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ORIGINAL ARTICLE

Simultaneous single-trajectory endoscopic biopsy and third ventriculostomy in pediatric pineal region tumors

Wei Liu[1] · Raynald[2] · Yongji Tian[1] · Jian Gong[1] · Zhenyu Ma[1] · Lukman Ma'ruf[3] · Chunde Li[1]

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Abstract

Pineal region tumors have different pathological tumors and their optimal management remains controversial. Advancements in neuroendoscopy have led to the ability to simultaneously treat the hydrocephalus and obtain a tissue diagnosis. A retrospective review of 34 patients with pineal region tumors in Beijing Tiantan hospital from the year 2016 to 2018 was undertaken. A single bur hole for both procedures was used successfully in all patients. Once pathologic diagnosis is made, the subsequent management of different tumors is dependent on response to therapy, the tumor markers and original pathology. Follow-up period was 4–26 months. All 34 cases presented with hydrocephalus and increased intracranial pressure manifestations. Elevated blood tumor markers were found in seven cases. The neuroendoscopic biopsy was diagnostic in 32 samples (94.1%) and nondiagnostic (gliosis) in two patients. 21 cases were germinomas, five cases were tectal astrocytomas, two cases were pineoblastomas, two cases were non-germinomatous germ-cell tumours (NG-GCTs) and 1 case immature teratoma and glioblastoma respectively. During the follow-up period, all germinomas but one case with elevated blood α-fetoprotein received craniotomy with a final diagnosis of NG-GCT received radiotherapy and chemotherapy. Four tectal astocytomas, two pineoblastomas and two NG-GCTs received subsequent open surgery due to progressive development, the pathological data was concordant with the initial endoscopic biopsy sample. An additional VP shunt was inserted in one tectal astrocytoma who have hydrocephalus after craniotomy. Except for 18 cases of transient fever and a case with intratumoral hemorrhage, there was no other significant complications, cognitive disorder and no death. The simultaneous single-trajectory endoscopic technique permits not only to control hydrocephalus but also to obtain histological diagnosis with a low incidence of complication and higher safety. Providing meaningful pathological data, endoscopic biopsies could lead to an appropriate management decision. Especially, it is favored as an early step in the management of patients with marker-negative tumors.

Keywords Pineal tumors · Germ cell tumors · Hydrocephalus · Endoscopic third ventriculostomy · Endoscopic biopsy

Introduction

Tumor located in the posterior third ventricle or pineal area often cause obstructive hydrocephalus and thus necessitate a CSF diversion procedure such as endoscopic third ventriculostomy (ETV) [1]. The pathological differential diagnosis for tumor located in this area includes germ cell tumors, astrocytomas, pineal parenchymal tumors or others and a tumor biopsy is often indicated [2]. In the past, dual procedure is more recommended, the trajectory for ETV is more anteriorly to avoid injury to the fornix while an endoscopic biopsy (EB) prefer more posteriorly trajection to make sure the exposure for the tumors and avoid injury to the venous angle at Monro foramen [2]. Recently, more various advances techniques have been suggested to combine ETV and EB with either only one entry points or two entry points, using rigid and/or flexible endoscope [3–10]. In the current study, we present our experience performing EB after ETV procedure using a rigid endoscope with only a single trajectory. We found that this method is quite safe and effective for simultaneous EB and ETV.

✉ Chunde Li
lichunde@hotmail.com

[1] Department of Neurosurgery, Beijing Tiantan Hospital, Capital Medical University, Beijing 100050, China

[2] NeuroIntervention Center, Beijing Tiantan Hospital Capital Medical University, Beijing 100050, China

[3] Department of Neurosurgery, Gatot Subroto Central Army Hospital, Jakarta 10410, Indonesia

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Patients and methods

Patients

From January 2016 to December 2018, 34 pediatric patients with tumor located in the posterior third ventricle or pineal area (Fig. 1a–c) underwent neuroendoscopic procedures for CSF diversion and tumor biopsy in our hospital. A retrospective review of patient characteristics and clinical findings are summarized in Table 1. Patient data including age, sex, sign and symptoms, pre-operative tumor marker, pre-operative diagnosis, the presence of hydrocephalus, pathological findings and post-operative treatment were recorded. The follow-up data were collected by telephone or clinical follow-ups. This study was approved by the Ethics Committee of Beijing Tiantan Hospital, Capital Medical University. Informed consent was obtained from all participants or their parent or legal guardian.

