Efficacy of neuroendoscopic procedures in minimally invasive preferential management of pineal region tumors: a prospective study

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Object. This prospective study is based on a consecutive series of 20 patients with pineal region tumors who underwent minimally invasive preferential management. The purpose of this report is to discuss the role of neuroendoscopic procedures in the management of pineal region tumors.

Methods. If the tumor markers α-fetoprotein and human chorionic gonadotropin were not detected in serum and there was significant ventricular dilation visualized on neuroimaging, neuroendoscopic surgery was first applied for tumor debulking with tissue diagnosis and gross morphological analysis of the tumor and the intraventricular structures, followed by third ventriculostomy.

Subsequent procedures were determined on the basis of verified individual tumors. For treatment of germinomas and pineoblastomas, if no tumor dissemination was confirmed by pre-, intra-, or postoperative findings, stereotactic radiotherapy or radiosurgery was performed after one course of chemotherapy with the ICE regimen (isofomid, cisplatin, and etoposide) and followed by two additional courses of chemotherapy. For treatment of malignant germ cell tumors, after extensive surgery, adjuvant chemotherapy with the ICE regimen was performed in three courses in all cases. Then radiotherapy was started using various methods, depending on the evidence of tumor dissemination. For treatment of teratomatous and neuroectodermal tumors other than pineoblastomas, extensive surgical removal was performed. As for adjuvant therapy, if the tumor was a low-grade glioma or if the patient was younger than 5 years of age, postoperative treatment did not include radiotherapy. If the tumor was a malignant teratoma or high-grade glioma, conventional focal radiotherapy was performed, followed by chemotherapy with ICE for 1 year.

All but two treated patients had ventriculomegaly. Neuroendoscopic procedures were performed in six of 15 treated patients. Neuroendoscopic biopsy with tumor debulking offered enough material for tissue diagnosis, including immunohistochemical analysis and, in one case, revealed evidence of tumor dissemination undetectable on neuroimaging. With one exception, no shunt was required in any patient undergoing endoscopic third ventriculostomy. Stereotactic radiotherapy was performed in indicated cases. Favorable therapeutic outcomes were obtained in all cases of germinoma and pineoblastoma, with follow-up periods ranging from 24 months to 6.5 years.

Conclusions. Our minimally invasive preferential regimen clarified the precise indication for neuroendoscopic procedures, and the majority of our patients with dilated ventricles and no evidence of tumor markers were treated satisfactorily with effective neuroendoscopic procedures as the initial procedure, avoiding unnecessary craniotomy and radiotherapy and promising excellent therapeutic outcomes. The treatment for malignant pineal region tumors remains a subject for further study.

Key Words • pineal region tumor • neuroendoscopic surgery • radiosurgery • chemotherapy

Various aspects of the therapeutic regimen for pineal region tumors have been discussed. There are more than 17 different pathological tumor types in the pineal region, and the therapeutic approach differs for each. Some tumors can be treated by radical surgical resection alone, but most tumors require adjuvant therapy—radiotherapy, chemotherapy, or both. Germinoma is the most common type, accounting for more than 80% of pineal region tumors occurring in patients between 15 and 35 years of age in the Japanese population. This tumor is extremely radiosensitive and curable only by radiotherapy. Its epidemiological characteristics are now known to be identical to those in the Korean population as well. The low-dose radiation test or radiotherapy is still recommended as the initial treatment step in management of pineal region tumors by a number of Japanese and Korean neurosurgeons. However, during the course of radiotherapy, there is a risk of progression of the disease when this therapeutic regimen is used in certain types of radioresistant tumors. There is a tremendous racial difference in the patient population in

