ELSEVIER

Endoscopy

THE ROLE OF NEUROENDOSCOPY IN THE TREATMENT OF PINEAL REGION TUMORS

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The authors describe a technique for the initial management of patients with pineal region neoplams and symptomatic hydrocephalus. Endoscopic third ventriculostomy and, if possible, tumor biopsy are performed through a single precoronal burr hole. When indicated, formal tumor resection can be performed nonemergently, without the need for ventricular drainage or shunting.

KEY WORDS
Brain tumors, neuroendoscopy, hydrocephalus, ventriculoscope, pineal tumors.

Although improvements in neuroimaging and microsurgical technique have enhanced the safety and efficacy of pineal tumor surgery, the optimal treatment for pineal tumors and the often associated noncommunicating hydrocephalus remains controversial. Histopathologic diagnosis is essential for individualizing management of the wide assortment of lesions arising in the pineal region. Conventional techniques to obtain tissue diagnosis include stereotactic biopsy and various "open" procedures. Limitations of stereotactic biopsy include sampling error, which can be particularly problematic in the pineal region because of the heterogeneity of many tumors occurring here, and the risk of hemorrhage, because of proximity of the major deep venous drainage of the brain. Direct surgical resection is frequently indicated, but obligates the patient to a major procedure with its attendant risks, when less invasive alternate therapies may exist, such as radiation therapy for germinoma. Hydrocephalus, when present, should be controlled before a formal tumor resection is performed.

Approximately 90% of patients with pineal region tumors have hydrocephalus at the time of presentation [6]. Many patients are acutely ill from increased intracranial pressure and require urgent treatment of hydrocephalus. Traditionally, hydrocephalus has been controlled with either an external ventricular drain or a ventriculoperitoneal shunt. Ventricular drains and shunts, however, carry associated risks of infection and malfunction, and, in fact, the incidence of shunt malfunction in patients with pineal tumors and hydrocephalus is significant. In one series, nearly 20% of patients with pineal tumors and hydrocephalus required a shunt revision because of a malfunction in the postoperative period [6]. Presumably, this high malfunction rate is related to elevated cerebrospinal fluid (CSF) protein and cellular debris.

Ventricular shunts may contribute to dissemination of some pineal neoplasms. In patients with malignant germ cell tumors or pineoblastoma there exists a low but definite risk of peritoneal metastasis following shunting [2–5,7]. Although millipore filters have been used on occasion to prevent tumor seeding, they have not generally been helpful because of the significantly increased rate of ventricular shunt malfunction [1,6].

We report an alternative surgical strategy for managing certain patients with pineal region neoplasms that allows treatment of the symptomatic hydrocephalus as well as safe tumor biopsy under direct vision in the same sitting. Patients presenting with increased intracranial pressure from noncommunicating hydrocephalus undergo emergent endoscopic third ventriculostomy through a precoronal burr hole. This permits rapid control of symptomatic hydrocephalus without the need for an external ventricular drain or shunt. Through the same operative exposure, the posterior third ventricular tumor is biopsied under direct vision, and samples of CSF are collected for tumor markers and cytology. Definitive surgical extirpation of the neoplasm, if

