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Is additional mesial temporal resection necessary for intractable epilepsy with cavernous malformations in the temporal neocortex?

Yumi Kashida [a,b], Naotaka Usui [b,*], Kazumi Matsuda [b], Kiyohito Terada [b], Koichi Baba [b], Akihiko Kondo [b], Daisuke Hirozawa [b], Takayasu Tottori [b], Tadahiro Mihara [b], Ryosuke Hanaya [a], Kazunori Arita [a], Yushi Inoue [b]

[a] Department of Neurosurgery, Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima, Japan
[b] National Epilepsy Center, Shizuoka Institute of Epilepsy and Neurological Disorders, Shizuoka, Japan

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ABSTRACT

Purpose: Cavernous malformation (CM) in the temporal neocortex causes intractable epilepsy. Whether to resect additional mesial temporal structures in addition to the lesionectomy is a still controversial issue. To clarify the need for the procedure, we retrospectively analyzed pre- and postoperative clinical data of patients with surgically removed CM.

Subjects and methods: We included data from 18 patients with CM in the temporal neocortex who presented with intractable epilepsy. Eleven patients of our early series were treated with extended resection, i.e., lesionectomy and the resection of additional mesial temporal structures. Seven patients underwent lesionectomy, i.e., removal of the CM and of hemosiderin-stained surrounding brain tissue. Pathological assessments of the resected hippocampus were performed. Chronic intracranial electroencephalography (EEG) recordings were obtained in 6 patients. We performed perioperative neuropsychological assessments in all patients.

Results: The seizure outcome was recorded as Engel class I in 17 patients (94.4%); Ia = 12 (66.7%) Ib = 2 (11.1%), Ic = 1 (5.6%), Id = 2 (11.1%), and class IIb in one patient (5.6%). Adding resection of the mesial temporal structures to lesionectomy did not alter the seizure outcome. Pathology of hippocampus revealed limited neuronal loss in CA4. Ictal onsets in the ipsilateral lateral cortex were detected in all 6 patients who underwent intracranial EEG. In 4 patients each, we also detected ictal onsets from the ipsilateral mesial temporal structures and from the contralateral temporal lobe. Postoperatively, in the patients where their CM was located in the language-dominant hemisphere (n = 10), the full-scale intelligence quotient (IQ) and the performance IQ increased ($p < 0.05$), whereas the verbal memory (WMS-R) deteriorated in two of 5 patients.

Conclusion: Excellent seizure outcomes were obtained even the lesionectomy alone. To confirm appropriate surgical strategy for lateral temporal CM with intractable epilepsy, further studies in large sample size are needed.

1. Introduction

Cavernous malformations (CMs) in the central nervous system are benign vascular malformations; they are found on magnetic resonance imaging (MRI) studies in 0.4% to 0.9% of the population [1–3]. About half of patients with a central nervous system CM had at least one seizure before the diagnosis [1–5]. The seizure recurrence rate is 5.5% per patient-year [3]. Although seizures can be medically controlled in 47% to 60% of patients [6,7], surgery has been recommended as the most effective treatment in patients with drug-resistant epilepsy [8]. The reported rate of postoperative freedom from seizures is 62.5% to 88.3% [9–12]. The cause of surgical failure is still unclear, and it has been an issue of debate whether adding mesial temporal resection to lesionectomy would benefit patients with cavernoma in the temporal neocortex. Several authors reported the usefulness of electrocorticography (ECoG) for identifying the region to be resected, and proposed that extended resection based on ECoG may improve surgical outcome [13–15]. To clarify the optimal surgical strategy for these patients, we retrospectively assessed the relationship between the surgical outcome and clinical, electrophysiological, and pathological data.

2. Subjects and methods

From March 1987 through March 2014, 38 patients with intractable CM-related epilepsy underwent resective surgery at National Epilepsy Center, Shizuoka Institute of Epilepsy and Neurological Disorders. Of these, 18 met our inclusion criteria: the lesion was evaluated on MRI scans, it was located lateral to the collateral sulcus, and the postoperative follow-up period was 2 years or longer.

* Corresponding author at: Department of Neurosurgery, National Epilepsy Center, Shizuoka Institute of Epilepsy and Neurological Disorders, Shizuoka 420-8688, Japan.
E-mail address: usui-nsu@umin.ac.jp (N. Usui).

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All 18 patients underwent noninvasive investigations, including long-term video-electroencephalography (EEG) monitoring, neuroimaging studies (MRI and computed tomography), and neuropsychological tests. The magnetic field intensity of the MRI studies was 0.3 T in the 4 early patients (cases 1–4) and 1.5 T in the other patients (cases 5–18). The MRI sequences of fluid-attenuated inversion recovery (FLAIR), T1 weighted images, T2 weighted images, and T2 star weighted images were applied. Neuropsychological tests included the Wechsler Adult Intelligence Scale (WAIS)/WAIS-R/WAIS-III and the Wechsler Memory Scale (WMS)/WMS-R. The language-dominant side was determined with the Wada test in all patients.

This study was approved by the ethics committee of National Epilepsy Center, Shizuoka Institute of Epilepsy and Neurological Disorders.

2.1. Surgical procedures and postoperative seizure outcomes

Patients with intractable epilepsy and CM in the lateral temporal lobe who were treated from 1987 through 1999 underwent extended resection regardless of intracranial EEG findings (lesionectomy plus resection of the anteromesial part of the temporal lobe). Six patients in our early series underwent intracranial EEG recordings. The resected area included the amygdala, 2.5–3.0 cm of the anterior part of the hippocampus, and the adjacent parahippocampal gyrus (Fig. 1). From 2000 through 2004, we chose either extended resection or lesionectomy alone. Lesionectomy consisted of resection of the cavernoma and surrounding hemosiderin-stained tissue (Fig. 2). From 2005 on, lesionectomy became the first treatment choice. Exceptionally in Patient 15, to make him seizure-free was of utmost importance considering the individual situation of the patient. Therefore, we chose extended resection.