Abbreviations used in this paper: AFP = α-fetoprotein; CSF = cerebrospinal fluid; CT = computerized tomography; EVD = external ventricular drainage; HCG = human chorionic gonadotropin; ICP = intracranial pressure; MR = magnetic resonance; WBRT = whole-brain radiation therapy; WNRT = whole-neuraxis radiation therapy.
with a median age of 30.4 years at diagnosis. There were 16 male and 4 female patients ranging from 10 to 73 years of age, with a median age of 30.4 years at diagnosis. This is the major reason why radical surgery with tissue diagnosis is performed in these countries, as opposed to the regimen performed in Japan and Korea.31

Recently, minimally invasive procedures, including neuroendoscopic surgery, stereotactic surgical procedures, and such treatments, radical surgical removal was performed after one course of chemotherapy with the ICE regimen (isofomid, cisplatin, and etoposide). The radiation doses administered by gamma knife radiosurgery were 26 Gy in the central and 13 to 2.6 Gy in the peripheral zone. If there was evidence of tumor dissemination, the patient underwent WBRT or WNR if spinal metastasis was present, followed by three courses of ICE chemotherapy. If the patient was younger than 5 years of age, chemotherapy was started before radiation therapy and the extent of radiation prescribed was based on the patient’s response to chemotherapy. If there was residual tumor detected in the pineal region on MR imaging after these treatments, radical surgical removal was performed as the "second-look and resection" procedure.

TABLE 1
Prospective regimen for minimally invasive preferential management of pineal region tumors*

<table>
<thead>
<tr>
<th>Hydrocephalus</th>
<th>Tumor Marker (AFP or HCG)†</th>
<th>Multiplicity§</th>
<th>Radiological Specificity</th>
<th>Initial Procedure</th>
<th>Second Procedure</th>
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<tr>
<td>+ §</td>
<td>–</td>
<td>±</td>
<td>± (lateral extension)§</td>
<td>neuroendoscopic surgery regimen based on tumor type</td>
<td>stereotactic biopsy regime based on tumor type</td>
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<tr>
<td>±</td>
<td>+ §</td>
<td>+ §</td>
<td>+ (calcified firm mass or AV shunt)§</td>
<td>radical op regime based on tumor type</td>
<td>radical op regime based on tumor type</td>
</tr>
<tr>
<td>±</td>
<td>–</td>
<td>–</td>
<td>± (small cystic mass)§</td>
<td>radical op</td>
<td>observation</td>
</tr>
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</table>

* AV = arteriovenous; chemo = chemotherapy; CNS = central nervous system; RT = radiotherapy; + = yes; – = no; ± = either yes or no.
† In serum or CSF.
‡ On MR imaging.
§ Determining factor in selecting initial procedure.

Clinical Material and Methods
From 1993 to 1998, 20 patients were cared for prospectively by following a policy of minimally invasive preferential prospective regimen in our institutions. The regimen is summarized in Table 1. There were 16 male and 4 female patients ranging from 10 to 73 years of age, with a median age of 30.4 years at diagnosis.

Initial Procedure
If the tumor markers AFP and HCG were undetected in serum and ventriculomegaly was found on CT or MR imaging, neuroendoscopic surgery was first applied (Table 1) for tumor debulking and tissue diagnosis, with gross morphological analyses of the tumor and intraventricular and infracisternal structures. Information on the gross appearance of the tumor and the presence of tumor dissemination was obtained, following which endoscopic third ventriculostomy was performed in the standard fashion (Fig. 1).10,17 An EVD tube was inserted at the same time. Neuroendoscopic surgery was not performed in patients with small ventricles; in these patients stereotactic surgery was applied. If serum proved to be positive for tumor marker(s), extensive surgery was first attempted for radical total removal of tumor, as long as there was no evidence of tumor dissemination. In patients in this group in whom there was tumor dissemination, immediate adjuvant chemotherapy was selected as the initial procedure and was followed by WNRT. An EVD system was used for postoperative management in all patients with ventriculomegaly who had undergone third ventriculostomy or craniotomy. A daily CSF specimen was obtained for cytological analysis. The EVD system was kept open even in patients in whom there was no intraoperative evidence of tumor dissemination. After confirmation of cytological findings negative for tumor tissue in CSF for several days after the procedure, continuous ICP monitoring was performed to check the patency of the third ventriculostomy or the reopened aqueduct. If the CSF cytological analysis proved positive postoperatively, the EVD system continued to be used as long as possible, along with chemotherapy, in all patients treated with any surgical procedure.