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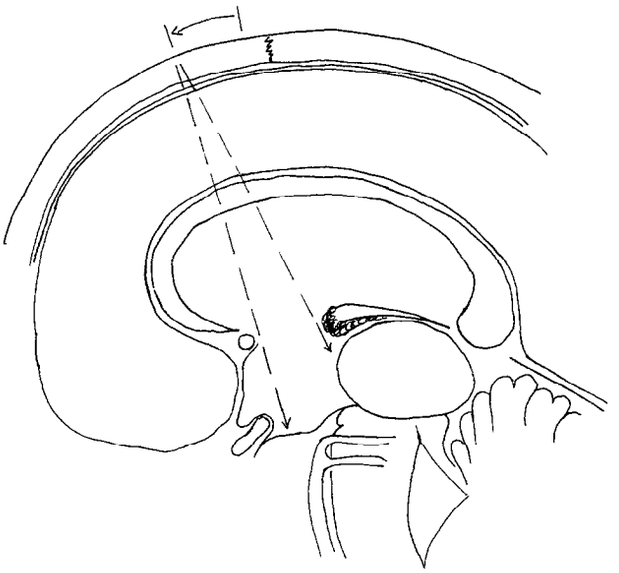
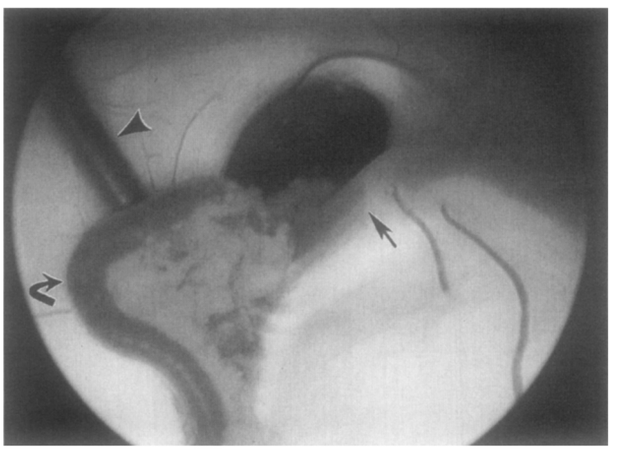


1 Trajectory: the standard coronal burr hole for a third ventriculostomy is in the midpupillary line, just anterior to the coronal suture. This trajectory provides a direct approach through the foramen of Monro to the floor of the third ventricle, but a poor approach to the posterior third ventricle. When third ventriculostomy is combined with biopsy of a pineal region mass, the burr hole is moved anteriorly, using the preoperative sagittal MRI as a guide. This allows a trajectory to both the floor of the third ventricle and to the posterior third ventricle.

indicated, is conducted electively through an appropriate traditional open approach to the pineal region. During the open microsurgical tumor resection, visualization of the lesion and surrounding structures may be enhanced by the use of the endoscope.

Operative Technique

A burr hole is made anterior to the coronal suture in the midpupillary line. We prefer to use a rigid endoscope because, in general, its optics and working channels are superior to those provided by the flexible fiberoptic endscopes. The tradeoff, however, is a reduction in steerability, and because of this the standard coronal burr hole must be modified to allow the operator access to both the anterior third ventricular floor and the posterior third ventricular tumor from the same entry site. The standard coronal burr hole usually provides a direct approach through the foramen of Monro to the floor of the anterior third ventricle, but a poor approach to the tumor situated in the posterior third ventricle. When endoscopic third ventriculostomy is combined with biopsy of a pineal region mass, the burr hole is moved a bit more anterior than

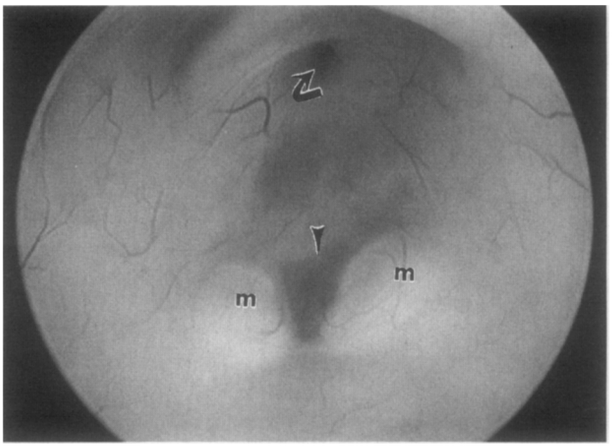


2 Endoscopic view: right foramen of Monro. Arrowhead denotes the septal vein, curved arrow the choroid plexus, and straight arrow the thalamostriate vein.

