with normal or high weight. Therefore, the weight is a limitation for successful tumor resection owing to bleeding intolerance. In addition, all these four situations could be complicated by a difficult anatomic position, such as tumor being much closer to vital structures, precluding complete resection. Regarding the anatomical distribution of GPIT, we observed a predominance in the supratentorial compartment, occurring in 14 of our study patients (70% of cases), which differed from the series published by Guo *et al*.,[5] wherein 44 (73%) out of 60 consecutive cases of children with GPIT had tumor in the infratentorial compartment. However, Oliveira *et al*.[2] selected only supratentorial tumors and studied 23 children with similar histological distribution. This discrepancy could be explained based on the small samples of studies regarding GPIT and the tumor features. In the present study, we observed great variations in the histological types of GPIT, with medulloblastomas, choroid plexus carcinoma, anaplastic ependymoma, and teratoid rhabdoid tumors being the most frequent malignant tumors. Notably, the proportion of histological types varied greatly among studies. Guo *et al*.[5] observed medulloblastomas in most patients and observed only one with rhabdoid teratoid tumor among the 60 patients studied. Furthermore, a study observed a higher incidence of choroid plexus carcinoma in a series of 23 children with

**Table 2: The strategy of surgical management of 20 children with giant intracranial tumors**

| Case | Number of operations | Resection | Blood transfusion (mL/kg) | S1 (days) | S2 (days) | S3 (days) | Complication | Adjuvant treatment | Follow-up (months) | GOS |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 2 | 1BT/1T | 0 / 5.26 | 22 | - | - | No | No | 40 | 5 |
| 2 | 3 | 2ST/1T | 13.6 / 22.7 / 0 | 21 | 365 | - | Liquoric leakage | No | 54 | 5 |
| 3 | 4 | 3ST/1T | 6.66 / 8.75 / 15 / 4.11 | 74 | 70 | 189 | No | No | 68 | 5 |
| 4 | 2 | 1ST/1T | 0 / 0 | 58 | - | - | Hemiparesis | QT | 33 | 5 |
| 5 | 1 | 1ST | 12.71 | - | - | - | Pneumonia | No | 1 | 1 |
| 6 | 1 | 1ST | 0 | - | - | - | No | No | 22 | 5 |
| 7 | 2 | 2ST | 0 | 181 | - | - | Hemiparesis | Cabergoline | 63 | 5 |
| 8 | 2 | 1ST/1T | 12.8/30 | 30 | - | - | No | QT | 8 | 5 |
| 9 | 2 | 1ST/1T | 0 / 0 | 95 | - | - | Dysphagia | No | 8 | 3 |
| 10 | 2 | 2ST | 0 / 8.1 | 8 | - | - | Sepsis | No | 3 | 1 |
| 11 | 1 | 1PT | 18.3 | - | - | - | DVT | No | 1 | 1 |
| 12 | 2 | 1ST/1T | 0/0 | 38 | - | - | Dysphonia | Chemo | 12 | 4 |
| 13 | 3 | 2ST/1T | 10/16.6/6.4 | 16 | 171 | - | Hemiparesis | Rx + Chemo | 13 | 1 |
| 14 | 1 | 1ST | 10.2 | - | - | - | No | Chemo | 3 | 5 |
| 15 | 1 | 1BT | 0 | - | - | - | No | No | 48 | 4 |
| 16 | 2 | 2ST | 0/5.5 | 30 | - | - | No | Chemo | 5 | 1 |
| 17 | 2 | 2ST | 100/83.3 | 14 | - | - | No | Chemo | 4 | 1 |
| 18 | 1 | 1PT | 110 | - | - | - | Instability | No | 1 | 1 |
| 19 | 3 | 2ST/1T | 14/10/15 | 10 | 120 | - | No | Chemo | 8 | 1 |
| 20 | 2 | 1BT/1ST | 0/0 | 34 | - | - | SBW | Chemo | 2 | 5 |

BT = biopsy, PT = partial resection, ST = subtotal resection, T = total resection, S = time between the operations, DVT = deep venous thrombosis, Rx = radiotherapy, BSW = salt brain wasting, GOS = Glasgow outcome scale

supratentorial tumors.[2] Hence, these discrepancies reinforce the great histological heterogenicity of these tumors. Therefore, there has been a surge in staged resection as a treatment strategy, wherein the purpose is to achieve the best cytorreduction by using more accurate hemostasis technique along with the clinical restoration of the patient. Ideally, if the tumor is slow growing, this technique is more effective. However, in malignant tumors, this strategy should be applied with less duration of patient recovery [Figure 3 and Table 2].

