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CLINICAL STUDY – PATIENT STUDY

Favorable long-term outcome of low-grade oligodendrogliomas irrespective of 1p/19q status when treated without radiotherapy

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Abstract Despite the accumulating evidences of high chemosensitivity especially in anaplastic oligodendrogliomas with loss of chromosomes 1p and 19q, the optimal management strategy for low-grade tumors using the 1p/19q information remains controversial. We have treated all low-grade oligodendrogliomas by a chemotherapy-preceding strategy without radiotherapy, and here we analyzed the survival outcomes of 36 consecutive patients in relation to 1p/19q status. The treatment protocol was as follows: (1) simple observation after gross total resection, and (2) modified PCV chemotherapy for postoperative residual tumors or recurrence after total resection. The 1p and 19q status were analyzed by fluorescence in situ hybridization. The median follow-up period was 7.5 years and no patient was lost during the follow-up periods. 1p/19q co-deletion was observed in 72% of the patients, and there was no significant association between 1p/19q co-deletion and chemotherapy response rate. The 5- and 10-year progression-free survival (PFS) rate was 75.1 and 46.9%, respectively, and the median PFS was 121 months for 1p/19q-deleted tumors and 101 months for non-deleted tumors (log-rank test: $P = 0.894$). Extent of surgery did not affect PFS ($P = 0.685$). In contrast, the elder patients (>50) had significantly shorter PFS ($P = 0.0458$). Recurrent tumors were well controlled by chemotherapy irrespective of 1p/19q status, and 35 out of 36 patients survived without receiving radiotherapy. The 5- and 10-year overall survival rates were 100 and 93.8%, respectively. Two of the patients in their sixties (29%) suffered from severe cognitive dysfunctions and marked brain atrophy following chemotherapy alone. These results show that low-grade oligodendrogliomas could be successfully treated by surgical resection and nitrosourea-based chemotherapy alone without radiotherapy irrespective of 1p/19q status.

Keywords 1p/19q · Chemotherapy · Leukoencephalopathy · Neurotoxicity · Oligodendroglial tumor · PCV

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Introduction

The therapeutic strategy for adult low-grade gliomas, especially as regards the choice and timing of radiotherapy, is still controversial [1–4]. Although radiotherapy is undoubtedly beneficial for a subset of patients with low-grade gliomas, the natural history of gliomas when not irradiated after surgery is largely unknown. Only four prospective randomized trials have been conducted regarding the efficacy of radiotherapy for low-grade gliomas, and none of them could demonstrate any significant benefits on overall survival (OS). The EORTC 22845 randomized trial suggested that immediate postoperative radiotherapy for any residual tumors has advantages in terms of progression-free survival (PFS) but not in terms of OS [1, 3]. On the other hand, radiation-induced toxicities such as delayed cognitive dysfunction and leukoencephalopathy are important factors to determine treatment strategy [5, 6].

Stratification or personalization of the treatment strategy based on some markers is expected. Among gliomas, deletions of chromosomes 1p and 19q are shown to be associated with tumors including oligodendroglial components [7]. The co-deletion has also been associated with

responsiveness of anaplastic oligodendroglial tumors to radiotherapy and chemotherapy as well as with prolonged survival of the patients [8, 9]. However, this predictive and prognostic relevance of the 1p/19q co-deletion are more controversial for low-grade tumors [10–17]. To elucidate this issue, a long follow-up period is necessary because the patients with low-grade oligodendroglial tumors usually have more favorable outcome than anaplastic tumors.

In addition to the controversy in the application of radiotherapy, it has been reported that low-grade oligodendroglial tumors respond well to chemotherapy [18–21]. Therefore, we have treated all patients without using radiotherapy and have applied a nitrosourea-based chemotherapy (PAV, a modified PCV) when postoperative progressing tumors were verified [19]. The aim of this study was to elucidate the long-term outcome of low-grade oligodendrogliomas treated with chemotherapy-preceding strategy without radiotherapy in relation to 1p/19q co-deletion.

Methods

Patients and treatment

Since 1995, we have prospectively treated all patients having low-grade oligodendrogliomas by a radiotherapy-deferring and chemotherapy-preceding strategy using a standard nitrosourea-based chemotherapy (PAV, a modified PCV). The classic oligodendroglioma histological features were defined by areas composed of uniform and round nuclei surrounded by perinuclear halos and in an even tissue distribution [15]. The treatment protocol was: (1) simple observation after complete resection of tumors, and (2) PAV for postoperative residual tumors or recurrence after total resection. In this chemotherapy, lomustine (CCNU) was replaced with nimustine (ACNU; [1-(4-amino-2-methyl-5-pyrimidinyl)-methyl-(2-chloroethyl)-3-nitrosourea hydrochloride] which is a water- and lipid-soluble nitrosourea derivative. The chemotherapy protocol was ACNU 75 mg/m^2 on day 1, vincristine 1 mg/m^2 on days 8 and 29, and procarbazine 100 mg/day on days 8–21; this cycle was administered four times a year for 2 years [19]. Patients were required to provide written informed consent before receiving the chemotherapy.

Data collection

All patients histologically confirmed to have oligodendroglioma or oligoastrocytoma were enrolled in this study. Age, sex, tumor location, tumor size, pathological diagnosis, and extents of resection were recorded. None of the patients was excluded from analysis because of early recurrence within 1 year after surgery. Magnetic resonance imaging (MRI) studies were performed preoperatively, postoperatively within 2 weeks, and after every course of chemotherapy. Tumor volume was estimated as the product of the three largest perpendicular diameters of all measurable lesions on fluid-attenuated inversion recovery (FLAIR) with reference to pre- and postgadolinium T1-weighted MRI. Regarding the extent of surgery, gross total resection was defined as a disappearance of the tumor on MRI, and subtotal resection as a $\geq$70% reduction of the tumor size. Responses to chemotherapy were determined in the patients with postoperative residual tumors using the modified Macdonald criteria [22], in which complete response (CR) was defined as disappearance of all measurable disease, and partial response (PR) was defined as $\geq$50% decrease in the measured tumor size compared with baseline. Progressive disease (PD) was defined as $\geq$25% increase of the tumor size and stable disease (SD) was applied to all other situations. Toxicity was graded according to the National Cancer Institute's Common Toxicity Criteria version 3.0.

The histological diagnosis was confirmed by a neuropathologist other than the initial diagnostician. Chromosome 1p- and 19q-deletion analyses were done using a standard fluorescence in situ hybridization (FISH) of fixed cytogenetic preparation from fresh tumor tissues [23]. FISH probes for 1p were the target region of 1p36 with a control region of 1q25, and those for 19q were the control region of 19p13 with the target region of 19q13. The total number of signals was counted, and the ratio of 1p:1q or 19q:19p of $<$0.75 was diagnosed as loss.

Statistical analysis

Progression-free survival was calculated from the date of diagnosis until the first sign of radiological progression, death, or last follow-up. OS was calculated from the date of diagnosis until the date of death or last follow-up. The Kaplan–Meier method was used to estimate survival rates and the log-rank test was applied to compare the survival differences using StatView software (SAS Institute, Cary, NC, USA). A Fisher exact test was performed to determine the association between 1p/19q co-deletion and chemotherapy response rate. Cox's proportional hazard regression model was used to perform multivariate analysis for the possible prognostic variables including age, extent of resection, 1p19q status (SPSS, Chicago, IL, USA).

Results

Thirty-six consecutive patients with histologically proven low-grade oligodendrogliomas were treated between 1995

Table 1 Patient characteristics

Age	
Mean	43
Range	22–68
>50	14 (39%)
Sex (%)	
Male	24 (67)
Female	12 (33)
Karnofsky performance score (%)	
≧70	35 (97)
<70	1 (3)
Histology (%)	
Oligodendroglioma	33 (92)
Oligoastrocytoma	3 (8)
1p/19q deletion (%)	
Yes	23 (72)
No	8 (22)
Extent of surgery (%)	
Gross total	15 (42)
Subtotal/partial	21 (58)
Chemotherapy (%)	
Yes	26 (72)
No	10 (28)
Recurrence (%)	
Yes	15 (42)
No	21 (58)

and 2008 (Table 1). Thirty-three patients had oligodendrogliomas and three had oligoastrocytomas. There were 24 men and 12 women with a mean age of 43 years (range 22–68 years). The patients were followed up with for a median period of 7.5 years and no patient was lost during the follow-up period. Fifteen patients (42%) underwent gross total resection, 10 patients (28%) underwent subtotal tumor resection, and the other 11 (30%) underwent partial resection. Twenty-six patients were treated with chemotherapy. Tumor recurrence occurred in 15 patients (42%); 5 patients after total resection (5/15: 33%), 4 after subtotal resection (4/10: 40%), and 6 after partial resection (6/11: 55%).