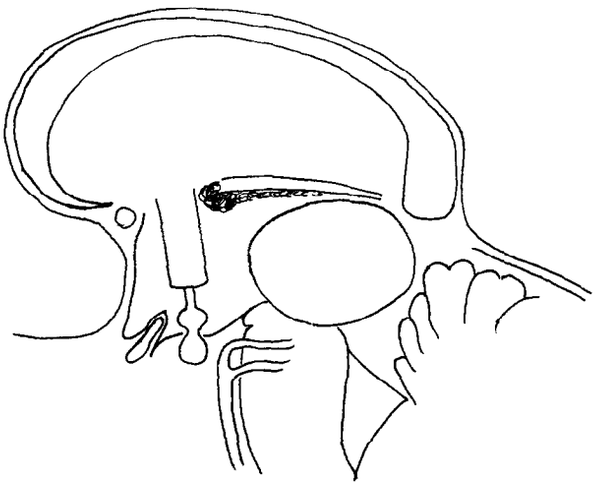
usual, using the preoperative sagittal magnetic resonance imaging (MRI) as a guide (Figure 1). This usually allows one to have a satisfactory trajectory through the foramen of Monro to both the floor of the anterior third ventricle and to the posterior third ventricular tumor.

A Gaab rigid endoscope sheath (Karl Storz, Tuttlingen, Germany) is used to cannulate the lateral ventricle. The obturator is removed and CSF is collected for tumor markers and cytology. The ventricular anatomy is visualized using a 4 mm diameter 0° straightforward viewing lens inserted into the endoscope sheath. The lens is connected via a microchip camera to a television monitor. Standard anatomic landmarks are identified including the choroid plexus, septal and thalamostriate veins, and the foramen of Monro (Figure 2). The endoscope is advanced through the foramen of Monro into the third ventricle, and the anatomic landmarks along the floor of the third ventricle are identified (Figure 3).

The third ventriculostomy is performed first. The viewing lens is removed and a smaller diameter lens and working channel system is inserted into the rigid endoscope sheath. A blunt probe is used under direct visual guidance to puncture the floor of the third ventricle in the midline just anterior to the mammillary bodies. We have refrained from using laser or radiofrequency energy along the third ventricular floor because of the possibility of injury to the basilar artery that lies under the thinned tuber cinereum. The basilar artery can usually be seen pulsating beneath the translucent floor. Great care is taken to place the fenestration anterior to the basilar apex. A no. 3 French Fogarty balloon catheter is used to widen the fenestration (Figure 4). The



3 Endoscopic view, floor of the third ventricle. Curved arrow denotes the infundibular recess, and the optic recess is just anterior to this. *M* denotes the mammillary bodies. The pulsatile basilar artery (arrowhead) can be seen through the thinned tuber cinereum. The floor has not yet been perforated. The site for perforation is in the midline anterior to the basilar artery.



4 Balloon catheter: a Fogarty balloon catheter introduced through the working channel of the endoscope is advanced through the small opening in the floor of the third ventricle made by the blunt probe. The balloon is repeatedly inflated and deflated to enlarge the fenestration.

balloon is repeatedly inflated and deflated, until a window has been created in both the ependyma and the subjacent arachnoid membrane (Figure 5).

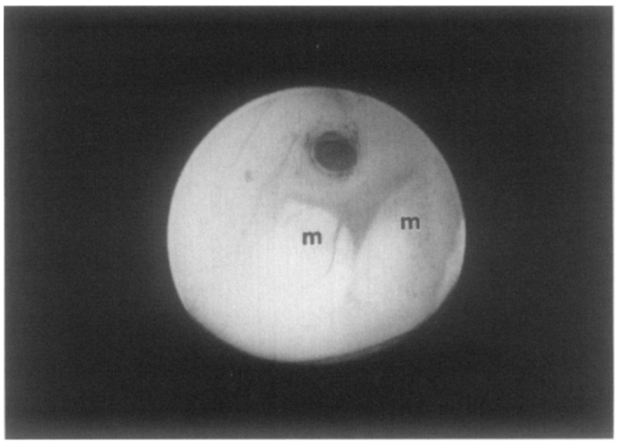
The endoscope is then directed posteriorly toward the aqueduct to visualize the tumor in the pineal region. Care is taken to avoid injury to the fornix and the periforaminal veins. Biopsy forceps are used to obtain tissue from the lesion. The bipolar cautery can be used to coagulate vessels on the surface of the tumor, if necessary. If the tumor appears highly vascular, a biopsy is not taken. The ventricle is irrigated with warm lactated Ringer's solution through one of the working channels in the endoscope sheath. The endoscope is removed and a piece of gelfoam is placed at the burr hole site. The scalp is closed in layers.