The postoperative seizure outcome was assessed based on the Engel classification and the International League Against Epilepsy (ILAE) seizure outcome classification. We analyzed the relationship between the seizure outcome and possible prognostic factors such as the lesion side, the lesion size, the seizure semiology, the age at seizure onset, the age at surgery, the seizure frequency, scalp EEG findings, use of chronic intracranial EEG, and the extent of resection. Unitemporal spikes were defined as more than 90% of spikes recorded over the affected temporal region, and bitemporal spikes as others. Seizure onset on ictal EEG was defined by the occurrence of localized, sustained, rhythmic, or spiking EEG pattern, visually distinguished from background activity. The laterality and distribution of the ictal abnormalities were noted.

2.2. Intracranial EEG analysis

Intracranial EEG electrodes were placed on the bilateral temporal lobes by using a combination of depth and subdural electrodes [16]. Depth electrodes were stereotactically placed in the bilateral hippocampi and amygdala. One week later, video-EEG monitoring was started and continued for 6 to 11 days to record at least 3 clinical seizures.

We defined the seizure onset site as the following [17]: (1) ipsilateral lateral onset, discharge originating from lateral cortex ipsilateral to the lesion and recorded by subdural electrodes; (2) ipsilateral mesial onset, discharge originating from the ipsilateral hippocampus and/or amygdala and recorded by depth electrodes; (3) contralateral onset, discharge originating from the contralateral temporal lobe; (4) unlocalized, the laterality of the ictal discharge could be assessed but we could not determine whether it originated from mesial or lateral cortex; and

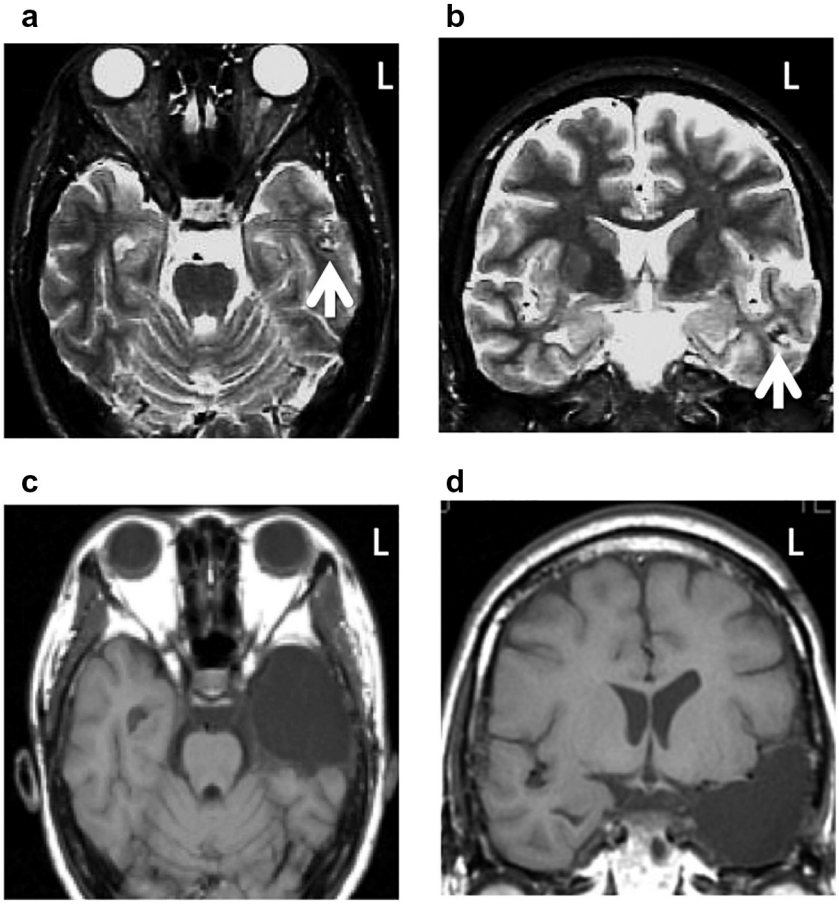

Fig. 1. Patient 7. Magnetic resonance images. This patient underwent extended resection. (a, b) Preoperative T2-weighted axial (a) and coronal (b) images. The cavernous malformation (CM) was located in the left middle temporal gyrus (white arrows). (c,d) Postoperative T1-weighted axial (c) and coronal (d) images. The anterior temporal lobe including the CM and mesial temporal structures was removed.