The 5- and 10-year PFS rates were 75.1 and 46.9%, respectively, and the median PFS was 101 months (Fig. 1a). There was no significant difference of PFS between the patients who were observed after total resection and those with incomplete resection followed by the chemotherapy (median PFS, 121 vs 93 months, respectively, $P = 0.685$) (Fig. 1b). In contrast, the elder patients (>50) had significantly shorter PFS ($P = 0.0458$) (Fig. 1c). There was no difference in clinical course including PFS between the patients with oligodendroglioma and oligoastrocytoma. A salvage second surgery was performed in

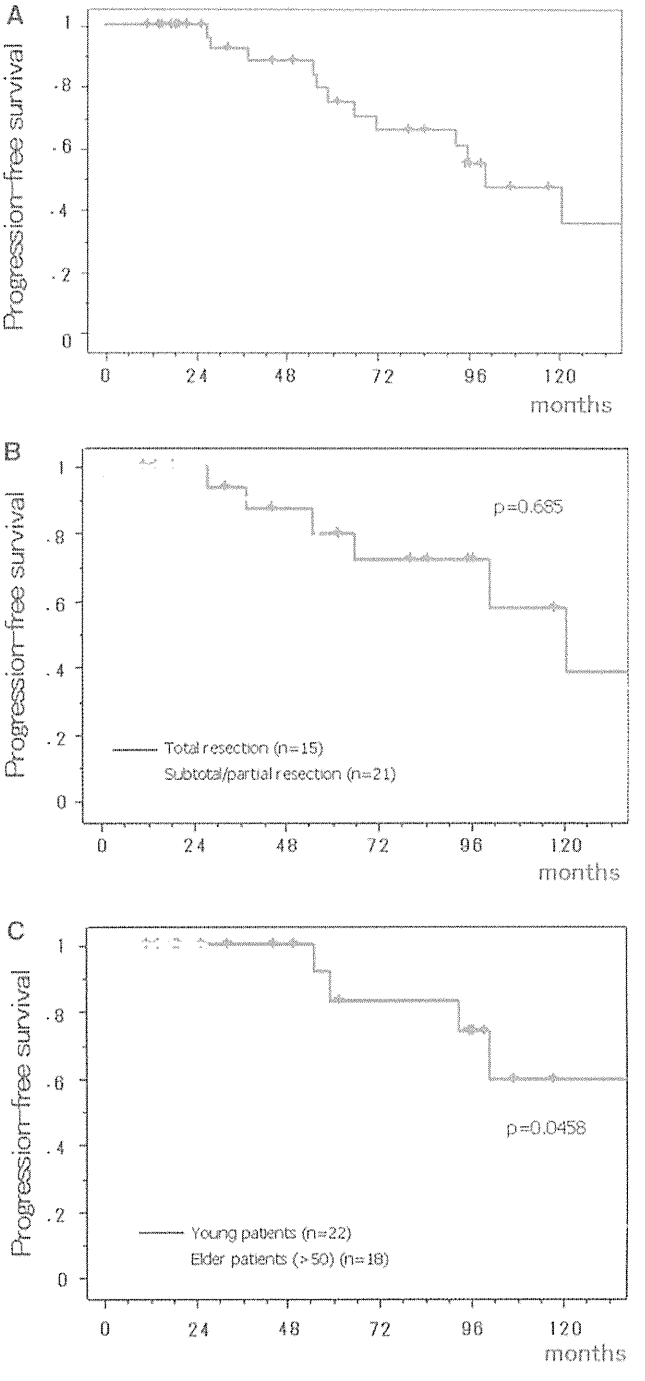

Fig. 1 Kaplan–Meier analyses for the progression-free survival of all 36 patients with low-grade oligodendrogliomas (**a**), and those comparing by extent of surgery (**b**) and age (**c**) are shown. *Tick marks* indicate last follow-up

seven cases, and malignant transformation was not observed in the present non-irradiated series. There was a patient whose tumor had 1p/19q loss but finally could not be controlled by chemotherapy. This patient refused radiotherapy and died at 81 months after surgery. Therefore, no patient in the present study received radiotherapy, and 35 out of 36 patients survived without receiving

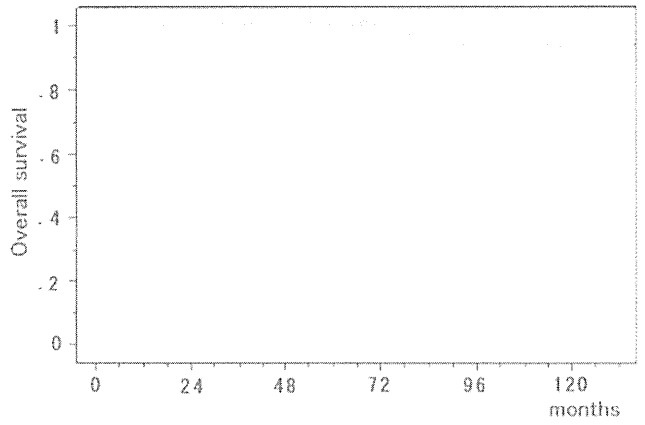

Fig. 2 Kaplan–Meier analyses for the overall survival of all 36 patients with low-grade oligodendrogliomas treated by surgical resection and chemotherapy without radiotherapy is shown. *Tick marks* indicate last follow-up

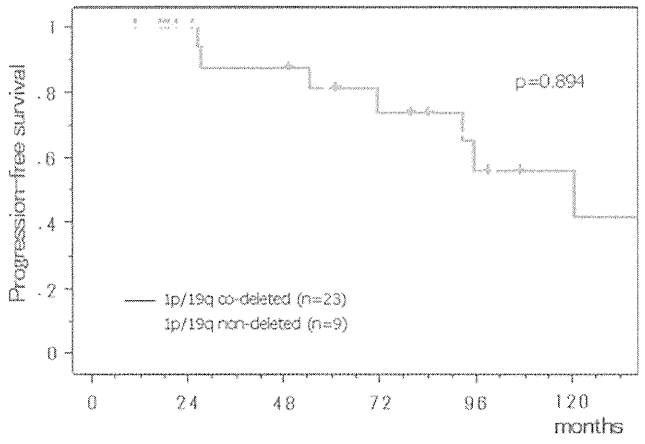

Fig. 3 Kaplan–Meier analyses for the progression-free survival of patients with low-grade oligodendrogliomas with and without 1p19q co-deletion are shown. *Tick marks* indicate last follow-up

radiotherapy at the follow-up period of 10 years; 5- and 10-year OS rates were 100 and 93.8%, respectively (Fig. 2).

1p/19q co-deletion was observed in 23 of 32 cases (72%) analyzed with FISH. Isolated loss of 1p or 19q was not observed in the present series. Median PFS rate for the patients with 1p/19q co-deleted tumors was 121 months and that for non-deleted tumors was 101 months. There was no significant difference in PFS between the patients with 1p/19q co-deleted tumors and those without co-deletion ($P = 0.894$) (Fig. 3). The multivariate analysis showed that neither of age, extent of resection, nor 1p/19q status was significantly associated with the length of PFS (Table 2).

Two patients in their sixties manifested marked brain atrophy without tumor recurrence 4–5 years after the initiation of chemotherapy (Fig. 4). These patients required intensive nursing care and observation because of their developing cognitive deficits. The MRI finding of tight high-convexity, which is typical for normal pressure hydrocephalus, was not observed and the CSF tap test was negative in the patients. A grade 3 or 4 leukopenia mandating a treatment delay occurred in two patients (9%).

Table 2 Multivariate analyses for the possible prognostic factors

	P
Age (<50 vs ≥50)	0.1274
Extent of resection (total vs non-total)	0.7089
1p19q co-deletion (deleted vs non-deleted)	0.3995

Discussion

The present study showed that, when treated with a radiotherapy-deferring and chemotherapy-preceding strategy using modified PCV chemotherapy, the 10-year OS rates of low-grade oligodendrogliomas were over 90% irrespective of 1p/19q status. This outcome compares favorably with those of previous reports including immediate postoperative radiotherapy without chemotherapy; the median survival times were within 5.3–14.9 years [24–27, 31], and 5- and 10-year OS rates were 52–95% [24–31] and 24–85% [24, 25, 27–29, 31], respectively. The median times to tumor progression were within 5.6–13.2 years [26, 31], and the 5-year PFS rate was reported as 67% [30]. In addition, it was reported that neither PFS and OS were significantly improved by radiotherapy in retrospective studies employing chemotherapy [32–34]. As a new therapeutic strategy for low-grade oligodendrogliomas, the effectiveness of PCV chemotherapy has been reported [18–21, 35–38], and some authors have concluded that radiotherapy could be postponed until malignant transformation occurs [3, 18–21, 32, 35]. The present result is in accordance with these studies. In contrast, although PCV chemotherapy for low-grade oligodendrogliomas achieved stabilization or shrinkage of tumors, its efficacy was not curative in many cases, as shown by the increased recurrence rate at 10-year follow-up. A longer observation period in a larger cohort would be necessary to clarify the validity of the radiotherapy-deferring and chemotherapy-preceding strategy against low-grade oligodendrogliomas.

