

Treatments for obstructive hydrocephalus secondary to malignant midline intracranial tumors during the perioperative period – a retrospective study of 372 pediatric patients from a single institution

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Abstract

Objective

Common treatments for obstructive hydrocephalus caused by malignant midline intracranial tumors during the perioperative period include ventriculoperitoneal shunt (VPS) placement/endoscopic third ventriculostomy (ETV) and direct tumor resection, but which of these treatments is superior remains unclear. The purpose of this study is to explore the management of hydrocephalus during the perioperative period and subsequent outcomes.

Methods

Data from 372 patients with obstructive hydrocephalus due to malignant midline intracranial tumors under the age of 18 years referred to the Department of Pediatric Neurosurgery at Beijing Tiantan Hospital between January 2018 and September 2019 were collected. We also collected their clinical features and outcomes for further statistical analysis.

Results

A total of 372 pediatric patients were treated for obstructive hydrocephalus. In total, 215 patients underwent preoperative VPS placement; the effectiveness of preoperative VPS placement was 98.1% (211/215), and the mean duration of relapse was 63.5 ± 15.7 days. Forty children underwent ETV before tumor removal; the effectiveness of preoperative ETV was 90.0% (36/40), and the mean duration of relapse was 53.8 ± 44.9 days. A total of 117 patients underwent direct tumor resection after being diagnosed; the recurrence rate of hydrocephalus was 20.5% (24/117), and the mean duration of relapse was 125.0 ± 170.8 days. There was a significant difference between preoperative VPS placement followed by resection and postoperative VPS placement and preoperative ETV followed by resection and postoperative VPS placement ($p = 0.013$).

Conclusion

Malignant midline intracranial tumors in pediatric patients usually lead to obstructive hydrocephalus, and preoperative intervention for hydrocephalus (VPS or ETV) will improve patient outcomes. The optimal management strategy for obstructive hydrocephalus due to malignant midline intracranial tumors is preoperative VPS placement or ETV due to their low hydrocephalic recurrence rates and high effectiveness.

Introduction

Hydrocephalus is the most common condition treated by pediatric neurosurgeons[10]. Obstructive hydrocephalus (also known as noncommunicating hydrocephalus) occurs when there is obstructed cerebrospinal fluid (CSF) flow within the ventricular system[15], especially in the intraventricular, paraventricular[16] and other midline regions. Therefore, obstructive hydrocephalus is one of the most common complications of midline tumors, leading to an abnormal accumulation of CSF in the central nervous system[20] and eventually increased intracranial pressure (ICP). For malignant midline tumors, subsequent chemotherapy and radiotherapy are often required after resection, introducing more considerations about how to relieve the recurrence of hydrocephalus.

To relieve the symptoms of obstructive hydrocephalus caused by malignant midline intracranial tumors, neurosurgeons often prefer surgery to remove the tumors and recover CSF circulation. Nevertheless, avoiding acute encephalocele and ensuring the recovery CSF circulation during surgery is not guaranteed. Furthermore, how to prevent hydrocephalus relapse during subsequent therapy is still unclear.

Thus, ventriculoperitoneal shunts (VPSs) have become one of the conventional treatments[7, 26] and have undergone many advances since their first use in the mid-1950s[24]. However, the potential complications were significant, including foreign material implantation, shunt malfunction, infections, and cognitive impairment, which remained a constant source of concern for the child, parents, and family[4, 18, 23, 26].

In the 1990s, endoscopic third ventriculostomy (ETV) emerged as an effective alternative treatment for hydrocephalus, along with improvements in endoscopy and camera technologies[4, 9]. The primary advantage of ETV is freedom from foreign material implantation, but this approach cannot ensure whether the stoma closes early.

Therefore, which of these treatments is superior is still widely discussed and remains unclear. Neurosurgeons are usually expected to rely on their experience[8]. To address this problem, we reviewed 372 pediatric patients who were treated for obstructive hydrocephalus at a single center to describe the management of hydrocephalus during the perioperative period and the subsequent outcomes.