Surgical technique

All procedures were performed under general anesthesia with the patient in a supine position. The head is elevated 15° to facilitate venous drainage. A 3–4 cm slightly curved or straight line skin incisions were done over ~ 2.5 cm anterior to the coronal suture and lateral to the midline is performed. Then a frontal burr hole was made to provide an adequate trajectory for ETV and biopsy. A 4 mm outer diameter and 0° or 6° rigid endoscope (Karl Storz or B.Braun Aesculap, Germany) was introduced into the right or left lateral ventricle through the frontal lobe, reaching the third ventricle, posterior part of the third ventricle and pineal area. At the time of initial ventricular cannulation, CSF was collected for biochemical analysis.

An ETV was performed using a monopolar probe (with or without current as needed), followed by enlargement of the orifice using the endoscopic forceps or 3-French Fogarty balloon catheter. The Liliequist membrane must be opened and the prepontine subarachnoid space was communicated (Fig. 1d, e). After ETV procedure, the

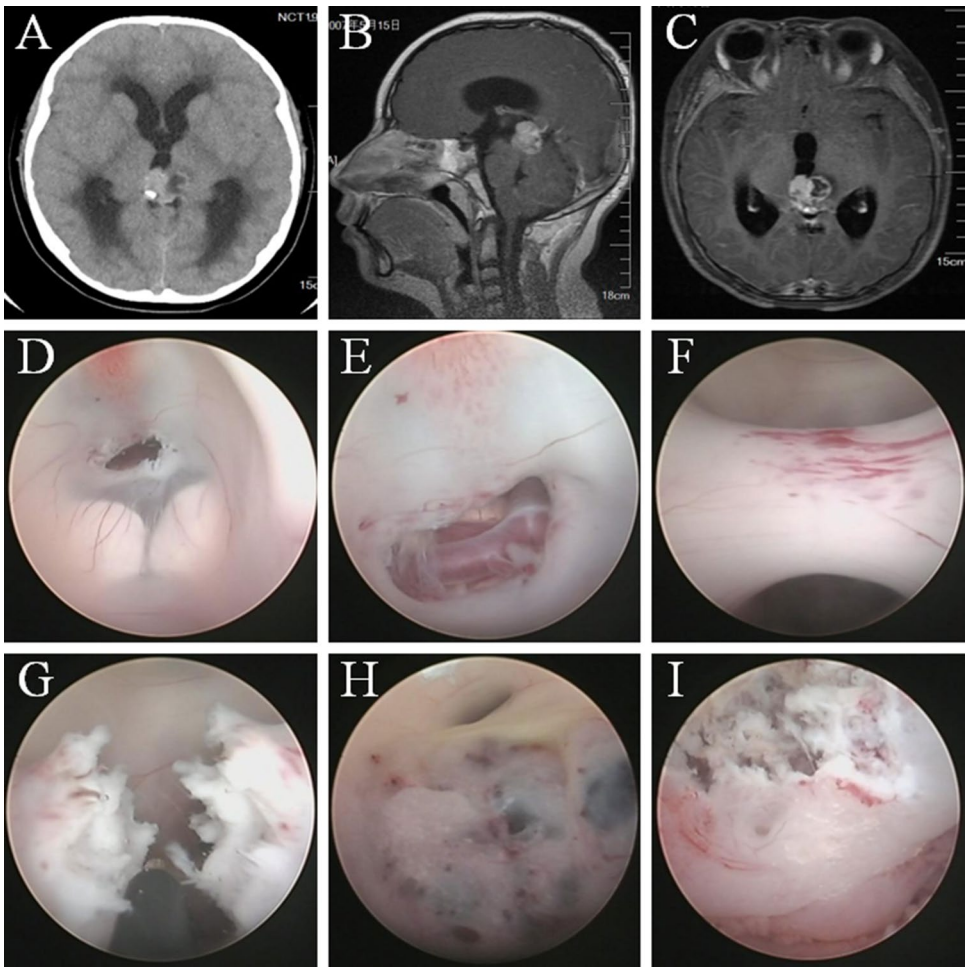

Fig. 1 **a**–**c** CT and MR images of the posterior third ventricle was obtained in an 11-year-old boy presenting with headache and lethargy. **d** ETV was performed on the floor of third ventricular. **e** Ventriculostomy was confirmed after Liliquist membrane was opened and the basilar artery can be visualized. **f** Massa intermedia was visualized after the angle of the endoscope was adjusted which hinder the posterior third ventricle. **g** Massa intermedia was cut off to expose the posterior third ventricle. **h** The pineal region tumor was exposed. **i** No bleeding was seen after biopsy

Table 1 Characteristics of patients

No	Age	Sex	Sign and symptoms	Pre-op tumor marker	Pathology	Preoperative hydrocephalus	Postoperative treatment	Postoperative V–P shunt	Follow-up duration	Outcome
1	10 y 4 m	M	Headache, vomiting	Blood AFP 700	Germinoma	Yes	CT → open surgery	No	5	Alive
2	4 y	M	Headache, nausea, vomiting, gait disturbance	N/A	Astrocytoma	Yes	Open surgery	Yes	29	Alive
3	5 y 5 m	M	Nausea,vomiting	Blood and CSF: normal	Astrocytoma	Yes	RT → open surgery	No	28	Alive