Subsequent Procedures in Individual Tumors

Germinoma. If no tumor dissemination was confirmed pre-, intra-, or postoperatively, gamma knife stereotactic radiosurgery or frameless stereotactic radiotherapy was performed after one course of chemotherapy with the ICE regimen (isofomid, cisplatin, and etoposide). The radiation doses administered by gamma knife radiosurgery were 26 Gy in the central and 13 to 2.6 Gy in the peripheral zone. If there was evidence of tumor dissemination, the patient underwent WBRT or WNR if spinal metastasis was present, followed by three courses of ICE chemotherapy. If the patient was younger than 5 years of age, chemotherapy was started before radiation therapy and the extent of radiation prescribed was based on the patient’s response to chemotherapy. If there was residual tumor detected in the pineal region on MR imaging after these treatments, radical surgical removal was performed as the "second-look and resection" procedure.

Malignant Germ Cell Tumors. When AFP and/or HCG were found in various combinations, a certain type of malignant germ cell tumor was suggested. Even if the tumor...
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markers are not detected, the tissue diagnosis obtained during the neuroendoscopic procedure may suggest malignant or immature teratoma. After extensive surgery, adjuvant chemotherapy was performed in three courses. Various methods of radiotherapy were started, depending on the patient's response to chemotherapy and the evidence of tumor dissemination. If there was any evidence of tumor dissemination in the spinal canal, WNRT was performed; if no metastasis was evident, WBRT was performed. Chemotherapy was continued for a total of 1 year, including before and after radiotherapy. The practical application of the total course of chemotherapy was decided based on the patient's condition, especially the degree of bone marrow suppression. Granulocyte colony-stimulating factor was used in a routine manner as indicated.

Benign Teratoma. When tissue diagnosis confirmed the presence of benign teratoma or a mixed type of germ-cell tumor with a teratomatous component, extensive surgical removal was performed. Additional pathological analysis of the surgical specimen was performed using specific immunohistochemical staining. Subsequent therapeutic steps were initiated if any other tumor component was present.

Neuroectodermal Tumors

Pineoblastoma. Using the surgical specimen obtained by the neuroendoscopic procedure, an extensive immunohistochemical study was undertaken—during which the presence of synaptophysin, MIB-1 (Ki-67 antigen), S-100 protein, glial fibrillary acidic protein, vimentine, cytokeratin, and other factors were determined—to diagnose the cell differential character of the tumor. The therapeutic modality for this type of tumor is essentially the same as that used in treating germinoma.

Neuroectodermal Tumors Other Than Pineoblastoma. If the tissue diagnosis indicated astrocytoma or another type of glioma, or if cerebral angiography demonstrated glioblastoma with specific findings, extensive surgical removal was performed. As for adjuvant therapy, if the tumor was a low-grade glioma or if the patient was younger than 5 years of age, the postoperative course did not include radiotherapy or chemotherapy. If the tumor was malignant or a high-grade glioma, conventional focal radiotherapy was performed, followed by ICE chemotherapy for 1 year.