Methods

Clinical criteria

Over 1,000 pediatric patients are admitted to the Department of Pediatric Neurosurgery, Beijing Tiantan Hospital every year; more than 80% of them are children with intracranial tumors, and approximately half are complicated with obstructive hydrocephalus. In total, we retrospectively reviewed 372 consecutive pediatric patients during the study period from January 2018 to September 2019. All patients had undergone preoperative and postoperative neurological and radiological evaluations. The inclusion criteria were as follows: 1) under 18 years of age; 2) initial neuroimaging showed solid midline intracranial tumors (Ommaya reservoirs rather than ETV/VPS placement were preferred for cystic tumors), complicated with enlarged ventricles as well as paraventricular edema (Fig 1); 3) postoperative

pathology including glioma, germ cell tumors, medulloblastoma, anaplastic ependymoma, etc.; and 4) initial VPS placement or ETV was implemented preoperatively or the tumor was directly resected after diagnosis to relieve hydrocephalus. Clinical characteristics were collected from medical records, such as age at the first operation, sex, tumor location, pathology, preoperative and postoperative therapeutic schedule, date of the initial procedure, date of resection, date of every subsequent procedure, date of hydrocephalus relapse, date of the last follow-up, and outcomes. Regular follow-up data regarding postoperative symptoms and outcomes were obtained from 1 year to 3 years after surgery via telephone. The criterion to define an effective operation that relieved hydrocephalus was mainly the absence of signs or symptoms of increased ICP, including an improved level of consciousness, resolution of eye movement abnormalities, and relief from headache, vomiting, and urinary incontinence. Follow-up neuroimaging was not considered crucial because on imaging, the ventricles often do not show a remarkable reduction in size postoperatively compared to preoperatively[4]. In contrast, the criterion for hydrocephalus recurrence was relapse of the signs and symptoms above, and neuroimaging indicated absolute enlargement of the ventricles.

Statistical analysis

For clinical parameters, continuous variables are presented as means (\pm standard deviations), and categorical variables are presented as numbers of patients and frequencies. The differences in clinical parameters were analyzed by t-tests or chi-square tests. SPSS software version 17.0.0 (IBM Corp., Armonk, New York, USA) was used for statistical analyses. A $p < 0.05$ was used as a threshold for statistical significance, and all tests were two-tailed.

Results

Clinical characteristics

A total of 372 pediatric patients were treated for obstructive hydrocephalus at our department from January 2018 to September 2019, and their conditions were all caused by malignant midline intracranial tumors. There was an obvious preponderance of boys (65.1%; Table 1). The mean age at the first surgery was 7.6 ± 4.1 years. The midline tumors originated from three locations, including suprasellar (9.7%), pineal region (26.1%), and the fourth ventricle (64.2%). Moreover, the most common pathology was medulloblastoma (36.0%), followed by germ cell tumor (18.8%), glioma (18.0%), other types of tumors (17.5%), and anaplastic ependymoma (9.7%).

Furthermore, the sex ratio (0.7, 4.4, 1.6, respectively, $p < 0.001$; Table 2), as well as the mean age at first surgery (7.0 ± 4.3 , 9.4 ± 4.1 , 7.0 ± 3.8 , respectively, $p < 0.001$), was significantly different among the three locations of suprasellar, pineal region and the fourth ventricles. The main pathology in suprasellar was glioma (66.7%), whereas the most common pathology in the pineal region was germ cell tumors (63.9%), and the fourth ventricle showed a predominance for medulloblastoma (56.1%), which led to significant differences in pathology among the three locations ($p < 0.001$).

Among the 372 patients, 117 underwent direct excision after diagnosis (31.4%; Table 3), 40 underwent ETV preoperatively (10.8%), and 215 underwent VPS placement (57.8%). After tumor resection, 3 children underwent ETV (1 tumor in suprasellar (5.6%), 2 in the fourth ventricle (0.8%)), and 31 underwent VPS placement (6 tumors in the suprasellar are (16.7%), 9 in the pineal region (9.3%), 16 in the fourth ventricle (6.7%)) due to the recurrence of hydrocephalus.

Outcomes of initial VPS placement or ETV

VPS placement was performed as the first-line treatment in 215 patients with obstructive hydrocephalus. In our analysis, sex and age at the first surgery were significantly different among the three locations ($p = 0.021$ and 0.010 , respectively; Table 4). The outcomes of these 215 patients were optimistic; only 4 children experienced recurrence of hydrocephalus because of shunt blockage (2 tumors in the suprasellar and 1 in the fourth ventricle underwent VPS placement again after resection, and 1 from the fourth ventricle underwent ETV). The effectiveness of preoperative VPS placement was 98.1% (211/215), and the mean duration of relapse was 63.5 ± 15.7 days.

