Surgical Management and Prognostic Factors Based on 50 Tectal Plate Gliomas

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Abstract

Background

The management and prognostic factors of tectal glioma (TG) remain ambiguous, because it is an extremely rare neoplasm that occurs predominantly in the pediatric population. The objective of this study was to evaluate the risk factors for progression-free survival (PFS) in TG patients after ETV operation, elucidate the radiological features of TG, and propose a treatment protocol.

Methods

From 2002 to 2018, 50 patients that preoperative imaging manifestations were low-grade TGs were treated at our institute. Clinical features, treatments, radiologic findings, biopsies, and pertinent risk factors were evaluated.

Results

A total of 50 patients with a diagnosis of TG were identified. Twenty-six (52%) patients were males. The median age at diagnosis was 11.5 years (range 0.5–19 years). All patients had symptoms related to obstructive hydrocephalus and were treated with endoscopic third ventriculostomy (ETV). After a median follow-up duration of 59 months (range 11.0–208.0 months), progression occurred in six patients (12%), with a median PFS time of 18.0 months (range 4.0–56.0 months). Twelve patients (24%) underwent a biopsy, one patient (8.3%) was diagnosed with anaplastic oligodendroglioma, one patient (8.3%) was diagnosed with astrocytoma (WHO grade II-III), five patients (41.7%) were diagnosed with pilocytic astrocytoma, and the type of tumor could not be confirmed in five patients (41.7%) due to the small amount of tumor sample, thus, these patients were diagnosed with gliosis. PFS rates at 1 and 5 years were 91.2% ± 4.2% and 84.9% ± 5.9%, respectively. A multivariate model demonstrated that a large tumor size and cystic changes are risk factors for progression.

Conclusion

ETV has been uniformly successful in the management of hydrocephalus caused by TG. A large tumor size and cystic changes are risk factors for progression. Under the condition of safety, a biopsy should be performed. For patients with low-grade TG, ETV is often the only surgical procedure that most patients require.

Highlights

Tectal gliomas are generally low-grade gliomas with a favorable prognosis.

The only surgical procedure that most patients with tectal glioma require is ETV.

Under the condition of safety, neuroendoscopy for a pathological diagnosis should be performed.

A large tumor size and cystic changes are risk factors for progression.

Background

Tectal glioma (TG) represents a unique subset of typically low-grade gliomas arising in the tectal region at the roof of the brainstem.[1, 2] The clinical presentation is often related to symptoms of obstructive hydrocephalus from the compression of the cerebral aqueduct, including headache and nausea typically attributed to increased intracranial pressure.[3–5] Endoscopic third ventriculostomy (ETV) is a neurosurgical approach used to redirect cerebrospinal flow and is currently the most often used approach for the treatment of obstructive hydrocephalus. [6–8]Given the paucity of information regarding TG in published studies, its management and prognostic factors remain ambiguous, and few studies have systematically summarized the clinical outcome of TG patients treated with ETV. [4, 9–12]Therefore, we retrospectively reviewed patients whose preoperative imaging manifestations were consistent with low-grade TG and who underwent ETV in our institute. The goal of this study was to evaluate the risk factors for progression-free survival (PFS), elucidate the radiological features of TG, and propose a treatment protocol based on 50 TG patients who received ETV treatment.

Methods

Patient Population

From 2002 to 2018, 50 patients whose preoperative imaging manifestations were consistent with low-grade TG and who underwent ETV at our institute were enrolled in this study. The study was performed under an institutional review board-approved protocol in compliance with regulations set by Beijing Tiantan Hospital (BTH) for the study of human subjects with their informed consent. Radiographic and pathological data were collected from picture archiving and communications systems (PACSs). A comprehensive review of medical charts, pertinent radiographic data, and operative reports was conducted. Clinical records and imaging studies were reviewed to confirm the presence of TG and the symptoms of the patients. A standardized report form was used to extract clinical data, including sex, age, main preoperative complaint, symptom duration, and any follow-up data, from the medical records.

Radiological Analysis

Tumor volumes were assessed for T1 and T2 signal intensity and circumscription, and calculated using the cubature formula as follows: volume = abc/2, in which a, b, and c were mutually orthogonal and represented the maximal diameters (width, thickness, and height) measured on axial, sagittal, and coronal magnetic resonance imaging (MRI) scans. Each tumor was graded for the proportions of cystic and/or enhancement avidity at each time -point. Changes in tumor size are given as the percentage of the two greatest perpendicular diameters compared to baseline, and an increase of $\geq$ 25% was categorized as progressive disease.

Surgical Management

For patients with TG in this study, all suffered from the clinical symptoms caused by hydrocephalus. ETV was the first intervention to treat obstructive hydrocephalus, and a biopsy was performed with safety and no bleeding. Craniotomy was performed when the tumor progressed obviously and the symptoms gradually worsened after ETV.

Pathological Examination

Fresh paraffin-embedded tumor tissue was cut into 5-μm slices and stained with hematoxylin and eosin (HE). Immunohistochemical staining was performed for glial fibrillary acidic protein (GFAP), Ki-67 protein (Ki-67), oligodendrocyte lineage transcription factor (Olig2), epithelial membrane antigen (EMA), cytokeratin (CK), carcinoembryonic antigen (CEA), vimentin, and S-100. Two independent neuropathologists reviewed the microscopic pathologies of TG samples.

Follow-up and Statistical Analysis

A clinical and radiographic follow-up was performed every 6 months within the first year and yearly thereafter. Four patients were lost to follow up, and 46 (92%) patients were available for PFS analysis. The pertinent risk factors were evaluated by univariate and multivariate Cox regression analyses. Secondary outcomes were PFS in subgroups with significant risk factors, and the pertinent estimated mean PFS time was calculated using the Kaplan-Meier method (log-rank test). $P < 0.05$ was considered significant. Analyses were performed with SPSS software (version 25.0, IBM Corp.).