Techniques of Neuroendoscopic Surgery

The neuroendoscopic instrumentation included a rigid-rod endoscope (Gaab system; Codman, Boston, MA) for morphological analyses and a steerable flexible-rod endoscope (Codman) for the surgical maneuver. Two burr holes were made in the right frontal region on the pupil line, one at the coronal suture and the other behind the hair line. Ventricular taps were made by using a manometric ventricular trocar (Mizuho, Tokyo, Japan) directed toward the right foramen of Monro from each burr hole, and the intraventricular pressure was measured and a CSF sample was obtained. The trocar was replaced by a No. 14 French peel-away sheath (Cook, Inc., Bloomington, IN) and inserted in both tracks. First, the rigid-rod endoscope was introduced to determine the intraventricular structure and gross appearance of the tumor. From the frontal burr hole through the foramen of Monro, the pineal region occupied by tumor was under direct vision, which

![Fig. 1. Schematic illustration demonstrating the technique of neuroendoscopic surgery used to treat pineal region tumors. A rigid-rod endoscope is first inserted into the right lower frontal burr hole and moved into the lateral ventricle to observe the gross morphological characteristics of the ventricle. Then the endoscope is introduced into the third ventricle, and the gross appearance of the tumor under and over the massa intermedia (thalamic adhesion) is analyzed. Next, a steerable flexible-rod-fiber endoscope is used to perform debulking of the tumor, and a sufficient number of tumor specimens is obtained from the various parts of the tumor. Using the other burr hole made at the coronal suture, the same procedure for gross morphological analysis with the aid of the rigid-rod endoscope is repeated. Then the steerable flexible endoscope is used to perform third ventriculostomy in the usual fashion.]

focused under or over the massa intermedia (Fig. 2). The floor of the third ventricle was observed via the coronal approach by using the bilateral mamillary bodies and the infundibular recess as landmarks (Fig. 3). Multiple rigid-rod endoscopes with different view angles (0°, 30°, 70°, and 120°) were used to observe the entire third ventricle and the anterior horn, body, and triangle of the right lateral ventricle, especially to detect the gross appearance of tumor dissemination.

A steerable flexible-rod endoscope was used for the therapeutic procedures. The tumor was debulked, and a satisfactory amount of tissue was obtained from various parts of the tumor. During this procedure, constant irrigation was performed using artificial CSF (Otsuka, Tokushima, Japan) or Haltman solution, which passed through an EVD tube guided from the other trajectory (Fig. 2 upper left) to keep the operative field clear and to control the bleeding. Tumor removal was essentially performed using biopsy microforceps measuring 3 mm when opened. If the endoscopic and MR examination of the ventricles confirmed no tumor dissemination, third ventriculostomy was performed in the standard fashion. The center of a triangle formed by the infundibular recess and bilateral mamillary bodies was penetrated with a microforceps, and the hole was dilated using a No. 2 French catheter balloon (Medi-tech, Watertown, MA), which could be inflated up
to 4 mm. Communication between the third ventricle and the basal cistern was then confirmed, and the morphological characteristics of the cistern were again examined with the aid of the rigid-rod endoscope to rule out tumor dissemination (Fig. 3).

The EVD tube was kept in place for postoperative continuous ICP monitoring during the next several days in cases in which there was no tumor dissemination. If there was any evidence of tumor dissemination, the EVD tube was kept in place for a course of chemotherapy with continuous CSF drainage.

Results
Diagnostic Findings and Decision Making

In 20 patients a mass lesion was diagnosed in the pineal region by neuroimaging. Thirteen of 20 patients were initially symptomatic; in all but one of these patients a relatively large mass in the pineal region with significant ventriculomegaly was demonstrated on CT and MR images at the time of the initial diagnosis. Two of seven asymptomatic patients became symptomatic, experiencing headaches or upward-gaze palsy, and some enlargement of the mass but with no evidence of ventriculomegaly on follow-up MR images. In three patients findings positive for serum tumor markers were found: two patients with AFP and one with both AFP and HCG. In all 13 initially symptomatic patients, CT and MR images demonstrated a solid mass lesion with or without small cystic components and various degrees of contrast enhancement. In one patient there was calcification in the majority of the mass lesion. In five asymptomatic patients with relatively small cystic lesions, there was no evidence of tumor growth or ventriculomegaly on serial MR images obtained during the follow-up periods, which ranged from 2.5 to 6.5 years, with a median follow-up period of 4.5 years.