Since a subset of low-grade gliomas progresses to malignant tumors, some stratification or personalization in the treatment planning are expected. In addition to the diagnostic relevance for oligodendroglial tumors, the prognostic role of 1p/19q loss is well defined for anaplastic oligodendrogliomas [8, 9]. For grade III tumors, 1p/19q loss may characterize a less malignant variant of the tumor, and the gene products lost as a consequence of 1p/19q loss may be mediators of resistance to genotoxic therapies [14]. In contrast, the prognostic relevance is less defined for

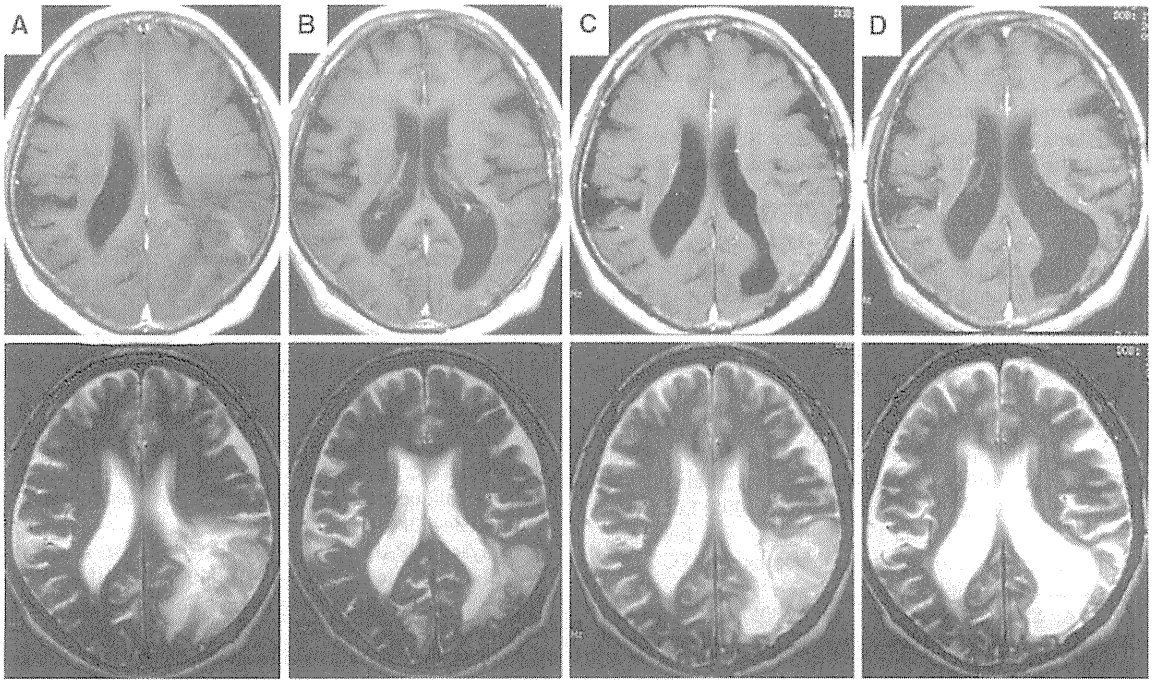

Fig. 4 The representative MRI pictures (*upper panel*; gadolinium-enhanced T1 weighted images, *lower*; T2-weighted images) of a patient aged 68 years. A left parietal tumor at initial diagnosis (**a**) was completely resected after surgery (**b**), and the tumor recurred 2.5 years after the surgery (**c**). Although chemotherapy with ACNU, vincristine and procarbazine achieved a complete response, the patient's neurological condition gradually worsened. Marked enlargement of the cortical sulci and lateral ventricles was observed without tumor recurrence at 7 years from diagnosis (**d**)

low-grade oligodendroglial tumors [10–17]. Our result showed that the outcome of patients with histologically typical low-grade oligodendrogliomas was generally favorable irrespective of 1p/19q status when treated without radiotherapy. Although 1p/19q loss is one of the major genetic alterations in oligodendroglial tumors [7, 23], other important genetic alterations would exist as an early event. The previous contradictory results may be partly due to heterogeneity in histology and treatments [10–17]. Radiotherapy would negatively modify the survival results of the patients having tumors without 1p/19q deletions [23]. However, the small sample size may have contributed to this result, and a future prospective study including more patients with 1p/19q information is needed.

Recently, temozolomide (TMZ) has been frequently used as the initial treatment for oligodendrogliomas with high response rates almost equivalent to those of PCV chemotherapy [10, 16]. Both of these chemotherapy regimens would be effective for low-grade oligodendrogliomas. TMZ is advantageous due to its safety profile especially with regard to hematologic toxicity. Standard 42-day PCV chemotherapy induces significant hematologic toxicity, requiring a dose reduction and/or a cycle delay [19, 36]. Therefore, we applied a prolonged-cycle interval schedule to avoid the cumulative hematologic toxicity of PAV, and the incidence rate of grade 3 or 4 leukopenia was acceptably low.

In the present study, the other adverse effect following the modified PAV chemotherapy was found after long-term observations. Two patients in their sixties underwent marked brain atrophy following chemotherapy without receiving radiotherapy. Other causes of brain atrophy due to aging, such as normal pressure hydrocephalus or multiple cerebral infarctions, could not be completely excluded. However, the MRI findings of tight high-convexity and the CSF tap test were both negative, and they had not had the risk factors for cerebral infarction. Although neurotoxicities of an intensive PCV regimen have been reported [38, 39], this is the first report of a potential neurotoxicity following a standard nitrosourea-based chemotherapy alone. This adverse effect could not be detected within short-term follow-up periods. Careful application of chemotherapy for patients older than 60 years is recommended. In contrast, the recurrence rate was higher in older patients than in younger patients, which highlighted the importance of surgical resection. Attempting the greatest possible surgical resection without neurological deteriorations followed by simple observation may be the best way to treat low-grade oligodendrogliomas, especially for the elder patients.

Conflict of interest There are no financial disclosures from the authors.

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Surgical Treatment of a Calcified Rathke's Cleft Cyst With Endoscopic Extended Transsphenoidal Surgery

—Case Report—

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Abstract

A 34-year-old male presented with a rare case of Rathke's cleft cyst (RCC) with calcification manifesting as persistent high fever and impaired consciousness. Physical findings revealed panhypopituitarism and bitemporal hemianopsia. Computed tomography showed mass lesions with marked calcification within the sella turcica and the suprasellar region. Magnetic resonance imaging showed solid and cystic components compressing the optic nerve. The preoperative diagnosis was craniopharyngioma. Initial endonasal transsphenoidal surgery (TSS) was performed with a surgical microscope, but the mass was extremely hard, so only partial removal was possible. Second endonasal extended TSS was performed with a neuroendoscope. The solid components were totally removed, but calcifications adhering to the optic nerve could not be removed completely. The histological diagnosis was RCC with marked granulation reaction. RCC with calcification is rare and difficult to differentiate from craniopharyngioma on neuroimages. Extremely thick calcification of the sella turcica enclosing granulation tissue and the cyst similar to armor, here called "armor-like calcification," is a characteristic imaging finding of RCC with calcification. The most important aspect is choosing a surgical approach to carefully and effectively relieve pressure upon the optic nerve. Endonasal extended TSS with an endoscope was effective in the present case.

Key words: calcification, extended transsphenoidal surgery, neuroendoscopy, pathology, Rathke's cleft cyst

Introduction

Rathke's cleft cyst (RCC) is a non-neoplastic intrasellar cyst covered by cuboidal or columnar epithelium with cilia and goblet cells.[2] Magnetic resonance (MR) imaging shows RCC as a cystic mass extending into the sella turcica or suprasellar region, with various levels of intensity and imaging findings depending on the cyst content and the nature of the cyst wall.[4,7,11-13] In contrast, RCC with calcification or ossification is rare,[6,8,9,11] with 13% of all cases of RCC.[11] Differentiation of RCC with calcification from a craniopharyngioma is crucial among the sellar lesions with calcification, but the preoperative diagnosis has been craniopharyngioma in previous cases, so differentiation is difficult.[6,8,9] Calcification in an RCC is presumed to have formed by cholesterin granulation tissue organizing as a result of repeated inflammation and bleeding. Neuroimaging findings have revealed a central portion consisting of solid and cystic components and a thick calcification enclosing structure similar to armor, here called "armor-like calcification," characteristic of RCC with calcification and ossification.[8,9]

In the present case, the preoperative diagnosis, treatment, and histological diagnosis of an RCC with severe

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calcification were difficult. This RCC was an extremely hard mass, and removal with conventional endonasal transsphenoidal surgery (TSS) was not possible. Additional surgery in the form of endoscopic extended TSS was performed.