Summary of Cases

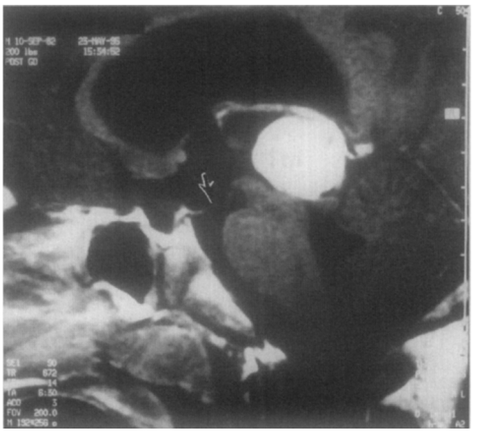
The surgical strategy outlined above has been used to treat four patients with hydrocephalus and tumors of the pineal region. In each case, noncommunicating hydrocephalus was controlled by the third ventriculostomy, without the need for ventricular shunt placement. Three of the four tumors were successfully biopsied endoscopically. One patient had a mixed malignant germ cell tumor (Case 1), one had an epidermoid tumor (Case 2), and one had a low grade astrocytoma of the midbrain (Case 3). A biopsy was not obtained in one patient (Case 4). He was a 12-year-old boy with symptomatic hydrocephalus from a large enhancing posterior third ventricular tumor, whose hydrocephalus was successfully controlled by endoscopic third ventriculostomy. Although the posterior third ventricular tumor could be seen endoscopically, it could not be biopsied because of technical difficulties working around an enlarged massa intermedia. This tumor, which proved to be a germinoma, was successfully removed in a second sitting via an anterior transcallosal craniotomy and subchoroidal transvelum interpositum approach. The patient is receiving adjuvant chemotherapy and remains well without radiographic evidence of tumor 7 months after surgery.

Three of the four patients subsequently underwent formal microsurgical tumor removal. The patient not undergoing further surgery (Case 3) was a 24-year-old woman who had presented in the second trimester of pregnancy with progressive visual loss and bilateral optic nerve atrophy. She underwent third ventriculostomy and drainage of a cystic midbrain tumor, with biopsy suggesting a low-grade astrocytoma. She was able to carry her pregnancy to term, and 8 months after endoscopic surgery there has been limited improvement in her vision, the lesion has remained stable, and her hydrocephalus has not recurred.

There were no operative complications. The patient with the epidermoid lesion (Case 2) developed a late onset recurrence of tumor. He had presented initially at age 11 years with headache and papilledema, and underwent successful endoscopic third ventriculostomy and tumor biopsy. The tumor was



5 Endoscopic view, completed fenestration. *M* denotes the mammillary bodies. Both the ependyma and arachnoid have been opened. The pulsatile basilar artery can often be in the interpeduncular cistern.



6 Mixed malignant germ cell tumor (Case 1). Sagittal T_1-weighted gadolinium-enhanced MRI demonstrates a 2.5 cm diameter round enhancing pineal region mass compressing the collicular plate, obstructing the aqueduct of Sylvius, producing non-communicating hydrocephalus. Note the inferior bowing of the floor of the third ventricle (arrow) secondary to the hydrocephalus.

