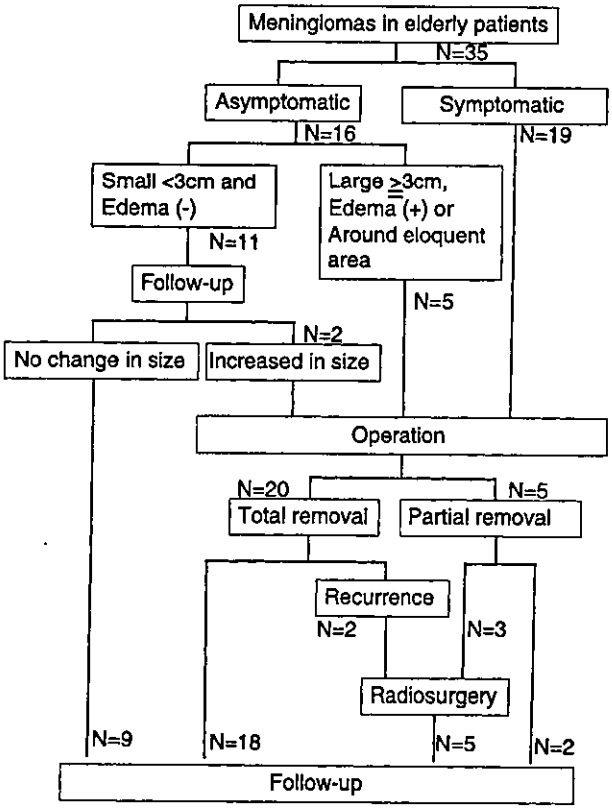

Fig. 1. Our strategy for treating meningiomas in elderly patients

found in patients between 70 and 84 years of age (mean, 73.4 years); these patients, 23 women (65.7%) and 12 men (34.3%), were enrolled in our protocol. We used the Karnofsky performance scale (KPS) for standardization of the patients' pre- and postoperative condition [6]. Clinical data on the 35 patients are presented in Tables 1 and 2.

Results

Patient characteristics

Our treatment strategy is presented in Fig. 1. Of the 35 patients, 19 (54.3%) were initially symptomatic and underwent surgical treatment. One patient (case 25) was asymptomatic at the time of meningioma diagnosis. However, this 70-year-old man became symptomatic during the course of conservative treatment and underwent surgery.

Of the 16 asymptomatic tumors, 5 were removed at the time of diagnosis; 3 of these were large (cases 21, 22, and 24) and 2 (cases 20 and 23) were located around eloquent areas. The large tumor in case 21 manifested peritumoral edema. The other 11 asymptomatic tumors were treated conservatively and monitored by MRI at 3–6 month intervals.

During the 13-month (average) follow-up period, 2 initially asymptomatic tumors increased in size; one (case 25) was operated on, in the other (case 26) we continued follow-up due to associated disease (COPD). The remaining 9 asymptomatic, conservatively treated tumors did not increase in size during a 23.2-month (average) follow-up period. Ultimately, 25 of the 35 (71.4%) elderly patients underwent surgical treatment. Their tumors ranged in size from 20–70 mm; 8 were located at the convexity and 5 were parasagittal tumors. The medical history of 5 patients (20%) included hypertension. In all but 5 patients the preoperative KPS was 80% or higher. The low KPS of the 5 patients was attributable to tumor symptomatology. Total resection was performed in 20 cases (Simpson I, $n=11$; Simpson II, $n=9$), partial resection in 5 (Simpson III, $n=1$, Simpson IV, $n=4$). Three of the partially resected symptomatic meningiomas (one each petroclival, falcotentorial, and clinoidal) required additional gamma knife surgery.

Histologically, of the 25 surgically treated tumors, 8 were meningotheliomatous, 10 were fibrous, 2 were transitional, 2 were psammomatous, 1 was angiomatous, and 2 were anaplastic meningiomas.

Operative morbidity (Table 3)

Postoperative complications were encountered in 4 patients (16%); 2 suffered permanent morbidity consisting of hemiparesis (cases 17 and 14). The other 2 manifested transient mild 7th nerve palsy (case 11) or cerebrospinal fluid leakage (case 15). Of the 4 patients with operative morbidity, 2 suffered additional postoperative medical complications. Patient 17, a 71-year-old man with a large olfactory groove meningioma developed pneumonia. Patient 14, a 76-year-old woman whose tumor was located at the convexity manifested pulmonary embolism. There was no operative morbidity among the 6 asymptomatic patients.

Operative mortality

Only one patient (case 9), a 78-year-old man with severe visual disturbance and hemiparesis whose preoperative KPS was 50%, died within 30 days of total removal of a large (60 mm) sphenoid ridge meningioma. The cause of death was cerebral infarction that occurred 2 weeks after surgery. Overall, the mortality rate for the 25 "operated" patients was 4%.

Postoperative KPS

At the time of discharge, 9 of the 25 "operated" patients (36%) manifested an improved KPS, in 13

Table 1. *Intracranial meningiomas in elderly patients treated by surgery*

Case no.	Age/sex	Tumor location	Size (mm)	Edema	Symptom	Medical history	KPS on admission	Tumor resection (simpson)	KPS on discharge	Histology	KPS during follow-up	Postop follow-up (months)	Adjuvant therapy
1	71/F	petroclival	25	–	cerebellar ataxia	not relevant	60%	IV	60%	meningotheliomatous	D	74	gamma knife
2	75/F	convexity	60	–	trigeminal neuralgia	not relevant	90%	I	100%	fibrous	100%	110	–
3	71/M	convexity	60	+	motor weakness	not relevant	90%	I	100%	meningotheliomatous	ND	ND	–
4	71/F	parasagittal	40	+	visual disturbance	not relevant	90%	II	100%	transitional	ND	ND	–
5	71/F	falcotentorial	50	–	dementia	not relevant	70%	IV	90%	fibrous	100%	96	gamma knife
6	71/F	parasagittal	40	–	headache	breast cancer	100%	II	100%	meningotheliomatous	ND	ND	–
7	71/M	tuberculum sellae	35	–	visual disturbance	not relevant	80%	II	80%	meningotheliomatous	80%	81	–
8	75/F	convexity	45	+	headache	gastric ulcer	100%	I	100%	angiomatous	ND	ND	–
9	78/M	sphenoid ridge	60	+	visual disturbance paresis	hypertension	50%	I	20%	meningotheliomatous	D	NA	–
10	74/F	parasagittal	50	++	headache, vertigo	hypertension	80%	I	100%	anaplastic	D	14	gamma knife (recurrent tumor)
11	71/F	cerebellopontine angle	20	–	dizziness	diabetes mellitus	90%	II	90%	fibrous	90%	57	–
12	72/M	clinoidal	40	–	visual disturbance	not relevant	80%	III	100%	meningotheliomatous	100%	59	gamma knife
13	72/F	cerebellopontine angle	25	–	vertigo	not relevant	90%	II	100%	fibrous	100%	54	–
14	76/F	convexity	70	++	convulsion	not relevant	100%	I	50%	anaplastic	D	28	**
15	73/F	tentorial	50	–	dizziness	hypertension	100%	IV	100%	fibrous	100%	38	–
16	71/F	convexity	40	–	tinnitis	not relevant	90%	II	90%	fibrous	100%	12	–
17	71/M	olfactory groove	70	–	visual disturbance	hypertension	70%	IV	50%	fibrous	D	7	–
18	72/F	convexity	40	–	cerebellar ataxia	not relevant	90%	I	100%	psammomatous	100%	8	–
19	71/F	foramen magnum	20	–	dizziness	not relevant	90%	II	90%	fibrous	100%	3	–
20	78/F	parasagittal	20	–	asymptomatic	not relevant	100%	II	100%	meningotheliomatous	ND	ND	–
21	73/M	convexity	35	++	asymptomatic	not relevant	100%	I	100%	transitional	100%	60	–
22	71/F	parasagittal	40	–	asymptomatic	uterine cancer	100%	II	100%	psammomatous	100%	12	–
23	78/M	tentorial	20	–	asymptomatic	not relevant	100%	I	100%	meningotheliomatous	100%	10	–
24	76/F	convexity	40	–	asymptomatic	not relevant	100%	I	100%	fibrous	100%	6	–
25	70/M	lateral ventricle	50*	–	dementia*	hypertension	50%	I	80%	fibrous	ND	ND	–

* This initially asymptomatic meningioma subsequently increased in size and became symptomatic.
** The tumor recurred 25 months after operation.
D Dead, *ND* not done, *NA* not applicable.