Forty children underwent ETV before tumor resection; sex and age at the first surgery were not significantly different among the locations ($p = 0.069$ and 0.078 , respectively; Table 5). Hydrocephalus recurred in 3 patients with germ cell tumors and 1 with anaplastic ependymoma, so VPS placement was performed after tumor resection (3 from the pineal region and 1 from the fourth ventricle), so the effectiveness of preoperative ETV was 90.0% (36/40), and the mean duration of relapse was 53.8 ± 44.9 days. Therefore, the effectiveness of preoperative VPS placement and ETV were both over 90%, but there was a significant difference between preoperative VPS placement followed by resection and postoperative VPS placement and preoperative ETV followed by resection and postoperative VPS placement ($p=0.013$).

Outcomes of direct resection

Furthermore, 117 patients underwent direct resection after diagnosis instead of VPS placement or ETV. The sex ratio was significantly different among the three locations ($p = 0.003$; Table 6), while age at the first surgery was not different ($p = 0.155$). According to our statistics, 20.5% (24/117) of patients (seven gliomas, seven medulloblastomas, four germ cell tumors, four anaplastic ependymomas, and two other malignant tumors) underwent VPS placement after tumor resection because of recurrence of hydrocephalus. Interestingly, two (1.7%) of these patients underwent ETV after the hydrocephalus recurred, but the symptoms were not relieved, and they finally underwent VPS placement to relieve their condition. The mean duration of relapse was 125.0 ± 170.8 days, the maximum and minimum durations were 710 and 7 days, respectively, and the median was 42 days. It is worth emphasizing that 22 of the 24 patients suspended their treatment due to sudden hydrocephalus relapse during chemoradiotherapy.

TABLE 1. Summary of the clinical characteristics of 372 pediatric patients with an initial presentation of hydrocephalus caused by malignant midline intracranial tumors

Clinical characteristics	Patients n (%)
Gender	
Male	242 (65.1)
Female	130 (34.9)
Age (years)	7.6 ± 4.1
Locations of tumor	
Suprasellar	36 (9.7)
Pineal region	97 (26.1)
Fourth ventricle	239 (64.2)
Pathology	
Glioma	67 (18.0)
Germ cell tumor	70 (18.8)
Medulloblastoma	134 (36.0)
Anaplastic ependymoma	39 (9.7)
Others	65 (17.5)

TABLE 2. Clinical characteristics of 372 pediatric patients with hydrocephalus caused by malignant midline intracranial tumors in 3 different locations

Clinical characteristics	Location of tumors (n)			<i>p</i>
	Suprasellar (36)	Pineal region (97)	Fourth ventricle (239)	
Gender				<0.001
Male	15 (41.7)	79 (81.4)	148 (61.9)	
Female	21 (58.3)	18 (18.6)	91 (38.1)	
Age (years)	7.0 ± 4.3	9.4 ± 4.1	7.0 ± 3.8	<0.001
Pathology				<0.001
Glioma	24 (66.7)	6 (6.2)	37 (15.5)	
Germ cell tumor	7 (19.4)	62 (63.9)	1 (0.4)	
Medulloblastoma	0 (0.0)	0 (0.0)	134 (56.1)	
Anaplastic ependymoma	0 (0.0)	2 (2.1)	34 (14.2)	
Others	5 (13.9)	27 (27.8)	33 (13.8)	

TABLE 3. Treatment for 372 pediatric patients with hydrocephalus caused by tumors located in 3 different regions

Treatments	Location of tumors (n)		
	Suprasellar (36)	Pineal region (97)	Fourth ventricle (239)
Direct resection 117	14 (36.1)	24 (24.7)	79 (33.1)
Preop. ETV 40	1 (2.8)	32 (33.0)	7 (2.9)
Preop. VPS 215	21 (61.1)	41 (42.3)	153 (64.0)
Postop. ETV 3	1 (5.6)	0 (0.0)	2 (0.8)
Postop. VPS 31	6 (16.7)	9 (9.3)	16 (6.7)