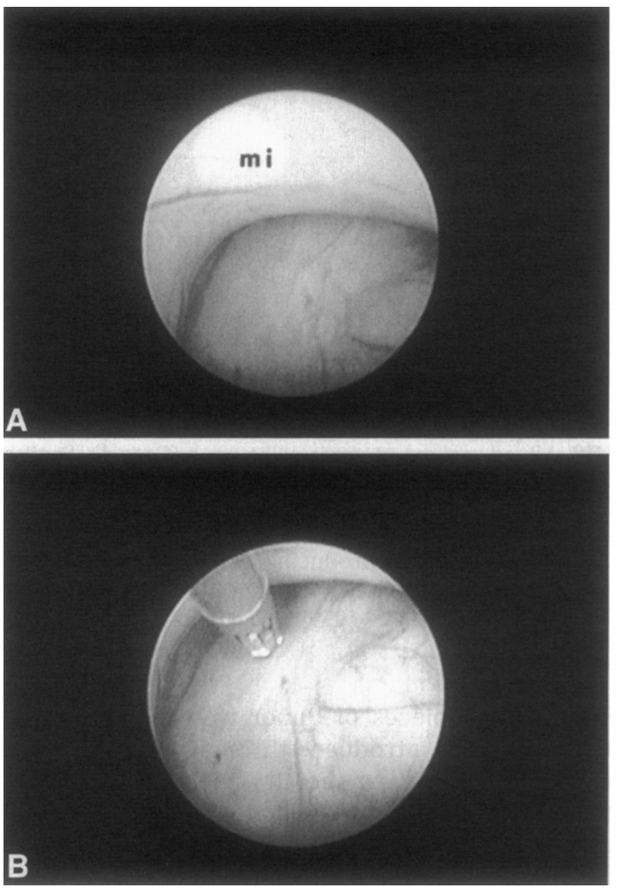
resected 1 week later via an infratentorial supracerebellar approach, and all tumor was removed except for a small fragment adherent to the vein of Galen. Histopathology from the open tumor resection was epidermoid, identical to that found endoscopically. The patient did well for 15 months, but then developed recurrent symptoms of increased intracranial pressure and was found to have a large enhancing tumor filling the third ventricle that was removed via anterior transcallosal craniotomy, with placement of a ventriculoperitoneal shunt. Pathology this time was mixed mature teratoma and germinoma. He is currently well 18 months from initial diagnosis, receiving chemotherapy followed by radiation. Presumably, this patient's recurrence as a different histologic lesion is the result of an initial sampling error. It is interesting, though, that there was no evidence of germinoma on analysis of tissue from both the endoscopic biopsy and the formal supracerebellar resection.

Illustrative Case

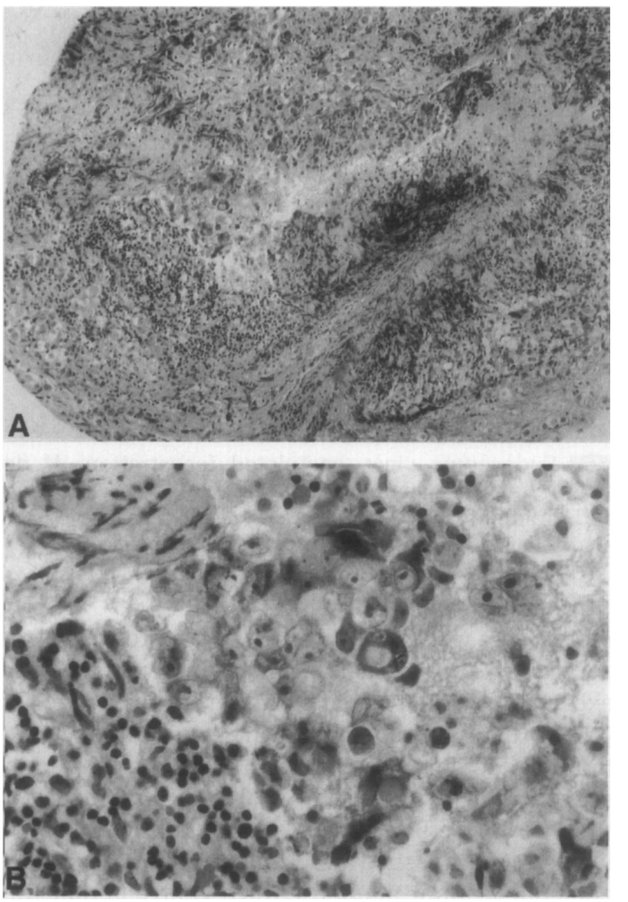
This 12-year-old boy (Case 1) presented to the emergency room with a 3 week history of headache, nausea, vomiting, and diplopia. Examination showed an obese boy in moderate discomfort with lethargy, bilateral papilledema, and Parinaud's syndrome. Cranial MRI showed a large enhancing pineal mass and noncommunicating hydrocephalus (Figure 6). The patient was brought to surgery emergently for endoscopic third ventriculostomy and biopsy of the lesion, both of which were performed through a single precoronal burr hole. The tumor had a grayish capsule with fine vessels on its surface, and pieces of tumor were removed with biopsy forceps introduced through a working channel in the endoscope sheath (Figure 7). Postoperatively, the patient's headache, papilledema, and diplopia resolved, and the Parinaud syndrome improved. Repeat cranial MRI with cine-flow analysis showed the ventricles were slightly smaller in size, and there was CSF flow across the fenestration in the floor of the third ventricle.