Case Report

A 34-year-old male had fever of around 38°C that had persisted since the end of June 2009. He was admitted to another hospital for further investigations because of fever of unknown origin on July 2, 2009. His consciousness deteriorated on July 5, 2009. MR imaging performed on the same day suggested pituitary apoplexy, and the patient was transferred by ambulance to our hospital later that day.

On admission, his level of consciousness was 10 (E2V3M5) on the Glasgow Coma Scale. The patient's temperature was 38.6°C and blood tests revealed hyponatremia and inflammatory reaction. A hormone loading test revealed panhypopituitarism. Visual acuity was 1.2 in the right eye and 0.8 in the left eye, and a visual field test revealed bitemporal hemianopsia. Computed tomography showed mass lesions with extremely thick calcification extending from within the sella turcica to the suprasellar region (Fig. 1A, B). The sella turcica was enlarged. MR imaging revealed well-demarcated anterior solid and posterior cystic components. Solid components had advanced into the suprasellar region and were compressing the optic nerve. Solid components were isointense on T_1-weighted and hypo- to hyperintense on T_2-weighted MR images, and the cystic components were hyperintense on T_1-weighted and hypo- to hyperintense on T_2-weighted images (Fig. 1C). T_1-weighted MR imaging with gadolinium revealed heterogeneous enhancement of the solid components (Fig. 1D). The initial diagnosis was intrasellar craniopharyngioma, and the differential diagnosis included pituitary abscess and pituitary apoplexy.

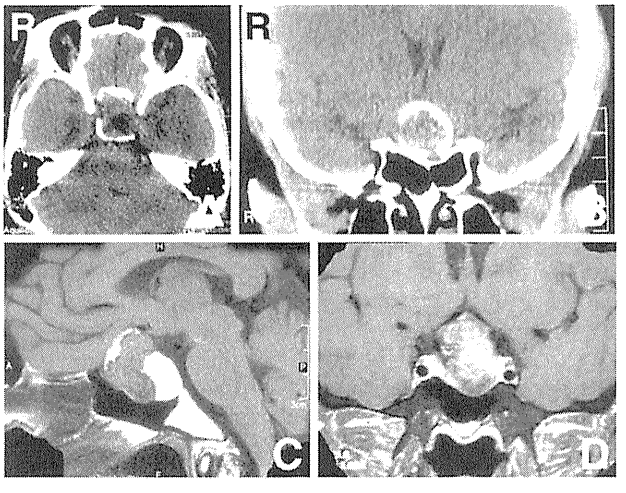

Fig. 1 A, B: Preoperative axial (A) and coronal (B) computed tomography scans showing mass lesions with extremely thick calcification, here called "armor-like calcification," extending from within the sella turcica to the suprasellar region. C: Preoperative sagittal T_1-weighted magnetic resonance image showing well-demarcated anterior solid and posterior cystic components. D: Preoperative coronal T_1-weighted magnetic resonance image with gadolinium showing heterogeneous enhancement of the solid components.

Two-stage surgery was planned. In the initial surgery, a definitive diagnosis would be obtained and pressure upon the optic nerve would be relieved via endonasal TSS. In the second surgery, the residual tumor would be removed via a craniotomy. On day 53 of hospitalization, endonasal TSS was performed with a surgical microscope. Opening the sellar floor in accordance with conventional TSS exposed the solid components. Removal of the solid components was difficult because of the presence of extremely elastic and hard granulation tissue (Fig. 2A), which was removed piecemeal using micro scissors and a Cavitron ultrasonic surgical aspirator (CUSA). During removal, opening the cyst resulted in the outflow of a motor oil-like fluid. Postoperative MR imaging revealed only partial removal of the solid components and opening of the cystic components. Postoperatively, visual field loss did not improve.

The second surgery was performed 3 months after the initial surgery. In light of the perioperative findings from the initial surgery, the initial plans were changed to a surgical approach in the form of endoscopic extended TSS. Initially, a wide surgical field was obtained by resecting the anterior wall of the sphenoid sinus from the frontal base of the skull to the clivus and laterally until the carotid prominence was exposed (Fig. 2B). The sella turcica was opened further utilizing the opening from the initial surgery. As in the initial surgery, removal of granulation tissue and calcified components was difficult because of hardness. Granulation tissue was completely excised using excision forceps, a punch, and CUSA (Fig. 2C). The calcification extending into the suprasellar region was extremely hard and had firmly adhered to the optic nerve (Fig. 2D). Most of the granulation tissue and the calcification were located in the intra-arachnoidal space. The optic nerve was confirmed to be pulsating, at which point relief of pressure on the optic nerve was presumably achieved. The calcifications adhering to the optic nerve could not be detached, so subtotal removal was completed. The sellar floor was reconstructed using a nasal septal flap and a sinus balloon was put in place.

Most specimens resected by the initial surgery consisted of granulation tissue containing cholesterin crystals. Some specimens contained cyst wall covered with a layer of ciliated epithelium (Fig. 3A). Squamous metaplasia was also present in some areas. Below the epithelium, granulation reaction was observed with clusters of foamy macrophages and deposition of cholesterin crystals and hemosiderin (Fig. 3B). No findings suggestive of craniopharyngioma was found. Most of the mass lesion was resected at the second surgery. The specimens consisted of similar granulation tissue with cholesterin crystals, and did not contain cystic walls. The diagnosis was RCC with marked granulation reaction.

Postoperative T_1-weighted MR imaging with gadolini-

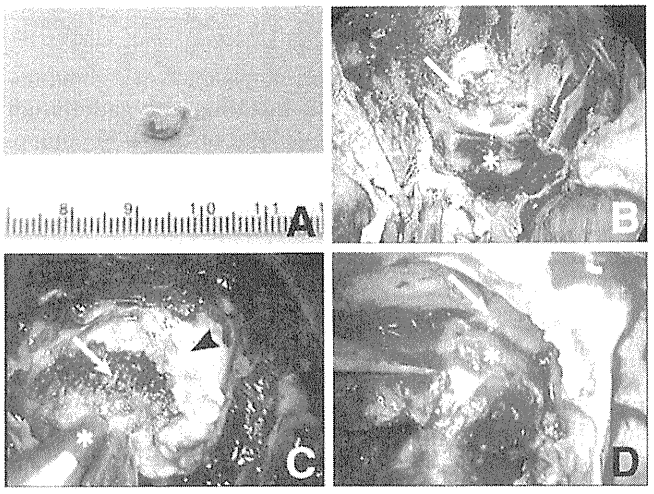

Fig. 2 A: Photograph showing the granulation tissue removed at the initial surgery. B–D: Intraoperative photographs demonstrating the surgical procedure of endonasal extended transsphenoidal surgery with the neuroendoscope. Wide surgical field showing the bone window of the sella turcica made at the initial surgery (*arrow* in B) and the clivus (*asterisk* in B). Granulation tissue (*arrow* in C) was completely removed using Cavitron ultrasonic surgical aspirator (*asterisk* in C). *Arrowhead* in C showing the dura mater of the sella floor. Thick calcification (*asterisk* in D) was firmly adhered to the left optic nerve (*arrow* in D).

Fig. 3 Photomicrographs showing the ciliated epithelium and part of a cyst wall. The cyst wall was covered with a layer of ciliated epithelium (A). Below the ciliated epithelium, clusters of foamy macrophages and a granulation reaction were noted (B). Hematoxylin and eosin stain, original magnification A: ×400, B: ×100.

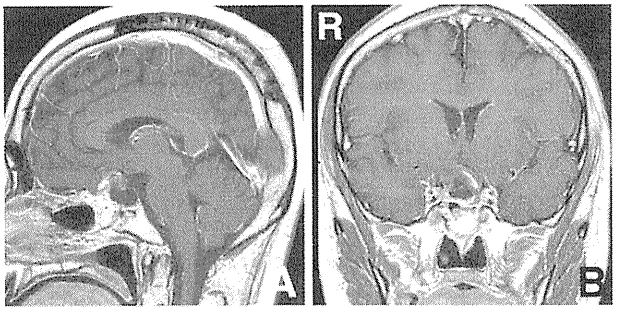

Fig. 4 Postoperative sagittal (A) and coronal (B) T_1-weighted magnetic resonance images with gadolinium showing the small residual mass within the suprasellar region. The solid and cystic components within the sella turcica were totally removed.

um revealed a small residual mass within the suprasellar region. The solid and cystic components within the sella turcica were totally removed (Fig. 4). Postoperatively, visual acuity was unchanged and bitemporal hemianopsia slightly improved. The patient has currently returned to work while undergoing hormone replacement therapy with hydrocortisone and levothyroxine sodium hydrate.