Results

Participants and Descriptive Data

The present cohort included 26 males and 24 females, with a median age of 11.5 years (range 0.5–19 years) at the initial diagnosis. The mean duration of symptoms was 9.1 months (range 0.3–36 months), and the most common preoperative symptom was headache (38 cases), followed by balance problems and ataxia (27 cases), nausea and vomiting (21 cases), visual complaints (8 cases), seizures (7 cases), urinary incontinence (4 cases), and developmental delay (4 cases) (Table 1).

Table 1
Clinical data from our series

Variable	Cases
No. of patients	50
Sex, no. (%)	
Male	26 (52.0)
Female	24 (48.0)
Age in years	
Median	11.5
Mean ± SD	10.4 ± 4.8
Main complaint, no. (%)	
Headache	38 (76)
Balance problems/Ataxia	27 (54)
Nausea/Vomiting	21 (42)
Visual complaints	8 (16)
Urinary incontinence	4 (8)
Developmental delay	4 (8)
Seizures	7 (14)
Duration of symptoms in months	
Median	6
Mean ± SD	9.1 ± 9.5
Pathology, no. (%)	
Gliosis	5 (41.7)
Low-grade glioma (WHO I-II)	5 (41.7)
High-grade glioma (WHO II-III)	2 (16.6)
FU duration in months	
Range	11.0-208.0
Median	57.0
Mean ± SD	72.9 ± 55.0

Radiographic Evaluation

All patients underwent preoperative MRI scans. The most common manifestations on MRI were hypointensity on T1-weighted images (44 cases [88%]) and hyperintensity on T2-weighted images (43 cases [86%]) (Fig. 1). Two lesions (4%) were heterogeneously enhanced on contrast images, and one lesion (2%) was homogeneously enhanced on contrast images. Cystic changes occurred in five lesions (10%). The mean tumor measurement at diagnosis was 2.8 ± 1.3 cm^3 (range 1.0-5.8 cm^3) (Table 2).

Table 2
Tumor characteristics

Characteristic	No. (%)
Lesion volume in cm^3	
Mean ± SD	2.8 ± 1.3
Range	1.0-5.8
MRI feature	50 (100)
TI & T2 signals	
Hypo T1 & hyper T2	42 (84)
Hypo T1 & mixed iso/hyper T2	2 (4)
Mixed iso/hypo T1 & mixed iso/hyper T2	4 (8)
Iso T1 & hyper T2	1 (2)
Iso T1 & mixed iso/hyper T2	1 (2)
Enhancement	
Heterogeneous	2 (4)
Homogeneous	1 (2)
Cystic changes	5 (10)
hyper = hyperintensity; hypo = hypointensity; iso = isointensity	

Treatment Strategies

All patients underwent ETV to treat obstructive hydrocephalus, and 12 patients (24%) underwent a biopsy. Successful ETV was achieved in all patients, and there were no intraoperative complications. A successful ETV procedure was defined as freedom from a shunt, an improvement in symptoms, and a reduced ventricular size.

Radiological progression eventually occurred in 6 of 46 patients. Four out of six patients who exhibited radiological progression underwent surgical resection, one patient received radiotherapy, and the other patient did not receive any treatment after ETV. The 40 patients without radiological progression did not receive any other treatment after ETV.

Pathological Diagnosis

Twelve patients (24%) underwent a biopsy. One sample (1/12, 8.3%) displayed histopathologies similar to those of anaplastic oligodendroglioma (WHO grade□), one sample (1/12, 8.3%) displayed histopathologies similar to those of astrocytoma (WHO grade II-III), and five samples (5/12, 41.7%) displayed histopathologies similar to those of pilocytic astrocytoma (WHO grade□). The type of tumor could not be confirmed in five samples (5/12, 41.7%) due to the limited tumor sample size; thus, these patients were diagnosed with gliosis (Fig. 2).

Follow-up

The median follow-up period was 57 months (range 11–208 months). At the end of follow-up, all of the patients were shunt-free, and the clinical symptoms related to hpdrocephalus had disappeared or were relieved. The symptom of headache disappeared in 28/38 (73.7%) patients who had a preoperative headache, and the symptom of headache in another 10 patients (26.3%) was relieved. All 27 patients (100%) who had preoperative balance problems or ataxia were asymptomatic after ETV and had normal gait. The 7 patients who had preoperative seizures were all asymptomatic for seizures after ETV. All postoperative imaging studies revealed a reduction in the ventricular size.

In the radiological progression group, the four patients who underwent surgical resection suffered from postoperative complications: two patients suffered from visual field defects and Parinaud syndrome, and the other two suffered from mutism. The patient who received only radiotherapy remained progression-free for two years after the completion of radiosurgery and his biopsy revealed astrocytoma (WHO grade II-III). The patient who did not receive chemotherapy or radiotherapy after ETV died three years later, and his biopsy revealed anaplastic oligodendroglioma (WHO grade□).

ETV failure was reported in one patient one year after the first intervention, the patient experienced balance problems again, and ETV was repeated. During surgery, we found that the stoma was closed. The symptoms disappeared after the second ETV operation.

PFS and Risk Factors

In our series, radiological progression occurred in 6 patients (12%). The results of the univariate Cox regression analysis (including age, sex, duration of symptoms, lesion volume, contrast enhancement, cystic changes and tumor circumscription) showed that a large tumor size (> 2.8 cm^3, P = 0.02) and cystic changes (P = 0.01) were independent adverse factors for PFS. Other radiologic parameters and clinical parameters were not significantly associated with PFS. PFS rates at 1 and 5 years were 91.2% ± 4.2% and 84.9% ± 5.9%, respectively. The estimated median survival time for PFS was 4 years (Fig. 3).

