

Pineal region tumors: Long-term results of endoscopic third ventriculostomy and concurrent tumor biopsy with a single entry approach in a series of 64 cases

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ARTICLE INFO

Keywords:

Pineal region tumors
Endoscopic third ventriculostomy
Tumor biopsy
Hydrocephalus

ABSTRACT

Objectives: Endoscopic third ventriculostomy and concurrent biopsy is increasingly used in management of the pineal region tumors. Our objective was to assess the results of single entry approach to surgically manage the tumors of the pineal region.

Patients and methods: A retrospective study was designed, and a series of 64 consecutive patients (31 male, 33 female) with pineal region tumor undergoing endoscopic third ventriculostomy and concurrent biopsy of the tumor was undertaken.

Results: A total of 64 patients underwent simultaneous endoscopic third ventriculostomy and biopsy of the pineal tumors with a single entry approach. A positive initial diagnosis was established in 97% of patients. 5 patients (7%) required the insertion of an external ventricular drain which was removed in all patients after 72 h but in one case (1%) undergoing permanent VP shunt insertion. The postoperative complications were divided into two transient and permanent complications. The transient complications included intraventricular hemorrhage (18%), seizure (1 to two episodes of seizure) (5%), diabetes insipidus (3%) and meningitis (3%) all were successfully managed. The only permanent complication was memory deficits occurred in one patient (1%). There was no mortality rate in current study.

Conclusion: The results of this study support the safety and efficacy of endoscopic third ventriculostomy and concurrent biopsy of the pineal region tumors as a less invasive surgical method associated with low morbidity and mortality rate. Our data demonstrated how simultaneous endoscopic third ventriculostomy and biopsy of the pineal region tumors with a single entry approach can produce favorable results.

1. Introduction

Tumors of the pineal or adjacent tectal region are relatively rare accounting for less than 1% of brain tumors in adults and approximately 5% of all intracranial tumors in children [1–4]. Approximately, 90% of patients with these masses present with obstructive hydrocephalus and thus the associated signs and symptoms are present owing to the anatomic location of these lesions [5,6]. Different treatment strategies have been suggested to surgically treat hydrocephalus resulting from mass effect of these lesions including ventriculoperitoneal (VP) shunting or external ventricular drainage; however, since the

earliest use of neuroendoscopy in treatment of patients with pineal region tumors reported by Fukushima [7], simultaneous endoscopic third ventriculostomy and biopsy of pineal lesion has become established as a surgical method to treat these tumors which is now the preferred approach due to the following advantages: taking a biopsy sample in addition to CSF diversion, taking a CSF sample for analysis of CSF tumor marker, and ability to minimize bleeding from the highly vascularized structures under direct vision [8–12]. Here, we present one of the largest retrospective studies of simultaneous endoscopic third ventriculostomy and biopsy of the pineal region tumors in 64 patients presenting to the neurosurgical unit of Loghman Hakim hospital

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Table 1
Preoperative demographic data.

Demographics	Frequency, %
Sex	
Male	48
Female	52
Average age, years	
Male	36.8
Female	35.9
Clinical presentation	
Headache	78
Vomiting	14
Gait instability	6
Parinaud's syndrome	1
Diabetes insipidus	1
Precocious puberty	1

between the years of 2005 and 2018.