4	5 y	F	Progressive gait disturbance	N/A	Pilomyxoid astrocytoma	Yes	Open surgery	No	21	Alive
5	3 y	M	Intermittent headache, vomiting, lethargy	N/A	Immature teratoma	Yes	No	No	20	Alive
6	9 y	M	Relapsing headache and neck pain, nausea, vomiting	Blood AFP 7.47, hCG 88.92; CSF AFP normal, hCG 80.25	Germinoma + choriocarcinoma	Yes	CT	No	18	Alive
7	6 y	M	Intermittent headache, vomiting	Blood and CSF: normal	Germinoma	Yes	Radio and chemo	No	18	Alive
8	14 y	M	Headache, vomiting	AFP 84.03, hCG < 0.1	Mature teratoma	Yes	open surgery → RT + CT	No	18	Alive
9	13 y	M	Lethargy, tumor recurrence after 4 years	Blood: Normal AFP < 0.605, hCG < 0.1	Glioblastoma	Yes	No	No	17	Die
10	15 y	M	Headache, vomiting	Blood: normal AFP (< 0.1, hCG 1.43), CSF: normal (< 0.605, hCG 2.15)	Germinoma	Yes	RT and CT	No	17	Alive
11	10 y	M	Headache, vomiting, gait disturbance	N/A	Astrocytoma	Yes	No	No	16	Alive
12	10 y	M	Headache, vomiting	Blood and CSF: normal	Germinoma	Yes	Radio and chemotherapy	No	16	Alive
13	12 y	M	Headache, vomiting, lethargy	Blood: normal	Germinoma	Yes	RT and CT	No	15	Alive
14	4 y	M	Headache, vomiting	Blood: normal, CSF: hCG slightly high 5.26	Pinealoblastoma	Yes	Open surgery	No	15	Alive
15	15 y	M	Headache, vomiting	Blood and CSF: normal	Germinoma	Yes	RT and CT	No	14	Alive
16	1 y 9 m	M	Headache, vomiting, lethargy	N/A	Astrocytoma WHO grade II	Yes	Open surgery	No	13	Alive
17	9 y	M	Headache, diplopia, weakness on right extremities	N/A	Astrocytoma	Yes	No	No	13	Alive
18	15 y	M	Headache, nausea, vomiting	Blood: normal, CSF: hCG slightly high 6.75	Germinoma	Yes	RT and CT	No	13	Alive
19	11 y	M	Headache, nausea, vomiting	Blood: normal	Germinoma	Yes	RT and CT	No	11	Alive
20	15 y	M	Headache, nausea, vomiting	Blood and CSF: normal	Germinoma	Yes	RT and CT	No	11	Alive
21	11 y	M	Headache, nausea, vomiting	Blood: normal	Mixed GCT	Yes	open surgery → RT + CT	No	11	Alive
22	10 y	M	Headache, vomiting	Negative	Pinealoblastoma	Yes	Endoscopic resection	No	9	Alive
23	11 y	M	Headache, vomiting	Blood and CSF: normal	Germinoma	Yes	RT and CT	No	8	Alive
24	15 y	M	Lethargic, amaurosis	Blood: normal	Germinoma	Yes	RT and CT	No	8	Alive
25	11 y	M	Lethargy, attention deficit	Blood: normal	Astrocytoma WHO grade II	Yes	Open surgery	No	5	Alive