The endoscopic biopsy revealed a mixed germ cell tumor consisting of germinoma, endodermal sinus tumor, and immature teratoma (Figure 8). The germinoma component had sheets of large epithelioid cells with prominent central nucleoli mixed with small reactive appearing lymphocytes. The endodermal sinus component displayed nests of pleomorphic cuboidal epithelial cells forming papillae and Schiller Duval bodies. Immunostaining was positive for alpha-fetoprotein (α-FP) and beta-human chorionic gonadotropin (β-HCG) in the endodermal sinus component, and placental alkaline phosphatase in the germinoma component. CSF cytology was negative. The CSF levels of β-HCG and α-FP were within the normal range. Cerebral angiogram showed a minimal tumor blush and posterior displacement of the precentral cerebellar vein. MRI of the spine was normal.

Several days later, the tumor was resected through an infratentorial supracerebellar approach. Surgery was uncomplicated and the postoperative course was smooth. Pathology once again showed a mixed malignant germ cell tumor. Elements of embryonal cell carcinoma were identified



7 Mixed malignant germ cell tumor (Case 1). (**A**) Endoscopic view as seen through a zero-degree straightforward endoscope lens: the lesion projected anteriorly from the posterior third ventricle, and bulged underneath the massa intermedia (*mi*); (**B**) endoscopic biopsy: through the working channel of the endoscope, biopsy forceps were advanced to the surface of the lesion and biopsies were obtained.



8 Mixed malignant germ cell tumor (Case 1), histopathology. (**A**) Low magnification photomicrograph shows the tumor is predominantly comprised of an admixture of large epithelioid cells and lymphocytes consistent with a germinoma; (**B**) high magnification photomicrograph shows an area of highly pleomorphic cohesive epithelioid cells with prominent, often multiple nucleoli, indicative of embryonal cell carcinoma. Other areas of this tumor consisted of endodermal sinus (yolk sac) tumor and immature teratoma.

as well. Repeat cranial MRI confirmed gross total resection of the tumor. The patient's vertical gaze palsy resolved completely and he returned to his premorbid baseline, and began adjuvant chemotherapy.

Discussion

The optimal management of patients with symptomatic pineal region tumors includes control of the frequently associated hydrocephalus and the safe acquisition of tissue for histologic diagnosis. The traditional use of ventricular drainage or shunting to control hydrocephalus can be associated with a host of complications, and direct microsurgical attack on the tumor, often the standard of care, is not safe unless the increased intracranial pressure has been controlled.