Table 2. *Asymptomatic intracranial meningiomas in elderly patients treated conservatively*

Case no.	Age/sex	Tumor location	Size (mm)	Follow-up (months)	Follow-up results	Medical history	KPS at diagnosis	KPS at follow-up
25	70/M	lateral ventricle	20	33	growth (at 10 mos)	hypertension	90%	*50%
26	71/M	clinoidal	25	30	growth (at 16 mos)	COPD	80%	80%
27	84/M	clinoidal	35	22	no change	not relevant	100%	100%
28	80/M	sphenoid ridge	30	21	no change	not relevant	100%	100%
29	70/F	olfactory groove	20	29	no change	not relevant	100%	100%
30	75/M	sphenoid ridge	30	30	no change	not relevant	100%	100%
31	70/F	sphenoid ridge	20	30	no change	angina	100%	100%
32	77/F	convexity	15	25	no change	parkinsonism	80%	80%
33	76/F	falx	20	13	no change	hypertension	100%	100%
34	73/F	parasagittal	15	34	no change	hypertension	100%	100%
35	75/F	tentorial	14	5	no change	diabetes mellitus	100%	100%

* The KPS of this patient worsened during follow-up due to enlargement of the tumor and he subsequently underwent surgery.

Table 3. *Summary of treatment-related (30 day) morbidity in elderly surgically treated meningioma patients*

Case no.	Age/sex	Tumor site	Surgical complication	Medical complication
17	71/M	olfactory groove	hemiparesis (permanent)	pneumonia
14	76/F	convexity	hemiparesis (permanent)	pulmonary embolism
15	73/F	tentorial	CSF leakage (transient)	
11	71/F	cerebellopontine	7th nerve palsy (transient)	

(52%) it was unchanged, and in 3 (12%) is was worse than their preoperative score. None of the 6 asymptomatic patients experienced postoperative neurological deterioration.

Follow up evaluation

Of the 5 partially resected meningiomas, 3 required gamma knife surgery 3–6 months after the initial operation. Follow-up MRI studies were performed in 18 patients. During a mean follow-up period of 33.1 months, 2 of 20 totally resected tumors (10.0%) recurred. The average interval between treatment and recurrence was 18.5 months. Of 2 operated anaplastic meningiomas, 1 (case 10) was also treated by gamma knife surgery. The other patient with a surgically treated anaplastic meningioma (case 14) had an admission KPS score of 100%; it fell to 50% and she died without receiving further treatment 28 months after establishment of her diagnosis. A total of 4 patients (residual tumors, n = 3; recurrent tumor, n = 1) underwent gamma knife surgery which resulted in very good tumor control; all 3 residual tumors decreased in size during a mean follow-up period of 73.3 months. The cause of death in 3 patients (cases 1, 10, and 17) was due to associated disease. At the time of this writing, we are continuing to monitor 10 asymptomatic patients by MRI (mean follow-up period 23.3 months).

Discussion

High morbidity and mortality rates raise doubts about the advisability of surgical intervention in elderly meningioma patients. Following the introduction of CT scanning, 2.2–45.0 of elderly patients succumbed to operative mortality; 30–52% suffered perioperative morbidity (Table 4) [1, 2, 5, 9, 14, 16]. Advances in MRI and microsurgical techniques, neuroanesthetics, and intensive care management have led to better results [3, 4, 8, 12]. Some [3, 12] have reported that there is no significant difference in the morbidity rate of younger and older patients and surgical removal has been recommended even in aged patients with symptomatic meningiomas [3, 11]. The introduction of gamma knife surgery not only led to changes in the treatment of benign tumors but also provided a useful tool for dealing with residual and recurrent

Table 4. *Operated intracranial meningiomas in the elderly reported in the literature*

Author and year	Patient age	No. of cases	30-day mortality	Perioperative morbidity
Papo (1983)	>70	50	45%	NA
Awad *et al.* (1989)	>65	25	8%	52%
Cornu *et al.* (1990)	>65	96	16%	43%
Arienta *et al.* (1990)	>70	34	12%	44%
Umansky *et al.* (1992)	>70	37	5.4%	41%
Maurice-Williams and Kitchen (1992)	>65	46	2.2%	30%
Nishizaki *et al.* (1994)	>70	78	13%	
Black *et al.* (1998)	>65	57	1.5%	11%
Kuratsu *et al.* (2000)	>70	30	0%	23%
Buhl *et al.* (2000)	>70	66	7.6%	18%
Our series	>70	25	4%	16%

tumors [7]. In patients with adhering tumors and those with tumors adjacent to important structures we can reduce postoperative morbidity by subsequent gamma knife surgery. We treated our 19 patients with symptomatic meningiomas by surgery alone or by combined surgery and gamma knife surgery. Two meningiomas (cases 25 and 26) were initially asymptomatic but subsequently increased in size and became symptomatic during follow-up; one of these patients (case 25) was treated by total resection, the other (case 26) received conservative treatment due to associated disease (COPD). Of the 35 patients reported here, 20 (57.1%) were initially or subsequently recorded as symptomatic and treated by surgical resection. A single patient (case 9), a 78-year-old man with a meningotheliomatous tumor at the sphenoid ridge, succumbed to operative mortality. The cause of death was cerebral infarction. Operative morbidity occurred in 4 (16%) of our patients, 2 (8%) suffered permanent neurological morbidity.

The surgical indication in elderly patients with asymptomatic meningiomas demands careful evaluation. Regarding the natural history of asymptomatic meningiomas [8, 11, 13, 17], 22–35% of these tumors increased in size and there was no significant difference with respect to age, tumor size, and gender between patients with and without tumor growth during the follow-up period [8]. Asymptomatic meningiomas with CT evidence of calcification and/or hypo-intensity on T2-weighted MRI scans reportedly have a slower growth rate [8].

In our series, 2 of 11 (18.2%) conservatively treated asymptomatic tumors increased in size over a 23.2-month follow-up period (cases 25 and 26). This tumor growth rate is somewhat lower than that reported previously (Table 5), possibly because our strategy addresses high-risk asymptomatic meningiomas at the time of diagnosis. Like others [10, 11], we consider large meningiomas and those with peritumoral edema as high-risk tumors. When we encounter meningiomas around eloquent areas we carefully weigh our treatment options because resection of these tumors carries a high risk of morbidity. In our series, all 6 such asymptomatic tumors were totally removed and none of these patients succumbed to operative mortality or morbidity.

Table 5. *Studies on the natural history of asymptomatic meningiomas*

Author and year	Mean age	No. of cases	Tumor growth rate
Olivero *et al.* (1995)	66	45	22.0%
Niiro *et al.* (2000)	76.1	40	35.0%
Yoneoka *et al.* (2000)	61	37	24.3%
Kuratsu *et al.* (2000)	66.5	63	31.7%
Our series	74.6	11	18.2%

We assessed our treatment strategy not only by the patients' discharge KPS but also by their final morbidity and mortality rates. Of 25 "operated" patients, 21 (84%) had a good KPS ($\leq$80%)at discharge. In addition, 10 of our 11 conservatively treated elderly meningioma patients manifested a high KPS throughout follow-up, suggesting that repeated routine MRI scanning is highly useful in this group of meningioma patients.

Conclusions

The most important treatment aim in elderly meningioma patients is tumor control and the maintenance of their ability to pursue their activities of daily life. With this in mind, we developed our multimodal treatment strategy comprised of surgery, gamma knife surgery, and careful follow-up.

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Comments

The authors present a series of 35 elderly patients (70 to 84 years) treated for meningioma. Reading the report through and through, a neurosurgically thinking reader does not get a clear message. Even the conclusions are very general: "*The most important treatment goal in elderly meningioma patients is tumor control and the maintenance of their ability to pursue the activities of daily life. With this in mind, we developed our multimodal treatment strategy comprised of surgery, gamma knife surgery, and careful follow-up.*" A neurologically minded reader might swallow this, since for him a petroclival meningioma or a left-sided parasagittal parietal meningioma, or a giant tuberculum sellae meningioma, do not represent very different categories, but just an intracranial meningioma. However, for a neurosurgical reader no doubt the age does indeed count, but much more do: the location, the size, and the conflict of the lesion with the vital neighbouring structures. There is no doubt that, not only for elderly meningioma patients but also (and even more so) for younger meningioma patients, their ability to pursue the activities of daily life after the treatment is most important. I am always questioning myself when the experts are "quoting careful follow-up" in whatever disease. Is it a good strategy or is it just waiting to minimize our responsibility in the act of treatment, since when we are treating a symptomatic patient, we certainly are not under such a burden as when we are treating a symptom-less patient. In other words, surgical or any other treatment of a symptom-less meningioma patient should have an end-result within the lowest margin of morbidity (less than 1–2%), and with no mortality.

It goes without saying that in any age group any residual meningioma should be additionally treated, most probably optimally by radiosurgery. However, to treat a large meningioma (over 3 cm in diameter) only with radiosurgery – unless other medical conditions of the patient do not allow surgery – is not a justifiable option. Since we do still believe that meningioma represents a benign disease, in my opinion, surgery is the first option for all meningiomas, over 2.5 cm in diameter. Furthermore, the location, and the conflict with neural and vascular structures have to be dealt with prior to surgery. In cases of parasagittal meningiomas, venography is inevitable, and again, all the veins should be preserved despite difficulties at surgery. To leave a part of meningioma around the bridging veins is far better than to risk the rupture of this extremely important drainage without collateral. And then additional gamma-knife treatment is the option, particularly in elderly patients.