2. Patients and methods

We conducted a retrospective review of clinical documents of the patients admitted in our department of neurosurgery at the Loghman Hakim Hospital from 2005 to 2018 to identify all patients with the diagnosis of the pineal region tumors (Figure, left) undergoing endoscopic third ventriculostomy and concurrent tumor biopsy. A total of 64 patients were included (31 male and 33 female) in the study (Table 1). All patients had preoperative computed tomography scan, magnetic resonance imaging and detailed clinical history on admission, the data from medication documents, nursing and doctors' notes, and discharge summaries. Patient data were derived from clinical history, operation records and endoscopy database, medication documents, imaging and nursing and doctors' notes. The following clinical data were collected for each patient: age, sex, number of previous ventricular shunts, clinical presentation, germ cell markers, and histology, control and relapse rates. The rate of mortality, meningitis, bleeding, and infection, and shunt insertion and cytology of tumors were also collected. The diagnosis of a pineal region tumor was established based on the clinical signs and symptoms, physical examinations and imaging data. The patients' clinical presentations are divided into three groups: 1. High ICP-related signs and symptoms due to the mass effect of the lesion resulting in obstructive hydrocephalus including headache, vomiting, and gait instability 2. Signs and symptoms of pressure on nearby nervous structures such as Parinaud's syndrome 3. Signs and symptoms of an endocrine imbalance such as diabetes insipidus (DI) and precocious puberty. All 64 patients presented with hydrocephalus and the associated signs and symptoms due to mass effect of the pineal region tumors (Fig. 1, middle) undergoing ETV and concurrent tumor biopsy. In

all patients ETV was successful in restoring the CSF pathway (Fig. 1, right) but in one patient undergoing VP shunt insertion as the second option for CSF diversion (Table 3).

Both serum and CSF tumor markers including human chorionic gonadotropin (beta-HCG) and alpha-fetoprotein (AFP) were evaluated in all 64 patients. 48 out of 64 patients (75%) had negative tumor markers. In the remaining 16 patients (25%) tumor markers were reported positive in either the serum, CSF, or both (Table 4).

2.1. Surgical technique

Each patient was intubated under general anesthesia with his or her head in a neutral, flexed position and held in a 3-point MAYFIELD Skull Clamp head fixation frame (Integra Life-Sciences Services, Saint Priest, France). A preoperative brain MRI and CT scan were obtained in all patients. A rigid endoscope with a main and a side working channel and 0° viewing angle by Storz GAAB (Tuttlingen, Germany) was used. In the beginning, a 3.5 cm frontal precoronal burr-hole was made 3.5 cm from the midline until 2010. From 2010 onward, we used magnetic resonance (MR) navigation to determine the optimized trajectory as well as the most accurate location of a single burr-hole on individual basis in order to provide the most appropriate access to the pineal lesion and to prevent damage to the adjacent neuronal structures, particularly the head of caudate nucleus and fornices. In the case of a thick cranium, the burr-hole edge was trimmed to change the direction of working sheet trajectory. An appropriate trajectory allowed for visualization of the posterior wall of the third ventricle without injury to the boundaries of the foramen of Monro. After entry into the lateral ventricle via a single burr-hole trajectory and identification of the foramen of Monro and the other main landmarks of the lateral ventricle such as choroid plexus, fornix, and veins (Fig. 2) (Video1), the endoscopic sheath was forwarded through the foramen of Monro to the third ventricle in order to perform ETV carried out in all patients in current study prior to biopsy sampling to avoid obscuration of the field caused by bleeding occurring during the biopsy acquisition leading to prolonged duration of surgical procedure (Video1). After ETV was performed and the functionality of ETV perforation was ensured, the endoscopic sheath was backwarded through the foramen of Monro to the lateral ventricle to visualize the anatomy of the foramen of Monro and the nearby vascular structures (thalamostriate and septal veins) in order to detect any probable damage to the foramen of Monro or the surrounding vascular structures. CSF samples for tumor markers were obtained during the procedure of CSF diversion. The third ventricle was then entered again through the foramen of Monro to approach the posterior wall of the third ventricle in order to perform the concurrent biopsy of the pineal tumor. To reduce the risk of hemorrhage, we coagulated specific regions of the tumor beforehand. 6–10 biopsy specimens were harvested in each