Cerebral angiography was performed in all symptomatic patients, and the findings confirmed avascular mass lesions in all except one patient, in whom an extremely vascular tumor with an arteriovenous shunt was demonstrated, suggesting specific patterns of glioblastoma.

Based on clinical findings, the initial procedure was decided on a case-by-case basis. Consequently, the neuroendoscopic procedure was performed in six patients in whom there was no evidence of tumor markers. Extensive open surgery was performed in five patients, in three of whom there was positive evidence for tumor markers, in one patient with a mainly calcified lesion, and in one with an extremely vascular tumor. Radiotherapy was undertaken in one elderly high-risk patient with primary cancer and one patient with multiple intracranial lesions. No therapeutic procedure was performed in five asymptomatic patients who harbored relatively small cystic lesions with a likely diagnosis of pineal cyst.

Immediate Outcome After Neuroendoscopic Surgery as the Initial Procedure

Among the six patients who underwent neuroendoscop-
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ic surgery, the pathological findings were compatible with germinoma in four and pineoblastoma in two patients. Following the neuroendoscopic procedure, the patients underwent specific therapeutic regimens for their individual tumor types. There were no significant postoperative complications. Postoperative ICP monitoring after third ventriculostomy showed normalized ICP, and neuroimaging demonstrated normalized ventricular size (Fig. 4) in all patients, except one in whom intermittent mild-pressure waves and an ipsilateral subdural fluid collection were demonstrated on CT scans. Consequently, a VP shunt was implanted in this patient.

Final Outcome in Individual Tumor Types

Germinoma. A tissue diagnosis of germinoma was obtained in eight patients, and germinoma was suggested by radiological findings of a double tumor in one patient. Tissue diagnosis was performed by neuroendoscopic procedure in four patients, stereotactic biopsy in two, and extensive surgery in one patient. There was no evidence suggestive of tumor dissemination in five patients, and these patients underwent stereotactic radiosurgery (gamma knife surgery) or frameless stereotactic radiotherapy (p Reference). Four of these patients also underwent three courses of chemotherapy. Two patients underwent WBRT. All patients had no residual tumor and remained intact neurologically after the treatment (Table 2).

Malignant Germ Cell Tumors. Immediately after the extensive operation, a combined course of chemo- and radiotherapy was started. Radiotherapy was undertaken essentially in the manner of WBRT after three courses of chemotherapy. There was no evidence of tumor metastasis on MR images before the extensive operation in any patient. Complete remission of clinical symptoms was obtained in all patients after chemotherapy, with complete disappearance of tumors on CT scans and normalized levels of serum tumor markers. One patient has been alive without neurological deficit for more than 6.5 years after treatment. However, diffuse tumor dissemination occurred in the entire central nervous system during radiotherapy in two other patients and both died within 1 year after the initial diagnosis (Table 2).

Neuroectodermal Tumors. The surgical specimens obtained by neuroendoscopic surgery were also sufficient for immunohistochemical study. Findings were compatible with pineoblastoma in two patients, one of whom underwent gamma knife radiosurgery and chemotherapy. The other patient was diagnosed as having tumor dissemination by neuroendoscopic observation, even though MR imaging was nondiagnostic for this finding, and the patient underwent WBRT. The former patient underwent neuroendoscopic third ventriculostomy, but postoperative ICP monitoring demonstrated occasional pressure waves. Follow-up CT scanning revealed a subdural fluid collec-
tion with persistent ventriculomegaly. The subdural fluid collection was irrigated and a VP shunt was placed on the right side. Both patients completed a full course of chemotherapy and have recovered well, with complete remission for 3.5 years after the initial treatment. One patient in whom radiological findings were compatible with glioblastoma underwent an extensive operation followed by chemo- and radiotherapy but died 5 months after the initial procedure (Table 2).