TABLE 4. Outcomes of 215 pediatric patients with hydrocephalus who underwent VPS placement preoperatively

Clinical characteristics & Outcomes	Location of tumors (n)			p
	Suprasellar (21)	Pineal region (41)	Fourth ventricle (153)	
Gender (M : F)	11:10	34:7	94:59	0.021
Ages (years)	7.5 ± 4.5	9.2 ± 4.2	7.1 ± 3.9	0.010
Postop. VPS	2 (9.5)	0 (0.0)	1 (0.7)	0.042
Postop. ETV	0 (0.0)	0 (0.0)	1 (0.7)	-

TABLE 5. Outcomes of 40 pediatric patients with hydrocephalus who underwent ETV preoperatively

Clinical characteristics & Outcomes	Location of tumors (n)			p
	Suprasellar (1)	Pineal region (32)	Fourth ventricle (7)	
Gender (M : F)	1:0	27:5	3:4	0.069
Ages (years)	15.0	10.3 ± 4.2	7.0 ± 3.4	0.078
Postop. VPS	0 (0.0)	3 (9.4)	1 (14.3)	0.838
Postop. ETV	0 (0.0)	0 (0.0)	0 (0.0)	-

TABLE 6. Outcomes of 117 pediatric patients with hydrocephalus who did not undergo with VPS placement or ETV preoperatively

Clinical characteristics & Outcomes	Location of tumors (n)			p
	Suprasellar (14)	Pineal region (24)	Fourth ventricle (79)	
Gender (M : F)	3:11	18:6	51:28	0.003
Ages (years)	6.3 ± 3.2	8.4 ± 3.8	6.9 ± 3.8	0.155
Postop. VPS	4 (28.6)	6 (25.0)	14 (17.7)	0.540
Postop. ETV	1 (7.1)	0 (0.0)	1 (1.3)	-

Discussion

The mechanisms of hydrocephalus have not yet been fully illuminated, but it has been proven that the deterioration of CSF dynamics may play a role[2]. This study mainly discussed acquired hydrocephalus; some pathophysiological processes that affect ventricular outflow and subarachnoid absorption as well as brain compliance may contribute to the occurrence and development of this condition[10]. It has been reported in the literature that intraventricular hemorrhage is the most common cause of acquired hydrocephalus in infants, including premature babies. After this period, tumors become the most frequent etiology of acquired hydrocephalus, especially midline tumors in the fourth ventricle[2, 3, 10]. These tumors obstruct the CSF circulation, leading to acquired hydrocephalus, and therefore, this condition is classified as obstructive hydrocephalus. Similarly, we found that malignant midline intracranial tumors in pediatric patients usually lead to obstructive hydrocephalus, which is consistent with previous reports. Furthermore, by analyzing the patient characteristics, it was clear that the types of the tumor differed among locations, and the sex ratio and age at first surgery were also different for different types of tumors.

This large series demonstrated several findings regarding treatments as well. Direct tumor resection was able to re-establish CSF circulation and avoid a second operation. Nevertheless, this situation may be

temporary, as hydrocephalus relapse can be caused by residual tumor tissue, blood clots, hemostatic material, or partial brain swelling, which are hard to predict. Therefore, if the tumors were directly resected after the diagnosis, without using any method to relieve the hydrocephalus in advance, there is a high probability that the hydrocephalus would immediately recur. This situation would not only interrupt subsequent radiotherapy or chemotherapy but also can be life-threatening in some cases. The treatment method cannot predict the subsequent changes in patient condition; hence, a specific method is not recommended in clinical practice. According to the outcomes of 117 patients who underwent direct tumor resection in this study, the recurrence rate of hydrocephalus was as high as 20.5%, and the shortest duration was only 7 days. A retrospective study in 2018 found that the recurrence rate after direct resection of tumors in midline regions, such as posterior fossa tumors, in children was 8.4%^[3], and this rate was even over 25% in other reports^[21].