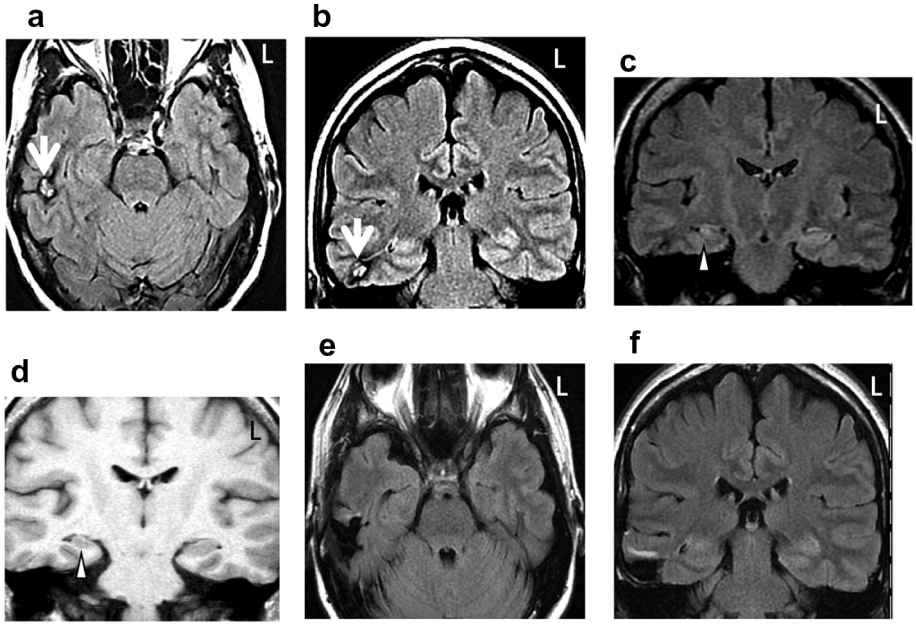

Fig. 2. Patient 13. This patient underwent lesionectomy only. (a, b) Preoperative fluid-attenuated inversion recovery (FLAIR) images. The cavernous malformation (CM) was located in the right inferior temporal gyrus (white arrows). (c, d) Preoperative coronal FLAIR and T1 weighted images. Slight atrophy of the right hippocampus is suggested (white arrowheads) (e, f) Postoperative FLAIR images. The CM and surrounding hemosiderin-stained area were removed. Mesial temporal structures of the temporal lobe were preserved.

(5) unlateralized, the laterality of the ictal discharge could not be identified. When the site of origin of ictal discharge was identified as equivalent to (1), (2), or (3) but the discharge propagated to other regions within 1 s, the onset site was judged to be uncertain, and the case was classified as (4) or (5).

Interictal discharges in the ipsilateral mesial temporal structure were also assessed. The spikes were graded as (++) when their mean frequency was 5 or more spikes per 10 s, as (+) when there were 4 or fewer per 10 s, and as (−) when no or only ambiguous spikes were detected.

2.3. Pathology of the resected hippocampus

A sufficient amount of hippocampal tissue for pathologic assessment was obtained in 6 of 11 patients who underwent extended resection. The cell density of each hippocampal subfield (the fascia dentate, the hilus of the dentate gyrus (CA4), CA3, CA2, CA1, prosubiculum, subiculum, presubiculum, and parahippocampal gyrus) was evaluated using the Klüver–Barrera staining method. Less than 70% decrease of pyramidal or granular cell density compared with normal controls was defined as "significant neuronal loss" [18].

2.4. Neuropsychological assessments

All patients underwent neuropsychological intelligence tests before and 2 years after surgery. In the early period of our series, we used the WAIS, then the WAIS-R, and in the later period, we used the WAIS-III test. For memory evaluation, we applied the WMS test in the early period (case1–7); in the later periods, we used the WMS-R test (case8–18); WMS-R includes various subcategories (visual memory index,

Table 1
Clinical profiles of the 18 patients.

Pt	Age at onset	Age at surgery	Lesion side	Size (mm)	Clinical seizures				Scalp EEG	
					Aura	Seizure manifestations	sGS	CPS*	Interictal	Ictal
1	23	34	Lt	25–30	Autonomic (EAS)	IC, OA, GA	No	2–3/M	BI	Nonlateralizing
2	22	26	Lt	20–25	No	IC, OA, GA	No	1–2/M	BI	Nonlateralizing
3	21	30	Lt	10–15	Psychic	IC, GA	No	2–3/M	BI	BI
4#	21	29	Lt	20–30	No	GA, hemiconvulsion	Yes	1/W	Lt T	Lt. T
5	27	36	Lt	20–25	Autonomic (flushing)	IC, OA, GA	No	2–3/M	BI	Nonlateralizing
6	19	49	Rt	10–15	Indescribable	IC, OA	Yes	1/W	BI	Nonlateralizing
7#	22	37	Lt	<10	No	IC, OA, GA	Yes	1–2/M	BI	BI
8	26	51	Rt	15–20	No	IC, GA	No	1–6/M	BI	Rt. T
9	22	36	Rt	25–30	Autonomic (palpitation)	IC, OA, GA	No	1/W	Rt T	Rt. T
10	22	24	Lt	5–10	No	IC	Yes	2–3/M	Lt T	Lt. T
11	18	41	Lt	15–20	Dysphasic	IC, OA	No	1–2/W	BI	BI
12	18	30	Rt	20–25	Autonomic (palpitation)	IC, OA, GA	Yes	1–2/W	Rt T	Rt. T
13	31	43	Rt	10–15	Somatosensory (lt. hand numbness)	IC, OA, GA	Yes	3/M	BI	Rt. T
14	33	45	Rt	15–20	Cephalic	IC, vocalization	Yes	2–3/W	Rt T	Rt. T
15	39	45	Rt	<10	No	IC, GA	Yes	2/M	BI	Rt. T
16	23	49	Lt	10–15	Indescribable	IC, OA	Yes	2–3/M	BI	Lt. T
17	25	28	Lt	10–15	Dysphasic	IC	No	Daily	No paroxysms	Lt. T
18	27	36	Rt	10–15	Autonomic (palpitation)	IC, OA	Yes	2–3/W	Rt T	Rt. T

Age at onset: age at the first seizure, Lt: left, Rt: right, T: temporal, CPS*: frequency of complex partial seizures, IC: impaired consciousness, EAS: epigastric ascending sensation, OA: oroalimentary automatism, GA: gestural automatism, sGS: secondarily generalized seizure, BI: bitemporal independent, W: week, M: month.
#: Patients 4 and 7 were included in our earlier study [17].