Discussion

Background Epidemiology

There are tremendous racial differences among patients harboring pineal region tumors, of which there are at least 17 histologically distinct types. The epidemiological characteristics were first delineated by Araki and Matsumoto with their extensive survey in 1969, in which pineal region tumors were shown to be significantly common in Japan. A nationwide epidemiological survey with a statistical study of brain tumors demonstrated that the majority of pineal region tumors are germinomas. The epidemiological characteristics of Japanese patients were obviously different from those of Caucasians or even other Asian populations such as the Chinese. We conducted a worldwide survey to analyze the patient population and management of pineal region tumors in 1992 and again in 1998. These surveys confirmed the epidemiological characteristics of pineal region tumors. Furthermore, the patient populations in Japan and Korea were found to be almost identical. An extremely high incidence of germ cell tumors was found, representing 71.2% in Japan and 80% in Korea, with a low incidence of neuroectodermal tumors, representing only 15.2% and 16.8% of all pineal region tumors, respectively. In Western countries 51% of pineal region tumors are germ cell tumors and 42.9% are neuroectodermal tumors.

Changes in Therapeutic Regimen in the Past

In 1968, Poppen and Marino reported that pineal region tumors should initially be managed using radiotherapy because of the high mortality rate associated with radical surgery. Until the late 1970s, this conservative regimen was the standard initial procedure for treating pineal region tumors in North America. At that time, it became the standard therapeutic regimen in Japan. In the 1980s, the approach to pineal region tumors started to shift to extensive radical surgery due to the development of diagnostic neuroimaging and microsurgery. The use of a variety of surgical techniques to gain access to the pineal region was further supported by the advantages presented by microneurosurgery. At the same time, detection of the tumor markers AFP and HCG became available as an aid to the diagnosis and management of these tumors as well as the more specific morphological detection offered by CT and MR imaging. It was also emphasized that among the 17 or more histologically different types of pineal tumors in Caucasian patient populations, some were radioresistant. It was believed that tissue diagnosis would be necessary before the specific regimen was started. However, these therapeutic concepts were not completely adopted in Japan and Korea and have remained controversial. In the results of the analysis of our first worldwide survey performed in 1992, it was clearly demonstrated that the determination of tumor histological type as an initial procedure was strongly supported by the majority of neurosurgeons in North and Central America and in Europe, whereas initial application of the radiation test was still the generally accepted first step in Asian countries and Egypt. We concluded at that time that these different opinions on therapeutic modalities in pineal region tumors were mainly based on racial differences in the patient population.

New Choices of Therapeutic Modalities

Our recent cooperative study showed that significant changes have occurred over the last several years, during which minimally invasive neurosurgery has developed rapidly. Extensive resection of tumor as the initial procedure is now supported by only a small number of neurosurgeons throughout the world, including North America and Europe, but histological verification of the tumor is thought to be essential by more than 60% of neurosurgeons both in Japan and in Korea. If the tissue diagnosis obtained during the initial procedure suggested nongerminomatous tumor, radical resection was almost always performed. However, it is now well recognized that the inci-
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TABLE 2
Procedures undertaken and therapeutic outcomes in 20 patients with pineal region tumors*  

<table>
<thead>
<tr>
<th>Pathological Diagnosis</th>
<th>No. of Cases</th>
<th>Initial</th>
<th>Second</th>
<th>Third</th>
<th>No. of Cases</th>
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* GKRS/SRT = gamma knife radiosurgery/frameless stereotactic RT; NEO = neuroendoscopic operation; obs = observation; rad test = radiation test; RO = radical operation; SO = spinal operation; STBs = stereotactic biopsy; TCD = tumor completely disappeared; TSR = tumor size reduced; TSU = tumor size unchanged; WSRT = whole-spine RT.
† WBRT or SO + WSRT.