Discussion

Symptomatic RCC often develops with hypopituitarism (66–81%), headaches (49–81%), and vision and visual field loss (28–55.8%).[4,5,11,13] To treat these problems, cyst drainage is normally performed with TSS.[1,3,10,11] Symptomatic RCC with calcification also tends to develop with vision and visual field disturbance.[6,9] Conventional cyst drainage is ineffective at treating a symptomatic RCC with calcification because the extremely hard granulation tissue and calcification compress the optic nerve. Therefore, tissue and calcification removal are essential to relieve pressure on the optic nerve. Previous reports mention various approaches, but all involved removal.[6,8,9] In such an event, the most important aspects of the surgical strategy to deal with symptomatic RCC with calcification are location of the solid components and direction of extension, thickness of the calcified components, and extent of compression of the optic nerve. The surgical approach must be chosen based on these findings.

In the present case, a plan was initially formulated to use TSS with the operating microscope in the first stage to relieve pressure on the optic nerve, obtain a definitive diagnosis, and remove the residual tumor via a craniotomy in the second stage. However, the initial surgery was limited to only partial removal of the hard granulation tissue enclosed in "armor-like calcification." Based on the initial perioperative findings, transcranial surgery in the second stage would presumably have meant that the calcification covering the severely displaced optic nerve and granulation tissue embedded in that calcification would have to be removed, inducing damage to the optic nerve. On the other hand, a wide surgical field and a bone window were essential to remove the hard granulation tissue. In addition, a close and bright surgical image was necessary to

observe the granulation tissue extending from within the sella turcica to the suprasellar region, and the calcification adhering the optic nerves. Endoscopic extended TSS has advantages over TSS with the operating microscope for these points. Therefore, endoscopic extended TSS was chosen as the surgical approach for the second stage of surgery that would best preserve the optic nerve. Moreover, enlargement of the sella turcica and the wide space between the right and left internal carotid arteries were reasons for choosing extended TSS.

As indicated by the intraoperative findings, the calcifications had firmly adhered to the optic nerve, so forcible removal of these portions was not performed to preserve visual function. As a result, the chosen approach allowed the relief of pressure without directly manipulating the optic nerve and resulted in restoration of visual function postoperatively, both of which were the greatest advantages of choosing this approach.

"Armor-like calcification" in the vicinity of the sella turcica is an imaging finding characteristic of an RCC with calcification and helps to differentiate the condition from a craniopharyngioma. In the surgical treatment of an RCC with calcification, extended TSS with a neuroendoscope is safe and effective surgical approach for optic nerve decompression.

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解剖を中心とした脳神経手術手技

Anatomical and Surgical Note

鞍結節髄膜腫に対する手術到達法の選択：高位か低位か？*

寺坂　俊介**，小林　浩之**，寶金　清博**

Key words anterior interhemispheric approach, extended transsphenoidal approach, surgical approach, tuberculum sellae meningioma, visual function

No Shinkei Geka 39(6): 553 - 562, 2011

Ⅰ．はじめに

鞍結節髄膜腫は鞍結節や視神経交叉溝から発生する髄膜腫で，その発生頻度は頭蓋内髄膜腫の3～10%といわれている[1,19,20,26,38]．多くの患者は片側，もしくは両側の視力低下や視野障害を呈し視機能の悪化が唯一の症状であることも少なくない．視機能の温存もしくは改善が手術の最大の目的となるが，過去の報告でも約20%に術後の視機能悪化例が発生するといわれている[2,6,10,16,27,32,35-37]．術後視機能の予後不良因子として腫瘍径，術前の視機能，罹病期間，手術到達法などが検討されているが未だ結論は出ていない[10,13,16,29,44]．しかし本疾患において手術操作が術後の視機能の結果に何らかの影響を与えていることは多くの術者の共通認識である．視機能悪化の原因としては視神経そのものに対する直接損傷と視神経・視交叉への栄養血管損傷の一方もしくは両方が関与していると考えられている[6,10,19,36]．

鞍結節髄膜腫では腫瘍の発生母地や進展形式から視神経は外上方へ，視交叉は後上方へ変位していることが多い．視神経や視交叉を上方へ圧迫，変位させる髄膜腫は鞍結節髄膜腫と鞍隔膜髄膜腫のみである．視神経管内では可動性の乏しい視神経が脳槽部では外上方に大きく変位するため視神経管入口部では視神経が菲薄化し，ときに屈曲している場合もある．視神経の直接損傷を回避するために腫瘍の適切な内減圧とともに腫瘍剝離操作前（手術早期）の視神経管開放を強調する報告も多い[29,30,33,34]．発生母地は近いが前床突起髄膜腫や蝶形骨縁内側髄膜腫，蝶形骨平面髄膜腫はいずれも視神経や視交叉を下方に変位させる．これらは腫瘍の大きさに比して視機能低下の程度が軽く，術中所見でも視神経の形態が正常に近い形で保たれていることが多い．腫瘍が視神経や視交叉の上方に位置するか，下方に位置するかは栄養血管の温存という側面からも重要である．内頚動脈から分岐した眼動脈と上下垂体動脈はいずれも視神経や視交叉の下面から栄養血管を分岐する．鞍結節髄膜腫の手術では視神経や視交叉下面から腫

*Surgical Approach for the Tuberculum Sellae Meningioma: High and Low?

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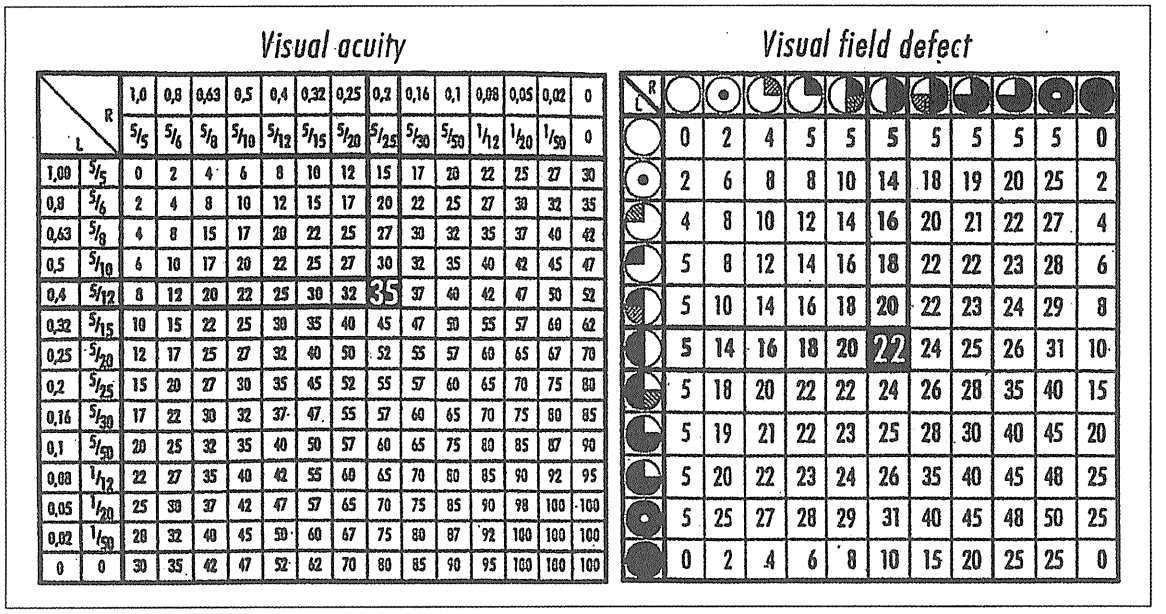

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0,1 5/50	20	25	32	35	40	50	57	60	65	75	80	85	87	90
0,08 1/12	22	27	35	40	42	55	60	65	70	80	85	90	92	95
0,05 1/20	25	30	37	42	47	57	65	70	75	85	90	98	100	100
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	5	19	21	22	23	25	28	30	40	45	20
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	5	25	27	28	29	31	40	45	48	50	25
	0	2	4	6	8	10	15	20	25	25	0

Fig. 1 A visual impairment score is provided by adding the scores in specific tables given for visual acuity and visual field defects. The score ranges from 0 (best) to 100 (worst).