Age does represents just one factor in meningioma patients, although certainly not the most important one, providing that the brain perfusion tests preoperatively are within normal limits. In our experience, anaesthesia – and any, even short-lasting, drops of mean arterial pressure may lead to serious consequences – is more dangerous than an appropriately designed and conducted microsurgical resection of a meningioma. Just for comparison: in meningiomas encasing the main draining veins at the parietal region or in meningiomas encasing the optic nerve and growing into the optic canal(s) and compressing the optic nerve(s) and similar situations all over the skull base, are always dangerous situations if handling at the time of the tumor resection is not optimal. Performing an optimal resection of the tumor at any location in a patient with generally diseased arteries in his 50s might be more dangerous than an optimal resection of meningioma in another patient in his 80s, when his arteries are in good condition. The age of the patient, according to his birth date is one thing, but the biological age of the patient is another thing. Age in meningioma patients is important, however it is not the most important factor in decision-making for surgery.

The authors should be congratulated for having opened up a problem which should be studied further, probably most appropriately in a cooperative study. The ideal would be to collect in such a study much larger groups of elderly patients with meningiomas at the same location. Personally, I am convinced that this study will continue, respecting all the important factors: location, size, conflicts with the vital structures, as well as regarding the type of meningioma.

Having personal experience with over 1000 intracranial meningiomas, I believe less and less that a meningioma is a benign disease – providing that the follow-up has been long enough. In this context, the age of the patient – when the disease is established – and the chosen modality of treatment have a different meaning, and management by "careful follow-up" in elderly patients, should be reconsidered.

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In this small series of patients over 70 years of age harbouring meningiomas, the authors have demonstrated that good clinical results can be achieved by a thoughtful and surgically conservative approach. I believe that most neurosurgeons would treat their elderly patients in a similar fashion. While similar and larger series are present in the bibliography, the present paper is well presented and has a nice summary of the literature on the subject.

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総説

テント上グリオーマの手術ステージ分類と手術方針

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A Proposed Staging System for Glioma Surgery

by
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Among the significant prognostic factors such as the patient's age, performance status, or tumor histopathology, the most important prognosticator for glioma patients is the degree of tumor removal. On the other hand, surgical removal should not induce aggravation of the patient's performance status. As a result, surgical planning for glioma should be carefully considered. However, there is no standard guide for preoperative planning at present. In this study, we tried to divide 390 gliomas into 5 stages according to the difficulty of surgery and then analyzed the relation between removal rate and each stage. The results demonstrated that the stage correlates with both the removal rate and the patient's survival. This grouping can be useful to discuss the feasibility of surgical planning among multiple neurosurgical institutions.

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Key words : glioma, surgery, MRI, stage, removal rate
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はじめに

グリオーマの予後因子に関する報告は以前より多数あるが，そのうち摘出度が予後に関係するか否かにおいては，賛否両論があった[1)2)6)7)9)10)11)14)]．しかしながら，近年MRIの普及により，摘出度の判定がより正確になり，それらをみるかぎりにおいては，摘出度は予後に有意に関係すると思われる[1)7)10)]．実際にLacroixら[10)]により，グリオーマの摘出率が98%以上であれば，有意に生存期間が延長するとの報告がなされている．したがって手術の目的は，可能なかぎり，最大限の摘出を目指すということになるが，摘出により患者のADLが明らかに低下すると予想される場合は，全摘出の適応にはならない．このことから，現時点でグリオーマの手術治療方針を検討するうえで問題になるのは，症状を増悪させないで腫瘍を摘出し得るかどうか判断することにある．しかしながら，それらの判断は各施設が独自に行っており，基準となるグローバルスタンダードは存在していない．そこで今回，厚生労働省「野村班，悪性神経膠腫の予後を改善するための標準的治療法の確立」における班員，班長

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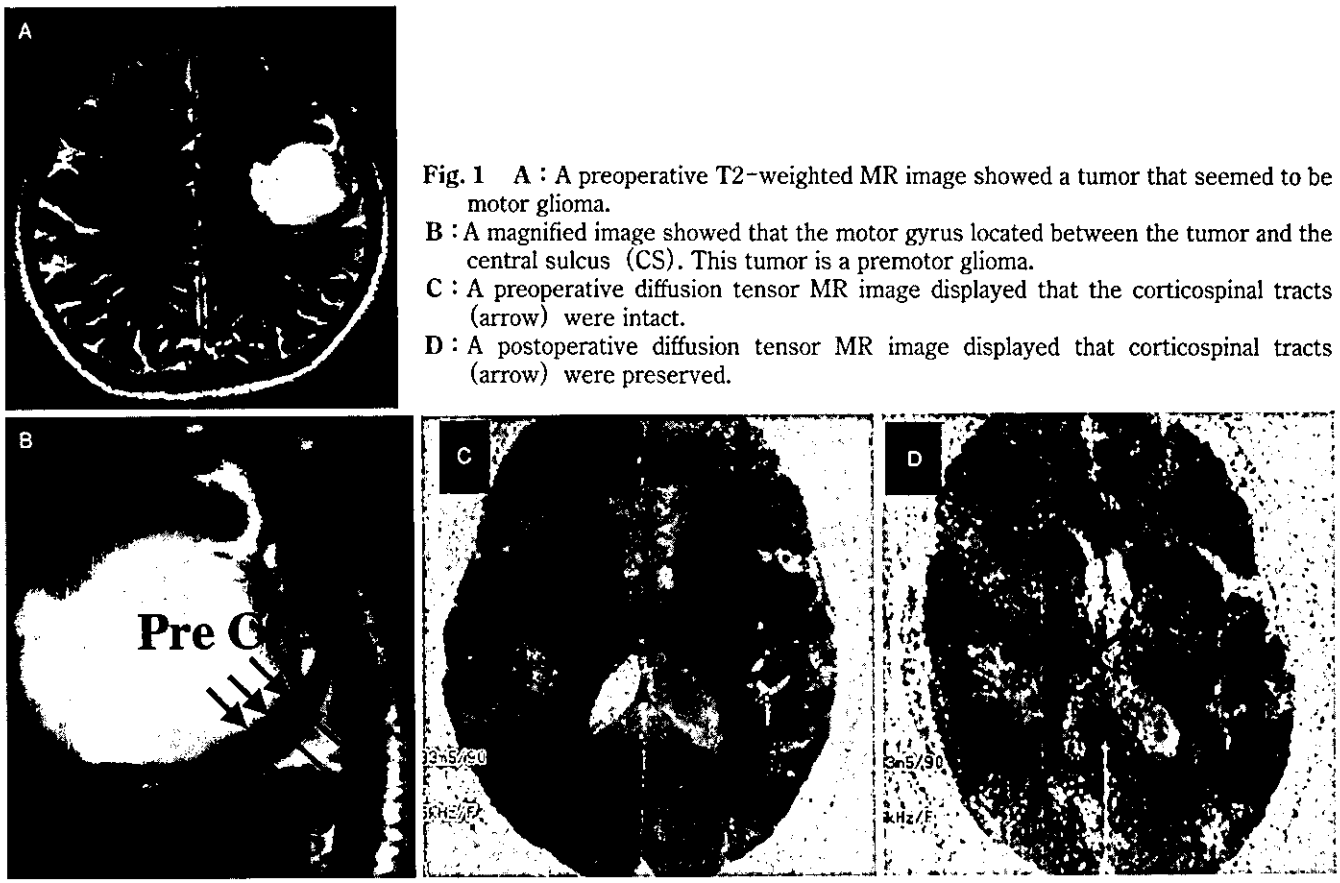

Fig. 1 A : A preoperative T2-weighted MR image showed a tumor that seemed to be motor glioma.
B : A magnified image showed that the motor gyrus located between the tumor and the central sulcus (CS). This tumor is a premotor glioma.
C : A preoperative diffusion tensor MR image displayed that the corticospinal tracts (arrow) were intact.
D : A postoperative diffusion tensor MR image displayed that corticospinal tracts (arrow) were preserved.

Table 1 Eloquent area

Motor and sensory cortex
Visual center
Speech center
Internal capsule
Basal ganglia
Hypothalamus or thalamus
Brain stem
Dentate nucleus

協力者に依頼し，各施設におけるグリオーマの術前の大きさ，存在部位，摘出度を検討することで共通のグリオーマの手術ステージ分類を作成することを試みた．

方 法

1 手術ステージ分類における問題点

ポイントは以下の3点である．

1) Tumor bulk の定義
2) Eloquent area の定義
3) Removal rate の定義

原則的には，腫瘍が T1 強調画像で造影される場合は，造影される領域を bulk と定義する．造影されない場合は T1 強調画像で，低信号の領域を bulk とする．最後に T2 強調画像でのみ所見がある場合は，T2 強調画像の高信号領域を bulk と定義する[10]．

2) Eloquent area の定義

さまざまな考え方があり，一定の見解がないが，基本的には手術前，手術後で患者の ADL を明らかに低下するものが eloquent area という考え方をすることができる．一般的には Table 1 のような領域が eloquent area として知られている[10]．しかしながら eloquent と思われる領域を摘出しても，術後症状の悪化しない症例等もあり，真の意味での eloquent area の定義は慎重でなくてはならない．eloquent area と鑑別すべき事例を提示する．

症 例：31 歳，男性．left frontal diffuse astrocytoma.