Table 1 (continued)

No	Age	Sex	Sign and symptoms	Pre-op tumor marker	Pathology	Preoperative hydrocephalus	Postoperative treatment	Postoperative V–P shunt	Follow-up duration	Outcome
26	13 y 2 m	M	Precocious puberty, headache, vomiting	Blood hCG: 192.2	Germinoma	Yes	RT and CT	No	4	Alive
27	15 y	M	Headache, vomiting, diplopia	Blood hCG: 3.02 (0–2.6); CSF hCG < 0.1	Germinoma	Yes	RT and CT	No	4	Alive
28	16 y	M	Headache, vomiting	Blood: normal	Germinoma	Yes	RT and CT	No	4	Alive
29	12 y	M	Lethargy	N/A	Germinoma	Yes	RT and CT	No	3	Alive
30	16 y	M	Headache, vomiting	Blood: normal	Germinoma	Yes	RT and CT	No	2	Alive
31	10 y	M	Dizziness, vomiting, lethargy	Normal	Germinoma	Yes	CT	No	1	Alive
32	16 y	M	Headache, dizziness	N/A	Germinoma	Yes	CT	No	1	Alive
33	7 y	F	Headache, vomiting	Blood AFP 1.76, hCG 5.39	Germinoma	Yes	CT	No	5	Alive
34	9 y	M	Weakness on upper extremities and tremor, gait disturbance	Blood AFP 2.54, hCG slightly high 3.2 (0–2.6), CSF AFP 0.719, hCG 34.38 (0–2.6)	Germinoma	Yes	CT	No	3	Alive

y year, *m* month, *M* male, *F* female, *RT* radiotherapy, *CT* chemotherapy, *N/A* not available

endoscope was delivered to the posterior third ventricle area. The massa intermedia identified (Fig. 1f) and then cut off (Fig. 1g) to have a better visualization of the posterior third ventricle structure. Identification of the tumor (Fig. 1h) and visual inspection of its growth patterns, careful coagulation of the surface of the neoplasm was performed and the tumor was sampled with cupped or grasping forceps (Fig. 1i). Local bleeds were controlled using irrigation and monopolar cauterization. As the possibility of tumors with mixed histology existed, attempts were made to obtain a sufficient quantity of tissue for pathological investigation. Tumor resection through the endoscopic procedure was performed in one patient. After completion of the tumor sampling and confirmation of the complete hemostasis, prolonged irrigation with Ringer's lactate solution was continued up to the final stages of the procedure to prevent ventricular collapse or income of air. Postoperative CT and MRI scans were obtained for all patients after operation. Slight injury to the fornix was occurred in some patients who had the relatively small size of the foramen monro (Fig. 2a). In all patients, postoperative image showed no abnormal manifestations of the foramen Monro and its surrounding structures, including veins and fornix (Fig. 2b, c).

Outcomes

We charted the histologic findings of the initial endoscopic biopsy samples, and compare them with the final biopsy samples at the end of the treatment. We evaluated the accuracy of the initial diagnosis and charted the subsequent management plans of those patients in which the diagnosis was inconclusive.

Results

Patient's clinical presentations and pre-op diagnosis

Patients ranged in age from 3 to 16 years old at the time of surgery. There were 32 male and 2 female patients. All cases presented with hydrocephalus and most had increased ICP manifestations, such headache, nausea and vomiting, and some were accompanied with dizziness, attention deficit and lethargy. Four patients had gait disturbance, 2 patients had weakness on extremities, 2 patients had diplopia and 1 patient had amaurosis. Elevated markers of a-fetoprotein (AFP) were found in 2 patients and slightly high β-human chorionic gonadotropin (β-HCG) marker was found in 3 patients.