Discussion

ETV can effectively relieve the symptoms of obstructive hydrocephalus caused by TG

The clinical symptoms of TG in patients are always caused by increased intracranial pressure from obstructive hydrocephalus.[13, 14] The natural history of these tumors is most often indolent. [11, 13–16]Thus, for most of these patients, the treatment of hydrocephalus is enough.[4, 17] ETV and shunt placement are currently the most widely used methods to relieve hydrocephalus. However, the risk of postoperative complications with shunt surgery is significantly higher than that of ETV.[3, 18] In our series, all of the patients were shunt-free during the follow-up period, and the symptoms caused by increased intracranial pressure disappeared or were relieved. For patients with low-grade TG, ETV is often the only surgical procedure that most patients require (Figs. 4 and 5).

Use of neuroendoscopy for a pathological diagnosis of TG

We can use neuroendoscopy for the pathological diagnosis of patients with TG.[19] Although most TGs are low-grade gliomas, there are also reports in the literature of TG that may also be a high-grade glioma. [3, 20] In our group, there were two patients whose preoperative imaging diagnoses were low-grade gliomas, but the pathological diagnoses were high-grade gliomas (WHO grade II-III), which indicates that imaging studies may not always accurately confirm the nature of the tumors.

The benefit of a pathological diagnosis is that it can identify the characteristics and grade of the tumor and guide subsequent treatment. [2, 19]The follow-up treatment of patients with TG is very important based on the pathological diagnosis.[5, 21] In our group of patients, one patient underwent ETV and received a biopsy. The pathology revealed anaplastic oligodendroglioma (WHO grade □). The patient did not receive chemoradiation or radiotherapy after the surgery. The symptoms of intracranial hypertension disappeared after ETV, but the patient died of glioma progression three years after ETV (Fig. 6). The pathological diagnosis of another patient who received ETV and biopsy was astrocytoma (WHO grade II-III). Six months later, the patient showed radiological progression and was treated with radiosurgery. The patient's vision improved after the ETV procedure, and the patient remained progression-free for two years after the completion of radiosurgery (Fig. 7).

During the operation of ETV, it is necessary to keep the surgical field clean as far as possible, and the bleeding during the operation is also very dangerous to the patient. So not all patients with TGs are eligible for a biopsy because of safety concerns, such as patients who have a small interventricular foramen or those in which the location of the tumor is not safe for assessing the pathology. In our study, 28 patients with TGs did not perform a biopsy due to the small interventricular foramen. More importantly, we found that tumor size greater than 2.8 cm^3 (P = 0.02) and cystic changes (P = 0.01) are significant predictors of progression. So patients with large size tectal gliomas and cystic changes should perform a biopsy under the condition of safety.

Prognosis of patients with TG treated with ETV.

It is believed that most TGs are low-grade gliomas, and the clinical course tends to be benign.[15, 22, 23] In our series, we analyzed the largest number of patients who underwent ETV to treat obstructive hydrocephalus caused by tectal plate gliomas to date. Our group of patients also confirmed that most TGs tend to be benign. Reisenauer et al. recently reviewed 44 patients at two institutions and found that the majority (36/44) required only cerebrospinal fluid (CSF) diversion procedures. Five of 44 patients (11.4%) received either radiotherapy (XRT) or chemotherapy. There was no significant difference in the initial tumor volume between patients with and without tumor growth. In our study, significant predictors of progression were a tumor size greater than 2.8 cm^3 ($P = 0.02$) and cystic changes ($P = 0.01$). In our group of patients, the clinical presentation of all TG was related to obstructive hydrocephalus, similar to other reports summarizing patients with TGs. The symptoms of the patients with TG and obstructive hydrocephalus were markedly relieved during the follow-up after ETV. Clinical symptoms disappeared or were relieved, and most of the tumors did not progress, indicating that the natural history of TG is most often indolent, and ETV is the only surgical procedure that most patients require.

Limitations

The main limitations of this study are its retrospective nature and limited sample size. Second, all patients in this study were enrolled from a single neurosurgery center. Third, the median follow-up and median PFS durations were not very different, which might underestimate the progression rate. Therefore, a multicenter study based on a larger cohort with a long-term follow-up is needed in the future.

Conclusion

In our surgical experience, ETV has been uniformly successful in the management of hydrocephalus caused by TG. Under the condition of ensuring the safety of patients, a biopsy should be performed. If the biopsy shows a high-grade glioma, the patient may receive comprehensive treatment to inhibit the progression of the tumor. Most of the pathology findings are low-grade gliomas, and the natural history of these tumors is most often indolent, so the treatment of hydrocephalus is the only surgical procedure that most patients require. A tumor size greater than 2.8 cm^3 and cystic changes are significant predictors of progression. No additional treatment for low grade TG gliomas after ETV is required until the tumor is found to progress.

Abbreviations

TG: tectal glioma; ETV: endoscopic third ventriculostomy; PFS: progression-free survival; BTH: Beijing Tiantan Hospital; PACs: picture archiving and communications systems; HE:hematoxylin and eosin; GFAP: glial fibrillary acidic protein; Ki-67: Ki-67 protein; Olig2: oligodendrocyte lineage transcription factor; EMA: epithelial membrane antigen; CK: cytokeratin; CEA: carcinoembryonic antigen.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the principles of the Declaration of Helsinki, and the study protocol was approved by the ethics committee of Beijing Tiantan Hospital (BTH). Because of the retrospective nature of the study, patient consent for publication was waived.

Availability of data and material

All data generated or analysed during this study are included in this published article.

Competing interests

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

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Authors' contributions

Conception and design: Songbai Gui, Jie Kang, and Chuzhong Li; Acquisition of data: Jie Kang, Chuzhong Li, Peng Zhao, and Jiwei Bai; Analysis and interpretation of data: Songbai Gui, Jie Kang, Chunhui Liu, Lei Cao and Xinsheng Wang; Drafting the article: Jie Kang and Songbai Gui; Critically revising the article: all authors. Approved the final version of the manuscript on behalf of all authors: Songbai Gui. Study supervision: all authors.

