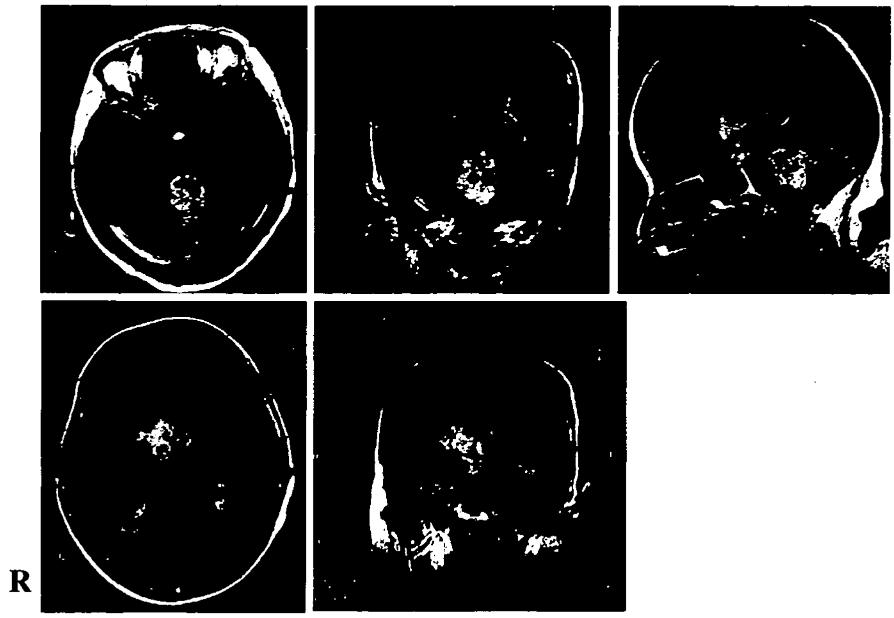

Fig. 4. MRI after whole-brain radiotherapy shows tumor progression as well as dissemination throughout the ventricular system

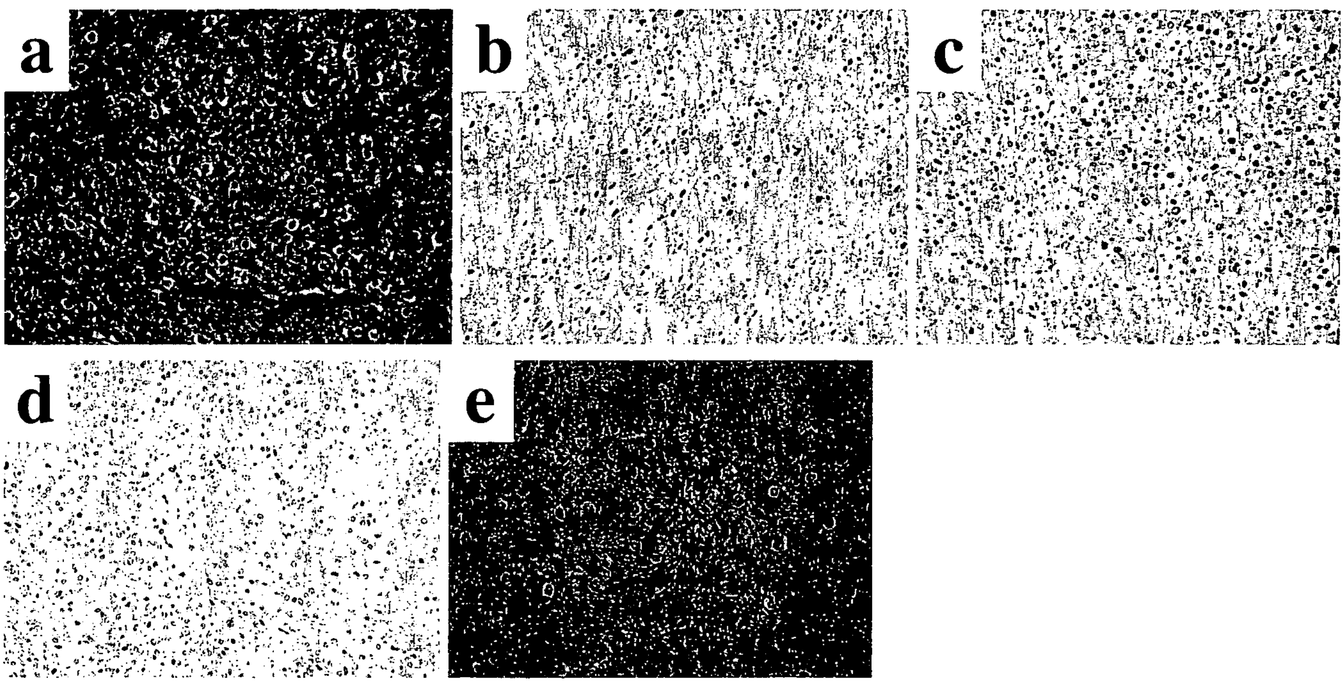

Fig. 5. The tumor cells had round or oval nuclei with finely speckled chromatin pattern with halos (**a**: H&E). Immunoreactivity for synaptophysin (**b**) and NSE (**c**) was positive; immunoreactivity for GFAP was negative (**d**); and MIB-1 LI was very low (**e**). **a–e** ×200

tumor was diagnosed as an oligodendroglioma at initial treatment.

We reexamined the tumor pathologically and diagnosed extraventricular neurocytoma based on the pathological findings and the patient's medical history (right frontal tumor). Some cases have been reported of neurocytoma with a poor clinical outcome, and anaplastic histological features, including apparent mitotic activity, microvascular proliferation, and necrosis, have sometimes been observed.[6–10] The MIB-1 LI varies from low to high. Soylemezoglu et al. reported that tumors with MIB-1 LI greater than 2% had a relapse rate of 63%, compared with a rate of 22% for tumors with a MIB-1 LI less than 2%.[11] They proposed considering CNs with a MIB-LI greater than 2% and/or vascular proliferation as "atypical central neurocytoma."[11]

In the present case, the MIB-1 LI was extremely high (80%), and mitoses and vascular proliferation were prominent; we therefore diagnosed neuroblastoma. Horten and Rubinstein collected and reviewed 35 cases with cerebral neuroblastoma. They proposed the criteria for the histological pattern of neuroblastoma.[12] According to the histologi-

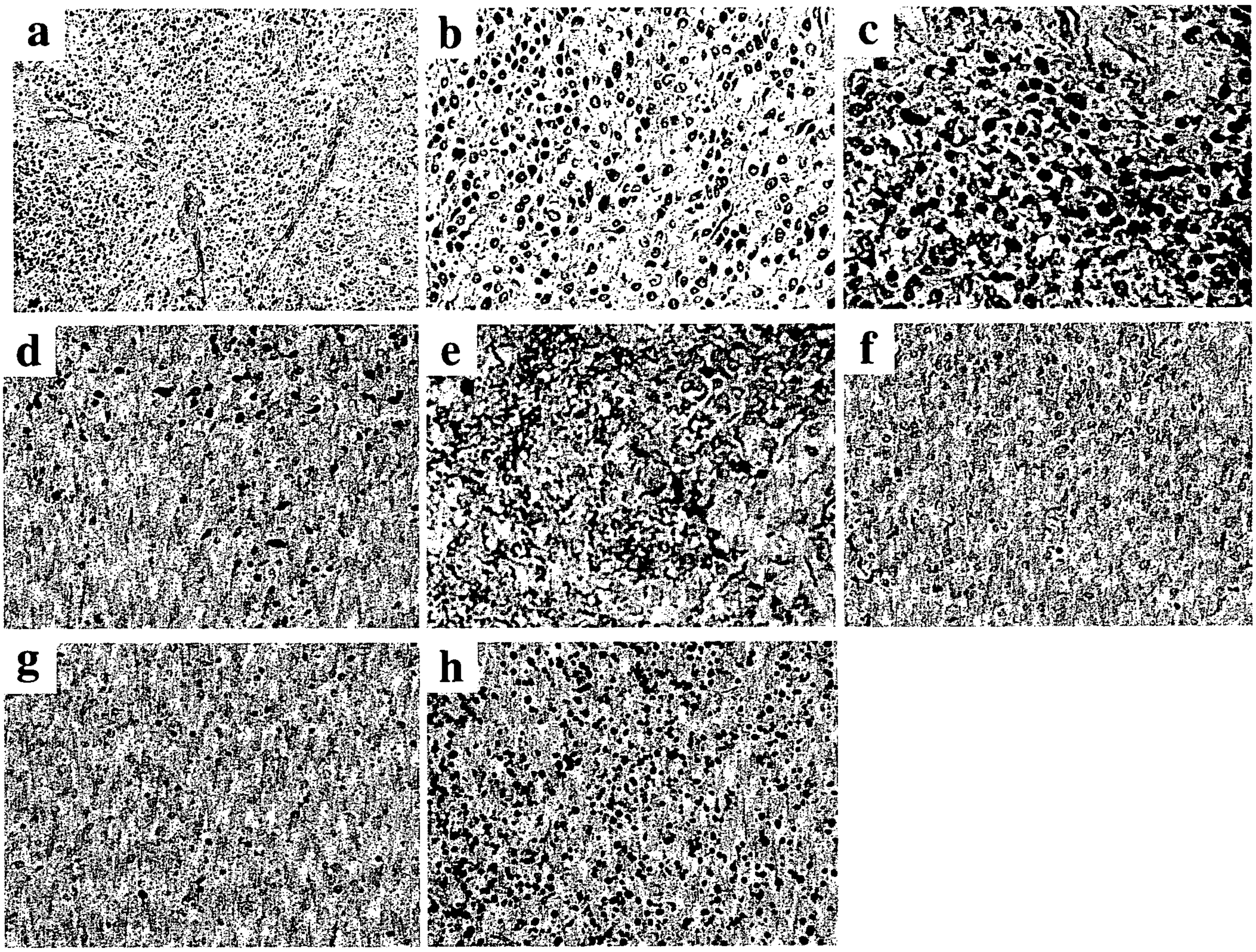

Fig. 6. Tumor cells display nuclear atypia, frequent mitoses, and microvascular proliferation (**a**, **b**: H&E). Immunoreactivity for synaptophysin (**c**), TUJ1 (**d**), and NFP (**e**) was positive; immunoreactivity for GFAP was partially positive (**f**); and immunoreactivity for OLG2 (**g**) was negative. MIB-1 LI was 80% (**h**). **a** ×40; **b**, **c**, **e** ×400; **d**, **f–h** ×200

cal classification of tumors of the central nervous system proposed by WHO in 2000, neuroblas toma is classified in the supratentorial primitive neuroectodermal tumor group with ganglioneuroblastoma.[13] Tong et al. reported that central neurocytomas are genetically distinct from neuroblastoma.[14]