画像上腫瘍は central sulcus (CS) に接し，motor area 上に存在しているように見える (Fig. 1A)．しかしながら MRI を詳細に検討してみると，腫瘍と CS の間には 1 つの gyrus が存在しており，premotor area の astrocytoma と考えられた (Fig. 1B)．結果的に腫瘍は全摘出され，術後の麻痺は認められなかった．自験例 30 例の検討で

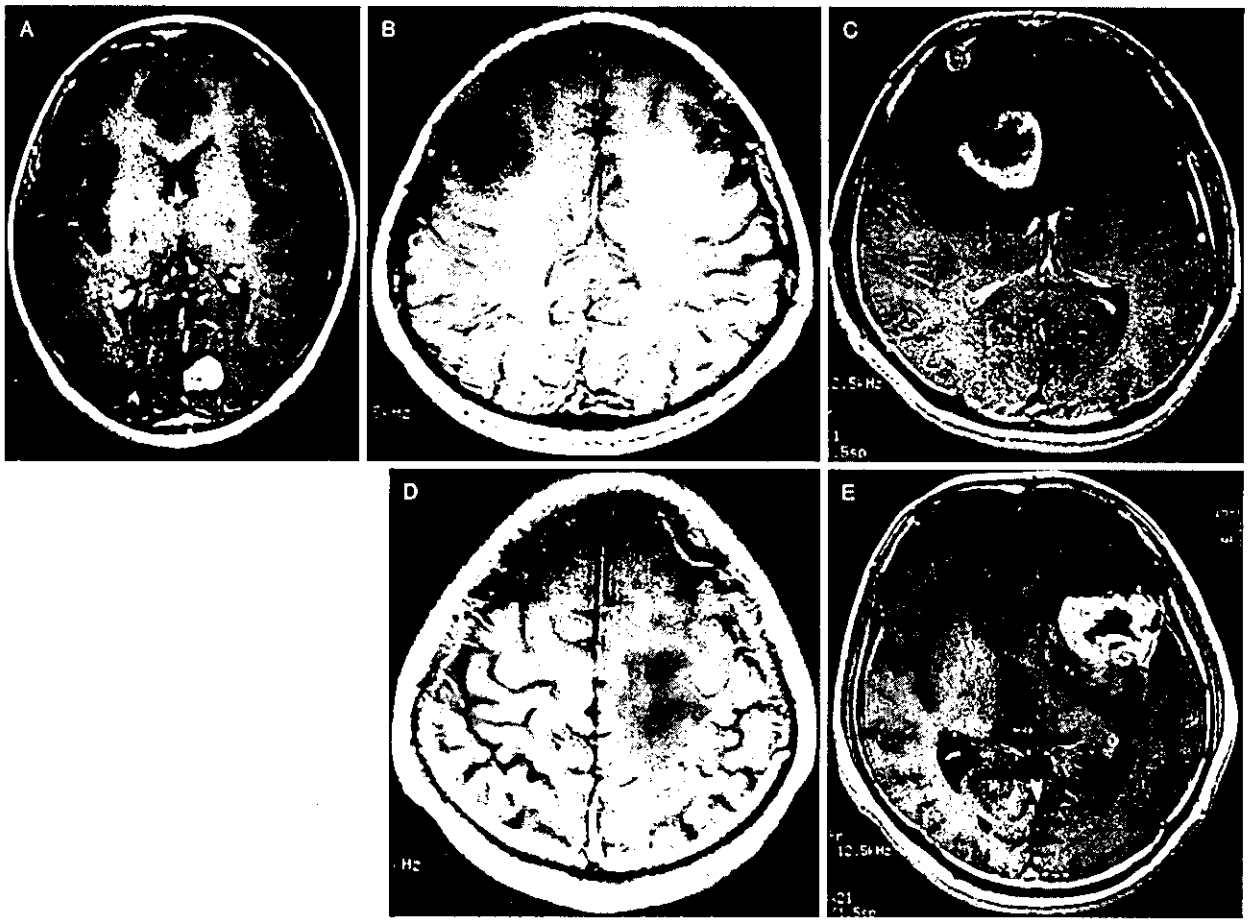

Fig. 2 A : Stage 1 glioma. A T1-weighted MR image with Gd-DTPA showed that the tumor was located within one gyrus in the non-eloquent area.
B : Stage 2 glioma. A T1-weighted MR image with Gd-DTPA showed that the tumor (2 cm) was located in the right frontal lobe.
C : Stage 3 glioma. A T1-weighted MR image with Gd-DTPA showed that the tumor (5 cm) was located in the right frontal lobe.
D : Stage 4 glioma. A T1-weighted MR image with Gd-DTPA showed that the tumor (3 cm) was located in the right fronto-parietal lobe. The tumor was beyond the eloquent area.
E : Stage 5 glioma. A T1-weighted MR image with Gd-DTPA showed that the tumor (4 cm) was located in the left fronto-temporal lobe. The tumor was beyond the sylvian fissure and extended to the basal ganglia.

Table 2 Surgical staging for glioma

Stage 1 : T size (≦1 cm) or within one gyrus
Stage 2 : Stage 1 (+1) or T size (1<T<3 cm)
Stage 3 : Stage 2 (+1) or T size (>3 cm)
Stage 4 : Stage 3 (+1) or Stage 2 (+1+1)
Stage 5 : Stage 3 (+1+1) or Stage 2 (+1+1+1) or Multiple lesions, Disseminated lesions, Extra CNS lesions
+1 : Eloquent area (motor, speech, visual) Thalamus, Basal ganglia, Bilateral lesions Sylvian fissure (insular cortex)

T : tumor, CNS : central nervous system

は，CT 上 motor area 近傍に腫瘍が存在するように見えても，MRI あるいは magnetoencephalography (MEG) より，実際に motor area に存在していた症例は 9 例 (30%) であった．次に深部白質の錐体路に関しても同様のことがいえる．腫瘍が錐体路にかかっているように見える症例でも，diffusion tensor MR image で，錐体路が intact に描出されることがある (Fig. 1C)．実際このような症例では麻痺の程度も軽いことが多く，本症例もほぼ全摘出し，麻痺の改善を認め，術後の tensor image でも錐体路は保たれていた (Fig. 1D)．このように詳細な検討を行い，eloquent area を同定することが必要である．

3) Removal rate の定義

問題になるのは，術後，摘出率を検討するためのその評価法である．MRI は必須の検査であり，かつ benign enhancement を除外するために，術後 72 時間以内に撮像

することが望ましい[1].

2 手術ステージ分類の作成

前述の問題点をふまえながらステージ分類を作成した．まず腫瘍の大きさから，Stage 1～3 に分類した（Table 2）．eloquent area（motor, speech, visual），視床，基底核に存在する病変，sylvian fissure を超え（insular cortex を含み）進展する病変，corpus callosum を超え対側に進展した病変に関しては Stage を 1 段階上げることとした．また多発病変，髄腔内播種，頭蓋外転移があるものは例外とし，大きさに関係なく Stage 5 とした．以上をまとめると Table 2 のようになった．

実際のステージ分類の例を紹介する．

症例 1：12 歳，女性．left occipital pleomorphic xanthoastrocytoma.

tumor size は 1 つの gyrus に限局しており，non-eloquent area に存在していた（Fig. 2A）．Stage 1 と判断し，腫瘍は全摘出された．

症例 2：24 歳，女性．right frontal astrocytoma.

tumor size は 1～3 cm で，non-eloquent area に存在していた（Fig. 2B）．Stage 2 と判断し，腫瘍は全摘出された．

症例 3：45 歳，男性，right frontal glioblastoma.

tumor size は 3 cm 以上で，non-eloquent area に存在していた（Fig. 2C）．Stage 3 と判断し，腫瘍は全摘出された．

症例 4：51 歳，女性．left fronto-parietal astrocytoma.

tumor size は 3 cm 以上であるが，eloquent area（motor area）に存在していた（Fig. 2D）．Stage 4 と判定し，部分摘出にとどまった．

症例 5：58 歳，男性．left fronto-temporal glioblastoma

tumor size は 3 cm 以上で，eloquent area かつ sylvian fissure を超えており Stage 5 と判定，biopsy を行い，診断を確定した．（Fig. 2E）

このような判定基準にのっとり，厚生労働省「野村班，悪性神経膠腫の予後を改善するための標準的治療法の確立」における班員，班長協力者を通じて 22 施設にステージ分類を依頼し，各施設において手術の施行された 390 例のグリオーマに関して，手術ステージ分類と摘出率の関係を検討した．同時に各症例の overall survival から他の因子とステージ分類の多変量解析を行い，Hazard ratio を計算した．