The placement of a VPS is a simple and safe surgery, and this device can effectively relieve various kinds of hydrocephalus. According to reports, the perioperative mortality rate of VPS placement is under 1%^[22], and the estimated 30-year VPS-related mortality rate is 5–10%^[10, 19]; moreover, some reports showed that the overall survival rate after VPS placement was 70% at 1 year, 58% at 10 years, and 49% at 20 years^[1], showing a decreasing trend year to year. According to our data analysis, the effectiveness of an initial VPS was 98.1% among 215 patients, and among those patients who failed initial ETV, a VPS can also solve the problem of hydrocephalus recurrence. Interestingly, a study in 2011 declared that patients with malignant tumors were less likely to experience VPS failure than those with benign tumors^[20], which may mean that patients with malignant tumors should be more inclined to choose a VPS preoperatively. Nevertheless, the disadvantages of VPSs are obvious as well. Foreign materials can be implanted for a long time, but whether these materials can be removed eventually remains to be explored. Moreover, obstruction is the most common cause of mechanical shunt failure^[1]. Previous studies have indicated that the rate of shunt infection is approximately 5–9%^[11, 12], and the first infection commonly occurs within 3 months after surgery.^[14, 27] With ETV, the problem of foreign material implantation is fundamentally avoided. The success rate of initial ETV ranges from 71% to over 90%^[6, 28], and the overall complication rate of ETV was shown to be 9% in recent meta-analyses^[17, 25]. According to our data, the effectiveness of preoperative ETV was 90.0%, which is consistent with previous reports. Regarding the disadvantages of this method, closure of the stoma secondary to gliosis usually presents within 2 years^[4]; therefore, whether hydrocephalus can be continuously alleviated in the postoperative and subsequent treatment period is unknown, necessitating the need for larger survey samples and a longer follow-up.

As a consequence, when choosing between VPS and ETV, we should not place more emphasis on ETV or even disregard VPS. According to our data analysis, VPS and ETV were equally able to relieve hydrocephalus, and the effectiveness of both was over 90%; however, upon deeper analysis, we found that preoperative VPS placement followed by resection and postoperative VPS placement was significantly different from preoperative ETV followed by resection and postoperative VPS placement, revealing that preoperative VPS placement led to a lower hydrocephalus recurrence rate and was more

effective. One of the longest follow-up surveys of pediatric patients with hydrocephalus declared that the long-term survival rate with a VPS was higher than that of ETV[1]; moreover, ETV failure occurred sooner than VPS failure according to another former study[5]. These previous results support our conclusion. Regarding those who are inclined to replace VPS placement with ETV, such views are mostly based on the skepticism and controversy about the higher complication rate, but even if shunt malfunctions and infections occur, careful aseptic techniques can decrease the rate of VPS-related infection[13], and the coating material and shunt design are also undergoing updates to reduce the possibility of obstruction[10]. Both VPS placement and ETV have their own advantages and disadvantages; therefore, it is highly unlikely that VPS placement will become an obsolete therapy in the foreseeable future; on the contrary, VPSs are crucial.

Conclusion

Malignant midline intracranial tumors in pediatric patients usually lead to obstructive hydrocephalus, and reliable and stable relief of hydrocephalus during the whole treatment period is the goal of comprehensive treatment for children.

We rarely recommend direct resection on account of a high recurrence rate. VPSs and ETV are two kinds of safe and effective treatments for obstructive hydrocephalus caused by midline tumors malignant, and both approaches can lay a solid foundation to ensure the safety of follow-up chemoradiotherapy. Therefore, VPSs and ETV can achieve a similarly high rate of effectiveness in the treatment of obstructive hydrocephalus secondary to malignant midline intracranial tumors during the perioperative period. Nevertheless, many patients who undergo initial ETV may experience hydrocephalus relapse and need to be rescued by a VPS.

Declarations

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Code availability: Not applicable.

Ethics approval: Not applicable.

Consent to participate: Not applicable.

Consent for publication: Not applicable.

Authors' contributions: Yunwei Ou and Kaiyu Fan contributed equally to this work. Jian Gong found out the problem according to clinical routine work. Zhiming Liu, Zhiyi Liao, Heng Zhang, Zhicen Li, Wenjian Zheng and Xueyi Guan collected the patients' data. Yunwei Ou analyzed and interpreted the data, Kaiyu Fan was a major contributor in writing the manuscript. All the authors read and approved the final manuscript.