瘍を剝離する操作が多く，その際に栄養血管を損傷する危険性は低くない[36]．一方視神経・視交叉上面と腫瘍との剝離が主となる蝶形骨平面髄膜腫などでは神経の直接損傷はあっても栄養血管損傷の可能性は低くなる．くも膜を温存しての腫瘍摘出（くも膜外摘出）は髄膜腫手術の基本であるが，本疾患においても視神経周囲のくも膜を温存できれば術後視機能低下の可能性は格段に低くなる．一見視神経が全周性に腫瘍に内包されているように見えても，十分な腫瘍の内減圧がなされると視神経と腫瘍の間にくも膜面が見えてくることはよく経験することである．

鞍結節髄膜腫に対する手術到達法にはさまざまな工夫や変法が報告されているが経頭蓋経由（上方）は，① pterional transsylvian approach，② unilateral subfrontal approach，③ bicoronal subfrontal approach，④ anterior interhemispheric approach の 4 つに大別される．下方からの手術到達法は拡大蝶形骨洞到達法で，ここ 2, 3 年の報告は極めて多い．

鞍結節髄膜腫に対する術前検査，手術到達法の選択，高位到達法として anterior interhemispheric approach[14,17,36,43]，低位到達法として拡大蝶形骨洞到達法[5,7-9,11,12,15]の手術手技とピットフォールに関して詳述する．

II. 術前検査

1. 視機能評価

前述したように本疾患の治療目的は視機能の温存もしくは改善であり術前術後の視機能の評価は必須である．われわれはドイツ眼科学会が用いている visual impairment score（VIS）を用いて術前後の視機能の評価を行っている（**Fig. 1**）．VIS は視力や視野障害のさまざまな組み合わせが点数化されており，合計点が VIS となる．視機能が正常であれば合計点は 0 点となり 100 点をカットオフ値としている．視力は最良の矯正視力を用い，視野はゴールドマン視野計にて測定する．評価時期は術前と術後 2 週間以内とし VIS が低下すれば視機能の改善，増加すれば悪化と判定する．

2. 画像診断

MRI では腫瘍と視神経との位置関係，視神経・視交叉の形態，腫瘍の視神経管への伸展程度を把

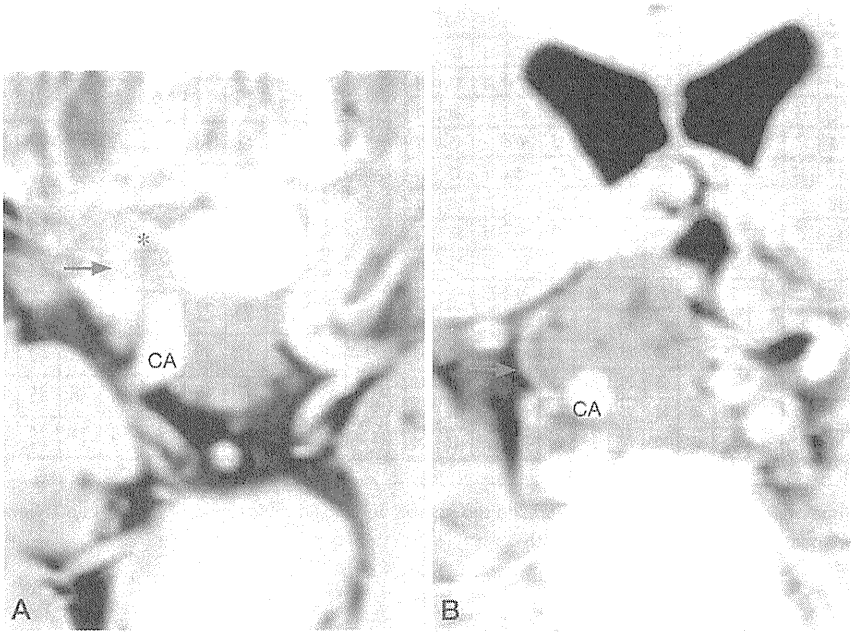

Fig. 2　A: An axial 3D heavily T2 weighted image depicted the tumor (**red asterisk**) extending to the medial aspect of the right optic canal. A **red arrow** shows the right optic nerve. B: The optic nerve is dislocated laterally with fanning configuration. **CA**: carotid artery.

握する．われわれは空間分解能に優れ，脳脊髄液のアーチファクトを抑えた3次元 heavily T2 強調画像（constructive interference in steady state：3D-CISS 法，TR/TE 12.25/5.9，FA 70°，FOV 180 mm，matrix 256×512，slab 40 mm，実効スライス圧 0.7 mm）の冠状断と軸位断を好んで用いている（Fig. 2A, B）．視力低下の著しい側ではときに視神経や視交叉が扇状になって腫瘍を取り囲んでいることがある．このような症例に側方からの手術到達法を適応すると術野の確保が非常に困難になる．腫瘍の視神経管への進展に関しては視神経管の開口部が正中に対して斜めであるという（視神経管開口部は内側が前方で外側は後方に位置する）解剖学的特徴の理解が必要である．鞍結節髄膜腫は多くの場合視神経の下内側から視神経管へ伸展するが，開口部内側が前方にあるため開口部付近の腫瘍は軸位断の MRI ではあたかも視神経管内に伸展しているように見えることがある．腫瘍の真の視神経管伸展例では視神経管開放が必要になることが多い．CT では腫瘍の石灰化の情報や各々の手術到達法に必要な情報を（蝶形骨洞の含気や前頭洞の発達など）収集する．

3. 内分泌学的検査

多くの論文でも報告されているように鞍結節髄膜腫では術前に内分泌異常を呈することは少ないといわれている[2,6,10]．自験例でも数値の異常を数%に認めたが内分泌異常の症状を呈した症例は1例もなかった．はっきりとした内分泌異常がある場合にはむしろ下垂体腺腫や頭蓋咽頭腫などを考慮すべきである．当施設では他疾患との鑑別のために下垂体前葉ホルモンの基礎値を測定しているが負荷試験は全例では行っていない．

III. 手術到達法の選択

鞍結節髄膜腫に対していかなる到達法を適応するかについては議論が尽きない．特に経頭蓋か経蝶形骨洞かという議論は学会や論文でも常に白熱する[3,8,9,28,32]．経蝶形骨洞到達法に対する批判的

意見は①腫瘍の摘出度に制限がある，②視神経管の開放が難しい，③腫瘍と穿通枝の剝離が難しい[5,24]，④髄液漏の危険性が高い[9,11]，の4点に大別される．しかしながら腫瘍が比較的小さく，正中部に限局するものを経蝶形骨洞到達法の適応症例とすれば批判の大部分は解決される．鞍結節髄膜腫は腫瘍経が小さくとも症候性になることが多く，また視機能の低下を予防する観点から無症候性であっても手術が許容される稀な疾患である．本到達法では鞍結節部の硬膜を十分に凝固・焼灼し，intercavernous sinus を含んだ硬膜を長方形型に切開すると小さな髄膜腫では腫瘍からの出血もほとんどなく，くも膜が保たれたまま腫瘍を娩出させるように摘出できる．硬膜内操作が30分以内のことも少なくない．本到達法では髄液漏の可能性は腫瘍の径にかかわらず高いがわれわれの鞍底形成の工夫を後述する．

経頭蓋到達法は unilateral subfrontal，pterional transsylvian，bicoronal subfrontal，anterior interhemispheric の順で選択されていることが多い．Unilateral subfrontal approach は片側の前頭開頭を行った後に前頭葉を挙上し，病変部に前外側から到達する．両側の視神経を術野に収めることが可能で硬膜内からではあるが視神経管を開放することもできる．腫瘍摘出は両側の視神経の間から行われるが，アプローチ側の視神経・視交叉の内側が死角になる．手技が簡素で腫瘍露出までの時間は短いが，上記以外に前頭洞が開放されること，前頭葉の牽引が強いこと（嗅神経の損傷の可能性），眼窩上壁が厚い場合には術野が狭いことが欠点として指摘されている．

Pterional transsylvian approach は脳神経外科医が最も慣れた手術到達法であり手術到達法に伴う合併症も最も少ない．大きくシルビウス裂を開放することによって前頭葉の可動性は増して牽引の程度は軽減する．腫瘍摘出のルートが両側視神経間と視神経と内頚動脈の間に増加する．硬膜外から視神経管を開放することも可能である．しかし根本的には術側の視神経や視交叉の内側が死角になることは解決されていない．また視神経内頚動脈間からの腫瘍摘出の際には視神経や内頚動脈からの穿通枝越しに腫瘍を摘出するため，術者の緊張度は非常に高くなる．多少の偏在はあるにせよ鞍結節髄膜腫は正中部に発生する腫瘍で周囲の重要組織は外側や後上方へ変位する．解剖学的に腫瘍への最も安全なルートは前方か下方である．

Bicoronal subfrontal approach は両側前頭開頭の後，上矢状洞を前方で結紮，切断し両側前頭葉を挙上して正中から腫瘍へ到達する．解剖学的指標の同定が容易で術野の死角も少なく，腫瘍へも直線的に到達できるが，前頭洞の開放，嗅神経の損傷，両側前頭葉障害が欠点とされている．腫瘍が鞍結節から鞍隔膜の方向に伸展している場合（ほとんどの症例で伸展している）には前頭葉を過度に牽引しなければ腫瘍を術野に収めることはできない．Nakamura らは上述した3つの到達法の比較検討を行い，理由は判然としないが bicoronal subfrontal approach の術後視機能が最も悪かったと報告している[32]．