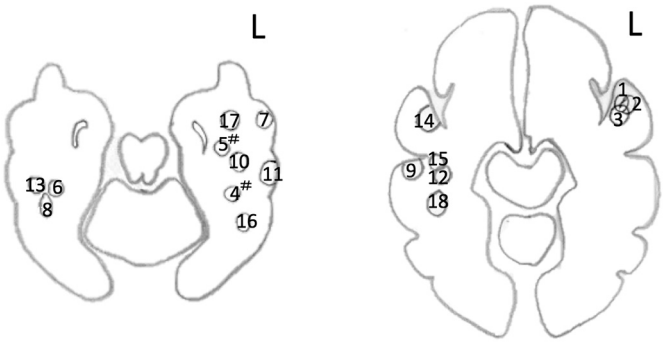

Fig. 3. Schematic representations of axial sections showing the cavernous malformation locations. Numbers are the case numbers. #: lesions in which surgery led to permanent postoperative neurological deficit (mild dysnomia).

verbal memory index, general memory index, attention/concentration, delayed-recall memory index) whereas WMS does not. Comparison of pre- and postoperative general and verbal memory scores was done in 11 patients who underwent WMS-R test.

2.5. Statistical analysis

Depending on the dataset characteristics, we applied the Fisher exact probability test or the Student *t*-test. Differences of $p < 0.05$ were considered statistically significant. Statistical analyses were performed using JMP 11.2 statistical software (SAS Institute, Cary, NC, USA).

3. Results

3.1. Clinical profiles (Table 1)

The mean age at seizure onset was 24.4 years (range, 18–39 years); at the time of surgery, it was 37.2 years (range, 24–51 years). No hippocampal abnormalities were seen on MRI scans from 17 out of patients. In the remaining case (Patient 13), atrophy of the hippocampus ipsilateral to the CM was observed. Since our basic surgical strategy for CM was "lesionectomy" at that time, lesionectomy was performed for this particular patient. In 10 patients, the CM was located in the language-dominant hemisphere, and in 8 patients, it was in the nondominant hemisphere (Fig. 3).

Auras were reported by 12 patients; they were autonomic in 5; dysphasic in 2; and somatosensory, psychic, or cephalic in one each. In 2 patients, they could not be classified, and were therefore defined as indescribable. All 18 patients had complex partial seizures, and 10 had a history of secondarily generalized seizures. The seizure frequency of complex partial seizure was monthly in 10 patients, weekly in 7, and daily in one.

Scalp EEG revealed interictal discharges in bitemporal regions in 11 patients; in 6 patients, they were unitemporal. The seizure onset was unilateral in 11, bitemporal independent in 3, and unlateralized in 4 patients.

3.2. Postoperative seizure outcome (Table 2)

Mean postoperative follow-up was 9.9 years (range, 2.0–26.6 years). At the latest follow-up, the seizure outcome was recorded as Engel class I in 17 patients (94.4%; Ia = 12 [66.7%], Ib = 2 [11.1%], Ic = 1 [5.6%], Id = 2 [11.1%]) (Table 2). In the remaining one patient, it was class IIb (5.6%). Of the 11 patients treated by extended resection, 10 were in Engel class I (90.9%) (Ia: 8 [72.7%], Ic: 1 [9.1%], Id: 1 [9.1%]), and the other was classified as being in Engel class IIb. No interictal EEG abnormalities were detected on postoperative EEG in this patient (Patient 9) who did not become seizure-free (class IIb). All 7 patients treated by lesionectomy alone were in Engel class I (Ia: 4 [57.2%], Ib: 2 [28.6%], Id: 1 [14.3%]). There was no significant difference in the rate of Engel class Ia seizure outcomes between patients treated with extended resection and with lesionectomy alone ($p = 0.63$, Fisher exact probability test).

At the latest follow-up, 2 patients (cases 4 and 5) presented with mild dysnomia. Both harbored lesions in the basal temporal region on the language-dominant side: the fusiform gyrus in case 4 and the inferior temporal gyrus in case 5 (Fig. 3). Both patients had undergone extended resection. Visual field defects (VFD) was also investigated. The data of postoperative visual field were available for all but one patient (Case 5). Asymptomatic upper quadrantanopia occurred in all patients (10/10, 100%) who underwent extended resection, whereas it occurred in 2/7 patients (28.6%) who underwent lesionectomy.

3.3. Prognostic factors

Assessment of the relationship between the postoperative seizure outcome and possible prognostic factors identified none (Table 3). Additional resection of the anteromesial part of the temporal lobe did not alter the seizure outcome.

Table 2
Surgical procedure, pathology, and outcome.