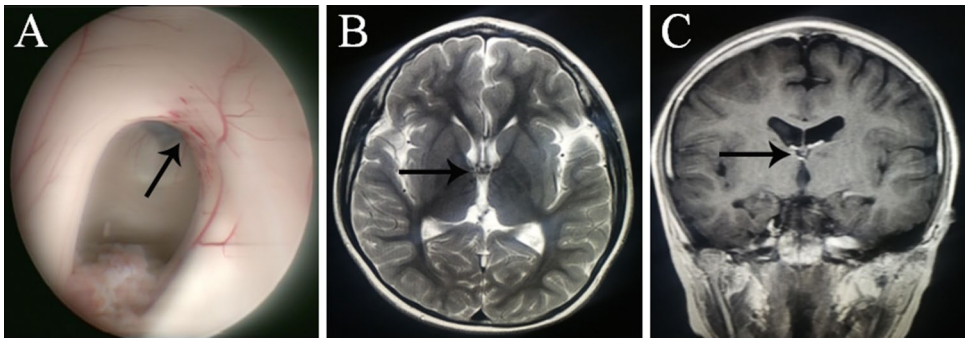

Fig. 2 **a** Slight injury to the fornix was seen intraoperatively. **b**, **c** Postoperatively, no abnormal manifestations of the foramen Monro and its surrounding structures, including veins and fornix were seen in the axial and coronal view of the T2WI MRI

Surgical outcome and complications

The ETV and biopsy were postoperatively uneventful in all cases. No navigation was used during the procedure, and only rigid endoscope was used for the whole procedure. The hydrocephalus was relieved in all patients. There were no technical difficulties during surgery. Further management included open surgery for tumor resection were performed in seven cases. The most common complication was a non-infectious fever in almost all cases. But the symptoms were alleviated 2–3 days later. All patient had an uneventful course and discharge without any neurological deficit.

Pathology

All specimens were diagnostic. Pathologies included germinoma was seen in 20 cases, two had mixed germ cell tumor one of them presented with germinoma with choriocarcinoma, two patients had teratoma (immature and mature, respectively). Astrocytoma (WHO grade II) was seen in five cases, and the other three patients had pilomyxoid astrocytoma, glioblastoma and pinealoblastoma, respectively. The open surgical pathology was concordant from the endoscopic pathology.

Postoperative treatment and follow-up

Twenty-four patients had postoperative radiotherapy and/or chemotherapy after confirmed biopsy diagnosis and the tumor was significantly disappeared during follow-up (Fig. 3). Seven of eight patients with astrocytoma pathological findings and one patient with pineoblastoma only had tumor resection surgery. The average follow-up was 11.65 months (range 1–29 months). During follow-up, thirty-one patients were alive during, except one patient died due to progression of the disease and his pathological finding was glioblastoma. Only one patient develop secondary hydrocephalus after craniotomy and require additional V–P shunt placement.

Discussion

In posterior third ventricle, pineal or tectal area tumor, cerebral aqueduct occlusion is common. CSF diversion procedure is often necessary. Neuroendoscope is being increasingly used in recently not only to relieve hydrocephalus but also to obtain a biopsy of the tumor. Generally, both procedures were performed separately due to limitations on the anatomical structure and often two trajectories with