For patients with typical neurocytomas, complete resection is considered the best treatment, and after incomplete resection patients benefit from radiotherapy. In our case, radiotherapy and gamma-knife radiosurgery were effective, although not curative. To our knowledge, there has been no previous report of transformation of neurocytoma to neuroblastoma. It is possible that the neuroblastoma originated from a different site or was a radiation-induced secondary tumor. However this may be, our case is of considerable interest from both pathological and clinical perspectives.

The most appropriate treatment for CN has yet to be clearly established. It has been suggested that radiation therapy is advisable in patients with recurring tumors and histological evidence of malignancy. The role of chemotherapy is less clear, and few reports have addressed this issue.[15–17] von Koch et al. reported that chemotherapy including procarbazine, CCNU, and vincristine was effective for recurrent central neurocytoma.[18] However, because our patient's general condition was already very poor at her final admission, we could not treat her with chemotherapy.

Long-term controlled studies are needed for evaluation of the efficacy of postoperative radiation therapy, and close, long-term follow-up is necessary for patients with extraventricular neurocytoma.

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Clinical Article

Surgical resection of tumors located in subcortex of language area

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Summary

Object. Although functional mapping facilitates the planning of surgery in and around eloquent areas, the resection of tumors adjacent to language areas remains challenging. In this report, we took notice that the language areas (Broca's and Wernicke's) present at the perisylvian fissure. We posit that if there is non-essential language area on the inner surface of the Sylvian fissure, safe tumor resection may be possible even if the tumor is located under the language cortex.

Methods. The study population consisted of 5 patients with intrinsic brain tumors (frontal glioma, $n = 3$; temporal cavernous angioma, $n = 1$; primary malignant central nervous system lymphoma, $n = 1$) located in the perisylvian subcortex, in the language-dominant hemisphere. All patients underwent awake surgery and we performed intra-operative bipolar cortical functional language mapping. When the tumor was located under the language area, the Sylvian fissure was opened and the inner surface of the opercular cortex was exposed with the patient asleep, and additional functional mapping of that cortex was performed. This enabled us to remove the tumor from the non-functioning cortex.

In our series, 4 of 5 patients had not language function on the inner surface of the operculum. Only one patient, a 52-year-old man with frontal glioblastoma (Case 3) had language function on the inner surface of the frontal operculum.

Conclusion. We suggest that even perisylvian tumors located in the subcortex of the language area may be resectable via the nonfunctioning intrasylvian cortex by a transopercular approach without resultant language dysfunction.

Keywords: Functional mapping; language area; operculum; brain tumor.

Introduction

To minimize the risk of postoperative language deficits in patients scheduled for surgery near the perisylvian cortex in the dominant hemisphere, knowing the localization of language function is important for planning the cortical trajectory and the resection area. While reports on language cortical and subcortical mapping using awake craniotomy and/or a sub-dural grid are available [13, 14, 19], surgical resection under the eloquent cortices continues to present a high risk of neurological sequelae. Neuro-imaging functional techniques are in development and are beginning to be efficient for cortical sensorimotor mapping, but still lack sensitivity and specificity for language mapping, and remain difficult to give real-time data during surgery [16].

The supratemporal plane is divided into the three parts (planum polare, Heschl gyrus, planum temporale), and contains the primary and association auditory system and a part of Wernicke's area. However, the language function of the inner surface of the operculum, and the clinical presentation and treatment of patients with lesions in these areas have rarely been described.

Here we present the results of functional mapping and surgery undergone by 5 patients with tumors located in and around the subcortex of the language area. These

Table 1a. *Summary of the 5 patients*

Case	Age (yr), sex	Diagnosis	Tumor localization	Handedness	Language dominancy	Initial symptom
1	49 F	malignant lymphoma	lt. temporal	Rt.	Lt.	epilepsy
2	31 F	astrocytoma	lt. frontal	Rt.	Lt.	inicidental
3	52 M	glioblastoma	lt. frontal	Rt.	Lt.	hemiparesis
4	55 M	oligodendroglioma	lt. frontal	Rt.	Lt.	epilepsy
5	44 F	cavernous angioma	lt. temporal	Rt.	Lt.	transient paraphasia

Table 1b. *Summary of the severity of aphasia in the 5 patients*

Case	Overall SLTA severity		Auditory comprehen-sion		Naming		Sentence repetition		Sentence reading aloud		Reading comprehen-sion		Kana letter dictation		Sentence dictation	
	pre	post	pre	post	pre	post	pre	post	pre	post	pre	post	pre	post	pre	post
1	10	10	7	9	16	18	3	5	4	5	7	9	10	8	5	5
2	10	10	10	10	20	20	5	4	5	5	10	10	10	10	5	5
3	5	9	1	1	14	14	3	4	5	5	1	1	6	8	1	1
4	10	10	9	8	18	18	4	4	5	5	10	10	10	10	5	5
5	10	10	10	10	20	20	4	4	5	5	8	8	10	10	5	5

lesions can be resected safely using functional mapping in patients undergoing awake surgery.

Methods

Subjects

There were 5 patients with intrinsic brain tumors (frontal glioma, $n = 3$; temporal cavernous angioma, $n = 1$; temporal primary central nervous system malignant lymphoma, $n = 1$) located in the perisylvian subcortex in the language-dominant hemisphere. They were 2 men and 3 women; their median age was 46 years (range 31–55 years) (Table 1a).

Language evaluation

The Standard Language Test of Aphasia (SLTA) was used to evaluate language functions. The SLTA is the standardized test battery most commonly used to evaluate Japanese aphasic patients [20]. The aphasia severity ratings (0 = most severe, 10 = normal) are based on the 19 SLTA sub-scores; these were used as the primary language measure in the present study [8, 11]. The following seven subscores of the SLTA were also included in the analysis: auditory comprehension (to obey verbal commands) (out of 10); naming (out of 20); sentence repetition (out of 5); reading aloud short sentences (out of 10); dictation of Kana letters (out of 10); and dictation of short sentences (out of 5). Each patient was given the SLTA twice; the aphasia severity ratings before and after the operation (approximately 1 to 3 months after the surgery) are shown in Table 1b.

Intra-operative cortical functional mapping

To determine whether the lesions were located in the dominant hemisphere, patients underwent pre-operative functional MRI and/or intracarotid amytal testing (Wada test). During awake surgery, intra-operative cortical mapping for language was performed in all patients following the previous reports [1, 10, 14]. Intravenous anesthesia (propofol) was used during craniotomy. After creating a cranial opening large enough to expose most of the lateral temporal and inferior frontal lobe, propofol administration was discontinued and the patient was allowed to awaken. Silver-tip bipolar electrodes spaced approximately 5 mm from each other were placed on the exposed cortical surface. Stimulation parameters are set at 60 Hz, biphasic square wave pulses (1 msec/phase), with variable peak-to-peak current amplitude between 2 to 12 mA (peak-peak amplitude). To avoid eliciting local seizure phenomena or false negative or false positive results, a current below the after-discharge threshold was used so that depolarization was not propagated to the nearby cortex. Before mapping, 10 to 20 sites were selected and marked with small tags. Sites for stimulation mapping were randomly selected to cover all of the exposed frontal or temporal lobe cortex, including areas thought to contain sites essential for language function and areas near and overlying the lesion site. Each patient was shown images of simple objects. Cortical stimulation, applied before the presentation of each image, was continued until there was a correct response or the next image was presented. Each pre-selected site was stimulated 3 to 4 times but never twice in succession. Sites where stimulation produced consistent speech arrest or anomia were considered essential language areas.

Case illustration

Case 1

This 49-year-old right-handed woman was in excellent health when she had her first generalized tonoclonic seizure. Preoperative MRI showed a round well-enhanced 2.5 cm lesion in the superior temporal gyrus. Intra-operative functional mapping of the essential speech cortex under awake surgery disclosed that the tumor was located just under the temporal language area. After exposing the posterior part of superior temporal plane by opening the Sylvian fissure, we performed intra-operative language mapping of the posterior part of the superior temporal plane. No language site was identified at that area. Unfortunately, we could not obtain an intra-operative pathological diagnosis, so we totally removed the lesion via a superior temporal plane cortical incision (Fig. 1). Postoperative histological diagnosis was primary CNS malignant lymphoma. This was treated with radio-chemotherapy as adjuvant therapy. Her postoperative SLTA score remained unchanged. She discharged from our hospital without any neurological deficits.