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Figures

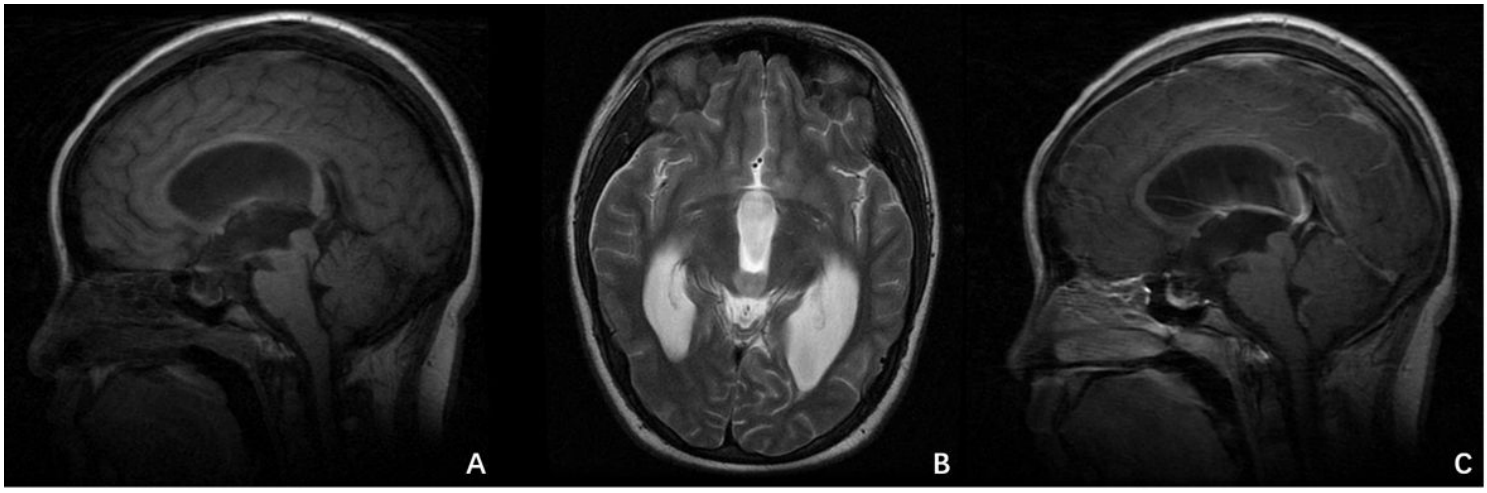

Figure 1

Typical MRI features of TG: A: T1 hypointense lesion obstructing the cerebral aqueduct; B: T2 hyperintensity of the lesion; C: Sagittal postcontrast T1-weighted image shows a typical nonenhancing

lesion.