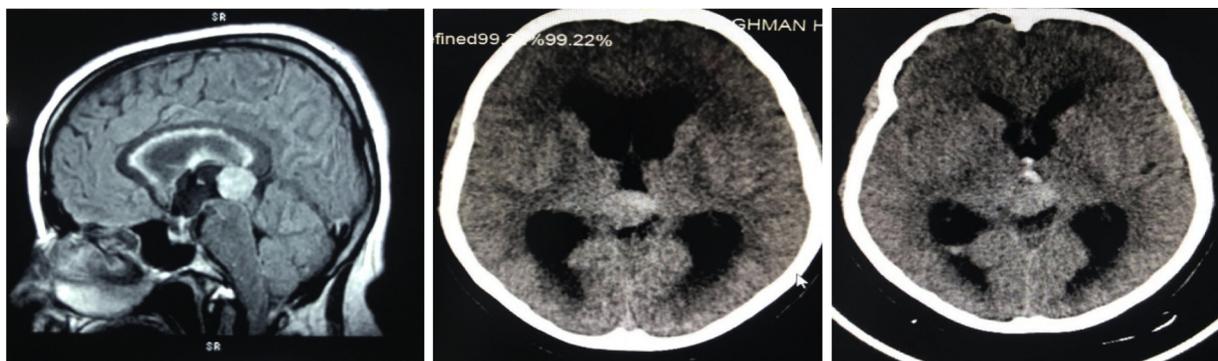


Fig. 1. View of a pineal region tumor with a hyperintense appearance on T1-weighted, gadolinium-enhanced sagittal magnetic resonance imaging (left). Axial computed tomography scan without contrast demonstrates a hyperdense lesion in posterior wall of the third ventricle resulting in bilateral ventriculomegaly (middle). The hydrocephalus of the patient is relieved after performing endoscopic third ventriculostomy and concurrent tumor biopsy. A small amount of clots is seen at the site of the biopsy (right).