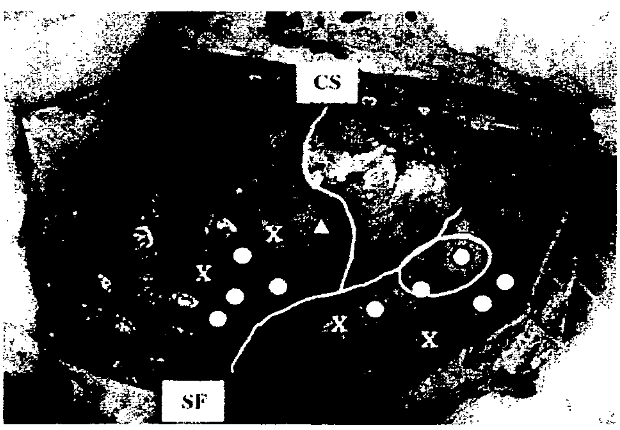

Fig. 1. *Case 1* – A 49-year-old woman with primary CNS malignant lymphoma. Intra-operative photograph of the brain map showing that the tumor is located under the Wernicke's area. ○ Speech arrest, △ dysarthria, × no response, *CS* central sulcus, *SF* Sylvian fissure

Case 2

This 31-year-old woman was in excellent health when she sustained a simple head injury. CT study incidentally disclosed an anomaly. Preoperative MRI revealed a round, non-enhancing, 3 cm lesion in the inferior frontal gyrus. With the patient awake, intra-operative cortical functional mapping of the essential speech cortex was performed. A frontal language area was identified; the tumor was located under the tongue motor area. We exposed the frontal operculum by opening the Sylvian fissure and performed intra-operative language mapping. No language function was identified at the inner surface of the posterior part of the frontal operculum; the tumor was removed from the non language area (Fig. 2). The histological diagnosis was low-grade astrocytoma. Although she suffered transient dysarthria, she fully recovered within several days.

Case 3

This 52-year-old right-handed man was admitted to our hospital with aphasia and right-hand loss of power to grip. MRI showed a ring-like enhanced lesion in the frontal lobe. Intra-operative cortical language mapping failed to identify a frontal language area. His inferior frontal gyrus was swollen. We exposed the inner surface

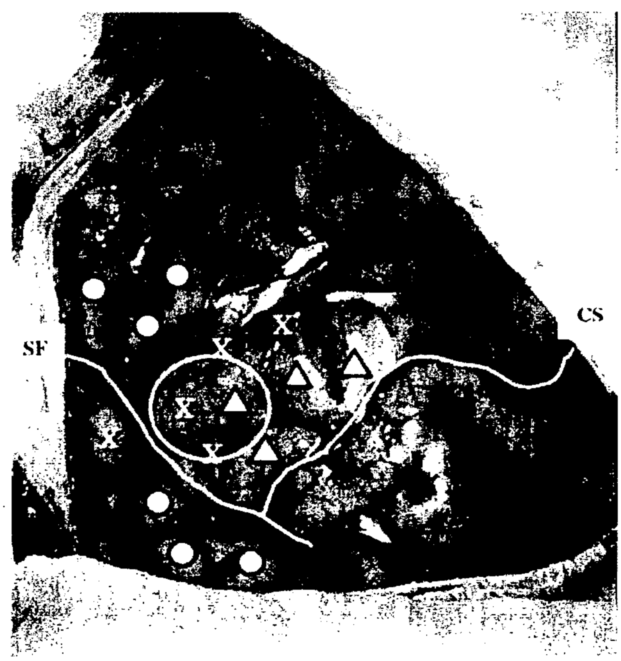

Fig. 2. *Case 2* – A 31-year-old woman with low-grade astrocytoma. Intra-operative photograph of the brain map showing that the tumor is located within the tongue motor area. ○ Speech arrest, △ dysarthria, × no response, *CS* central sulcus, *SF* Sylvian fissure

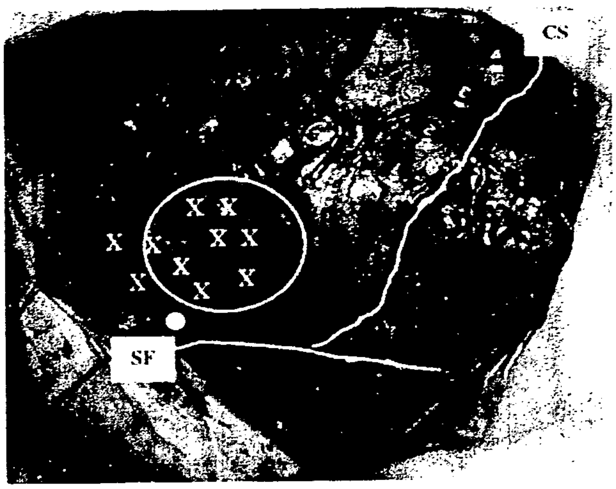

Fig. 3. *Case 3* – A 52-year-old man with frontal glioblastoma multiforme. Intra-operative photograph of the brain map showing that the Broca's area is located on the inside of the Sylvian fissure. ○ Speech arrest, Δ dysarthria, × no response, *CS* central sulcus, *SF* Sylvian fissure

of the frontal operculum by opening the Sylvian fissure and performed intra-operative language mapping again. The essential language area, located on the inner surface of the frontal operculum, was compressed by a tumor and shifted into the Sylvian fissure. We resected the tumor through the non-language cortex (Fig. 3). The language area was replaced to the surface of inferior frontal gyrus. The histological diagnosis was glioblastoma multiforme. His overall SLTA severity had worsened immediately after the operation, whereas it recovered and improved 3 months after surgery (Table 1b).

Case 4

This 55-year-old-man was admitted our hospital with transient epileptic motor aphasia. T1- and T2-weighed MRI showed a low- and a high-intensity lesion in the inferior frontal gyrus, respectively, which was not enhanced by gadolinium. His pre-operative interictal SLTA score was normal. During awake surgery, intra-operative functional mapping identified a frontal language area. The tumor was located under the language area. We opened the Sylvian fissure and performed intra-operative language mapping at the inside of the Sylvian fissure again. Because no essential language area was identified on the inner surface of the frontal operculum, we resected the tumor through this non-language area (Fig. 4). The histological diagnosis was oligodendroglioma. His postoperative SLTA score was also normal.

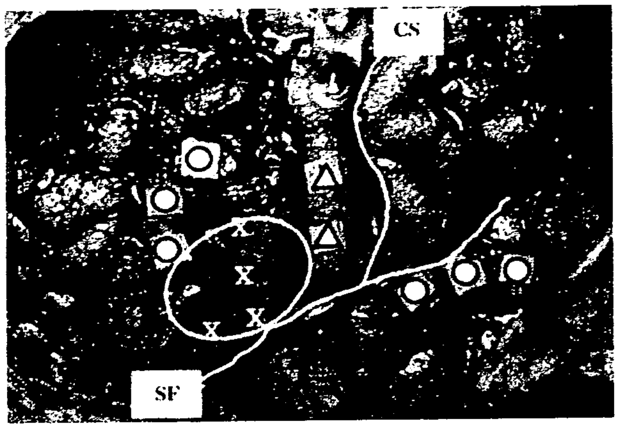

Fig. 4. *Case 4* – A 55-year-old man with oligodendroglioma. Intra-operative photograph of the brain map showing that the tumor is located under the Broca area. ○ Speech arrest, Δ dysarthria, × no response, *CS* central sulcus, *SF* Sylvian fissure

Case 5

This 44-year-old woman visited our hospital complaining of transient paraphasia. T2-weighted MRI showed a mixed-intensity lesion with a hypo-intense rim in the left superior temporal gyrus. Awake craniotomy was performed. Intra-operative functional mapping revealed that the tumor was located under Wernicke's area. We opened the Sylvian fissure and performed intra-operative language mapping of the planum temporale. No language function was identified at that area. We resected the tumor through the non-language area on the splanum temporale (Fig. 5). The diagnosis was cavernous angioma. Her postoperative SLTA score was normal.

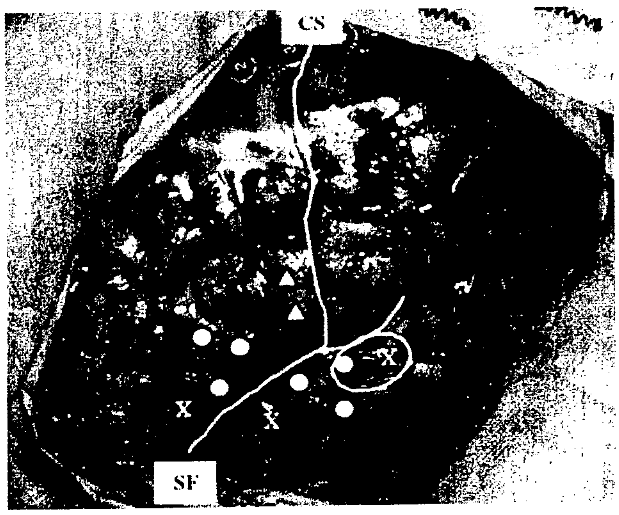

Fig. 5. *Case 5* – A 44-year-old woman with cavernous angioma. Intra-operative photograph of the brain map showing that the tumor is located under the Wernicke area. ○ Speech arrest, Δ dysarthria, × no response, *CS* central sulcus, *SF* Sylvian fissure