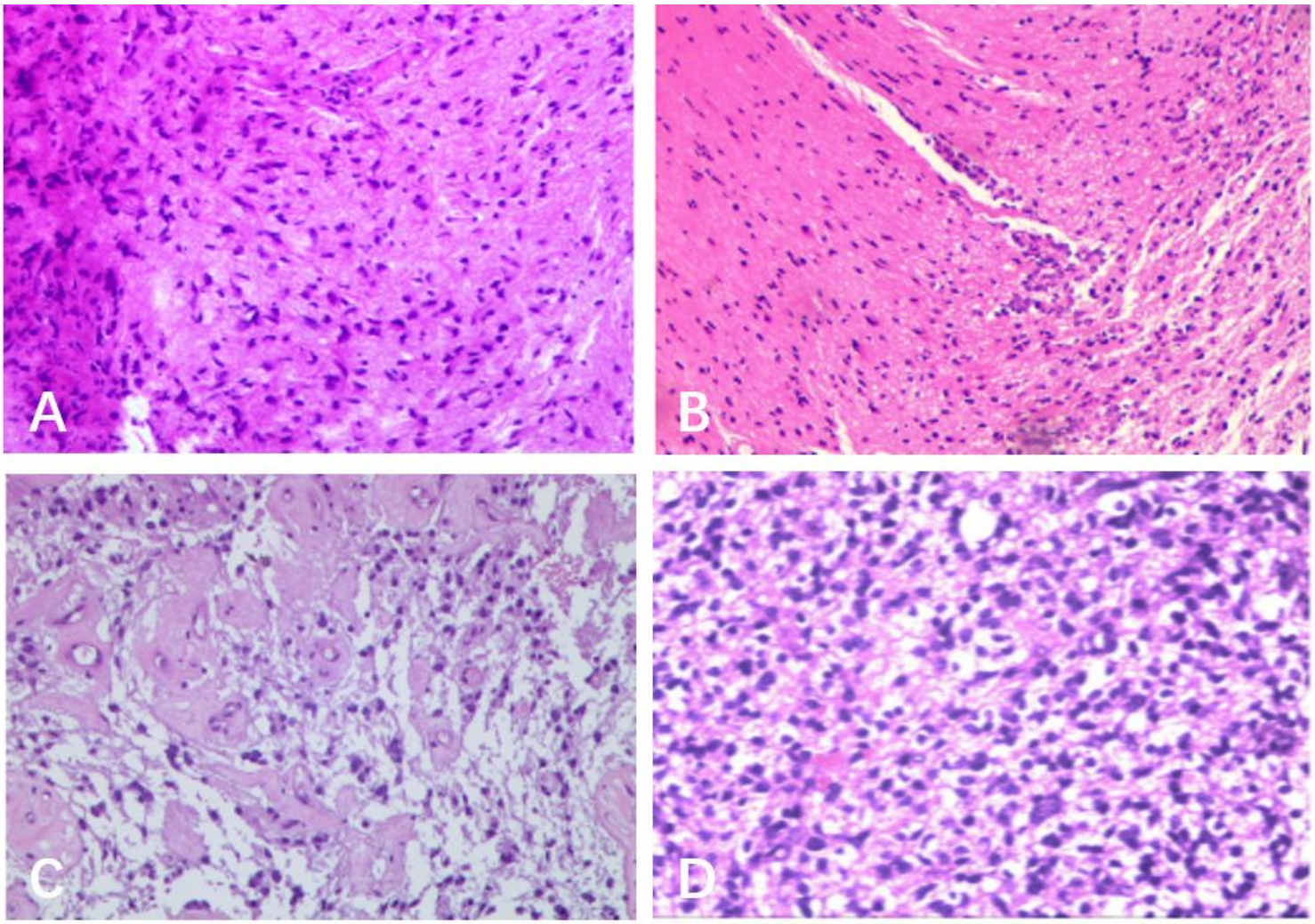

Figure 2

Biopsy of TG: A and B: Due to the small amount of tumor sample, the pathology could not confirm the type of tumor, and the patients were diagnosed with gliosis. The tumor cells are diffusely and strongly positive for GFAP and Olig2. Ki67 labeling is minimal. C: Typical morphologic features of pilocytic astrocytoma: Rosenthal fibers, sclerotic vessels, and an alternating loose and more compact architecture. The tumor cells are diffusely and strongly positive for GFAP and Olig2. Ki67 labeling is minimal. D: The pathology revealed anaplastic oligodendroglioma (WHO grade III). Tumor cells are extremely abundant, with a diverse morphology, increased nuclear and cytoplasmic proportions, and common mitotic signs. Tumor vascular endothelial hyperplasia is obvious, and there is tumor necrosis. The tumor cells are diffusely and strongly positive for GFAP and Olig2. Ki67 labeling is 40%.

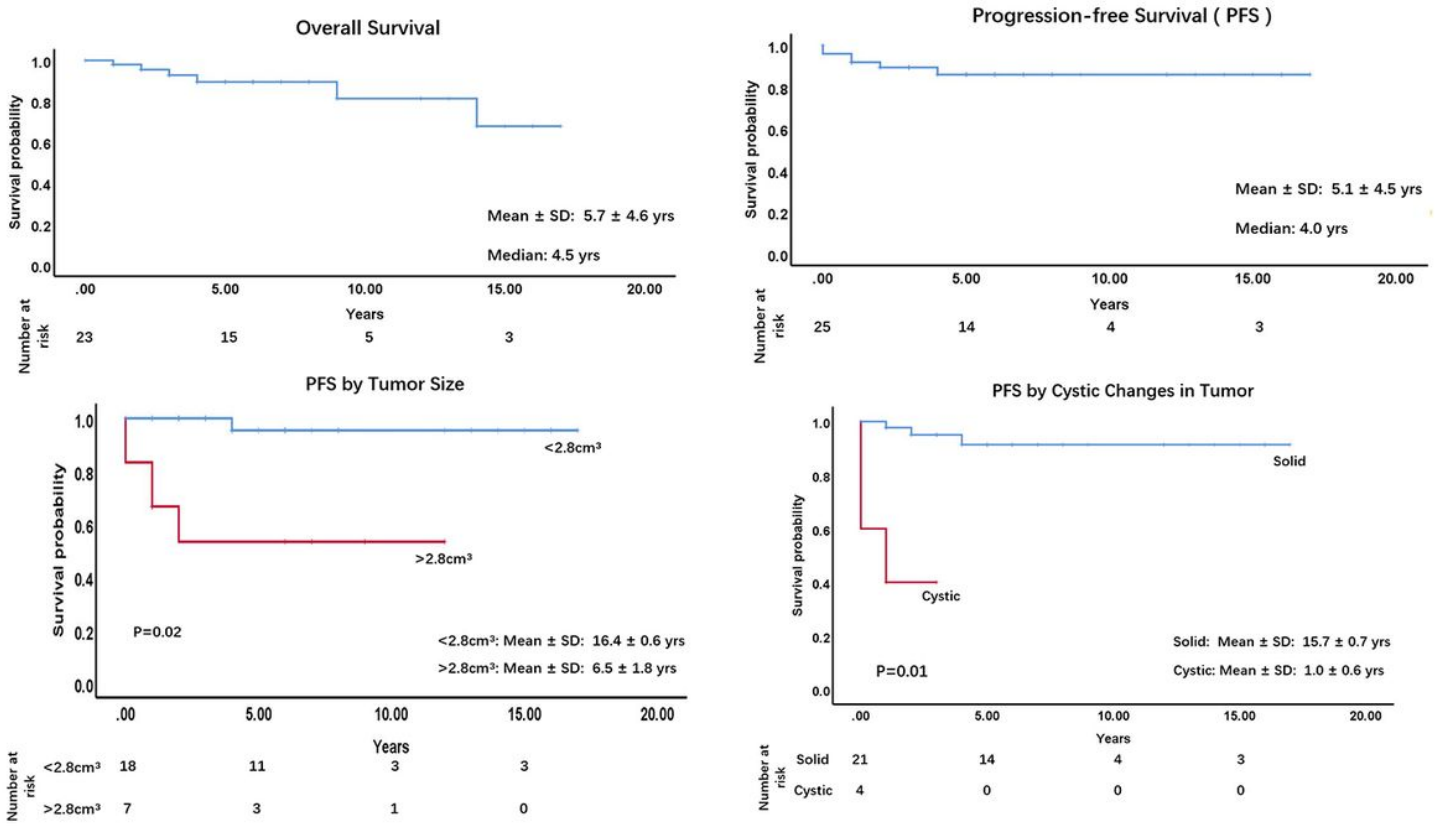

Figure 3

A, B: Kaplan-Meier curve showing the overall survival (OS) and PFS times of the patients. C: PFS of TG patients based on tumor size. D: PFS of TG patients based on cystic changes