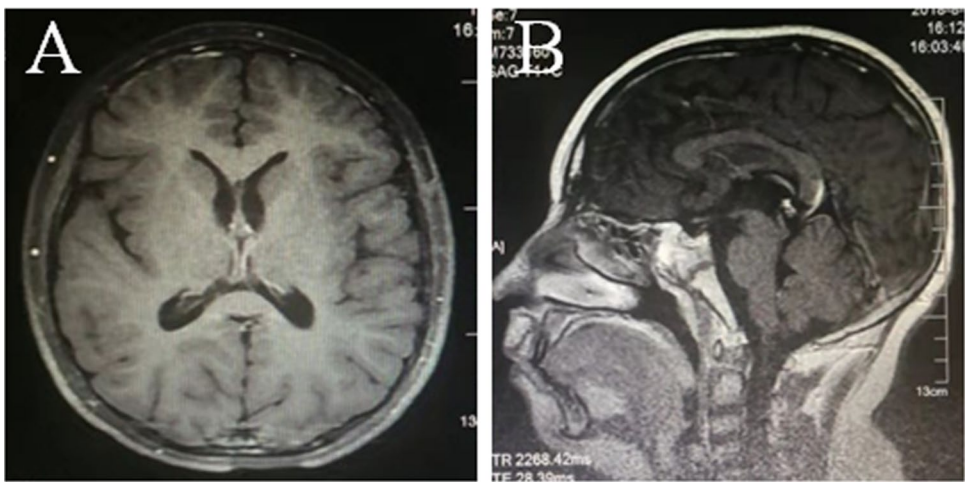

Fig. 3 **a** MRI examination showed hydrocephalus relieved after adjuvant therapy was given. **b** MRI examination showed a reduction of the tumor volume after adjuvant therapy was given

2 burr-holes is needed to provide good visualization and to reduce injury to the complex and important anatomical structure in the midline region. For ETV, an anterior trajectory is needed to avoid fornix and vascular injury because it is more or less parallel to the basilar artery. While, for EB, posterior trajectory is needed to enable a clear view and access to the tumor located in the posterior third ventricle, pineal or tectal area (Fig. 4) [1]. The ETV entry is usually at the midpupillary line and anteriorly to the coronal suture, while the EB entry is located more anteriorly at the hairline [10]. The angle different on both trajectory has limit the ability to use a single entry to perform both ETV and EB. However, with the advances in neuroendoscopic technique, both ETV and EB can be performed through single trajectory to overcome the major drawback of the need for 2 burr-holes and 2 separate transcortical passes [4–6, 10–12].

Several authors have suggested to performed one "compromised" burr-hole which is located midway between the two ideal entry sites [7, 9, 13–15]. However, there are several limitations such as more pressure to the fornix while performing ETV and posterior border of the foramen of Monro during EB procedure. Moreover, this technique is only suitable for large tumor located not too posteriorly [1]. Other authors suggested a flexible endoscope which has an advantage to reach both distance [3, 7, 8, 16–18]. Roth et al. [1] demonstrated a combined rigid and flexible endoscopy for ETV and EB through a single ideal trajectory. They use a rigid endoscope for anatomical inspection, evaluation tumor spread and performing an ETV, while flexible endoscope was used for performing EB. However, the inferior optical quality compared with the high definition rigid endoscopic system has become an important limitation of this flexible endoscopic system which may affect the ability to identify tumor spread [19, 20]. In addition, the flexible forceps are smaller than those of rigid endoscope and may affect the size of the biopsy specimen which is susceptible to sampling error [21, 22]. Although some authors reported that it did not reduce the accuracy rate of diagnosis using the flexible endoscope [3, 7, 18, 23].

Different with previously described technique, in this study we performed both ETV and EB with a rigid endoscope system through a single trajectory. In addition, we sacrifice the massa intermedia to get a better visualization and space during the EB procedure. Due to the various structure of the interventricular foramen, certain adjustment of the endoscope orientation is limited. Anatomically, the anterior border, medial part and posterior medial part of the interventricular foramen were constituted by the fornix. While the posterior border and posterior-lateral part were mainly constituted by the choroid plexus. Hence, during the procedure, posterior adjustment of the endoscope to expose the pineal tumor might injure the choroid plexus but not the fornix. Therefore, we put more concern to the venous bleeding complication from this procedure instead of the injury to the fornix. Slight injury to the fornix might occur in some patients with the relatively small size of foramen monro. However, this injury could not be seen in the post-operative MR imaging and accordingly additional neurologic deficits were not detectable in all patients.

We also found that this technique may benefit in small tumor and if the mass lesion located extremely posterior to the third ventricle. However, sacrificing the massa intermedia is not necessary when the tumor volume is bigger, because mostly, the tumor with more large volume is protruded anteriorly and may push the posterior wall of the third ventricle which cause the tumor can be seen obviously after we enter the third ventricle. In the present study, no significant neurological deficit or complication was found after we sacrifice the massa intermedia. However, further study to include evaluate the brain function including (motor, sensory, cognitive, intelligence and memory function) is needed for verification. We suggest that the massa intermedia can be sacrifice especially in pediatric patients, considering that they have a better recovery compared with adult patients.