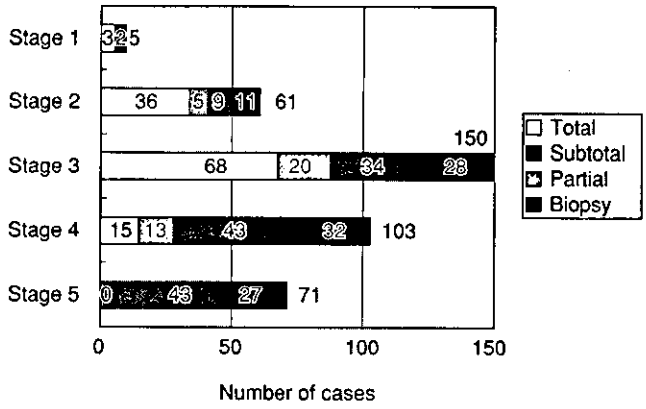

Fig. 3 Bar graph showing the number of cases for each stage

Table 3 Survival (multivariate analysis)

Sex	$p=0.3173$	Hazard ratio	0.859
Age	$p<0.0001$		1.025
AA	$p=0.0462$		1.760
GBM	$p<0.0001$		4.500
Partial	$p=0.0185$		0.629
Subtotal	$p=0.0153$		0.492
Total	$p=0.0004$		0.446
Stage	$p=0.0003$		1.424

AA：anaplastic astrocytoma
GBM：glioblastoma multiforme

結 果

各 Stage における症例数と摘出率の関係を Fig. 3 に示す．Stage 3 が最も多く，150 例（38%）を占めた．以下 Stage 4 が 103 例（26%），Stage 5 が 71 例（18%），Stage 2 が 61 例（16%）の順であり，Stage 1 は 5 例ときわめて稀であった．おおむね各施設間において摘出率に明らかな差はなかった（Fig. 3）．各 Stage での摘出率は Stage 1～3 までは，約 60%の症例で subtotal removal 以上が可能であった．一方で，Stage 4 では subtotal removal 以上の摘出率は 28%，Stage 5 では全例 partial removal 以下の摘出率であった．また多変量解析の結果では年齢，組織学的悪性度，摘出率などの従来から報告されている予後不良因子に加え，手術ステージ分類の Stage の高いものほど，予後不良である結果が示された（Table 3）．

考 察

脳腫瘍の病期分類に関しては，他臓器腫瘍と同様に UICC（International Union Against Cancer）による TMN 分類が提案された[16]．しかしながら N 因子がないことや脳の臓器としての特殊性から，一般的に普及しなかった．

また下垂体腺腫，聴神経鞘腫などの脳実質外腫瘍に対しては，独自の分類がそれぞれ提唱されている[5)13)]．

一方，グリオーマ等の脳実質内腫瘍における病期ステージ分類の試みは髄芽腫，脳幹グリオーマ，視床グリオーマで認められているが，一般的な広義のグリオーマにおいてはステージ分類は認められていない[4)8)15)]．その理由として，グリオーマは浸潤性に存在するとの考えからtumor bulkを同定することが，CT時代には困難であったからである．Burger[3)]の報告によれば，グリオーマはCTで造影される領域の周辺3 cmまで浸潤しているとされている．したがってCTの造影領域より判定される摘出度は，予後との関連があるという報告は散見されるものの，正確な摘出度を反映しているとはいいがたかった[2)]．しかしMRI出現後，その空間分解能の向上とともに，たとえグリオーマといえども，ある程度Tumor bulkの同定が可能になった．そこでわれわれは，Tumor bulkを同定したところ，グリオーマの約半数にてTumor bulkの同定がMRI上可能であることがわかった[12)]．この事実が今回の手術ステージ分類を可能にしたと考えている．

今回，考案したグリオーマの手術ステージ分類と手術摘出率の検討から，大きく分ければStage 3以下は全摘出が可能であり，Stage 4以上は全摘出が困難であるということが示唆された．それをふまえてStage 3以下で部分摘出以下になった症例を検討すると，次のようなことが原因になっていると考えられた．まず，診断目的でbiopsyを行っている症例に関しては，解析対象から除外できるものと考えられた．次にnon-eloquent areaに存在し，理論的にはsubtotal removal以上は可能ではあるがpartial removalになっている症例が，Stage 2で10例（50%），Stage 3で34例（55%）存在した．これに関しては，eloquent area近傍であった可能性などさまざまな問題点があり，今後の検討の必要がある．また，eloquent areaに存在しながら，total removalとなっている症例がStage 3で2例（3%），Stage 4において11例（73%）存在した．これに関してはeloquent areaの定義がきちんとなされていない可能性もあるが，年齢，組織学的悪性度，症例のKPSなど，各施設間における治療方針の違いなども考慮しなくてはならない．

手術ステージ分類と予後に相関があるという多変量解析の結果は，手術ステージ分類の当初の目的とは異なるものであるが，今後グリオーマの治療成績を議論するうえでも，ステージ分類が重要な因子になっていく可能性が示唆された．

今回の手術ステージ分類は，手術の難易度に関係する腫瘍の大きさ，存在部位に焦点を当てたものであるが，全国的な多施設における調査でも，手術ステージと摘出率には一定の傾向がみられた．今後さらにeloquent area等に関する詳細な基準を設定することで，より有用な分類法になる可能性がある．このようなグローバルスタンダードが，今後は必要になってくるものと思われた．

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要　旨

テント上グリオーマの手術ステージ分類と手術方針

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神経膠腫の予後を決定する因子として，手術の摘出度は最も重要な因子であり，最大限の摘出が望まれる．その一方で，腫瘍が eloquent area にある場合は，その部位の摘出は不可能とされる．したがって病変の摘出が可能であるかを判断する標準ガイドラインが必要である．そこで，腫瘍の存在部位，大きさから手術ステージ分類を作成し，国内の施設において実際に手術治療された神経膠腫をそれに基づき分類し，摘出率との関係を検討した．結果としてわれわれの作成した手術ステージ分類のステージが上がるにつれ，摘出率が下がる傾向が認められた．またステージ分類は患者の予後とも相関していた．神経膠腫の手術方針を決定するうえで，この手術ステージ分類が有用なグローバルスタンダードとなる可能性が示唆された．

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▨特集/脳ドックの新しい診療ガイドライン

4. 無症候性脳腫瘍*

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Key words：brain check, asymptomatic brain tumor, meningioma, pituitary tumor, incidentaloma

はじめに

脳の健康診断(通称：脳ドック)において腫瘍が発見されることは稀である。未破裂脳動脈瘤や無症候性脳梗塞と比べると，脳腫瘍は脳ドックの分野では'orphan disease'とも言える。しかし，腫瘍の場合は継時的に成長していく可能性があり，発見・診断時点で治療の必要性の判断が求められる。悪性腫瘍が疑われる場合は別として，無症候性の良性腫瘍の場合はその自然史が判明しないと治療の適応が決められない。しかし，MRIの一般普及後いまだ10数年であり，疾患の頻度が低いこともあって大規模な自然史研究の成果は極めて乏しい。

今回のガイドラインでは初めて「脳腫瘍および腫瘍様病変」がとりあげられた。しかし，上記のような理由でエビデンスに基づいた確たる指針は打ち出し難いのが現状である。そのため日常臨床上，比較的常識的と思われる内容となっている(表1)。

I. 無症候性脳腫瘍の種類と頻度

大きなシリーズでよく引用される論文は目下3つである。中村(1997)は，1,305例(1991年11月～1997年9月)の受診者(男843例，女462例)の中に，3例(0.2%)の脳腫瘍を発見した[11)]。内訳は，髄膜腫，下垂体腺腫および聴神経腫瘍が各1例である。Katzmanら(1999)は，1,000例(1996年5月～1997年6月)の健常者(男546例，女454例)のMRIを検討し，3例(0.3%)のグリオーマを発見した[5)]。組織学的には，low grade oligodendroglioma, pilocytic astrocytomaが各1例と，low grade glioma疑いが1例である。Onizukaら(2001)は，4,000例(1996年4月～2000年3月)の受診者(男1,987例，女2,013例)の中に，11例(0.3%)の脳腫瘍を診断した[12)]。内訳は，髄膜腫6例，下垂体腺腫3例，星細胞腫1例，類上皮腫1例である。

これら3編の論文はその対象群や検査法がそれぞれ異なっている。対象例の年齢や性別，職業や受診動機も異なるであろうし，検査法としてMRIの機種や撮像法も疾患発見率に大きな影響を与える。実際，Katzmanらの1,000例にグリオーマが3例みられ，髄膜腫がなかったというのも容易には納得しがたい。

ただ，いずれも脳腫瘍としての頻度が0.2～0.3%であったことは興味深い。一般人口における原発性脳腫瘍の年間発生頻度は人口10万人につき9.2例(0.0092%)と報告されている[1)]。そのため日常臨床ではおよそ人口1万人に1例(0.01%)と解釈している。もちろんこのような発生率と，主として中年以降の受診者における発見率とは意義が異なるが，数字の上では20～30倍という大きな隔たりがある。無症候例は無症候のままで長期間経過するものが多いことを想定させる頻度差である。