Summary of cases

Pre- and postoperative MRI of the 5 patients are shown in Fig. 6. Quality of resection was systemically evaluated using immediate (within 72 hr after the operation) post-operative MRI. We were able to remove all tumors totally without permanent new neurological deficits and without exacerbation of the patients' aphasia. Schematic drawings presented in Fig. 7 identify the localization of the 5 tumors and the language areas. Of the 5 patients, only case 3, a patient with

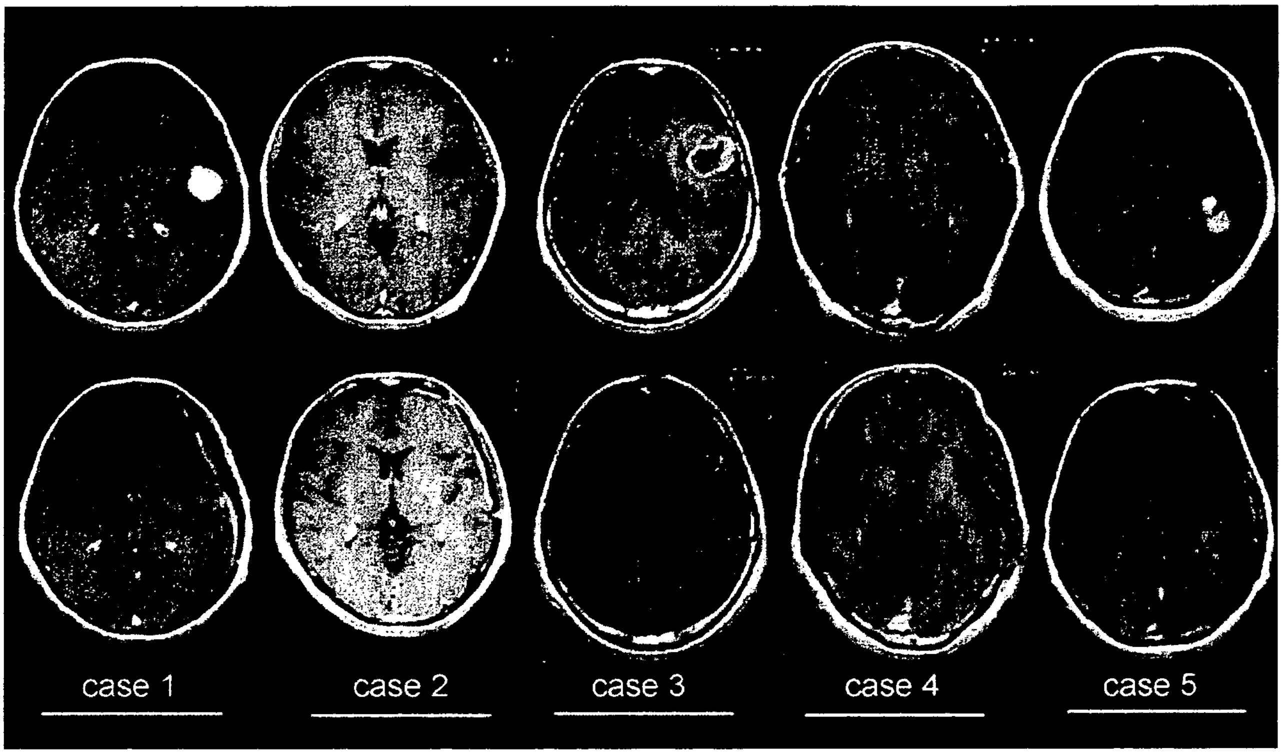

Fig. 6. Pre (*upper line*) – and post (*lower line*)-operative Gd-enhanced, T1-weighted magnetic resonance images obtained on the 5 patients. All tumors were removed almost totally

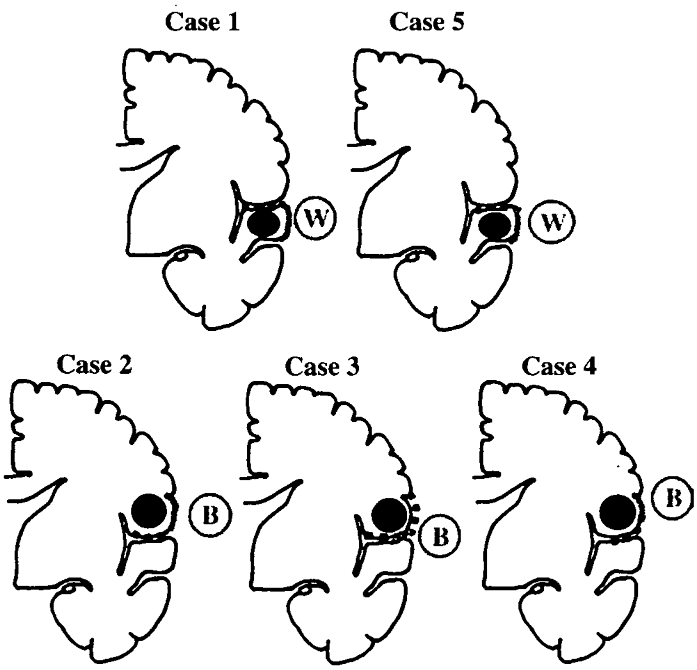

Fig. 7. Schematic drawing of the brain map of the 5 patients. *B* Broca's area, *W* Wernicke's area. The filled circles indicates the tumor. The dotted and gray lines encircle the functional- and non-functional areas, respectively

frontal glioblastoma manifested essential language function on the inner surface of the frontal or temporal operculum. This language area, located on the frontal operculum, appeared to be compressed and displaced by the tumor.

Discussion

Although functional mapping facilitates the planning of surgery in and around eloquent areas, the resection of tumors adjacent to language areas remains challenging. Ojemann and his associates reported that the essential language area localized to a focal areas of dominant hemisphere cortex of approximately 1 cm^2 [14, 15]. And the exact location of these sites in the left dominant hemisphere was found to vary substantially across the patient population. Haglund and colleagues reported that a margin of 7 to 10 mm around the language areas resulted in significantly fewer permanent postoperative linguistic deficits [9]. Recently, Duffau and colleagues noted no higher rate of definitive language worsening despite a resection coming in contact with the language sites (but higher rate of transient postoperative aphasia) [4]. Whittle IR *et al.* reported the incidence of iatrogenic dysphasia without intra-operative brain mapping is not dissimilar to that described after resection during use of awake craniotomy and intra-operative language testing [21]. They suggested that a large prospective study would be required to assess the usefulness of intra-operative language testing. Recently, Duffau H *et al.* reported that successful resection of a left insular cavernous angioma using intra-operative language mapping [5]. And Berger MS *et al.* mentioned that to maximize the extent of tumor resection while minimizing permanent language deficits, and recommended the using of cortical stimulation mapping [2]. Although this might be still controversial, we believe intra-operative language mapping is necessary to avoid surgical morbidity.

In this report, we took note that the language areas (Broca's and Wernicke's area) present at the perisylvian fissure. We posit that if there is non-essential language area on the inner surface of the Sylvian fissure, safe tumor resection may be possible even if the tumor is located under the language cortex. We operated on 3 patients with frontal gliomas without new neurological deficit except case 3 who experienced worsening of his aphasia transiently. But, his aphasia was improved 3 months after surgery.

The functional imaging studies allow detection of all the areas implicated in the realization of a task, but not the essential structures in these networks. There has been some work on the importance of the left frontal operculm for syntactic processing [6], and this region is activated during functional imaging studies of language. The functional imaging studies detected the distribution of 'essential' and 'participating' neuronal activity. But, the distribution of 'participating' neurons is substantially different to the focal, lateralized 'essential' sites identified by stimulation mapping for language. Noninvasive functional imaging modalities are an aid to the neurosurgeon, but the golden standard is still believed to be intra-operative monitoring. The evolution of better presurgical functional brain mapping techniques such as magnetic source imaging (MSI), fMRI, and probabilistic Diffuion Tensor imaging/fiber tracking methods will allow an estimation of the anatomical and functional cortex [7, 12]. These techniques may have the potential to promote functional neuronavigation as to an alternative to awake surgery.

The supratemporal plane of the temporal lobe in humans and subhuman primates contains the cortical representation of the primary and association auditory system and forms a part of Wernicke's area. However, the clinical presentation and treatment of patients with lesions in these areas have rarely been described. Silbergeld *et al.* who performed intra-operative cortical mapping during awake surgery on 2 patients subjected to resection of left-hemisphere Heschl gyrus gliomas, reported that neither patient manifested postoperative deficits [18]. Of 3 patients with non-dominant hemisphere Heschl's gyrus gliomas operated on by Russell and Golfinos [17], one presented with postoperative difficulty with music comprehension and production. In this report, we operated on 2 patients with left planum temporale tumors. We only examined language function intra-operatively. However, none of our 2 patients complained of auditory dysfunction and auditory change upon cortical stimulation. And we could remove the tumors without language dysfunction via non-functioning planum temporale cortex.

In our series, 4 of 5 patients had no essential language area on the inner surface of the operculum. Only one patient, a 52-year-old man with a frontal glioblastoma (Case 3) had language function on the inner surface of the frontal operculum. Duffau and colleagues reported 3 cases of inferior frontal gyrus (F3) glioma operated on without neurological deficits. They speculated that total F3 infiltration by glioma, thus a functional reorganization due to brain plasticity would explain the lack of deficit [3]. However, from intra-operative findings, after tumor removal, language cortex replaced on to the surface of the inferior frontal gyrus. We could not detect essential language area on the medial area of the essential language area, and so we speculated his language area was compressed and displaced, rather than that there was reorganization of a new language area.