We suggest a surgical strategy for the initial management of patients with non-communicating hydrocephalus from pineal tumors that eliminates the need for ventricular shunting and permits a tissue diagnosis to be obtained under direct vision. A rigid ventriculoscope is inserted through a precoronal burr hole, and a fenestration is made in the floor of the anterior third ventricle. In the same sitting, CSF is collected for routine studies as well as cytologic examination and tumor markers, and the endoscope is directed to the posterior third ventricle for biopsy of the tumor.

This management plan allows rapid, safe, and effective treatment of the obstructive noncommunicating hydrocephalus that accompanies pineal region tumors, and eliminates the need for external

ventricular drainage or shunting. The problems of infection and malfunction associated with external ventricular drains and shunts, as well as the risk of peritoneal metastasis, are eliminated. Third ventriculostomy allows the patient's CSF dynamics to normalize before definitive surgical resection, and permits completion of the patient's evaluation without the constraints of an external ventriculostomy. When formal tumor resection is necessary, it can be performed safely on a nonemergent basis through a traditional open approach. The endoscope can be used to enhance visualization of the pineal region during tumor resection, assisting the microsurgical exposure by permitting visualization around "blind" corners.

One technical problem associated with use of a rigid endoscope to perform both third ventriculostomy and pineal tumor biopsy is that of finding a trajectory to two different deep-seated targets from a single point of entry in the brain. The trajectory from a pre-coronal burr hole to the floor of the third ventricle is different from the path to the posterior third ventricle, although both must traverse the foramen of Monro. Using a rigid endoscope introduced through a standard precoronal burr hole usually gives an ideal trajectory through the foramen of Monro for third ventriculostomy, but may require dangerous stretching of the periforaminal structures to look back at the pineal region.

We have chosen to solve this problem by using the preoperative sagittal MRI to help plan the trajectory. By moving the burr hole site somewhat more anteriorly, one can usually gain access to both the anterior and posterior third ventricle, thus accomplishing the ventricular fenestration and tumor biopsy with the same exposure. We prefer the rigid endoscope because of the superior optics related to its solid rod lens. If there is difficulty visualizing the posterior third ventricle, one can substitute angled lenses, but there still may be difficulty reaching the lesion with instruments for biopsy. In such a situation, a flexible steerable fiberoptic endoscope can be used for both procedures, or the third ventriculostomy can be done with a rigid endoscope, and the biopsy with a flexible endoscope introduced through the rigid endoscope sheath.

Whichever endoscope system is selected, there may still be anatomic pitfalls related to this technique. If the massa intermedia is large, it can block access to the posterior third ventricle. This was the situation we encountered in the one instance (Case 4) that we were unable to biopsy. We did have good endoscopic visualization of the lesion, however, and because of this we selected an anterior transcallosal subchoroidal corridor when we removed it microsurgically. Another concern is postbiopsy hemorrhage. Tumors sitting within the ventricular system may bleed after biopsy, and such bleeding may be troublesome because it is not tamponaded by brain. The endoscope is helpful in this regard, since it allows direct visualization of the tumor surface. Small blood vessels can be controlled with endoscopic bipolar coagulation, and minor venous bleeding usually stops with warm irrigation. If the tumor appears highly vascular, however, it is our recommendation that endoscopic biopsy not be carried out.

In summary, neuroendoscopy contributes to the safe minimally invasive management of patients with neoplasms of the pineal region and symptomatic hydrocephalus. It is reasonable to consider endoscopic third ventriculostomy and tumor biopsy as the initial approach to some of these lesions.

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COMMENTARY

The authors report their unique experience with four patients with hydrocephalus and tumors of the pineal region. In each case, a noncommunicating hydrocephalus was controlled by endoscopic third ventriculostomy. In three cases they successfully carried out an endoscopic biopsy.