Patient	Language dominancy	Intracranial EEG	Surgery	Hippocampal neuron loss	Seizure outcome*	Follow-up (y)	Postoperative deficits #	
								VFD
1	ND	Performed	Extended	CA4	Ic (1)	26.4		HUQ (R)
2	D	Performed	Extended	CA4	Ia (1)	26.6		HUQ(R)
3	D	Performed	Extended	CA4	Ia (1)	26		HUQ(R)
4	D	Performed	Extended	Not available	Ia (1)	22.6	Dysnomia	HUQ(R)
5	D		Extended	Not available	Ia (1)	10	Dysnomia	Not available
6	ND		Extended	Not available	Id (1)	16.1		HUQ (L)
7	D	Performed	Extended	CA4	Ia (1)	7.5		HUQ(R)
8	ND		Extended	Not available	Ia (1)	7.8		HUQ (L)
9	ND		Extended	CA4	IIb (2)	12.5		HUQ(L)
10	D		Lesionectomy	Not applicable	Ia (1)	4.2		HUQ (R)
11	D	Performed	Lesionectomy	Not applicable	Ib (1)	2		HUQ(R)
12	ND		Extended	Not available	Ia (1)	2		HUQ(L)
13	ND		Lesionectomy	Not applicable	Ia (1)	5.1		HUQ(L)
14	ND		Lesionectomy	Not applicable	Ia (1)	2		No defect
15	D		Extended	CA1 & CA4	Ia (1)	2		HUQ(L)
16	ND		Lesionectomy	Not applicable	Ia (1)	2.1		No defect
17	D		Lesionectomy	Not applicable	Ib (1)	2		No defect
18	D		Lesionectomy	Not applicable	Id (1)	2		No defect

D: language-dominant hemisphere, ND: language-nondominant hemisphere, *: seizure outcome at the latest follow-up (Engel classification and last available outcome (ILAE classification) in parenthesis)), #: neurological deficit at the latest follow-up, Extended: extended resection, HUQ: homonymous upper quadrantanopia, L: left, R: right, VFD: visual field defect.

Table 3
Comparison of variables between patients with and without postoperative seizures.

Variables	All patients (n = 18)	Seizure-free (Engel class Ia) (n = 12)	Persistent seizures (n = 6)	p value
Gender (male/female)	8/10	6/6	2/4	0.64[a]
Mean age at surgery (range)	37.2 (24–51)	37.1 (24–51)	37.3 (28–49)	0.95[b]
Mean age at seizure onset (range)	24.4 (18–39)	25.4 (18–39)	22.3 (18–27)	0.19[b]
Mean seizure duration before surgery; years (SD)	11.3 (8.9)	10.3 (8.0)	13.3 (11.1)	0.57[b]
Mean seizure duration before surgery (≥10 y/<10 y)	9/9	6/6	3/3	1.00[a]
Mean seizure frequency per month (SD)	5.3 (6.7)	3.3 (2.5)	9.4 (10.1)	0.21[b]
Size of lesion (≥15 mm/<15 mm)	9/9	6/6	3/3	1.00[a]
sGS +/−	10/8	4/8	4/2	0.32[a]
Scalp EEG findings (unitemporal/bitemporal)	5/13	2/10	3/3	0.27[a]
Use of intracranial EEG	6/12	4/8	2/4	1.00[a]
Surgery (extended resection/lesionectomy)	11/7	8/4	3/3	0.63[a]

SD: standard deviation, sGS: secondarily generalized seizure. a: Fisher's exact probability test, b: Student's *t*-test, both for comparison of the seizure-free and persistent seizure groups.

3.4. Pathology of the hippocampus

None of the 6 hippocampal specimens subjected to pathologic study revealed severe neuronal loss in the CA1–CA4 subfields, as would be seen in hippocampal sclerosis ILAE type 1 [19] (Table 2). In cases 1, 2, 3, 7, and 9, we observed neuronal loss limited to the CA4 region (Fig. 4). In case 15, we noted neuron loss in CA1 and CA4.

3.5. Chronic intracranial EEG findings

In 6 patients (cases 1–4, 7, and 11), we performed chronic intracranial EEG recordings and identified the site and side of seizure onset (Table 4). A total of 43 complex partial seizures, 7 simple partial seizures, and 10 secondarily generalized seizures were recorded, as were approximately 140 subclinical seizures.

In all 6 patients, seizures with onset at the lateral cortex ipsilateral to the lesion were recorded. In 4 patients (cases 1, 2, 4, and 7), seizures originating at the ipsilateral mesial temporal structure were recorded (Fig. 5); in patients 1 and 4, these were clinical seizures, and in patients 2 and 7, they were subclinical seizures. Patients 2, 3, 7, and 11 experienced seizures that originated at a site contralateral to the lesion (Fig. 6); they were clinical in patients 2 and 11 and subclinical in patients 3 and 7.

In addition to spikes in ipsilateral lateral temporal cortex, all 6 patients manifested interictal spikes in the ipsilateral mesial temporal structures; in cases 3, 4, and 7, they were recorded as frequent (5 or more spikes per 10 s).

3.6. Neuropsychological assessments

We divided our 18 patients into groups that had undergone surgery on the language-dominant hemisphere (group 1, n = 10) and the non-dominant hemisphere (group 2, n = 8). Postoperatively, the full-scale intelligence quotient (FSIQ) and the performance IQ (PIQ) increased significantly from the preoperative level in group 1 ($p < 0.05$); the change in the verbal IQ score was not significant. Group 2 manifested no significant changes (Table 5). We also divided our patients into subgroups based on the hippocampus preservation in each group to clarify the effect of medial temporal structure resection (Table 5). No statistically significant perioperative changes were detected since the number of patients in each subgroup was small.

Fig. 7 shows the perioperative WMS-R scores of 11 patients. One of the 5 patients in group 1 experienced a decline in the general memory quotient of more than 10 points. Two of the 5 patients in group 1 manifested a decrease in the verbal memory quotient of more than 10 points; the patients had undergone lesionectomy only. None of the 6 patients in group 2 manifested a decrease of more than 10 points in either score.

4. Discussion

To clarify the need for extended resection of mesial temporal areas in patients with CM-associated intractable epilepsy, we retrospectively analyzed clinical, electrophysiological, neuropsychological, and pathological data in 18 patients who underwent surgical treatment for this condition. We did not find any indication that ECoG or extended resection improved outcomes in these patients.