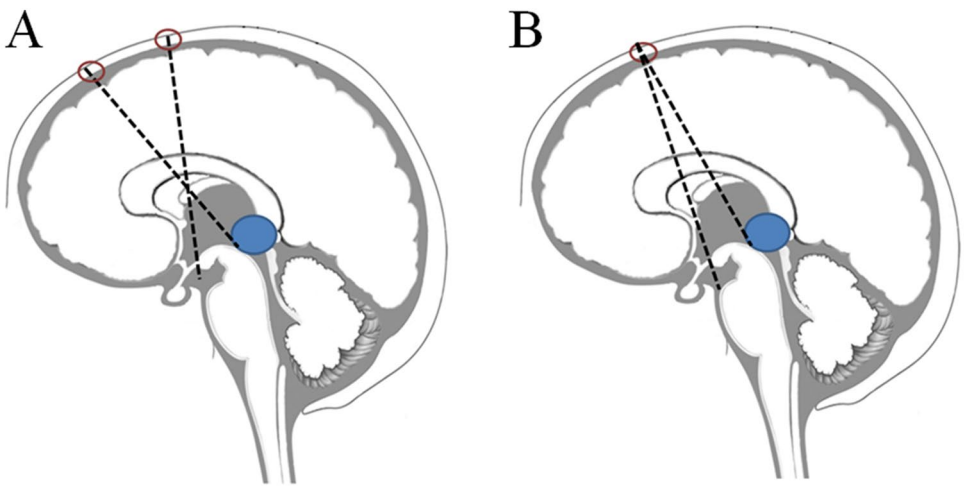

Fig. 4 **a** Two distinct and optimal entry sites for endoscopic third ventriculostomy (precoronal entry) and pineal region tumor biopsy (closer to the hairline frontal entry). **b** The single burr hole and single trajectory use in the present study

Regarding this matter, a comparison of neurological function between pediatric and adult population is urgent needed for verification.

Tumors of the posterior third ventricle or pineal region are histologically variable, such as germ cell tumors (germinomas, nongerminomatous GCTs and teratomas), tumors of the pineal origin (pineocytomas and pineoblastomas) and tumors of neuroepithelial origin (including gliomas of all grades) [24]. In children, approximately 60% of are germ cell origin [25], and the most common type is germinoma [26]. According to several authors, the prevalence of GCT is consistently higher in Asian population than western population [27–29]. In our series, 21 of 32 patients were pathologically diagnosis as germinoma. This result emphasizes the importance of ETV and EB by neuroendoscopy technique, especially a patient who had pre-operative AFP and HCG tumor marker negative. After biopsy was confirmed, radiotherapy and chemotherapy were given which result in good prognosis and no recurrence of the tumor during follow-up. Moreover, this ETV and EB are also effective for low-grade glioma patient as the disease progression was slow and no need for surgical resection.

In summary, ETV and EB through a single burr hole and a single trajectory frontal approach with a rigid endoscope system is safe and feasible in patient with posterior third ventricular or pineal region tumor. All patient in our series has uneventful postoperative course. They were discharged without any neurological deficit, only one patient had to undergo additional shunt procedure due to secondary hydrocephalus one year after first open surgery. One patient with pathological diagnosis of glioblastoma was died during follow-up due to progression of the disease. The main limitations in our study are that we did not perform detail and further examination to evaluate patient's neurological function because in our series we sacrifice the massa intermedia to get better exposure of the tumor and space during the neuroendoscopic procedure. Therefore, further prospective and comparative study with more comprehensive pre and postoperative neurological evaluation are needed in the future.

In conclusion, ETV and EB through a single trajectory are safe and feasible with low incidence of complications. The histological diagnosis obtained can provide a meaningful diagnosis for further appropriate treatment modalities. Therefore, this technique should be highly considered especially in patients with germinoma or tectal low-grade glioma.

Compliance with ethical standards

Conflict of interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge, or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval This study was approved by the Ethics Committee of Beijing Tiantan Hospital, Capital Medical University.

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