なお，本ガイドラインでは，真の腫瘍のみならず腫瘍と鑑別を要する様々な嚢胞性疾患を腫瘍様病変としてガイドラインの腫瘍の項に加えて論じている。

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* Asymptomatic Brain Tumor

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表1 無症候性脳腫瘍および腫瘍様病変
(脳ドックのガイドライン)

(推奨)
1) 下垂体部腫瘤が発見された場合，実質性でかつ鞍上進展(視神経に接触または軽度挙上)がみられれば手術(おもに経蝶形骨手術)が勧められる。嚢胞性病変およびより小さな実質性病変に対しては，当初6カ月毎に2回，以後年1回MRIによる経過観察を行う。この際同時に下垂体前葉機能を検査する。
2) 髄膜腫とみられる病変が発見された場合，蝶形骨縁内側型の腫瘍以外は，MRIで経過観察する。MRI検査の間隔は1)と同様である。蝶形骨縁内側型の髄膜腫は視力障害発症後はその回復が困難であるため，予防的な摘出術が勧められる。
3) 頭蓋内の様々な嚢胞性腫瘤(クモ膜嚢胞，コロイド嚢胞，松果体嚢胞など)が発見された場合，CTあるいはMRIで経過観察する。MRI検査の間隔は1)と同様である。
4) 1) 2) 3)とも，経過観察中に腫瘤の増大傾向あるいは個々の特殊な事情があれば，年齢，局在，手術リスクなどを考慮した上で患者に説明し，十分な理解を得て治療を行う。治療とは主として手術療法を指すが，1)と2)については定位的放射線療法(ガンマナイフなど)の適応も考慮する。
5) グリオーマを疑わせる病変が発見された場合，診断をある程度確定するための追加検査を行う。グリオーマが強く疑われる場合は手術により組織診断を確定させるが，摘出程度は発生部位によって異なる。疑診例に対しては，2カ月後再度MRIを行い，主に梗塞性病変と鑑別する。

II. 下垂体部腫瘤

下垂体の無症候性腫瘤には2つの意味がある。その1つは，従来から報告されているが，剖検下垂体における subclinical microadenoma のことである。その頻度は，大きなシリーズのみを挙げると，2.7% (27/1,000, Hardy, 1969)[4]，9.1% (145/1,600, McCormick and Halmi, 1971)[7]，22.5% (225/1,000, Costello, 1936)[2] とかなり大きな開きがある。これは'腺腫'の定義と検索の方法の差によるものと推測される。筆者らは以前(1981年)[16]，1,000例の剖検下垂体中に58例(5.8%)の subclinical microadenoma を見い出した。これらは'腺腫'例のみであるが，筆者らは直径2 mm以上の全ての腫瘍様病変を検討しなおしたところ(1994)[15]，1,000例中61例(6.1%)にこれが発見された。内訳は，ラトケ嚢胞37例，腺腫20例，出血2例，梗塞2例であった。2 mm以上の病変としたのは当時のMRIでの検出限界であり，ホルモン産生 microadenoma の画像診断上 false positive となる頻度を知ることが目的であった。

一方，通常の画像診断で偶然発見される下垂体病変は臨床用語として下垂体偶発腫(pituitary incidentaloma)と呼ばれる。この概念に包含されるものは，下垂体腺腫やラトケ嚢胞以外に，様々な嚢胞性疾患，下垂体過形成や下垂体炎(後2者はいずれも症候の乏しい病変)などである。CTスキャンのみの時代はルーチンの撮影が水平断である上，頭蓋底の骨によるアーチファクトで，下垂体病変の発見率は低かった。しかし，MRIでは鮮明な正中矢状断が基本的画像となったため，下垂体偶発腫が一躍注目されるようになった。

先にも述べたとおり，自然史がわからないと治療方針が立たないため，厚生労働省の間脳下垂体機能障害調査研究班では筆者を責任者としてその調査を実施した。その結果，下垂体疾患に関心の深い40施設から506症例が回答された。そのうち手術を施行した258例を除き，6カ月以上の間隔でMRIを行った248例について以下記述する[14,17]。

248例の内訳は，男性102例，女性146例，平均年齢48.7歳であり，追跡期間は6～173カ月(平均26.9カ月)であった。推定診断は，下垂体腺腫115例(46.4%)，ラトケ嚢胞98例(39.5%)，下垂体嚢胞8例(3.2%)，クモ膜嚢胞2例(0.8%)，生理的肥大6例(2.4%)，下垂体炎1例(0.4%)，その他18例であった。画像評価が可能であった242例において，腫瘤の経過は，不変180例(74.4%)，増大30例(12.4%)，縮小29例(12.0%)，縮小と増大を繰り返すもの3例であった。

一方，腺腫と診断した例(実質性成分主体の腫瘤)の

みで腫瘤容積の変化をみると，不変72%，増大20%，縮小10%であり，ラトケ嚢胞と診断した例では，それぞれ77%，5%，16%であった。

すなわち，腺腫と考えた例では2年強の追跡中に約20%が増大するのに対し，ラトケ嚢胞では約5%にすぎなかった。

以上の事実より，今回のガイドラインでは，実質性腫瘤で，かつ鞍上進展(視神経に接触または軽度挙上)がみられれば手術(主に経蝶形骨手術)が勧められる，とした。一方，ラトケ嚢胞を主体とする嚢胞性病変および上記よりも小さい実質性腫瘤に対しては，原則的に経過観察を勧めることとした。嚢胞性の腫瘤でももちろん増大はありうるが，視神経に対してはより圧迫が軽度であると思われる上，急激に増大する心配も少ないものと想定した。小さな実質性病変に関しては意見の分かれるところである。中高年者では経過観察でもよいが，若年者では，手術(経蝶形骨手術)を勧めるべきかもしれない。本ガイドラインでは，経過観察中に増大傾向がみられた場合に，様々な個人的背景を考慮した上で主として手術療法を行うとした。なお，実質性，嚢胞性を問わず，蝶形骨洞側に大きく進展した腫瘤に関しては言及していないが，やはり個別の事情に応じて治療適応を考慮すべきである。筆者自身としては，蝶形骨洞側へ大きく進展した実質性腫瘤はやはり経蝶形骨手術で摘除すべきであると考える。

経過観察の期間と内容であるが，当初は半年毎2回(1年)，以後は年1回のMRIと，下垂体前葉機能検査とした。最初のチェックを半年毎としたのは，稀に比較的早く増大する症例があるからである。内分泌検査は外来での採血であるので，各前葉ホルモンとともに甲状腺ホルモン(fT3とfT4)，副腎皮質ホルモン(cortisol)および性腺のホルモン(testosteroneまたはestradiol)を測定しておく。各々基礎値の単回検査であるので，末梢ホルモンのほうが意義が大きい。前葉ホルモンについてはプロラクチンの値が下垂体茎圧迫の程度を反映するが，他のホルモンは大きな変動がなければ数値自体は参考所見である。

III. 髄膜腫

無症候性の髄膜腫は，剖検時に2.3% (231/10,033)発見されるとの報告があるが(Nakasuら，1987)[8]，先にも述べたごとく，Onizukaらによると[12]脳ドックでは0.15% (6/4,000)の発見率である。剖検例では，より高齢者に多く，高齢者ほど腫瘍サイズも大きいとされているので，脳ドックの受診者の年齢層やMRIの撮像条件なども発見率に関与しているものと考えられる。

無症候性髄膜腫の自然史に関する大規模な研究はない。Kuratsuら[6]は，63例を平均2.3年みて，20例(32%)が増大したと報告した。Niiroら[10]は，高年齢者例を40例，平均3.5年みて，14例(35%)が増大，Goら[3]は，35例を平均6.2年みて，4例(11%)が増大，さらにOliveroら[13]は，45例を平均2.4年みて10例(22%)が増大したとそれぞれ報告している。観察期間や方法，増大の定義などは一定していないが，およそ2～3年の経過で20～30%の症例が増大を示すとみることができる。

増大に関与しうる因子としては，腫瘍の大きさ(大きい腫瘤)と周辺の浮腫が増大示唆要因として，腫瘍内石灰化とMRIのT2低信号が非増大示唆要因として挙げられている[3,6,9]。

無症候性髄膜腫の治療方針には未だ確たるものはないが，大半はまず経過観察でよいのではないかと考える。その観察方法はやはりMRIで当初半年毎2回，以後1年に1回とした。ただし，例外は蝶形骨縁内側型の髄膜腫である。この部位の髄膜腫は視神経管内に進展し，一度視力低下を発症すると手術により腫瘍を摘出しても視力の回復は難しい。そのため，蝶形骨縁内側型の髄膜腫が疑われた場合は，患者に十分説明をした上で予防的な腫瘍摘出術を行うことが勧められる。

IV. グリオーマ

グリオーマは基本的に悪性腫瘍であるため無症候で偶然発見されることは極めて稀である。確かにKatzmanら[5]は，1,000例中3例(0.3%)のいわゆるlow grade gliomaを発見しているが，一方でYueら[18]は，3,672例のMRIで1例もグリオーマを認めていない。Onizukaらの報告による[12]4,000例中1例(0.025%)のlow grade astrocytomaという頻度が妥当な上限ではないかと思われる。