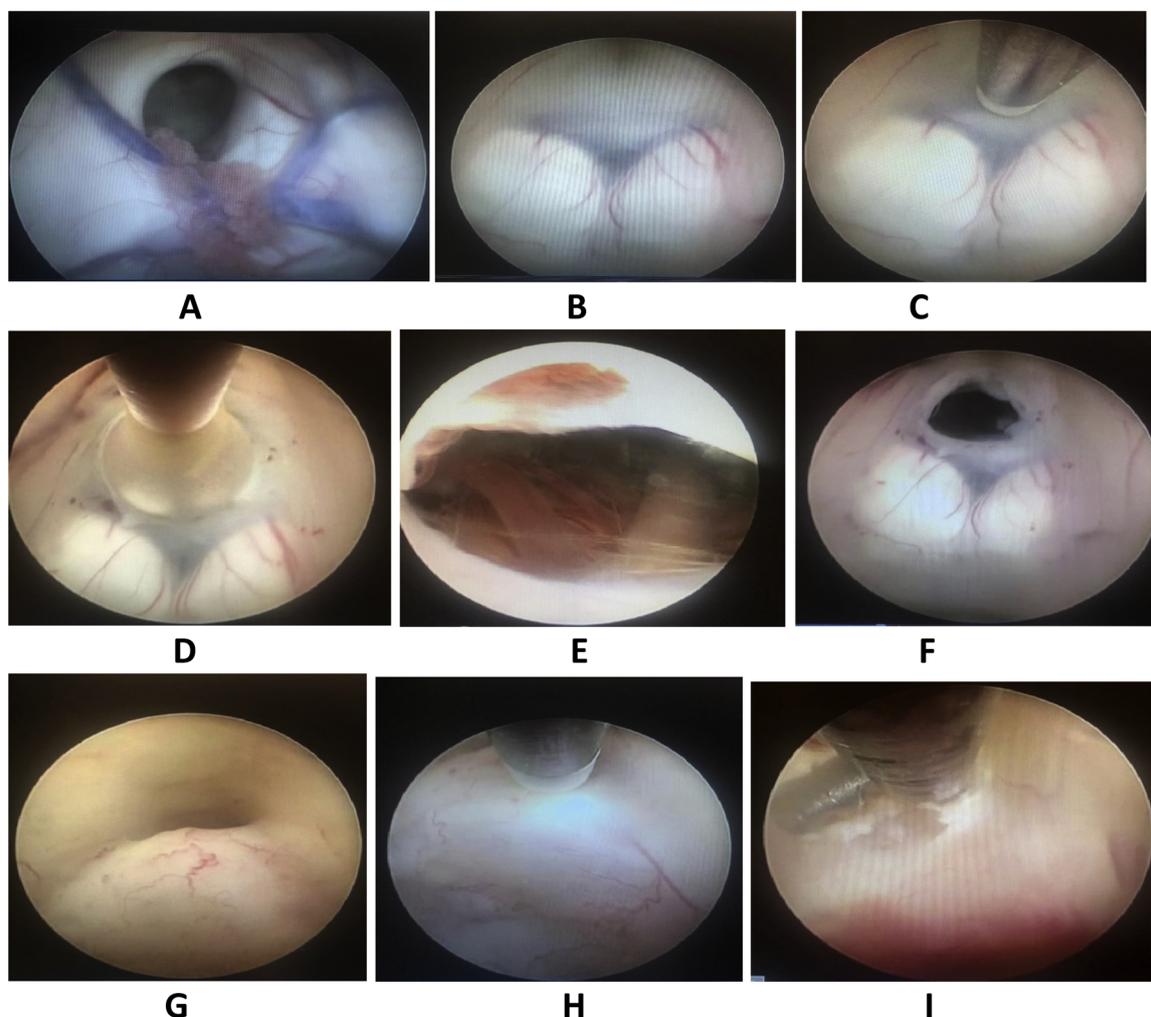


Fig. 2. View of the lateral ventricle, the foramen of Monro (A) and the floor of the third ventricle (B). Application of a rigid endoscopy device to perform endoscopic third ventriculostomy (ETV) (C). Enlarging the created ostomy using Fogarty balloon (D). View of the interpeduncular and prepontine cistern, basilar artery and its branches (E). View of the floor of the third ventricle, the created ostomy after performing ETV (F) and the pineal tumor located in the posterior wall of the third ventricle (G). Coagulation of the tumor surface to reduce the risk of bleeding while taking a biopsy (H). Application of a grasping forceps to make a tumor biopsy (I).

patient. In the case of a small amount of hemorrhage causing no impaired vision, we performed short irrigation and bipolar coagulation to stop bleeding. Prolonged hemorrhages caused by smaller blood vessels resulting in obscuration of the surgical field were all successfully stopped by constant irrigation with isothermic Ringer lactate and optional coagulation. The clots were then evacuated, if needed. Finally, the created ostomy was visualized again to ensure its functionality. If additional clearance of the CSF was necessary, EVD was placed. Five patients required EVD in our series (Table 3) which was removed after 72 h in all patients but in one case (1%) undergoing permanent VP shunt insertion. After the operation, the cortical hole of brain was plugged with Gelfoam (Pfizer, New York, New York, USA), and the cranial defect was covered with bone dust and/or titanium burr-hole plate.

3. Results

In this study, the results of simultaneous ETV and biopsy of the pineal lesion were evaluated in 64 patients with a diagnosis of pineal region tumor. A total of 31 cases were male with an average age of 36.8 years and 33 females with average age of 35.9 years. Patients were mean 36.35 years of age; the youngest was 6 and the oldest was 87 years old (Table 1).

All 64 cases underwent endoscopic third ventriculostomy and

concurrent biopsy of the lesion with a single entry approach without any cortical injury. A negative initial diagnosis was found in only 2 out of 64 patients (3%). In these two cases, the second biopsy samples were taken with the same approach reported positive in both (Table 3).

The histological type of pineal tumors determined with biopsy of the lesion is as follows:

Classic ependymal tumor (15%), Ependymoblastoma (11%), Pineocytoma (23%), Pineoblastoma (6%), Tectal plate glioma (12%), Germinoma (16%), Teratoma (8%), Mix germ cell tumor (6%) and Embryonal cell carcinoma (3%) (Table 2).

Table 2
Histologic feature of the tumors after an ETV and concurrent biopsy in the pineal region.

Histology of tumor	Frequency, %
Classic ependymal tumor	15
Ependymoblastoma	11
Pineocytoma	23
Pineoblastoma	6
Tectal plate glioma	12
Germ cell tumors	16
Teratoma	8
Mix germ cell tumor	6
Embryonal cell carcinoma	3

Table 3
Results.