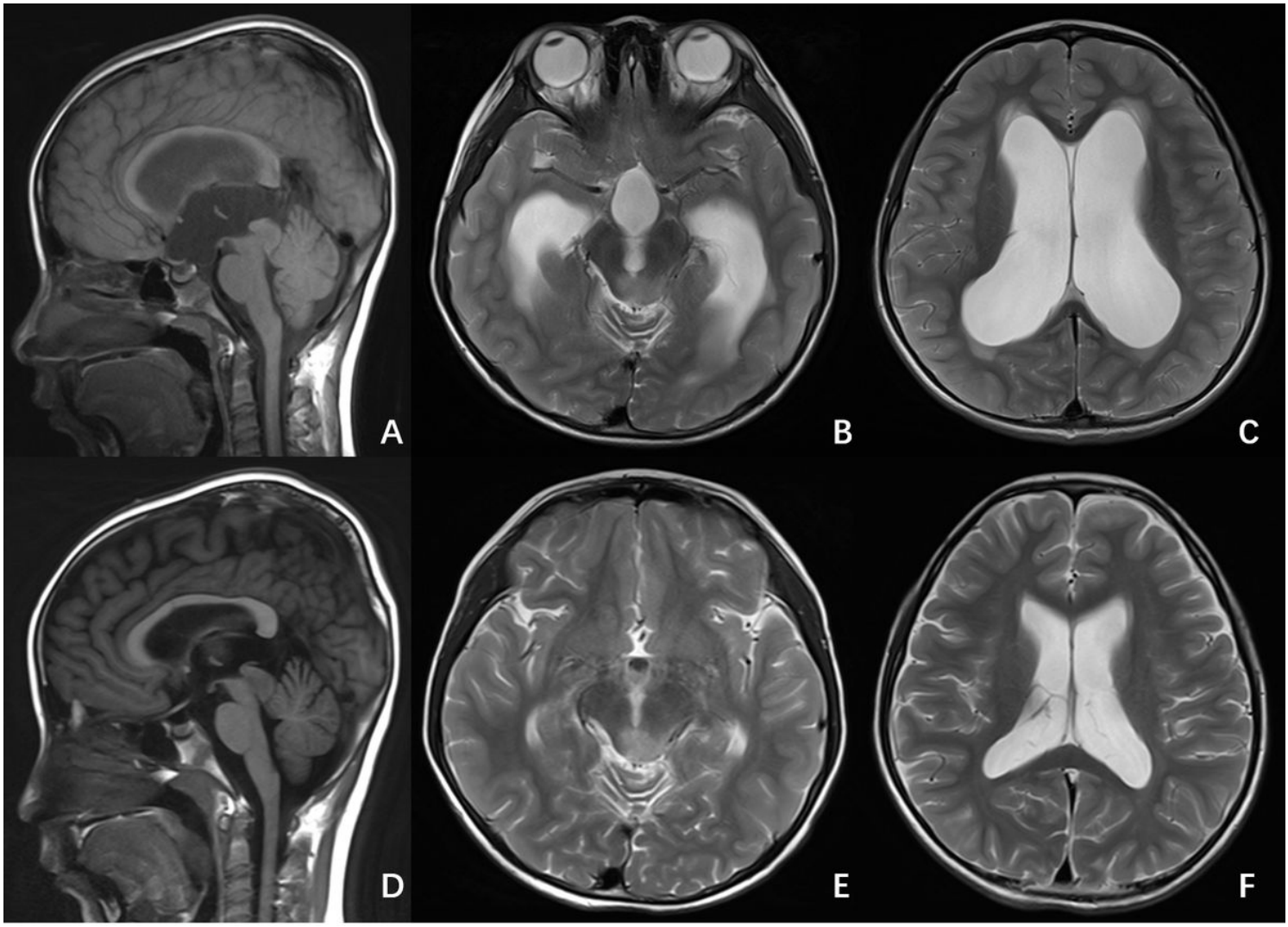

Figure 4

The patient experienced headache and nausea for 6 months before ETV. After the operation, the symptoms caused by hydrocephalus disappeared and the patient remained progression-free for six years after ETV. A, B, C: T1 hypointense lesion obstructing the cerebral aqueduct; T2 hyperintensity of the lesion. Note the dilated lateral and third ventricles. D, E, F: Six years after ETV, the reduced size of the lateral and third ventricles, with clear brain sulci can be observed, and the TG did not show radiological progression.