Bicoronal subfrontal approach の最大の欠点である過度の両側前頭葉の牽引を軽減した到達法が anterior interhemispheric approach である．本到達法はわが国では前交通動脈瘤に対する到達法として有名であるが[18]，鞍結節髄膜腫に応用した報告は意外に少ない[14,17,43]．本到達法は bicoronal subfrontal approach と同じ前方からの到達法ではあるが，顕微鏡の視入角が全く異なるため鞍隔膜近傍や内頚動脈近傍も死角にはならない．しかし大脳半球裂の剝離に長時間を要すること，架橋静脈の損傷の可能性があることがこの到達法特有の欠点である．

理論的には視神経・視交叉の直接損傷や栄養血管の障害の可能性が最も低いのが前方からの到達法ということになるが，実際には上述した各々の合併症の危険性，術者の慣れや技量が加味されて術式は決定される．当施設では基本的には前方からの到達法を選択することとし，腫瘍が大きければ anterior interhemispheric approach を選択し，小さければ拡大蝶形骨洞到達法を選択している．各々の到達法の手術手技とピットフォールを詳述する．

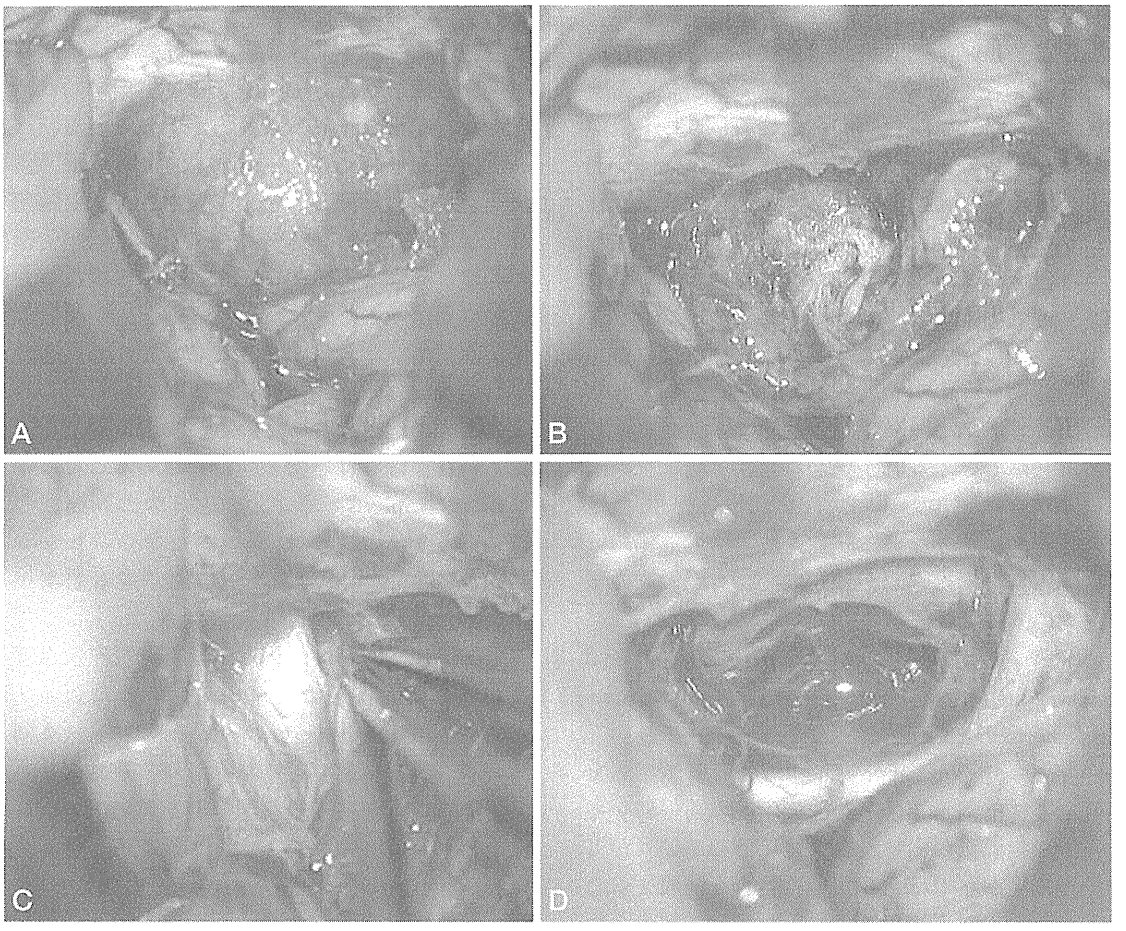

Fig. 3 A: After dissection of the anterior interhemispheric fissure, the tumor was exposed in the center of the surgical field. B: The tumor was first detached from its origin with bipolar cautery and debulked with an ultrasonic aspirator. During this step, main tumor feeders from the posterior ethmoidal artery and the superior hypophyseal artery were interrupted in most patients and devascularization of the tumor was also accomplished. C: The side of the optic nerve with better visual function was first dissected because of a better arachnoid plane. D: The tumor was totally removed while preserving the arachnoid plane and the small vessels.

IV. Anterior interhemispheric approach

1. 体位・開頭・前頭洞の処置

体位は仰臥位で背板は約 20° 挙上させる．頭部は床に水平としたまま首を前に出すようにして固定し（やや sniffing position となる）前頭部の頭髪線内側に冠状の皮膚切開を行う．皮膚，皮下の翻転時に骨膜は有茎弁として温存しておく．眼窩縁を外す必要はないが眼窩上縁が露出するところまで前頭骨を露出させた後に，正中部に切れ込むような両側前頭開頭を行う．前頭洞はほぼ全例で開放される．前頭洞の処置に関しては施設ごとに異なると思うが，われわれは前頭洞内の粘膜をすべて除去し前頭鼻管に筋膜を当て開頭時に採取した小骨片でこれを固定する．手術の最後に前頭洞の死腔には遊離脂肪片を挿入する方法を行っている．鶏冠を削除した後に上矢状洞をなるべく前方で結紮し離断して硬膜を W 型に切開する．大脳半球裂の剝離操作の前に背板をさらに挙上させ，前頭葉下面と嗅神経の剝離を行っておく．嗅神経の固定の是非に関しては意見の分かれるところで，最近はフィブリン糊での固定は行っていない．

Table Surgical outcome of visual function

Patient no.	Age(yr) /sex	Size (mm)	Preop VIS	Postop VIS	Outcome
1	57/F	26	15	10	improved
2	70/F	32	51	51	unchanged
3	56/F	22	44	25	improved
4	68/F	35	100	41	improved
5	58/F	35	100	42	improved
6	62/M	30	43	4	improved
7	57/F	45	77	26	improved
8	69/F	30	17	15	improved
9	83/F	20.5	58	22	improved

2. 大脳半球間裂の剝離

大脳半球間裂剝離の手術手技は前交通動脈瘤の場合と大差はないが[18,31,39,40]，われわれが本到達法の際に注意していることを記載する．本手術法の基本コンセプトは pericallosal cistern，chiasmatic cistern，lamina terminalis cistern を顕微鏡の視軸を変えながら順序よく開放していくことにある．第1ステップでは挙上していた背板をやや下げることにより患者を vertex down の頭位とし，術者は遠位部の帯状回を剝離し，脳梁膝部を露出させる．両側の脳梁周囲動脈を確認し，これを中枢側に追いながら帯状回を剝離すると trabeculae が比較的疎な pericallosal cistern に侵入する．Cistern が大きな場合には大脳半球間裂の沈み込みを防ぐ目的で gelfoam をこの空隙に挿入することもある．次に背板を挙上させ顕微鏡の視軸が蝶形骨洞平面に向かうようにする．脳べらを帯状回になるべく平行に当て，上方へ持ち上げるようにして張力をかけると trabeculae の可視性がよくなる．もともと直回近傍の trabeculae は短く切離が難しいが，腫瘍の場合には圧迫により大きく変位していることがあるので注意が必要である．直回を剝離するとくも膜を被った髄膜腫を確認できる．背板を下げ chiasmatic cistern と lamina terminalis cistern を連続させる本来の第3ステップは行わず，腫瘍を覆っているくも膜を切開したのちに顕微鏡を左右に倒し両側前頭葉下面と腫瘍との剝離を行う（**Fig. 3A**）．

3. 腫瘍の摘出

術野の正中に腫瘍は露出されるが，この時点では視神経や視交叉の同定は行わない．髄膜腫の手術の基本である腫瘍への栄養血管の遮断と腫瘍の発生母地からの切り離しを正中部から行う．この部位の髄膜腫は比較的軟らかいことが多いため吸引器で腫瘍を吸引しながら蝶形骨洞平面から鞍結節部の方向に硬膜を十分凝固しながら後篩骨動脈からの腫瘍栄養血管を遮断する．上曲のバイポーラーがこの部位の硬膜の凝固に適している．栄養血管が遮断されると腫瘍からの出血が急速に減少してくるのがわかる．腫瘍体積がおおよそ 1/2 になるまで内減圧を行ったのちに蝶形骨洞平面を外側に辿るように腫瘍を摘出して視神経管入口部で視神経の同定を行う（**Fig. 3B, C**）．おおよその視神経・視交叉の走行を確認したのちにさらに腫瘍の内減圧を進める．われわれはほとんどの症例で視機能の良好な側から視神経の剝離を始めているが，例外なく視力が良好な側にはよりしっかりしたくも膜面が残存している．このくも膜面をトレースするように視交叉からも腫瘍を剝離していく．鞍隔膜や下垂体茎と腫瘍の癒着は比較的少ない．最後に視力の悪い側の腫瘍を十分な時間をかけて剝離する（**Fig. 3D**）．視神経管開口部に残存腫瘍がある場合は 30° の硬性鏡を併用して摘出する．