4.1. Seizure outcomes and prognostic factors for seizure control

A main characteristic of our study is that we included only patients with intractable epilepsy, and we specifically selected CMs located in the temporal neocortex. In our series, the postoperative seizure outcomes were better than those reported in earlier series [10–12,20]. Engel class I was the surgical outcome in 94.4% of our 18 patients. We do not have a clear explanation for unfavorable outcome of one patient (Patient 9: class IIb). Although according to Rosenow et al. [8], the lesion size, seizure type, seizure frequency, epilepsy duration, and preoperative EEG findings are prognostic factors, we found no prognostic factors.

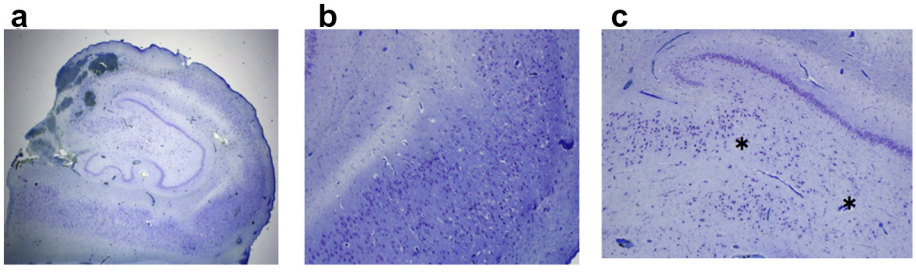

Fig. 4. Patient 2. Klüver–Barrera hippocampal staining. (a) Low magnification. (b) Neuron density in the CA1 segment was normal. (c) Neuronal loss (indicated with an *) was limited to the CA4 region.

Table 4
Number of seizure discharges recorded by intracranial EEG.

	Ictal discharges																				Interictal spikes
	Ipsilateral												Contralateral				Unlateralized				
	Lateral				Mesial				Unlocalized												
Patient	SPS	CPS	sGS	SCS	SPS	CPS	sGS	SCS	SPS	CPS	sGS	SCS	SPS	CPS	sGS	SCS	SPS	CPS	sGS	SCS	Ipsilateral mesial
1	3			6		5	1														+
2		4						1		3				3							+
3		7		1												16					++
4		2	1	40		5	1														++
7		6	2	>50				2							2			2	3		++
11		4		>50									4	2							+

SPS: simple partial seizure, CPS: complex partial seizure, sGS: secondarily generalized seizure, SCS: subclinical seizure.

We considered multifocal activity in the scalp EEG reflected the seizure arising from ipsilateral and contralateral temporal lobes. These are considered to be due to "secondary epileptogenesis (we discussed it in later section; 4.3 Intracranial EEG findings)", and this secondary epileptogenesis was of reversible status that would vanish after surgery ipsilateral to the CMs, so they did not correlate with seizure prognosis. Neither the extent of resection nor the use of intracranial EEG predicted an Engel class Ia surgical outcome in our study. Moreover, duration of epilepsy did not influence outcome. Some authors found that longer duration of epilepsy negatively influenced the seizure outcome [8,10,13,21]. The reason why no prognostic factor was found may be because of the small sample size of our study. Further studies with an increased number of patients will be necessary.

Whether the resection of brain tissue immediately surrounding the CM leads to a better seizure outcome remains controversial [8,22]. In all of our patients, we resected the hemosiderin-stained tissue surrounding the CM; consistent with the results of Baumann et al. [20], this method yielded good seizure outcomes. Although this issue remains still controversial, the ILAE the task force recommended resection of the gliotic hemosiderin stained tissue whenever possible from the point of the pathophysiology, as seizures do not arise in the CM itself, which contain no neurons, but rather in the surrounding gliotic tissue with hemosiderin. [8].

4.2. Hippocampal pathology

A pathologic study revealed no typical hippocampal sclerosis in any of our 6 specimens; although in 5, we noted neuron loss limited to CA4. Neuronal loss in CA4 has been called "endfolium sclerosis" [23–25]. This limited neuronal loss in CA4 tends to be seen in patients with temporal lobe epilepsy accompanied by a mass lesion [19]; it may be the result of frequent seizures rather than a cause of epilepsy. In patients with epilepsy caused by CM, hippocampal resection may not be necessary.

4.3. Intracranial EEG findings

Few chronic intracranial EEG recordings have been reported in patients with CM [17,26]. Sevy et al. [26] reported 6 cases of patients who underwent intracranial EEG and suggested that the relationship between the CM and the epileptogenic zone is potentially complex. However, resection was done only in 2 of the 6 patients, and the