Incidence of radio- and chemosensitive tumors is quite high and that these tumors tend to disseminate throughout the central nervous system. The major treatment choice is not extensive surgery because it may not be sufficiently extensive; rather, adjuvant therapy is more often the more reliable therapeutic method in these patient populations. Our study revealed that tissue diagnosis is now performed more often in a minimally invasive fashion by using either stereotactic or neuroendoscopic procedures. With the high incidence of radio- and chemosensitive tumors, the majority of Japanese or Korean patients with pineal region tumors can be cured with subsequent adjuvant therapy.

As for the chemotherapy currently used for germ cell tumors, therapy combining cisplatin, vinblastin, and bleomycin has been replaced by a regimen of carboplatin combined with etoposide with or without ifosfamide (ICE). The oncolytic effect of these regimens has been confirmed in germ cell tumors in our present study as well, although their combination with other treatment modalities remains to be investigated. Additional therapeutic regimens should be determined, along with specific treatment guidelines, for each subgroup of germ cell tumors and other pineal region tumors.

Neuroendoscopic Procedures for Management of Pineal Region Tumors

Neuroendoscopic procedures have great advantages in dealing with tissue sampling, gross morphological analysis of tumor and ventricular and cisternal structures, and hydrocephalus. Neuroendoscopic surgery for brain tumors developed mainly as an approach to intraventricular lesions, in particular third ventricular tumors. It can be used for radical surgery in certain lesions such as colloid cysts. However, we found no reports supporting neuroendoscopic radical resection of tumors located in the pineal region. Gaab and Schroeder emphasized that a limiting factor in endoscopic tumor resection is the size of the lesion: a solid tumor should not exceed 2 cm in diameter if the procedure is to be applied. Using our technique, we have found that tumor debulking by neuroendoscopic surgery has always been possible in the pineal region, but the tumor size is always greater than 2 cm in diameter when it becomes symptomatic or causes obstruction of the aqueduct. The major purpose of applying neuroendoscopy as the initial procedure in the management of pineal region tumors is to identify the pathological characteristics of the tumor because of the high possibility of chemoresistance or radiosensitivity. The anterior neuroendoscopic approach to pineal region tumors is ideal for analyzing the gross appearance of the mass and to obtain tissue samples from multiple parts of the tumor. It can be useful to study the different parts of the tumor by using histological or immunohistochemical analysis to rule out the mixed type of tumor components. The only structure that interferes with the procedure when the anterior approach is used is the massa intermedia or interthalamic adhesion. When the neuroendoscopic approach follows the route below the massa intermedia, the inferior or ventral portion of the tumor compressing the aqueduct is obtained (Fig. 2 lower right). On the other hand, if the approach follows the route above this structure, the major part of the tumor is posteriorly surrounded by veins of the galenic system and the choroid plexus (Fig. 2 lower left). Technically, a single burr hole placed just in front of the coronal suture may allow the neurosurgeon to perform both the endoscopic third ventriculostomy and the pineal region biopsy safely. However, a low frontal approach provides a definite advantage by allowing observation of the entire tumor within the aforementioned intraventricular structures, as well as allowing tissue samples to be obtained from various parts of the tumor while avoiding any vascular regions. Some neurosurgeons may support performing third ventriculostomy before the tumor biopsy. We use irrigation through the EVD tubes placed via the coronal burr.
hole during and after manipulation of the tumor to prevent dissemination of tumor tissue in the CSF. After irrigation is completed and clear CSF is obtained in the ventricle, the floor of the third ventricle is opened. It is helpful to assess the gross morphological characteristics of the ventricle and cistern after third ventriculostomy. We treated a case in which intraventricular metastatic lesions had been undetectable on preoperative neurodiagnostic imaging including gadolinium-enhanced MR images (Fig. 3). The pathological findings in this case were compatible with a pineoblastoma. Tumor extension to the floor of the third ventricle may be observed in certain types of germ cell tumors, such as synchronous germinoma or malignant germ cell tumors, although we had no such cases in our series. Gross morphological analysis performed using a neuroendoscope offered extremely useful information for deciding which therapeutic steps should follow this initial procedure. The choice covers the range from stereotactic biopsy to extensive surgery by craniotomy. In our technique, the EVD system is left to monitor the postoperative ICP dynamics after third ventriculostomy. There was one patient in whom persistent intermittently high ICP was recorded and the EVD system was internalized. We had no patient in whom tumor dissemination developed after neuroendoscopic surgery, but we used extensive intraoperative irrigation via the EVD tube that had been inserted into the second burr hole for the subsequent third ventriculostomy procedure. Before removal of the EVD tube during the postoperative days, CSF could be obtained from the ventricle for cytological analysis as well. We believe that adjuvant chemotherapy will also deal with this possibility successfully. A nationwide cooperative study is now being conducted to analyze this issue statistically (K Moritake, et al., unpublished data). The biportal approach, which includes an additional burr hole in the low frontal region, is useful, especially when a rigid-rod endoscope is placed on a straight line via the foramen of Monro toward the pineal region. An approach via the burr hole on the coronal suture toward the posterior half of the third ventricle carries a risk of brain parenchymal injury (Fig. 2). The neuronavigational endoscopic approach may be useful, if only steerable flexible-fiber endoscopy is used via the burr hole on the coronal suture. It is essential to perform this operation by using a high-resolution endoscopic image. We hope that a more convenient and finer rigid-rod endoscope will be available in the near future.