In conclusion, we posit that there is non-essential language area on the inner surface of the Sylvian fissure. While studies on larger patient populations are necessary, we can remove the perisylvian tumors through overlying non-language cortex. We propose our (opercular) approach may be useful in patients requiring the resection of perisylvian tumors.

Conclusions

Of 5 patients with tumors in the perisylvian cortex, only one, a patient with a frontal glioblastoma, manifested essential language function on the inner surface of the frontal operculum. In this exceptional case, the language cortex was compressed by the tumor and displaced to the inside of the Sylvian fissure. Based on the functional mapping data we obtained, we suggest that even tumors located in the subcortex of the language area may be resectable through the nonfunctioning opercular cortex without inducing postoperative language dysfunction.

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Comment

This is an interesting study that emphasizes the value of intra-operative stimulation in awake patients during the resection of lesions adjacent to eloquent cortex. The authors hypothesize that even in the presence of lesions which seem unresectable because of location near Broca's or Wernicke's area, in selected cases a complete resection may be possible when the tumor is approached through a trans-opercular route of non-functional intrasylvian tissue on the inner' surface of the operculum.

In our opinion, however, awake craniotomy, while still regarded as the reference standard of surgery in eloquent cortex, should be considered an interim solution until the advent of better and more powerful functional imaging modalities that help us visualize functionally important brain tissue. We have experience with language MEG (magneto-encephalography) for over 5 years in about 120 cases operated upon for gliomas in the vicinity of Broca' and Wernicke's area with functional neuronavigation. From our experience we conclude that this may well be an alternative to intra-operative awake stimulation.

The evolution of better presurgical functional brain mapping techniques and probabilistic Diffusion Tensor Imaging/fibertracking methods will allow an estimation of the anatomical and functional cortex hitherto norknown. These techniques may have the potential to promote functional neuronavigation as to a true alternative to awake craniotomies.

More correlative studies will be warranted in the future to prove that these new techniques are as safe as the proven and tested method of intra-operative electrical stimulation.

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手術手技・周術期管理

斜台部腫瘍摘出における経鼻孔内視鏡手術の経験
―術式の工夫―

斎藤佑規　土谷大輔　櫻田香
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Technical Notes on Endoscopic Transnasal Transsphenoidal Approach for Clival Tumor

by

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Although there are various operative approaches for clival tumors, a transsphenoidal approach is one of choices when the main tumor extension is in an anterior-posterior direction with a slight lateral extension. However, this approach sometimes provides only narrow and deep operative fields. The recent development of a neuroendoscope and neuronavigation system allow for a wide operative field and easy identification of the surrounding important structures. As a result, an endoscopic transsphenoidal approach is now quite an effective approach for clival tumors. In this report, we discribe the effectiveness, technical problems, and solution of this approach based on our experience with a chondrosarcoma that was removed by endoscopic transsphenoidal approach.

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Key words : chondrosarcoma, clival tumor, endoscope, neuronavigation, transsphenoidal approach

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緒　言

頭蓋底の chondrosarcoma は浸潤性に発育することが多く，外科的切除は，transbasal approach, transmaxillary approach, transoral approach, transfacial approach, subtemporal approach, transsphenoidal approach など，多くの手術アプローチが報告されているが[1)7)9)]，いずれのアプローチでも広い術野を得ることは困難で，また周囲に存在する重要血管や脳神経が術野を制限するので，不十分な切除に終わることが少なくない[3)6)]．

斜台部腫瘍に対する transsphenoidal approach[4)10)]は，1960 年代[2)]から用いられているが，当時の手術用顕微鏡では視野の確保に制限があり，また閉創の困難さから髄液漏が問題となった[10)]．そのため，chordoma の手術アプローチとしてはあまり普及しなかった．今回は，最新の神経内視鏡システムを駆使し，transnasal transsphenoidal approach にて摘出を行った chondrosarcoma の 1 例を経験したので，内視鏡手術の有用性と限界について，われわれが行った技術的工夫を中心に本症例の手術に対して報告する．

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Fig. 1 Pathological specimen from the first operation. The diagnosis is chondrosarcoma (HE. ×200).

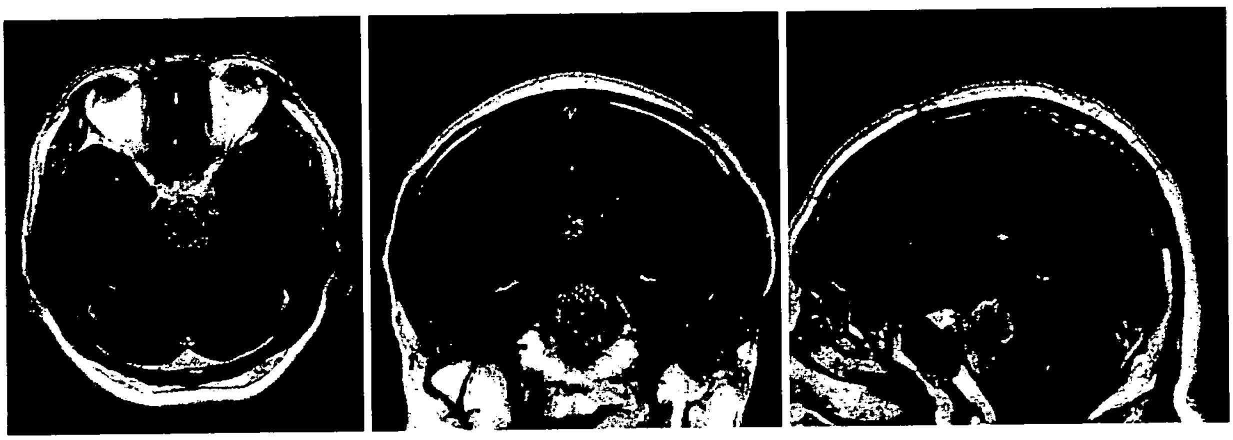

Fig. 2 MRI (T1-Gd enhanced) 33 months after the first operation. The residual tumor is regrowing.

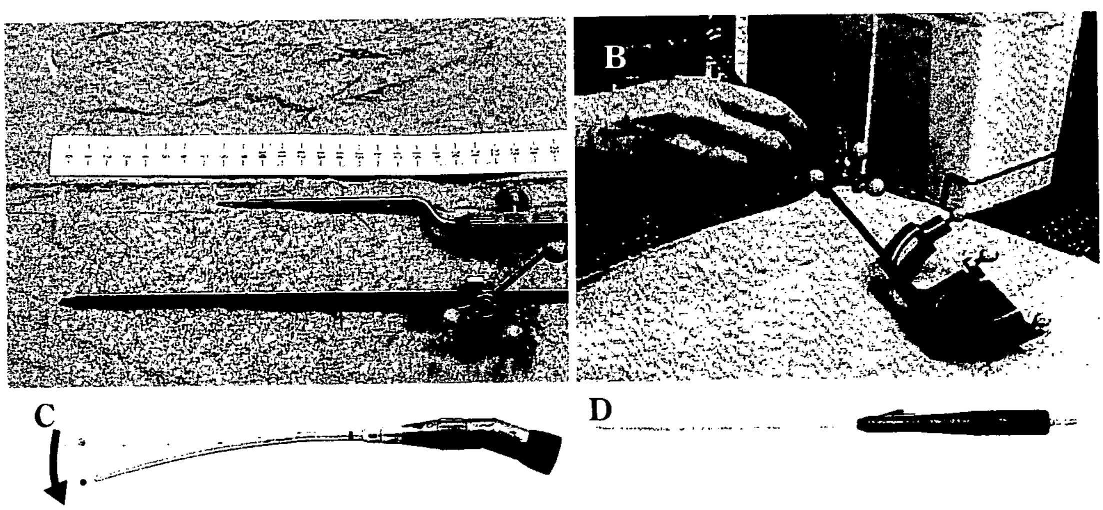

Fig. 3 An original long navigation pointer (**A**) registered by the Universal Instrument Integration system (**B**: VectorVision® : BrainLAB Co.,Ltd.) for this operation. Long and slim instruments we used for this operation, Primado® (**C**: Nakanishi Co.,Ltd.) and SONOPET® (**D**: M & M Co.,Ltd.).

Fig. 4 Intraoperative photograph. Basilar artery (＊), capule of tumor (#), and forceps (＋).