From a surgical point of view, I agree with the arguments of the authors that in case of a noncommunicating hydrocephalus, third ventriculostomy is preferable to a ventricular drain or to a ventricu-

loperitoneal or ventriculoatrial shunt procedure. Whenever the placement of a foreign body can be avoided, it should be avoided. I also agree with the authors' statement that before instituting any invasive treatment for pineal lesions, there must be a clear histopathologic diagnosis. However, I have quibbles as to the usefulness of an endoscope when obtaining a biopsy from a pineal tumor. "To someone with a new hammer, everything looks like a nail." Endoscopy to me is something like a new hammer. The endoscope is certainly a fine tool for the inspection of ventricular walls, for ventriculocisternostomy, and for cystic or cisternal lesions. Meticulous and careful three-dimensional planning of the approach to a pineal tumor, however, can be achieved using MRI and CT data, to avoid vascular structures. Very few pineal tumors present a tumor surface into the third ventricle and thus are accessible to the endoscope. The authors here report on difficulties with a large mass intermedia. We prefer careful three-dimensional planning of the trajectory using a workstation and CT/MRI data. To avoid any conflicts with internal veins, we usually prefer a lateral approach, in which an endoscope would be out of place.

In cases of a germinoma or other malignant germ cell tumor, we would prefer to use a ventricular drain until tumor regression is achieved by chemotherapy/radiotherapy. The authors correctly emphasize the usefulness of the endoscope for correcting the problem of a non-communicating hydrocephalus. I question, however, the usefulness of the endoscope for establishing the diagnosis of a pineal tumor.

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Endoscopic ventriculostomy is obviously the way to treat hydrocephalus in patients who have pineal region tumors. At the same time, one can endoscopically biopsy the tumor. The major problem in carrying out such biopsies is that many of the tumors in the pineal region are mixed, and a small biopsy taken with the endoscope does not necessarily give the full picture in regard to the pineal region tumor. However, as the authors point out, endoscopic biopsy is frequently the initial approach to some of these lesions.

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CSF diversion in obstructive hydrocephalus caused by pineal tumors is, in most cases, the first part of the treatment regimen for these lesions and may be achieved by inserting a ventricular drain or by implanting a shunting device, before relieving the aqueductal compression by removing the lesion itself. Endoscopic third ventriculostomy is a practical alternative to shunting procedures, allowing one to eliminate drawbacks such as shunt malfunction, and already has a rather long tradition [3–5]. This now well-established method [1,2,6] may prove to be superior to a ventricular drain alone, since in most cases aqueductal stenosis or compression will not be reversed after tumor removal, and besides the potential for infection and the necessity for careful management of an open drain, a shunting device must still be inserted.

It seems logical to use ventriculoscopy not only for fenestration of the floor of the third ventricle, but also to verify the histologic diagnosis of the pineal mass and to perform a biopsy. Because of the location and topography of the tumor, however, it may not always be possible to obtain a direct approach; the authors describe a more frontal burr hole that allows a better trajectory to the posterior part of the third ventricle. This may be possible for large tumors, and for those situated in the anterior part of the pineal region, but it may not be possible for smaller tumors (although this must be decided on a case-by-case basis). But all in all, even though in one of the four presented cases there was a sampling error from the biopsy, it seems reasonable to attempt this combined manoeuvre.

Principally, pineal region tumors should be treated by radical removal via a direct surgical approach, and decisions regarding adjuvant therapy should be made based on the proven histology. If radiation is considered, it should be used only for those tumors that have a tendency to see; chemotherapy and local radiosurgery can be used in cases that have no tendency for seeding but are not benign tumors, especially in the younger age groups. Radiation therapy, especially in the Western world where germinal tumors are a minority, should not be the initial treatment of choice, especially as microneurosurgery of these lesions has become a fairly safe procedure in the last 20 years.

Therefore, we agree that with associated hydrocephalus in pineal region tumors, the CSF dynamics should be stabilized before the surgical approach, and if possible, the nature of the tumor should be verified by endoscopic third ventriculoscopy and ventriculostomy. The sampling error in Case 2 is an exceptional experience in histologic sampling; it does not by any means disqualify the method of

primary neuroendoscopic ventriculostomy for biopsy.

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