Result	Frequency, %
Positive initial diagnosis	97
Negative initial diagnosis	3
Mortality	0
EVD	7
Permanent VP shunt	1
Postoperative complications	
Transient	
IVH	18
Seizure	5
Meningitis	3
DI	3
Permanent	
Memory deficits	1

Table 4
Summary of tumor marker levels.

Tumor Marker	Normal (%) Serum CSF	High (%) Serum CSF
Human chorionic gonadotropin	86 91	14 9
Alpha-fetoprotein	85 89	15 11

All 64 (100%) patients presented with hydrocephalus and the associated signs and symptoms. The clinical symptoms of the patients are categorized as three groups: patients with high-ICP related symptoms including headache (78%), vomiting (14%) and gait instability (6%), those with the symptoms due to pressure on the nearby nervous structures including Parinaud's syndrome (1%) and the last group are patients with endocrine imbalance symptoms including diabetes insipidus (DI) (1%) and precocious puberty (1%) (Table 1).

The average duration of surgery was 45 min. 5 patients (7%) underwent EVD which was removed after 72 h in all patients but in one case (1%) undergoing permanent VP shunt insertion (Table 3).

The mean length of hospital stay was 3 days and there was no rate of mortality (Table 3).

Postoperative complications are divided into transient and permanent complications. The transient complications included 12 cases of IVH (18%), 2 cases of meningitis (3%), 3 cases of seizure (1 to two episodes of seizure) (5%), 2 cases of DI (3%). Permanent complication included one case of memory deficits (1%) (Table 3).

All 64 patients underwent ETV and concurrent biopsy of the pineal region (Fig. 2) (Video1). We were not forced to convert to open microsurgical procedure in any patient.

4. Discussion

Pineal region tumors represent 5% of all intracranial tumors in children [1,4]; however, the incidence in adults is lower and these tumors account for less than 1% of brain tumors [2,3]. Tumors of pineal region are histologically divided into germ cell tumors (GCTs) (including germinomas, nongerminomatous GCTs and mature teratomas), tumors originating from pineal gland (including pineocytomas and pineoblastomas), tumors of neuroepithelial origin (including all grades of gliomas), and a wide spectrum of other tumors including metastases. Thus, tissue diagnosis of the pineal tumors would be necessary to determine the best management strategy, since variable responses to radiation therapy, chemotherapy, aggressive resection or combination of these treatment strategies have been reported for each of the aforementioned pineal masses [13–15]. Approximately, 90% of patients with tumors of pineal region present with obstructive hydrocephalus [5,6] necessitating an initial optimal surgical procedure to alleviate high intracranial pressure in those with severe acute high ICP-related signs and symptoms. Traditionally, ventriculoperitoneal shunting or external

ventricular drainage are the choices of surgical management to treat hydrocephalus in these patients; however, since the earliest performance of endoscopic strategy in patients with pineal lesions reported by Fukushima et al. [7], ETV and concurrent biopsy of the lesion has been established as a surgical procedure to restore the CSF pathway and also determine the histologic diagnosis of the pineal region tumors simultaneously. Endoscopic approach is now the preferred surgical method to harvest biopsy samples in pineal region, as it allows for direct visualization and thus, the ability to minimize bleeding from the highly vascularized structures, obtaining a CSF sample for CSF tumor marker analysis and simultaneous treatment of coexisting hydrocephalus. In addition, it is a minimal invasive approach and a diagnostically sensitive method [6,8,16,17]. Here, we performed endoscopic third ventriculostomy and concurrent biopsy in 64 patients using a single burr-hole trajectory. Our data suggested that the most common presenting features in patients with pineal region tumors are headache, vomiting and gait instability. IVH was the most common transient postoperative complication. Memory deficits was the only permanent postoperative complication occurred in one patient (Table 3).