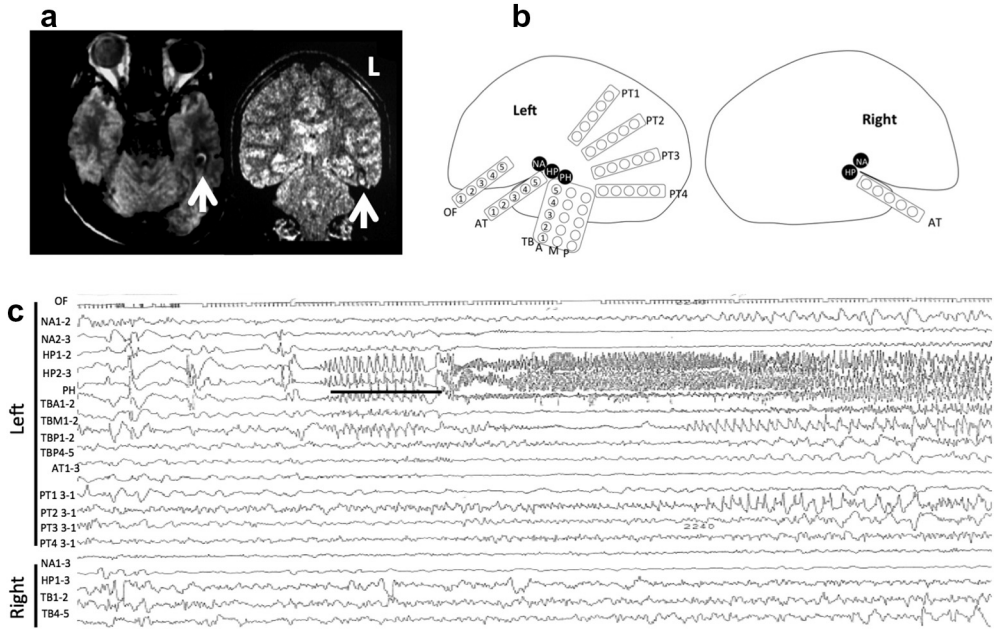

Fig. 5. Patient 4. Ictal discharges from the ipsilateral mesial temporal region were detected with chronic intracranial electroencephalography (EEG). (a) MRI showing a cavernous malformation in the left fusiform gyrus (white arrows). (b) Location of the intracranial electrodes. NA: depth electrodes in the amygdala, HP: depth electrodes in the hippocampus, PH: depth electrodes in the parahippocampal gyrus, OF: orbitofrontal region, AT: anterior temporal region, TBA: anterior temporal basal region, TBM: middle temporal basal region, TBP: posterior temporal basal region, PT: parietotemporal region. (c) Ictal EEG recorded during a complex partial seizure revealed fast, high-voltage activity in the left mesial temporal region. It spread over the adjacent temporal basal area.

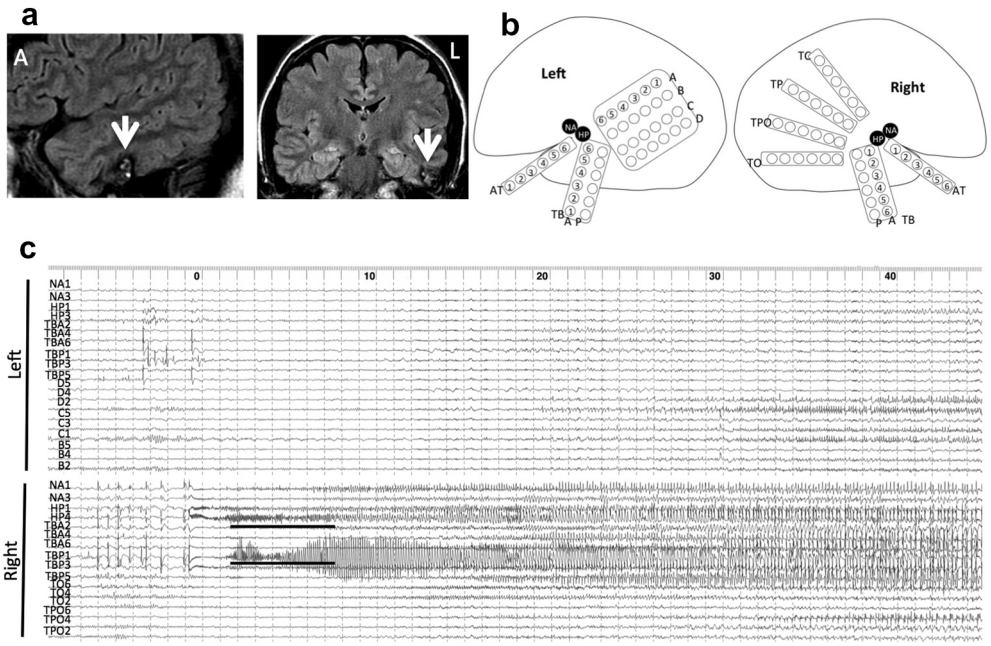

Fig. 6. Patient 11. Ictal discharges from the contralateral mesial temporal region detected by chronic intracranial EEG recordings. (a) MRI showed a cavernous malformation in the left inferior temporal gyrus (white arrows). (b) Location of the intracranial electrodes. NA: depth electrode in the amygdala, HP: depth electrode in the hippocampus, AT: anterior temporal region, TBA: anterior temporal basal region, TBP: posterior temporal basal region, TC: temporocentral region, TP: temporoparietal region, TPO: temporoparietaloccipital region, TO: temporooccipital region. (c) Intracranial EEG showed fast, high-voltage activity originating in the contralateral (right) mesial temporal structures. It spread over the right temporal lobe.

relationship between intracranial EEG findings and surgical outcome was not assessed.

In 4 of 6 patients with intracranial EEG, we recorded ictal discharges from the mesial temporal structure ipsilateral to the lesion. In our earlier study of patients with epilepsy with mass lesions in the temporal neocortex [17], which included 2 patients also included in the present study, we identified an ictal onset in the ipsilateral mesial temporal lobe in 7 of 15 patients (46.7%). This phenomenon is potentially explained by "secondary epileptogenesis" [27], but a preoperative MRI study showed no hippocampal abnormality in any of these patients. In addition, neuron loss was restricted to CA4 in hippocampal specimens from 3 of 4 patients with independent mesial-onset seizures in this series. Our earlier study of mass lesions in the temporal neocortex [17] also found that seizures with onset in the mesial temporal cortex were not associated with the typical hippocampal neuron loss. Therefore, even in patients with ipsilateral mesial temporal seizure onset recorded by intracranial EEG, additional hippocampal resection is not necessary.