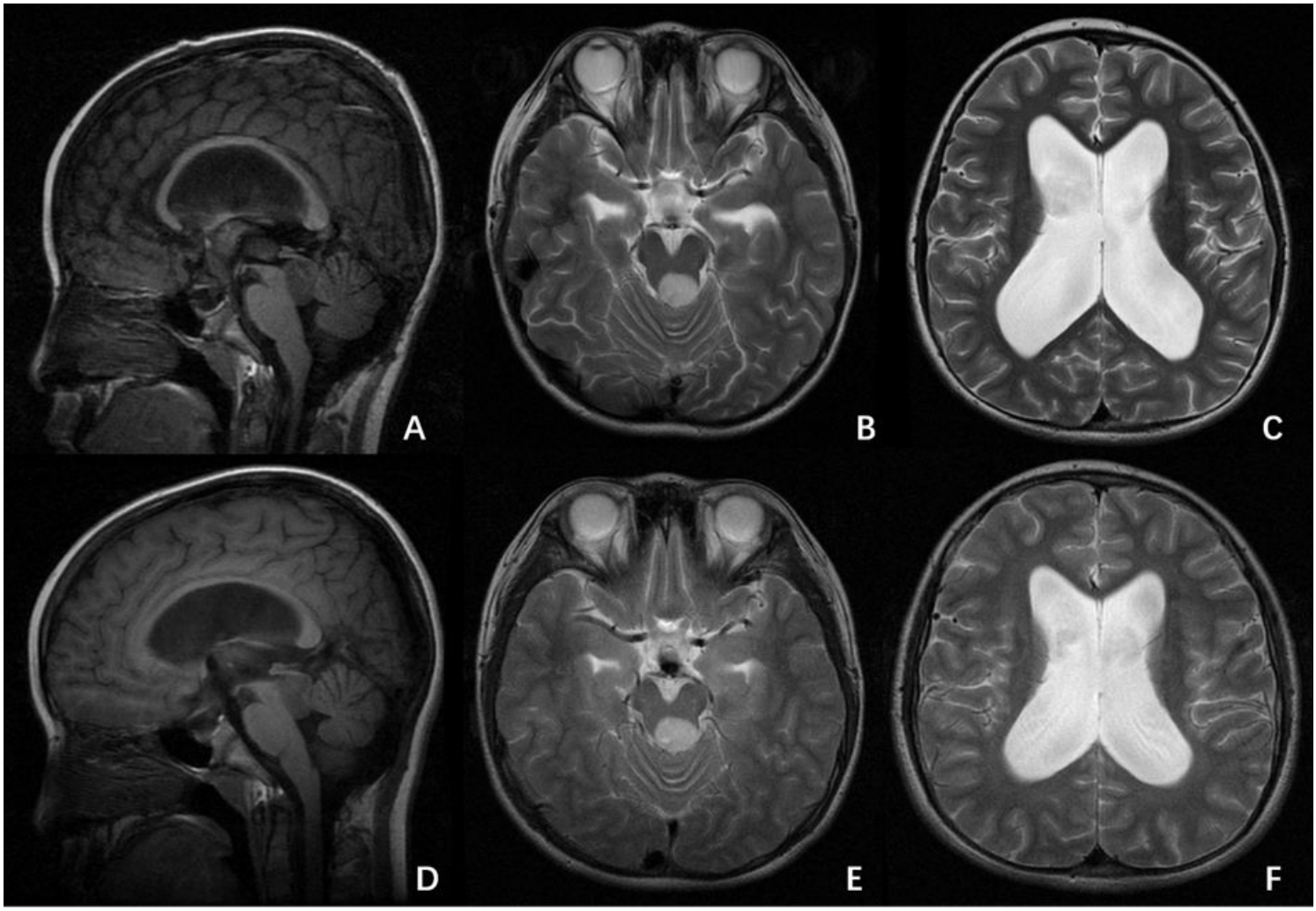

Figure 5

The patient experienced headache and balance problems for 2 months before ETV. After the operation, the symptoms disappeared and the patient remained progression-free for four years after ETV. A, B, C: T1 hypointense lesion obstructing the cerebral aqueduct; T2 hyperintensity of the lesion. Note the dilated lateral and third ventricles. D, E, F: Four years after ETV, we can see the reduced size of the lateral and third ventricles, and the TG did not show radiological progression.