症例提示

患　者：56 歳，男性

主　訴：複視

既往歴：特記事項なし

現病歴：2002 年より左方視時の複視を自覚するも放置していた．翌年 3 月に近医で眼精疲労と診断されていた．2004 年 8 月時点でも症状の改善を認めず，原因検索のため頭部 MRI を施行され，頭蓋内病変を指摘，当科紹介となった．

入院時現症：意識は Japan Coma Scale：0. 神経学的所見としては左の外転神経麻痺を認めた．

神経放射線学的所見：術前の頭部 MRI (T1-Gd) では，トルコ鞍から斜台にかけて後方に突出し，内部が不均一に増強される最大径 2.5 cm の腫瘍を認めた．橋は腫瘍により後方に強く圧排され，脳底動脈は右方に偏移していた．

第 1 回手術：斜台部 chondrosarcoma の術前診断の下，2003 年 3 月，Lt. subtemporal approach で摘出術を行った．手術は，ニューロナビゲーションにて腫瘍を確認しながら摘出を行い，右側に圧排された脳底動脈が確認できたところで摘出終了とした．腫瘍の病理診断は，術前診断どおり chondrosarcoma であった (**Fig. 1**)．

第 1 回術後経過：術後 MRI では残存腫瘍は内減圧されており，今後腫瘍が縮小し脳幹の減圧が期待されるため，後療法は行わず，自宅退院し経過観察となった．その後，およそ 4 カ月ごとに MRI による経過観察を行ったが，術後 33 カ月目の MRI で，明らかな腫瘍の再増大を認めた．

第 2 回手術：再発腫瘍は側方進展が少なく，後方進展が主体であったため，第 2 回手術は内視鏡下経鼻経蝶形骨洞手術で行うこととした (**Fig. 2**)．

手術には OLYMPUS 社製の 4 mm の 0 度，30 度，70 度の視野角を持つ硬性内視鏡と，BrainLAB 社製のニューロナビゲーションシステム (VectorVision®) を用いた．また通常のナビゲーション用ポインターは，本症例のように斜台より後方に進展する腫瘍の手術には短いため，任意の手術器械をナビゲーションポインターとして使用できるナビゲーションシステム付属の Universal Instrument Integration を用いて長いポインターを自作して使用した．さらに，狭い空間での斜台の掘削，斜台後方の腫瘍摘出のため，細経で長い経鼻手術用に開発されたハイスピードドリル (Primado®：ナカニシ社製)，ラパロスコープ用の超音波手術器 (SONOPET®：エムアンドエム社製) などの手術機器を用いた (**Fig. 3**)．

第 2 回手術所見：蝶形骨洞前壁を drill out し，蝶形骨内に進入すると，蝶形骨洞内に両側の内頸動脈隆起，トルコ鞍が確認された．また，それら 3 つの構造物に囲まれた斜台の骨は，腫瘍により一部破壊されていた．その部分をナビゲーションシステムにて確認し，これら重要構造物を傷つけないように開窓した．

腫瘍はもろく，出血も少なく，超音波手術器で容易に吸引可能であった．自作したポインターで摘出深度を確かめながら摘出を進め，脳底動脈を避けながら橋の前面まで到達し，クモ膜が摘出腔に下垂してきたところで摘出終了とした (**Fig. 4**)．摘出後，蝶形骨洞内を脂肪とフィブリン糊で充塡し，手術を終了した．

第 2 回術後経過：第 2 回術後の MRI では，斜台左上方部分に残存腫瘍が認められた．この部分は，今回用いた下垂体腫瘍に用いる硬性鏡の長さでは短く，視野角のついた内視鏡であっても blind となる部分であった (**Fig. 5**)．術後は，新たな神経脱落症状，髄液漏などの合併症もなく，自宅独歩退院し，現在も外来にて画像による経過観察を行っており，腫瘍増大時には定位放射線照射を行う予定である．

考　察

斜台部腫瘍に対する手術アプローチには，種々のものが報告されているが[1)7)9)]，腫瘍の側方進展が少ない場合，transsphenoidal approach は考慮されるべきアプローチである[5)]．

斜台部腫瘍に対する transsphenoidal approach は，古くは 1966 年の Bouche らの報告[2)]にさかのぼることができるが，当時の手術顕微鏡では側方の視野が確保できず，摘出に限界があり，斜台部腫瘍に対する transsphenoidal approach は普及しなかった．しかしながら，近年の神経

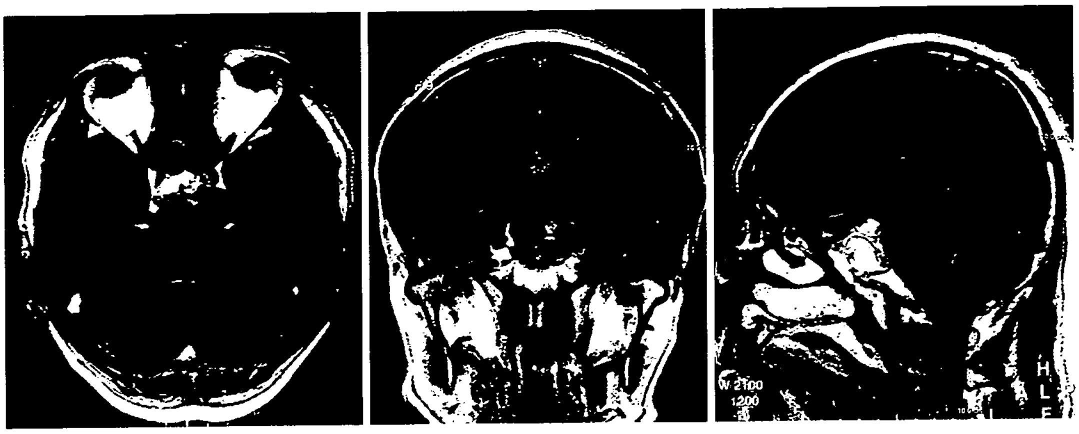

Fig. 5 MRI (T1-Gd enhanced) after the second operation. The remaining tumor was shown in the left superior portion. It seems to be a blind corner with the endoscope that we use, because the endoscope is too short to see there.

内視鏡の発達とともに，広い視野が確保され，摘出率が向上し，手術アプローチとして再評価されるようになった[8]．さらに今回症例で明らかとなったごとく，細径のドリルや超音波手術装置といった手術器械や，ニューロナビゲーションシステムといった最新の技術を応用することによって，より安全，確実に腫瘍摘出術が可能となった．今後，ますます斜台部腫瘍に対する内視鏡下経蝶形骨洞手術の適応が拡大するものと考えられる．ただし，今回の症例の経験から得られた問題点としては，現在トルコ鞍部の手術に用いられている硬性内視鏡では，斜台部後方に存在する腫瘍を側視鏡でみるには短く，blind となり摘出しきれない部位があることが明らかとなった(**Fig. 6**)．今回用いた内視鏡は，脳用の有効長 155〜160 mm，外径 4 mm のものであるが，例えば婦人科用としては有効長 280 mm，外径 3 mm のものも存在することから，有効長の長い内視鏡の開発は技術的には可能と考えられ，脳用の 160 mm を超える内視鏡の開発が必要である．また今回使用した超音波吸引器は，先端がまっすぐであるために直視下の腫瘍の摘出には効果を発揮するが，側方の腫瘍の摘出には限界がある．これは顕微鏡下の手術においても同様であり，内視鏡によって側方の視野がより確保されたとしても，側方に存在する腫瘍を摘出するための器材の開発も今後の課題である．

斜台部腫瘍摘出術に際しては，髄液漏が最も危惧される[3)6)10)]．斜台部腫瘍に対する内視鏡下経蝶形骨洞手術の報告は少ないが，Frank らの報告[5)]によると，chordoma，chondrosarcoma に対して内視鏡下経蝶形骨洞手術を行い，髄液漏は 11 例中 2 例（18%）に認めたのみで，その 2 例もフィブリン糊と脂肪組織の充填により治癒していることから，通常のトルコ鞍部の腫瘍摘出と同様の手技で髄液漏のコントロールは可能であると考えられる．しかしこの部位の腫瘍摘出に関して，髄液漏は最終的な手術の成否を分ける重要な合併症であり，症例によっては積極的な腰椎ドレナージの利用や，fascia を用いた硬膜の形成など，症例ごとに十分な髄液漏防止についての検討が必要なのはいうまでもない．また 11 例中 1 例（9 %）に腫瘍摘出時の内頸動脈損傷による出血を認めたと報告しているが，これは不用意にモノポーラ凝固装置を用いた結果とされており，ニューロナビゲーションシステムで内頸動脈を十分確認することで回避可能であったと推測され，術中の出血もコントロール可能な症例が多いと考えられる．内視鏡手術においては，止血方法が問題とされることが多いが，本論文からは，斜台部の chordoma，chondrosarcoma は出血が少なく，内視

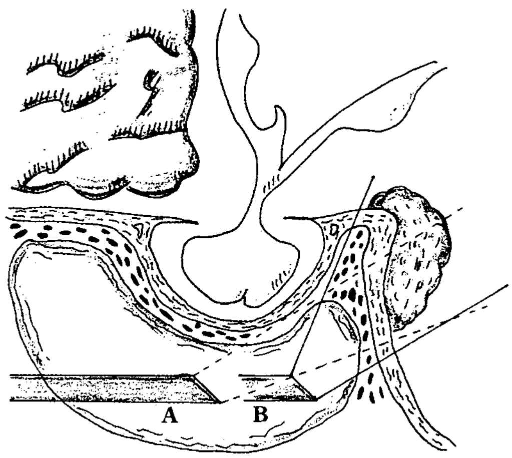

Fig. 6 Illusration showing the difference of range of the endoscopic visual field due to its lengths. **A** is the length we used this time. **B** is the ideal length.