しかし，他の偶発性腫瘤の大半が良性疾患であるのに対し，グリオーマは悪性疾患であるため，低頻度といえどもその対処には慎重でなくてはならない。主たるポイントは，low grade gliomaと脳梗塞との鑑別に求められる。そのため，グリオーマを疑わせる病変が発見された場合は，診断をある程度確定するための追加検査を行う必要がある。すなわち，MRI(ガドリニウム造影，diffusion，FLAIR)，MRS，CTスキャン(造影前後)などである。

これらの検査からグリオーマが強く疑われる場合は手術によって組織診断を確定させるが，その摘出程度は発生部位によって大きく異なる。一方，追加検査を

しても確定診断に至らない場合は，2～3カ月後に再度MRIを行う。梗塞性病変なら low intensity 病変周辺が萎縮しているが，グリオーマでは不変か何らかの進展，発育がみられる。

V. 様々な嚢胞性腫瘤など

頭蓋内には様々な嚢胞性病変が偶然発見されることが稀でない。これらの多くは非腫瘍性疾患であるが，中には腫瘍類似病変も含まれる。

具体的には，コロイド嚢胞，クモ膜嚢胞，松果体嚢胞が主であり，更には少し異なったものとして孔脳症(porencephaly)，透明中隔腔(cavum septi pellucidi)，ベルガ腔(cavum Vergae)などが挙げられる。しかし，これらの各論を述べるのは本稿の主旨ではないので省略する。

上記前3者のような頭蓋内の嚢胞性病変が無症候で発見された場合は，やはり前述したような間隔でCTスキャンあるいはMRIで経過観察を行う。

さらに，CTスキャンで low density を呈する疾患として，脂肪腫や類上皮腫があるが診療指針としては基本的に良性腫瘍のそれに準ずる。

おわりに

脳ドックの検診において脳腫瘍が発見されることは比較的稀である。もちろん広義の脳腫瘍の中には多くの種類の腫瘍類似病変も含まれる。しかし，中には真の neoplasm も存在し，これらは原則的には成長・増大する性格を有する。ただし，その成長速度や成長限界は未だ十分に知られていない。そのため今回日本脳ドック学会の示したガイドラインにおいても大半の例で経過観察を勧めている。

今後，脳ドックをはじめ画像検査で偶然発見された脳腫瘍の成長解析が進めば，より明確な診療方針を提唱できるものと考える。

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Treatment of low-grade oligodendroglial tumors without radiotherapy

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Abstract—The authors prospectively treated 18 consecutive patients with low-grade oligodendroglial tumors without postoperative radiotherapy. The treatment strategy was as follows: follow-up after total resection and chemotherapy after subtotal resection or biopsy. All patients were alive and 17 patients (94%) were progression-free after a median follow-up of 4.7 years. The results suggested that radiotherapy could be postponed until clinical progression in the treatment of low-grade oligodendroglial tumors.

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Oligodendroglioma is a rare intracranial tumor, which is conventionally treated with surgery with postoperative radiotherapy or follow-up.[1] Although many retrospective studies suggest that postoperative radiotherapy for oligodendrogliomas has some benefit,[2-5] the efficacy of radiotherapy is still unsettled. Radiation-induced toxicities, including dementia and radiation necrosis in particular, may occur in long-term survivors.

It has been recently reported that oligodendrogliomas including low-grade tumors respond to chemotherapy.[6] Since low-grade oligodendrogliomas can be indolent for years, some researchers recommend starting chemotherapy first to postpone radiotherapy until clinical progression.[1] In the present study, we prospectively treated patients with low-grade oligodendroglial tumors without radiotherapy. As a rule, chemotherapy was used to treat the incompletely resected tumors. We estimated the outcome of the patients as compared with the published reports, and discussed the necessity of radiotherapy for patients with low-grade oligodendroglial tumors.

Methods. Since 1995, we have treated patients with oligodendroglial tumors without postoperative radiotherapy according to the following protocol: follow-up after total resection and chemotherapy (ACNU 75 mg/m^2 for day 1, vincristine 1 mg/m^2 for days 8 and 29, procarbazine 100 mg/day for days 8 to 21; four cycles a year for 2 years) after subtotal/partial resection. In this study, the outcome of the patients was evaluated. The primary endpoints of our study were progression-free survival time and overall survival time. Patients were enrolled in this study if their tumors had been histologically confirmed as newly diagnosed low-grade oligodendroglioma or oligoastrocytoma. The patients were required to provide informed consent. The age, sex, original pathologic diagnosis, initial symptom, tumor location, imaging findings, and extent of resection were recorded. A minimum of 1 year of clinical follow-up information was required. The date of diagnosis was the date of initial surgery in 11 patients. However, in 7 patients abnormal imaging findings consistent with low-grade brain tumors were documented more than 1 year before obtaining pathologic material. In these patients, the initial imaging date was used as the date of diagnosis; and subsequently the diagnosis was pathologically confirmed as oligodendroglial tumor. The median interval from onset of symptoms to tissue diagnosis was 6 years for the seven patients. Tumor progression was defined as a change in the radiographic characteristics such as increased tumor size or new enhancement with or without clinical worsening. The progression-free and overall survival distributions were estimated using Kaplan-Meier methodology.

Results. Eighteen patients were treated and followed up for a median period of 4.7 years. There was no patient who was excluded from the analysis because of early recurrence within 1 year. Fifteen patients had oligodendrogliomas (grade 2) and three had oligoastrocytoma (grade 2). There were 13 men and 5 women. The tumors were frontal in eight patients, multilobular in four, temporal in five, and parietal in one. The patients' characteristics are summarized in table 1.

The initial presenting symptom was seizure in 7 (39%), headache in 4 (22%), memory disturbance in 2 (11%), and other neurologic deficits in 4. During this study, seizures developed in a total of 10 patients (56%). MRI and CT were obtained in all patients. Contrast enhancement was noted in 9 patients (50%). Calcification was noted in 10 patients (56%).

Five patients (27.8%) underwent total resection (postoperative MRI ensured tumor-free margin), and eight patients (44.4%) underwent subtotal tumor resection. Biopsy was carried out for five patients (27.8%) to avoid severe neurologic deficits after resection. No patient received radiotherapy.

Twelve patients received the chemotherapy immediately following the surgical resection. Although the patients who underwent biopsy or subtotal tumor removal were essentially candidates for adjuvant chemotherapy, one patient refused receiving chemotherapy after subtotal tumor removal. We estimated the tumor response to chemotherapy using MRI after the chemotherapy. We classified the response into three categories as follows: 1) responder, more than 50% reduction in volume; 2) nonresponder, more than 25% increment in volume; 3) no change, all other situations. Among the 12 tumors treated with chemotherapy, 7 (58.3%) including 2 oligoastrocytomas were responders and the other 5 cases were catego-

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Table 1 Patient characteristics

Characteristics	Values
n	18
M:F	13:5
Age at diagnosis, y, mean (range)	45.8 (9–69)
Age at operation, y, mean (range)	48.3 (23–69)
Follow-up period, y, median (range)	4.65 (1.0–15.6)
Tumor site	
Frontal	8
Temporal	5
Multilobular	4
Parietal	1

rized as no change. The chemotherapy was well tolerated. Although the primary toxicity experienced by patients during the chemotherapy was myelosuppression, grade 3 or 4 leukopenia that mandated treatment delay occurred only in two patients (11%).

All the patients were alive and did not have uncontrolled tumor progression (figure, A). Recurrence occurred in one patient with oligodendroglioma (5.6%) that had been completely resected, and the time for tumor progression was 2.5 years (figure, B). This patient had not received chemotherapy immediately after surgical resection. The recurrent tumor shrank after chemotherapy and was well controlled.

Discussion. We demonstrated that 94% of oligodendroglial tumors could be controlled without radiotherapy during a median follow-up of 4.7 years in our series. Although this follow-up period is not enough to give a definite conclusion, the 5-year survival rate in our study was favorable as compared with those in the previous reports[2-5] (table 2). It was suggested that radiotherapy could be postponed when tumor recurrence or progression occurred following surgical resection and chemotherapy. Large-scale clinical follow-up is required for determining the role of adjuvant radiotherapy in control of oligodendroglial tumors.

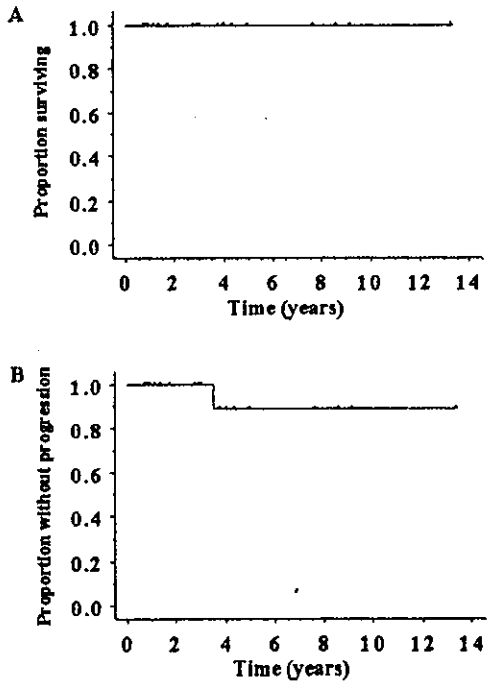

Figure. Kaplan-Meier curve shows overall (A) and progression free survival (B) of 18 patients. Tick mark indicates last follow-up.