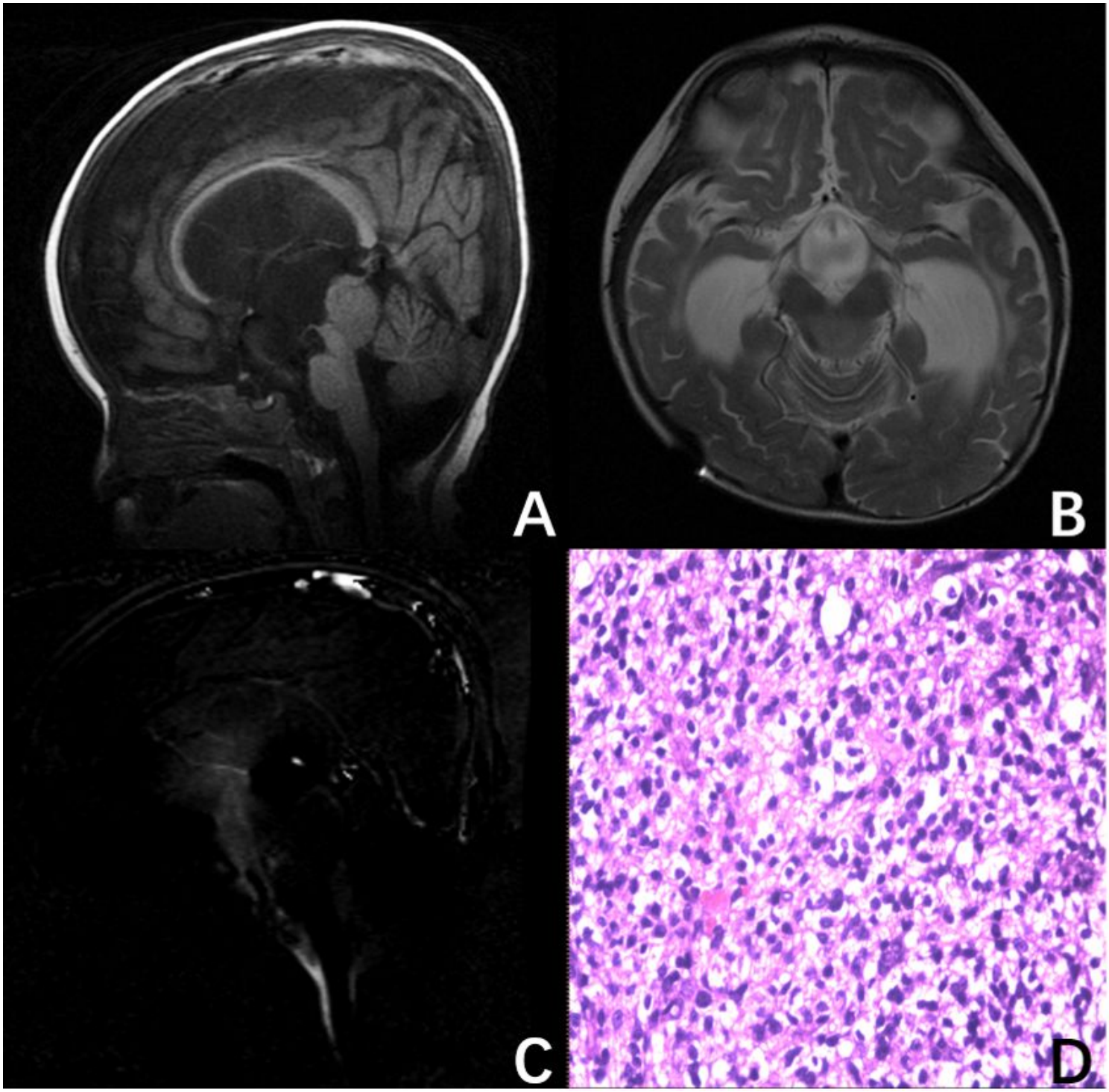

Figure 6

The patient’s symptoms consisted of a developmental delay, nausea, vomiting, and weak muscles of both legs preoperatively. She was treated with ETV and underwent a biopsy at the age of nine months. The patient recovered well after ETV, the symptoms of intracranial hypertension disappeared, and language and behavior developed normally. The pathology revealed anaplastic oligodendroglioma (WHO grade□). The patient did not receive chemoradiation or radiotherapy after the surgery. Three years later, the patient died of the glioma A, B: Note the dilated lateral and third ventricles. C: The direction and signal intensity of the CSF flow changed in PC-cine during the cardiac cycle. The direction of the flow was

downward during the systolic period and upward during the diastolic period. D: The pathology report indicated: anaplastic oligodendroglioma (WHO grade□).

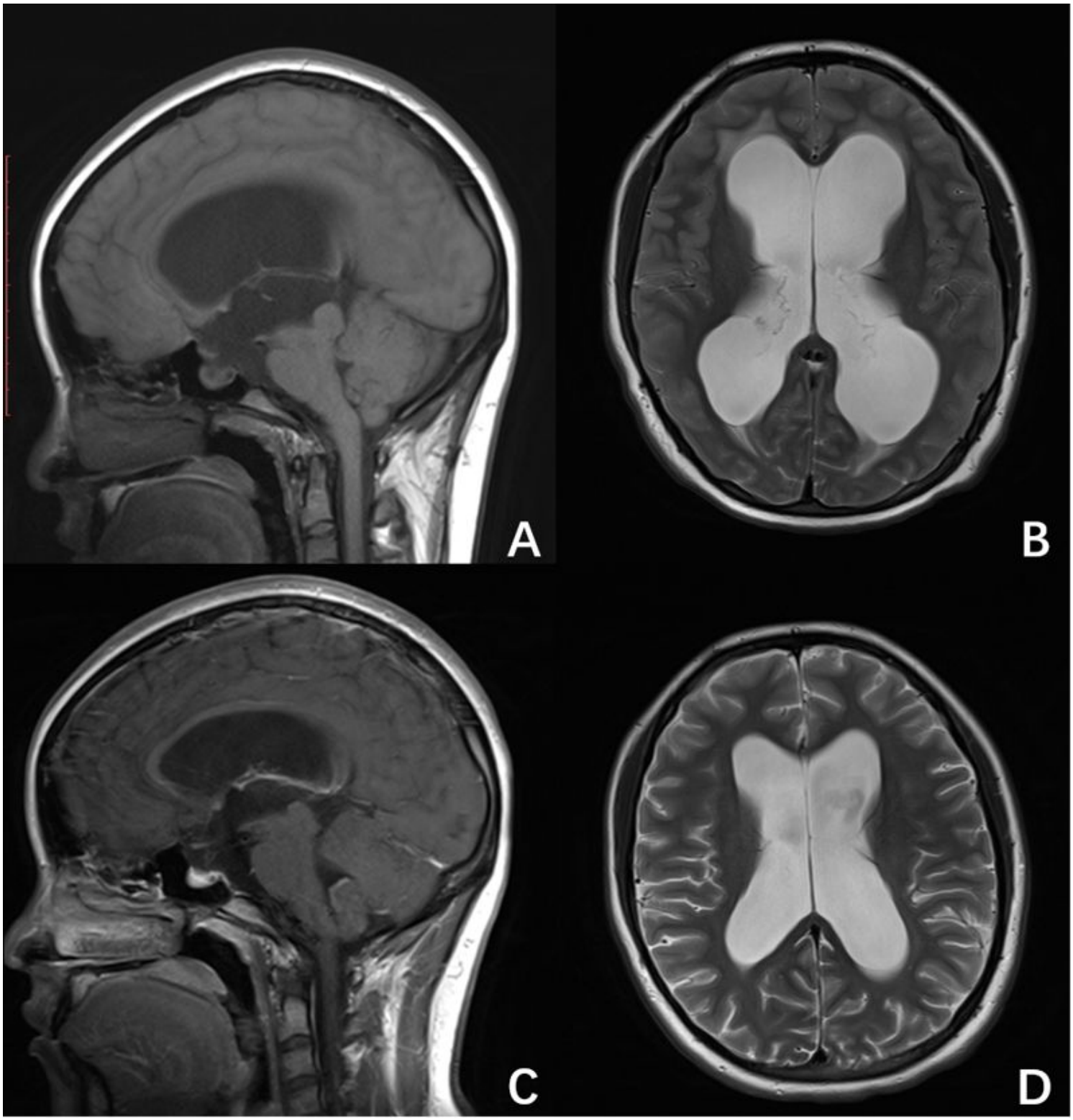

Figure 7

The patient experienced visual decline before the surgery. During ETV, the patient underwent a biopsy of the TG, which was significant for the pathological diagnosis of astrocytoma (WHO grade II-III). Six months later, the patient showed radiological progression and was treated with radiosurgery. The

patient's vision improved after the ETV procedure, and the patient remained progression-free for two years after the completion of radiosurgery. A, B: Note the dilated lateral and third ventricles. C, D: Two years after ETV and radiosurgery, we can see the reduced size of the lateral and third ventricles, with clear brain sulci.