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Figures

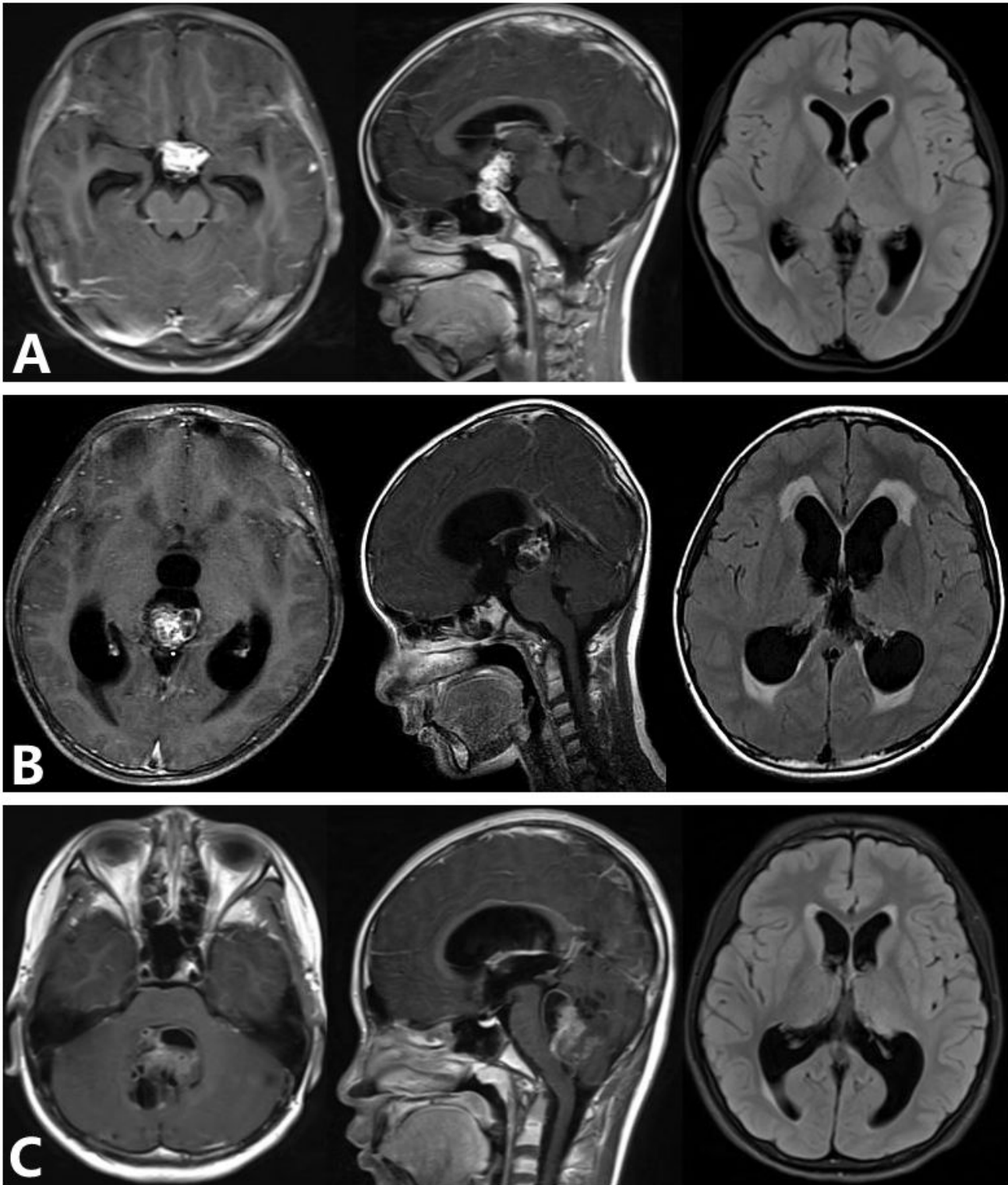


Figure 1

Preoperative magnetic resonance imaging (MRI) of the included children. There're axial, sagittal enhanced images and fluid attenuated inversion recovery (FLAIR) from left to right, respectively. A: Tumor in the suprasellar, its pathology was mixed germ cell tumor; B: Tumor in the pineal region, and the pathology was germinoma; C: Tumor in the fourth ventricle, and its pathology was medulloblastoma. All the midline tumors caused obstructive hydrocephalus with paraventricular edema.