4. 手術成績

本到達法を用いた連続9症例の視機能の成績を

提示する（Table）．術後に視機能が悪化した例は1例もなかったが，髄液鼻漏，静脈梗塞，嗅覚脱失が各々1例ずつ発生した．髄液鼻漏は術後10日目で発生し，再手術を行った．静脈梗塞は前頭部の硬膜切開時に誤って皮質静脈の1本を損傷した．症候性にはならなかった．嗅覚脱失は鶏冠の除去の際に片側の嗅神経を切断し，他側の嗅神経は術中問題なかったが術後に嗅覚が脱失した．本到達法では視神経管の開放は技術的にも，また髄液鼻漏の面からも容易には決断できない．術前画像診断にて視神経管内深くまで腫瘍が伸展しているような症例や嗅覚を絶対に担保しなければならないような症例では側方からのアプローチを選択することが望ましい．

V．拡大蝶形骨洞到達法

当施設では正中部に限局した鞍上部腫瘍に対して1990年代後半から本到達法をtranssphenoidal-transtuberculum sellae approachという名称で用いていた[23]．当初は顕微鏡単独にて手術を行っていたが，その後内視鏡やナビゲーションが導入された．本到達法の最大の合併症である髄液鼻漏に関しても，新たなシーラント材（デュラシール®，コヴィディエン，アイルランド），チタンクリップ（アナストクリップVCS®，レメイトバスキュラー日本，東京）サイナスバルーン®（ファイコンインターベック，東京）などの登場によって克服されようとしている．手術手技は未だ変化している領域なので基本術式と最近われわれが行っている頭蓋底再建の方法を述べる．

1．基本術式

体位は仰臥位で背板を約10°挙上し，手術台を術者側に約10°回旋させる．ナビゲーションを用いるため頭部はメイフィールドの3点固定を用いてやや首を傾げるようなsniffing positionで固定する．顕微鏡の場合には片側鼻腔，内視鏡では時に両側鼻腔を用いる．アプローチする鼻腔の中鼻甲介と上鼻甲介を十分外側に骨折させた後に自然孔より約15 mm手前の鼻中隔粘膜に通常の下垂体手術よりも長い縦切開を入れる．鼻中隔軟骨を対側に骨折させ鋤骨を露出し，蝶形骨洞前壁を大きく開窓する．下垂体手術よりも視軸が上を向くため後部篩骨洞の一部も同時に削除することが多い．蝶形骨洞内の粘膜を摘出し，トルコ鞍，頚動脈隆起，視神経管隆起を確認する．ナビゲーションを用いてdural tailを含むところまでの骨削除を試みるが，側方展開は海綿静脈洞内内頚動脈によって制限される．顕微鏡では蝶形骨洞平面の削除は7～8 mmが限度であるが，内視鏡を用いると格段に前頭蓋窩の骨削除の範囲は拡がる．骨削除はトルコ鞍前壁から開始するが，骨は菲薄化していないのでドリルで骨を薄くした後にケリソンロンジュールにて削除していくのが安全である．視神経管内への腫瘍伸展の有無にかかわらず視神経管開口部の骨削除を行うと腫瘍摘出が容易になる．骨削除が終わると視野の下1/4にanterior intercavernous sinusが見える術野になる．鞍結節部の硬膜を十分に焼灼した後に腫瘍の真下に硬膜切開を入れる．吸引器で腫瘍を吸引しながら硬膜切開を同心円状に徐々に広げていくと腫瘍が拍動しながら手前に出てくるのが確認できる．くも膜が見えるところまで硬膜切開を広げると腫瘍が分娩されるように摘出される（Fig. 4A）．術野正面には視神経，視交叉と前交通動脈が見える（Fig. 4B）．顕微鏡下では残存腫瘍の確認は難しく，30°もしくは70°の内視鏡で行うことが望ましい．本到達法での（下方からの）視神経鞘の開放は眼動脈損傷の可能性があり勧められない．手術成績はおおむね良好であるが，側方進展の強い症例に本手術法を適応し摘出部両端に腫瘍再発を認めた経験がある．

2．頭蓋底再建

この部位の頭蓋底再建はいわゆるwatertightの硬膜再建は目指していない．硬膜再建の方法はさまざまで，脂肪片やgelfoamのパッキング，生体膜やゴアテックス®を残存硬膜内に敷きこむinlay法，生体膜や生体適応性代用硬膜をフィブリン糊で固定するonlay法が挙げられる．またこれらを組み合わせたmultilayer法も報告されている[4]．最近では内視鏡下手術において鼻中隔粘膜を有茎弁として用いる方法が注目されているが

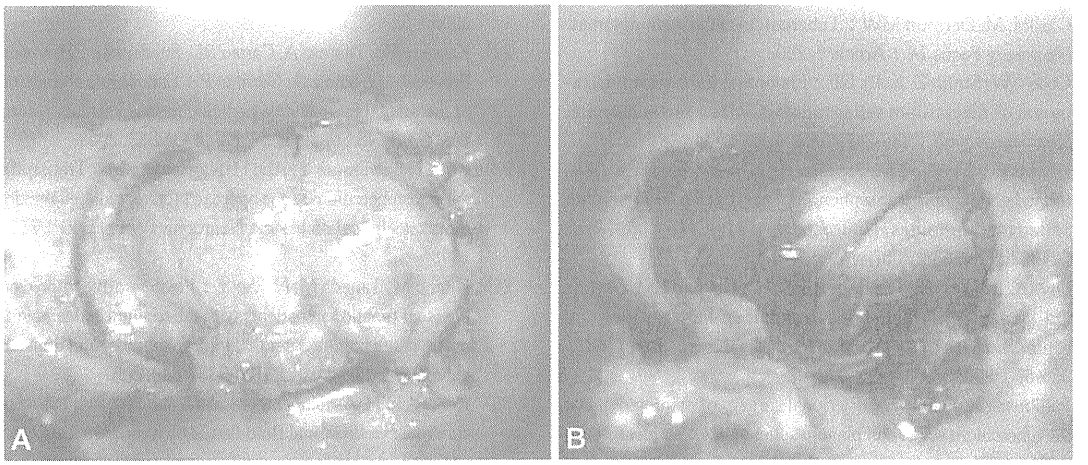

Fig. 4 A: After dural opening, the tumor spontaneously protruded into the surgical field. B: Direct surgical view of the undersurface of the chiasma was obtained at the end of this procedure.

[21,22]，本方法は栄養血管の温存や十分な長さの有茎弁が必要であるため術前から本法を計画した上で鼻腔内操作に臨むことになる．最近われわれは脂肪片から作製した生体膜＋アナストVCSクリップ＋ポリグルコール酸不織布フェルト（ネオベール®，グンゼ，京都）＋脂肪＋サイナスバルーンにて再建を行っているので紹介する．腋窩もしくは腹部から採取した脂肪の一部を濡れガーゼで包み，5分ほど圧迫を続けると線維成分のみが残った強度のある自家組織の膜ができる．これを硬膜欠損より大きめに裁断し，アナストクリップVCSにて断端硬膜と縫合する[25]．アナストクリップVCSはチタン製の非貫通性クリップで1本に35個のクリップが装填されているが5，6針かかると膜は安定する．非貫通性のため硬膜断端同士は外反する形状になる．長さが足りないときには，下垂体手術で用いるアリゲーター鉗子をクリップホルダーとしても使用できる．硬膜縫合部はフィブリン糊に浸したネオベール®にて補強する[41,42]．フィブリン糊をスプレー塗布した後に大きな脂肪片を蝶形骨洞内に挿入し，サイナスバルーンを挿入する．全例で1週間の脊髄ドレナージを行い，サイナスバルーンの抜去は術後10日以降にしている．

VI. おわりに

鞍結節髄膜腫では唯一の症状である視機能の悪化を深刻に捉えていない患者も多く，手術の難易度との間には大きな隔たりがある．手術到達法はいくつかあるが，各々に利点と欠点があり，術者側の要素と患者側の要素を勘案して総合的に決定すべきである．当施設では本疾患に対しては正中からの到達法を基本としており大脳半球間裂到達法と拡大蝶形骨洞到達法の詳細を報告した．

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