Future Prospects

Minimally invasive preferential management of pineal region tumors is a new treatment modality that may change therapeutic strategy in the near future. However, there are several aspects of this treatment strategy that still have to be improved.

First, there is still a possibility that neuroendoscopic procedures may cause dissemination of the tumor, although no cases have been reported in the literature and we have seen no such complication. In our experience, neuroendoscopic observation clearly showed that tumor tissue fragments were almost detached from the mass by some to-and-fro movement of CSF flow. This may suggest that there is a natural process of spontaneous dissemination of tumor with or without surgical intervention. We had two fatalities due to dissemination of malignant germ cell tumors. In both cases dissemination occurred after extensive radical surgery, but we noted no dissemination following neuroendoscopic procedures. We found no evidence that the neuroendoscopic procedure carries a higher risk of this complication. Extensive chemotherapy may play an important role in this issue. We expect that the results of the nationwide cooperative study will reveal the answer to this question.

Second, there are still some unsolved problems surrounding the judgment of shunt-independent arrested hydrocephalus after neuroendoscopic third ventriculostomy. We had one patient with persistent increased ICP after third ventriculostomy, requiring placement of a ventriculoperitoneal shunt. Postoperative continuous ICP monitoring via the EVD tube inserted after ventriculostomy is useful, and the aqueductal occlusion by tumor can be reopened using chemotherapy and stereotactic radiosurgery or radiotherapy while the EVD tube remains in place. If the tumor is large, compressing the midbrain with the basilar artery pushed forward, it may be technically difficult to make a satisfactory communication to the prepontine cistern. When tissue diagnosis proves that the tumor is chemo- or radiosensitive, appropriate treatment can be used as an alternative regimen.

Last, neuroendoscopic procedures have a great advantage in the management of chemo- or radiosensitive tumors, such as germinoma, pineoblastoma, or primitive neuroectodermal tumor. However, the second step of the regimen is still challenging in cases of malignant germ cell tumors, malignant gliomas, and other chemo- or radioresistant tumors. Although the patient populations of Japan and Korea are more suitable for minimally invasive preferential management, tumor management in different patient populations with a higher incidence of chemo- and radioresistant tumors remains a major ongoing subject of research in the development of a therapeutic regimen, especially for pineal region tumors in populations of North America and Europe.

References

Minimally invasive management of pineal tumors