4.1. Single and dual burr-holes and trajectories versus stereotactically guided biopsy

Endoscopic third ventriculostomy and concurrent biopsy of pineal region tumors could be performed through both single and two separate burr-holes. The risk of damage to nearby structures is reduced during this surgical method compared to stereotactically guided biopsy due to the direct vision of the lesion. The accuracy rate of diagnosis of stereotactically biopsy has been reported 91% with a morbidity rate of 3% [18], while there are several studies in which dual burr-holes and trajectories have been employed with an accuracy of diagnosis of 100% without a significant morbidity [3,9,19]; however, single entry approach has been reported to be associated with a negative initial diagnosis of 16% [20,21]. In another study [16], a negative initial diagnosis was found in only 1 out of 8 patients. The probable reasons of negative diagnosis in patients undergoing single burr-hole trajectory include the specific anatomical location of some pineal tumors resulting in technical limitation to access the tumor along with heterogeneity of pineal lesions [22–24]. The accuracy of endoscopic histological diagnosis has been shown to vary between 61% and 100% [5,6,8,21,25–28]. Several studies suggest two separate burr-holes for ETV and concurrent tumor biopsy [28–30] especially in the case of tumors located in posterior wall of the third ventricle [31]; however, Morgenstern et al. [31] reported that there were no significant differences between single and two trajectories in their series. Here, we performed one burr-hole for simultaneous ETV and tumor biopsy in our patients. In our study, a positive initial diagnosis was reported in 62 patients (97%) (Table 3). Tumors located posteriorly to the third ventricle are difficult to biopsy caused technical limitation during the surgical procedure, since stretching the origin of the internal cerebral vein increases the risk of major hemorrhage and venous infarction of the thalamostriate vein territory. In 2 out of 64 patients the initial diagnosis was found negative (3%). In these two patients the second biopsy samples were taken with the same approach; however we harvested larger biopsies and increased the number of samples as it has been shown that larger biopsies increase the diagnostic yield of the procedure [16]. The secondary biopsy samples were reported positive in both two patients. Increasing the number of samples is the other strategy to reduce the sampling error when taking a biopsy of the pineal region tumors [32]. Abbassy et al. [32] harvested six to eight biopsies for histopathology investigation in their series with a diagnostic rate of 81.8%. Chibbaro et al. [3] provided a minimum of 8 sample tissue for histological diagnosis and advised the acquisition of 8–12 samples. All tissue samples were diagnostic (100%) in their study. In current study, we harvested 6–10 biopsies for histological examination with a positive diagnosis rate of 97%. We do believe that one of the main reasons of the

high rate of positive tissue diagnosis in our series is the high number of samples taken as it has been documented in the abovementioned studies as well. Thus, a high rate of positive initial diagnosis could be achievable even in patients undergoing a single entry approach (Table 3).

In current study, all patients presented with hydrocephalus (Fig. 1, middle) and associated signs and symptoms successfully treated with single burr-hole trajectory (Fig. 1, right). 5 patients required (7%) a temporary EVD removed after 72 h but in one patient (1%) undergoing permanent VP shunt insertion (Table 3). This is in line with other recent studies [26,33]. Therefore, coexisting hydrocephalus could be successfully treated with single entry approach having the advantage of lower risk of infection and reduced potential seeding of the tumor compared to VP shunt insertion as well. There was no rate of mortality in our study. This is consistent with other studies [26,33]. Generally, multiple studies have demonstrated the safety of simultaneous ETV and biopsy of the pineal tumors and its lower morbidity and mortality compared to conventional approaches [1,6,27].