鏡手術のよい適応であると考えられる．今回の症例も出血が少なく，止血操作に難渋することはなかった．このように，側方進展の少ない斜台部の chordoma，chondrosarcoma は，内視鏡下経蝶形骨洞手術のよい適応疾患と考えられた．

結　語

Clival chondrosarcoma の内視鏡下経鼻経蝶形骨洞手術に際して，われわれが行った手術手技の工夫について報告した．内視鏡手術用に開発された手術機器とナビゲーションシステムの応用により，斜台部腫瘍を安全に摘出することができた．侵襲度が高い手術アプローチが多い斜台部腫瘍に対して，より低侵襲な内視鏡下経蝶形骨洞手術の適応拡大が期待される．

問題点としては，斜台部後上方や後下方に進展した腫瘍摘出のためには，現在のトルコ鞍部手術用の硬性内視鏡よりも長い内視鏡の開発が必要であると同時に，今後の課題としては，確保した側方視野に存在する腫瘍を摘出するための器械の開発が挙げられる．

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要　旨

斜台部腫瘍摘出における経鼻孔内視鏡手術の経験
—術式の工夫—

斎藤　佑規　　土谷　大輔　　櫻田　　香
佐藤　慎哉　　黒木　　亮　　嘉山　孝正

斜台部腫瘍への手術アプローチには種々の方法があるが，前後方向への進展が主体で側方進展が軽度の場合には，経蝶形骨洞手術も選択肢の１つである．従来の顕微鏡手術による本アプローチは，術野が狭く，手術アプローチとしては普及しなかった．しかし，近年の神経内視鏡やニューロナビゲーションシステムの発達は，広い術野の確保と周囲の重要構造物の同定に威力を発揮し，経蝶形骨洞手術の斜台部腫瘍への適応が拡大している．今回は，内視鏡下経蝶形骨手術にて摘出術を行った chondrosarcoma の１例を経験したので，その手術に際してわれわれが行った技術的工夫と手術における問題点につき報告する．

脳外誌　17：50-54，2008

BRAIN and NERVE 59(8)：881-886, 2007

症例報告

Isomorphic astrocytoma の 1 手術例

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An Operative Case of Isomorphic Astrocytoma

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Abstract

Diffuse astrocytomas are classified as WHO Grade II tumors. Recently, a subtype presenting with better prognosis has been proposed, and it is known as "isomorphic astrocytoma." A clinical case that we encountered was believed to be categorized as this subtype; it has been presented in this report.

The patient was a 20-year-old male with a chief complaint of intractable epileptic seizures. He experienced his first attack at 16 years of age in July 2001, and it was a generalized seizure. Anticonvulsants prescribed by a previous doctor had no effect on controlling the seizures. MRI performed in March 2004 showed a lesion approximately 2.0 cm in diameter in the left temporal lobe. The patient was referred to our institution for further investigation of the lesion and therapy.

Electroencephalography and magnetoencephalography were used to assess the lesion at seizure focus. The tumor was resected under awake surgery. The pathological diagnosis was diffuse astrocytoma, but this tumor was considered to be the isomorphic subtype. Some parts of the tumor showed a relatively high MIB-1 labeling index (LI) of 9.2%, and additional 50-Gy radiotherapy was performed. The postoperative course was uneventful and despite decreasing the anticonvulsant dosage, he has remained seizure free.

Isomorphic astrocytoma is characterized by prolonged epileptic seizures, a low MIB-1 LI, and better prognosis. In our case, since the MIB-1 LI was higher in some parts of the tumor, the appropriate therapy for WHO Grade II tumors was performed. However, this case was considered representative of isomorphic astrocytoma. No reports of this tumor subtype have been previously described in Japan. Therefore, this report is the first case of isomorphic astrocytoma reported to Japanese literature.

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Key words：diffuse astrocytoma, isomorphic astrocytoma, epilepsy

はじめに

Diffuse astrocytoma は星細胞腫群（astrocytic tumor）のうち，浸潤性に脳実質を侵す分化型グリオーマである。WHO 分類（2000）では，限局した発育を示す pilocytic astrocytoma との対比の意味で "diffuse" がつけられている。わが国では原発性脳腫瘍の 7.7%を占め，

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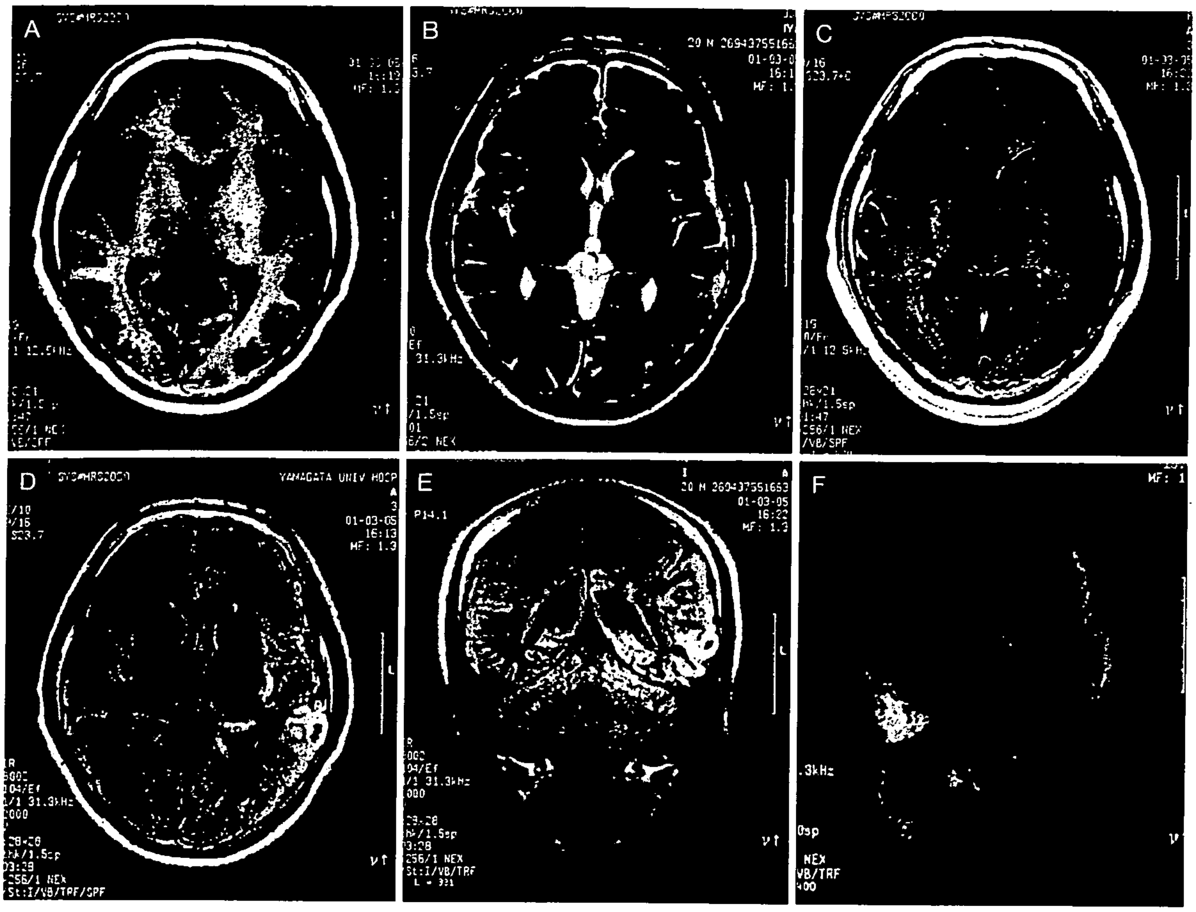

Fig. 1 Preoperative MRI

T_1-weighted (A), T_2-weighted (B), Gd-enhanced-(C), and FLAIR-(D, E, F) MRI showing a mass lesion in the left temporal lobe.

25〜59 歳に好発する。大脳半球，特に前頭葉に多く，次いで側頭葉，頭頂葉に発生する。臨床悪性度は WHO Grade II に属する。組織学的には 3 つの亜型に分類され，①線維性 (fibrillary)，②原形質性 (protoplasmic)，および③肥胖性 (gemistocytic) 星細胞腫がある。症状としては，脳実質へのびまん性の浸潤によりさまざまな局所症状が出やすく，頭蓋内圧亢進による症状は初期には出にくい。てんかん発作を起こすことが多いことも特徴の 1 つである[1]。

これまで diffuse astrocytoma と診断されていた星細胞腫のなかに，長期のてんかん歴を持ち，diffuse astrocytoma に比べて良好な予後をたどる一群，すなわち isomorphic astrocytoma が存在するとの報告がなされるようになった[2-4]。今回われわれは，この isomorphic astrocytoma と考えられた 1 例を経験したので報告する。

I．症　　例

患　者　20 歳，男性

主　訴　難治性てんかん

既往歴，家族歴　特記事項なし

現病歴　2001 年 7 月，全身性強直間代発作があり近医を受診した。MRI を施行されたが異常所見を指摘されず，バルプロ酸の内服を開始した。その後も数カ月に 1 回の頻度で複雑部分発作が出現し，ゾニサミドの併用を開始した。しかし発作のコントロールは不良で，月に 3，4 回の頻度に増加した。その後の MRI で異常を指摘され 2005 年 1 月，当科を紹介され受診した。

初診時神経学的所見　発作間欠期の状態では神経学的異常は認められなかった。複雑部分発作を月に 3，4 回の頻度で認めていた。当科外来受診後，カルバマゼピン投与も試みたが効果は認められなかった。