Table 2 Five-year survival rates of patients with oligodendroglial tumor in previous reports

		5-year survival rate, %	
Reference	n	With RT	Without RT
2	170	36	27
3	81	46 (<50 Gy)	63
		61 (>50 Gy)	
4	137	70	45
5	52	89	63

RT = radiotherapy.

Although many authors have suggested some benefit of radiotherapy in the treatment of oligodendrogliomas,[1-5] all those studies are retrospective. There are two prospective randomized studies on low-dose and high-dose fractionated radiotherapy for low-grade gliomas.[7,8] The authors demonstrated that the survival was significantly better in the patients with oligodendroglioma and oligodendroglioma-dominant histology, and that the low-dose radiotherapy is as effective as the high-dose for low-grade gliomas. The efficacy of early postoperative radiotherapy for patients with low-grade gliomas was also investigated.[9] The authors reported that early postoperative conventional radiotherapy improved the time to tumor progression, but not overall survival. Thus, the efficacy of early postoperative radiotherapy for oligodendrogliomas has not been established.

Patients with oligodendroglioma need care for radiation-related complications because they are relatively long survivors as compared with those with high-grade gliomas. It was reported that high frequency of radiation-induced toxicity, such as radiation necrosis and cognitive dysfunction, follows radiotherapy.[1] Since low-grade tumors can be indolent for years, the risk-benefit relationship of radiotherapy needs to be considered.

It has been demonstrated that anaplastic oligodendroglioma may be remarkably chemosensitive when associated with allelic loss of 1p/19q.[10] The molecular genetic analysis would be helpful to determine the therapeutic strategy especially for tumors with anaplastic components. Our results suggest that surgical resection and chemotherapy for residual tumors are generally enough for the initial treatment of low-grade oligodendrogliomas. It would be

better to postpone radiotherapy until tumor progression after chemotherapy becomes uncontrolled.

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process. As the scar matures, the continuous vascular regression may eventuallly transform the richly vascularized granulation tissue into a pale and avascular scar. Thus, the neomembrane of the fibrous capsule may not be seen if the time for vascular regression is long enough. In general, the capsules of chronic ICHs were commonly shown as ring enhancement after contrast medium injection,[1,2,7] but only faint enhancement was seen in our case. This may be attributed to vascular regression in the neomembrane.

How did the fibrous capsule undergo calcification and ossification? Based on the encephalomalacia changes in brain tissue adjacent to the haematoma, the patient might have suffered a severe brain trauma which caused progressive cell death and necrosis. Heterotopic bone formation tends to occur in necrotic tissue. The calcification of dead and necrotic tissue is frequently encountered and known as dystrophic calcification.[13] The membrane phospholipids of necrotic tissue, collagen fibrils or denatured proteins have been proven to be the centre for initiation of calcification.[13,14] Through the model of membrane-facilitated calcification,[15] the necrotic tissue around the hematoma underwent dystrophic calcification. Similar calcification phenomena could be found in chronic epidural and subdural haematomas.[10,11,16] The hematoma of the present case was a mixture of necrotic debris, cholesterol cleft, haemosiderin and sand-like calcification. The unabsorbed haematoma may be decomposed and degradation of red blood cells (RBCs) and white blood cells (WBCs) may occur over time causing deposition of haemosiderin and cholesterol, the latter being a component of cell membranes. The cholesterol cleft, haemosiderin and sand-like calcification of the semiliquid contents may be the result of insufficient degradation or clearance of RBCs, lipids and minerals.

The calcified chronic ICH in the present case was originally considered to be an extra-axial lesion. However, a thin layer of brain cortex covering over the lesion could be detected on the brain MRI (Fig. 1B). This was verified during surgery. The presentation of the intra-axial lesion as an extra-axial one on brain MRI may be attributed to the encephalomalacia changes in the surrounding brain tissue, which caused widening of the subarachnoid space. Comparing the MR images and skull plain film with the resected specimen, the upper and major portion of the mass showing intermediate signal intensity on T1WI and low signal intensity relative to the gray matter on T2WI was a mixture of necrotic debris, cholesterol cleft, haemosiderin and sand-like calcification (Figs. 1B and C and Fig. 2). The middle part of the lesion demonstrated low signal intensity on T1WI and high signal intensity on the T2WI, indicative of water contents (Figs. 1B and C and Fig. 2). The calcification, shown on the peripheral and lower portions of the mass in the skull plain film, appeared as high signal intensity on T1WI and T2WI (Fig. 1B–D and Fig. 2). The image characteristics are compatible with the gross appearance of the lesion and have not been reported previously.

In conclusion, in the present case, head injury or occult vascular malformation may be the cause of the initial intracerebral haemorrhage, and repeated haemorrhages from the fragile vessels of the neomembrane may have played a role in the expansion of the ICH. The neomembrane vessels may regress after a long period such as over the 28 years in our case. Calcification and ossification of the capsule were produced through the process of dystrophic calcification. It is recommended that in patients with encapsulated ICH, that the removed lesion and the adjacent brain tissue should be thoroughly examined to rule out the presence of any vascular malformation.

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A rare case of metastatic renal cell carcinoma resembling a nerve sheath tumor of the cauda equina

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Summary We present a rare case of solitary metastasis to the cauda equina from the kidney. The patient was a 68-year-old man with a two-year history of low back pain. His past medical history revealed a renal cell carcinoma diagnosed seven years earlier. His lumbosacral MR imaging showed a well-demarcated, intradural extramedullary mass at the L3 level. He underwent an L2-4 laminectomy. The operative findings of the tumor quite resembled that of a nerve sheath tumor. It did not infiltrate into the subarachnoid space and involved only one spinal nerve. Pathology of the tumor was a metastasis of the renal cell carcinoma. Only 10 cases with such a metastasis to the cauda equina have been reported in the English

literature. We added the 11th and reviewed the literature with reference to tumor pathologies, clinical findings and route of metastasis to the cauda equina.

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INTRODUCTION

The majorities of cauda equina tumors are of glial or nerve sheath origin,[3,5,7,15] and metastases from outside the central nervous system are extremely rare. We present a case of solitary metastasis to the cauda equina. His past medical history included renal cell carcinoma; nevertheless, the radiographic and the operative findings suggested a nerve sheath tumor. To our knowledge, only 10 cases with metastatic tumor of the cauda equina from outside the central nervous system have been reported in detail in the English literature.[1,2,4,6,8–12,14] The literature is reviewed with reference to tumor pathologies, clinical findings and route of metastasis to the cauda equina.

CASE REPORT

A 68-year-old male had a two-year history of low back pain, which worsened in recumbency or at sneezing and became progressively severe. His medical history revealed a renal cell carcinoma diagnosed seven years earlier and treated by a right nephrectomy. He had then three times undergone partial pneumonectomies for metastatic lung tumors from the primary lesion five years (left S1+2 resection), three years (right S2 resection) and one year (left S6 resection) prior to admission. On admission, he complained of low back pain projecting into the right L5 region. He had full muscle strength and intact sensation as to light touch, pinprick, and joint position sense. Deep tendon reflex showed no laterality. Straight leg raising test was limited on the right side. Plain X-ray films showed no abnormality. Lumbosacral MR imaging revealed an intradural extramedullary mass measured 2.5 cm craniocaudally by 1.3 cm anteroposteriorly at the L3 level (Fig. 1). The mass was well demarcated and demonstrated homogeneous enhancement. Abdominal MR images and radioisotope images revealed no tumor recurrence of the primary lesion and no tumor invasion to the intrapelvic or paraspinal organs.

He underwent an L2-4 laminectomy. Dural opening revealed an ocher-color ovarian-shape tumor. The tumor was elastic hard, well demarcated and did not infiltrate into the subarachnoid space. It involved only one spinal nerve that fanned out over the surface of the tumor. We resected the nerve proximal and distal to the tumor and could remove the tumor easily (Fig. 2). Pathology of the tumor was a metastatic renal cell carcinoma (Fig. 3). His postoperative course was excellent. He noticed a complete relief of radicular pain and left hospital on the twelfth postoperative day without neurological deficits. No recurrence was observed with a follow-up period of two years after surgery.

Fig. 1 Lumbosacral MR imaging (heavy T2 weighted image in sagittal plane) showing an intradural extramedullary mass located at L3 level.

Fig. 2 An operative view showing well demarcated tumor. The tumor did not infiltrate into the subarachnoid space and involved only one spinal nerve. It could be easily removed after resecting the nerve.

Fig. 3 Photograph showing the interface between the tumor and nerve root. Tightly packed clear cells are typical for renal cell carcinoma.

DISCUSSION

Spinal metastasis occurs in 10–60% of all carcinomas. However, intradural spinal metastasis is less common and represents only