4.2. Management of intraventricular hemorrhage during ETV and concurrent tumor biopsy

Most of intraventricular bleedings during endoscopic procedures are minor bleeding events without vision impairment controlled short after irrigation [34]. These short unavoidable bleedings during neuroendoscopy might not be counted as a complication and only those resulting in discontinuation of the surgical procedure or a conversion to microsurgery could be counted as complications [35,36]. Although severe intraventricular hemorrhages are rare, neuroendoscopists should be aware of them during intraventricular procedures to employ an effective strategy to manage them. Three consecutive steps are recommended to stop intraventricular bleeding events: first irrigation, then coagulation, and finally, more invasive methods have to be applied to manage IVH; however, most hemorrhages can be successfully stopped by sufficient irrigation and coagulation [35]. The most commonly recommended surgical technique to control a severe IVH is the switch to microsurgery [34,37,38] that is associated with some limitations. The origin of hemorrhage may not be inspected with microsurgical approach owing to limited visualization of the surgical field through the microscope. Thus, more invasive retraction would be necessary to detect the source of bleeding resulting in additional damage to the brain tissue. Some other strategies have been suggested to manage intraventricular hemorrhage. Cappabianca et al. [39] employed a small cotton pad through the working sheath as a tamponade under endoscopic inspection leading to a successful hemostasis after a short period of pressure. Nigasaka et al. [40] used a combined irrigation-coagulation suction cannula, the Nagasaka multifunctional suction cannula (Fujita Medical Instruments, Tokyo, Japan). The irrigation and suction volume can be balanced using a multifunctional suction cannula. The bleeding artery is then identified and coagulated under clear visualization. Nishihara et al. [41] applied a transparent sheath, a 10-cm-long tube made of clear acrylic plastic, to manage both intraventricular and intracerebral hematoma which improves the visualization of the surgical field through an endoscope inserted within. Oertel et al. [35] applied the dry field technique (DFT) to manage severe IVH with a successful outcome. This technique requires the aspiration of the entire intraventricular CSF to achieve clear visualization of the bleeding source. The coagulation is performed afterwards. In current study, IVH occurred as a transient complication in 18% of patients (Table 3). Here, to reduce the risk of hemorrhage, we coagulated specific regions of the tumor beforehand. In the case of a small amount of hemorrhage causing no impaired vision, we performed short irrigation and bipolar coagulation to stop bleeding. Prolonged hemorrhages caused by smaller blood vessels resulting in obscuration of the surgical field were all successfully stopped by constant irrigation with isothermic Ringer lactate and optional coagulation. The clots were then

evacuated, if needed. Finally, the created ostomy was visualized again to ensure its functionality. If additional clearance of the CSF was necessary, EVD was placed. Five patients required EVD in our series (Table 3) which was removed after 72 h in all patients but in one case (1%) undergoing permanent VP shunt insertion. Severe IVH, necessitating one of the abovementioned methods to control the bleeding, occurred in none of the patients in our series. Although the bleeding management and the fornix damage are of great concern to the neuroendoscopists in single entry approach to the third ventricle and the pineal region lesions, the intraventricular hemorrhage was successfully managed in our patients and no clinical signs and symptoms related to the fornix damage were found in our series. This is consistent with other recent studies [35,42–44]. The other transient complications included diabetes insipidus (3%) meningitis (3%), and seizure (1 to two episodes of seizure) (5%). IVH and diabetes insipidus were resolved short after surgical procedure (maximum one week after surgery). The patients with diabetes insipidus (3%) underwent medical treatment provided by a nephrologist. In the case of a meningitis, a 3-week medical treatment was administered by infectious disease specialist. All patients with meningitis were successfully managed without any neurological deficits. Those with seizure received medical treatment with phenytoin for 6–12 months (Table 3).

In current study, the only permanent postoperative complication was memory deficits occurred in only one patient (1%). The mean length of hospital stay in our study was 3 days. The significant reduction of costs related to a reduction in hospital stay as the accuracy of endoscopic biopsy has been well established [3,45,46].

5. Conclusion

The result of our series, one of the largest reported for simultaneous ETV and biopsy of pineal tumors, demonstrated the safety and efficacy of endoscopic procedure through single Burr-hole trajectory as a minimally invasive technique in management of pineal region tumors. Moreover, it allows for treatment of coexisting hydrocephalus as well as direct inspection of the highly-vascularized pineal lesions leading to lower risk of mortality and morbidity compared to stereotactic biopsy technique. The significant reduction of costs related to a reduction in hospital stay is the other advantage of this approach compared to other surgical methods. Based on our study, a number of 6–10 biopsy samples is highly recommended to be harvested in order to achieve a high rate of positive initial diagnosis.

Acknowledgements

The authors thank the Clinical Research Development Unit (CRDU) of Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran, for their support, cooperation, and assistance during this study.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.clineuro.2019.105418>.

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