神経放射線学的所見　2001 年に前医で MRI を施行さ

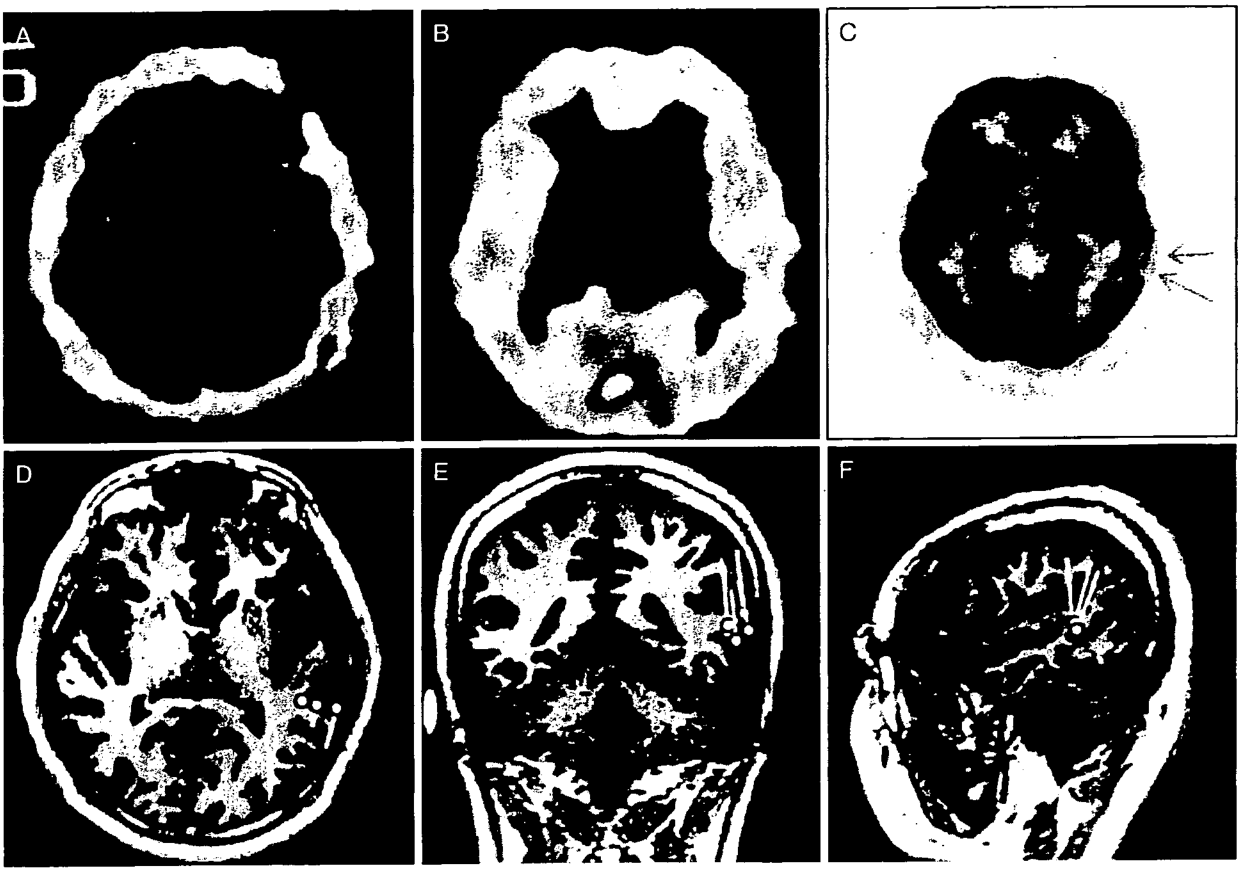

Fig. 2　SPECT, PET and MEG
Thallium-SPECT (A), Iomazenil-SPECT (B) and FDG-PET-(C) show a low-uptake lesion in the left temporal lobe. MEG results revealed that epileptic activity was detected in the left temporal lesion (D, E, F).

れているが，病変は指摘されなかった。われわれが retrospective に見直してみると T_2 強調画像で左側頭葉に内部が高信号，周辺部が等～高信号の病変が認められた。

当科初診時の CT では，単純，造影とも明らかな異常は指摘できなかった。

MRI では左側頭葉に皮質の腫大がみられ，内部は T_1 強調画像で低信号，T_2 強調画像では高信号である。周辺部は等～高信号である。造影効果は認められない（Fig. 1）。FLAIR の冠状断，矢状断をみると，病変は中側頭回後方に位置する。MRS（magnetic resonance spectroscopy）では NAA（N-acetyl aspartate）ピークの低下が認められる。明らかな choline ピークの上昇はみられず，low grade glioma のパターンと考えられた。

SPECT では，タリウムで病変部は低集積，イオマゼニルでも病変部位に一致した低集積が認められた。FDG（fluorodeoxyglucose）PET でも病変部位は低集積を示した。MEG によるてんかん焦点の検索を行うと，てんかん焦点は病変部に一致して推定された（Fig. 2）。

脳血管造影では明らかな腫瘍濃染などの異常所見はみられなかった。

手術所見　以上の結果から，術前診断として左側頭葉の low grade glioma，あるいは皮質形成異常による症候性てんかんと診断し，摘出術を施行することとした。

症例は生来右利きであり，言語有意半球の病変と考えられたため，言語野を同定しつつ摘出術を施行する目的で覚醒下手術を施行した。術中所見では病変部はやや赤色で腫大しており，皮質脳波では病変後方に spike の出現を認めた。Language mapping を行ったところ，病変の後下方の電気刺激によって picture naming の障害が出現した（Fig. 3）。

病変周囲の脳溝を鋭的に分け，病変切除を施行した。摘出後の皮質脳波で spike の消失を確認し手術を終了した。

術後経過　術後 MRI では，病変は全摘出されている（Fig. 4）。

術直後一過性の軽度の物品呼称の障害が出現したが，約 1 週間で完全に症状は消失した。WAIS-R では，術前は VIQ59，PIQ59，IQ52 であったものが，術後 1 カ月の

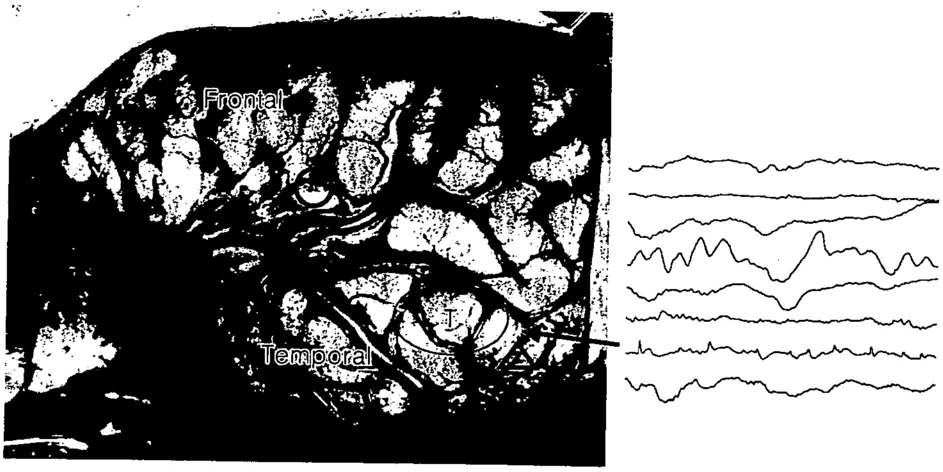

Fig. 3 Intraoperative photograph
The lesion showed swelling and was reddish. On the EEG rerealed spike activity in the posterior part of the lesion. T: tumor, ○: dysarthria, △: anomia.

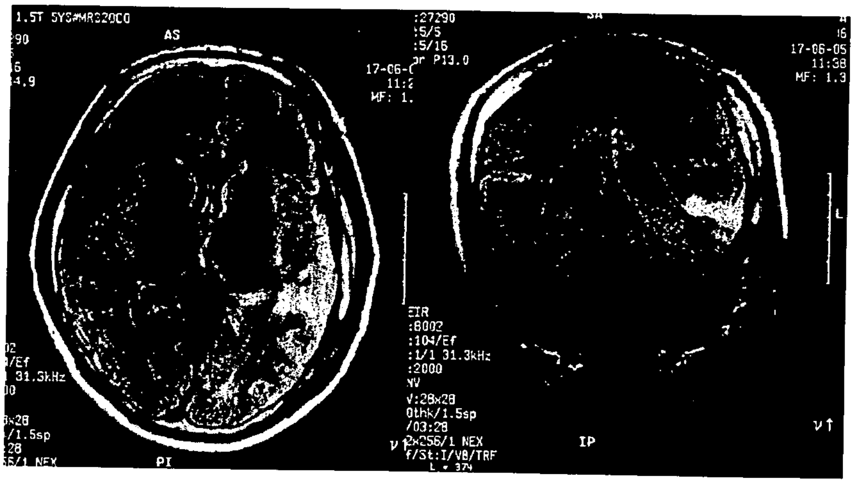

Fig. 4 Postoperative MRI
The lesion was removed completely.

時点ではVIQ72, PIQ70, IQ67と著明に改善した。てんかん発作に関しても術前はゾニサミド200 mg, バルプロ酸1,000 mg, カルバマゼピン400 mgでコントロールしていたが, 術後10カ月経過した現在, カルバマゼピン400 mgの内服のみで完全に消失している。

病理学的所見(Fig. 5) 病変部では腫瘤の形成はなく, 正常のグリア細胞とほぼ同大の核を持つ腫瘍細胞がびまん性に増生しており, 細胞密度が軽度に増加している。核の異型は乏しく核分裂像は認められない。核異型が乏しいため, 腫瘍細胞と背景のグリア細胞の鑑別はかなり困難である。既存の脳組織の破壊はなく, 反応性星細胞もみられない。免疫組織化学的には, GFAP(+/−), CD34, NeuN, NFPは陰性であった。MIB-1 LIは大部分で3%以下であったが, 最も高い部位で9.2%と軽度高値であった。

以上の病理学的所見より, 本例はdiffuse astrocytoma, WHO Grade IIと診断したが, 核異型の乏しさ, 免疫染色の結果, および病歴よりisomorphic astrocytomaと考えられた。しかし, 部分的にMIB-1 LIが軽度高値を示したため, 後療法としてWHO分類Grade IIの治療に準じて50 Gyの放射線照射を追加した。

II. 考 察

Isomorphic astrocytomaは, 2004年にSchrammらによってdiffuse astrocytomaのうち長期のてんかん歴を持ち, 組織学的にMIB-1 LIが低く, 臨床的にはdif-