The present study observed significant benefits of staged resection in almost all benign tumors and in some malignant tumors. Notably, giant intracranial benign tumors are slow growing and allow more time between the surgical procedures, facilitating the clinical restoration of children per their weight gain [Figure 4 and Table 2]. One study corroborated this impression and in a study involving three cases, Zhu *et al*.[1] argued that the approach of more than one operative procedure is beneficial in children with benign tumors because they are operated under better clinical conditions and with more time to recover between procedures. Another advantage of the step-by-step approach is the patient's weight gain between operating times, with a gain of up to 10 kg between interventions, making patients less susceptible to complications. Generally, the decision to time the resection stages is dependent on the tumor histology and the patient's clinical condition. Notably, malignant tumors should be addressed earlier, whereas the benign ones could be approached as patients recover.

Total resection of GPIT with a single procedure is often prevented by combination factors, such as patients' fragility and technical difficulties posed by tumors, and specially for malignant tumors like giant medulloblastomas, we had begun the resection debulking the tumor to achieve maximum and safe resection, and stopped the procedure only if there was a risk of hemodynamic instability because of the bleeding. Studies have revealed that subpial resection in monoblock is a valid option for giant tumors.[2,9] However, in our study case, this technique was not feasible either because of the tumor depth without an easily coagulable pedicle or the tumor size, preventing an external dissection of the tumor without causing excessive brain retraction or lesion to the veins on the brain surface. Moreover, in giant posterior fossa tumors, this technique was not feasible owing to the proximity to the brain stem structures and consequent worsening potentials during intraoperative monitoring.

Nevertheless, adequate control of intraoperative hemostasis is the primary factor limiting total resection at the first approach, especially in children with low

weight.[7,27,28] Although a previous study considered preoperative embolization to be useful, as a strategy to minimize hemorrhages, in managing choroid plexus carcinomas, in our experience this technique was not feasible in most situations for several reasons as follows: patient size, small size of the nourishing arteries, and clinical presentation with intracranial hypertension, without a prompt time for hemodynamic action.[29,30] The use of technologies like ultrasonic aspiration proved useful in tumors with a hard consistency because in addition to reducing the operating time, they minimized the retraction of neural structures. However, in tumors that were less consistent and more vascularized, the use of such technologies might cause loss of control over bleeding, and therefore, a piecemeal resection technique is preferred in such situations. Another intraoperative factor considered fundamental in controlling hemostasis and surgical duration was the communication between the pediatric neurosurgeon and the team of anesthesiologists and neurophysiologists. Notably, a previous case series study considered this communication crucial in minimizing fatal hemodynamic complications.[13]

Nevertheless, the mean hemotransfusion rate in this study was noted to be low (28.4 mL/kg), and hence, a staged resection combined with strategies to minimize blood loss proved effective. Studies have revealed a correlation between intraoperative hemorrhage during pediatric intracranial tumor surgeries and the increase in ICU hospitalization, as well as the need for mechanical ventilation and cardiovascular support.[7,31] Goobie *et al.*[32] considered a value of 60 mL/kg as the cutoff point, above which the outcome of craniosynostosis surgeries were worse.

Notably, among the complications observed in this study, motor alterations prevailed during the immediate postoperative period. However, these completely resolved in all patients within a week with increased corticotherapy and physiotherapy. In addition, intraoperative electrophysiological monitoring has proved to be an useful tool in minimizing permanent motor injuries. Notably, among the most commonly described complications are subdural effusion and endocrinological and metabolic disorders, either early or late.[3,14,33]

Nonetheless, this study had some limitations, such as the retrospective nature of data collection, impossibility to obtain quantitative data of tumor size, and nonusage of more accurate instruments to assess the patient's functional status during follow up. However, given that GPIT occurs less frequently than other intracranial tumors, the information provided by this study is meritworthy and will enable the acquisition of more future evidence.

The management of GPIT is a major challenge because of both the high technical complexity of tumor resection and the low tolerance of patients to hemorrhages and complications, especially in younger and low weight children with huge vascular tumors. Nevertheless, a detailed study of each child, meticulous planning of staged resection, and aiming maximum safe resection could improve a patient's survival by minimizing the risk of intraoperative catastrophic hemorrhages and enabling better recovery.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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