In addition, intracranial EEG recorded clinical seizures originating at a site contralateral to the CM in 4 of 6 patients; they disappeared after surgery on the lesional side (Engel class I). Clinical seizures originating from contralateral temporal lobe recorded by intracranial EEG have been reported by our previous study [17], and we considered this phenomenon due to "secondary epileptogenesis [27]". Our present data and our previous study showed excellent seizure outcome after ipsilateral surgery even for the patients with contralateral intracranial seizure patterns. Moreover, several scalp EEG studies [28,29] support our findings, so even if clinical seizures originating from the temporal lobe contralateral to the lesion are recorded by intracranial EEG, surgery ipsilateral to the CM is indicated.

Whether using ECoG during surgery for intractable epilepsy related to temporal lobe lesions is beneficial remains controversial [14,15,21,30]. We recorded interictal discharges in the mesial temporal structure in all 6 patients who underwent intracranial EEG. Nonetheless, in 1 of these 6 patients, lesionectomy with sparing of the mesial temporal structure achieved a favorable outcome (Engel class I). We conclude that interictal mesial temporal spikes by themselves cannot be used as an indicator for additional mesial temporal resection.

4.4. Neuropsychological outcome

Previous reports of CM-related epilepsy have not presented neuropsychological data. We found that the FSIQ and PIQ scores significantly

Table 5
Changes in WAIS scores (based on the hemisphere where the lesion was located).

Patient group		WAIS								
		FSIQ			VIQ			PIQ		
		Pre-op	Post-op (2 y)	p	Pre-op	Post-op (2 y)	p	Pre-op	Post-op (2 y)	p†
Language-dominant n = 10	Mean (SD)	87.7 (13.8)	91.6 (14.4)	0.0095	85.1 (15.1)	86.5 (15.1)	0.39	93.4 (12.5)	100.3 (13.6)	0.015
Extended resection (Hip. resected) n = 6		90.7 (12.9)	94.8 (11.8)	0.095	85.8 (13.8)	88.2 (13.4)	0.40	99.0 (9.82)	105.0 (11.6)	0.20
Lesionectomy (Hip. spared) n = 4		83.0 (6.16)	84.8 (8.38)	0.56	84.5 (10.1)	83.8 (10.9)	0.66	84.3 (5.38)	88.5 (4.65)	0.39
Language-nondominant n = 8	Mean (SD)	93.1 (13.3)	93.0 (10.6)	0.97	91.5 (14.6)	90.9 (10.5)	0.83	96 (9.7)	96.6 (11.8)	0.87
Extended resection (Hip. resected) n = 5		95.4 (18.8)	92.6 (17.4)	0.42	93.6 (21.1)	90.4 (19.1)	0.17	97.8 (13.3)	97.0 (13.1)	0.87
Lesionectomy (Hip. spared) n = 3		89.7 (13.6)	96.3 (10.7)	0.060	87.3 (15.0)	92.0 (5.20)	0.54	94.0 (10.4)	102 (16.5)	0.22

WAIS: Wechsler Adult Intelligence Scale, FSIQ: full-scale intelligence quotient, VIQ: verbal intelligence quotient, PIQ: performance intelligence quotient, op: operation.
† Student *t*-test.

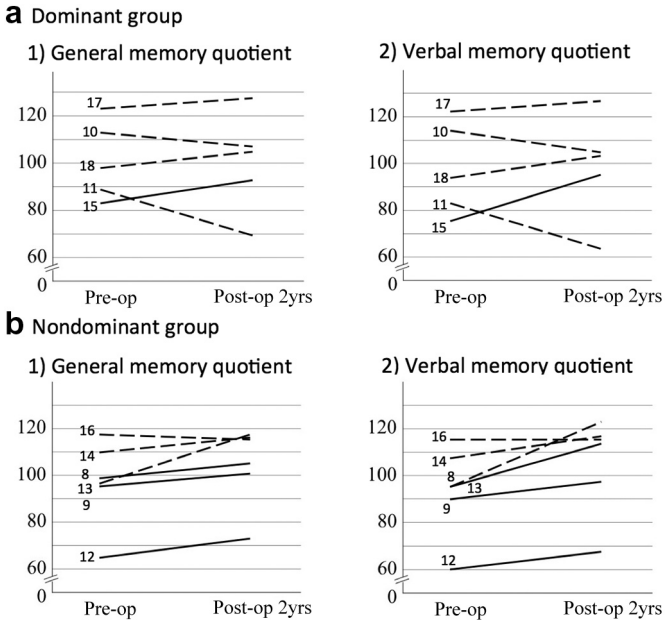

Fig. 7. Changes in the WMS-R scores. (a) Patients with lesions in the language-dominant hemisphere (group 1). (b) Patients with lesions in the language-nondominant hemisphere (group 2). Solid line: extended resection, dashed line: lesionectomy only. Pre-op, preoperative; post-op, postoperative.

increased postoperatively in patients whose CM was located in the temporal lobe of the language-dominant hemisphere. It is contemplated that the risk of IQ decline after surgery may be low even in patients with CM in the language-dominant hemisphere.

Unlike the IQ tests, pre- and postoperative memory function tests (WMS-R) showed a decline in verbal memory of greater than 10 points in two of 5 patients with language-dominant hemispheric involvement. Both patients had undergone lesionectomy. In case of mesial temporal lobe epilepsy, resection of the hippocampus results in the postoperative verbal memory deterioration in left-sided surgery [31], and anterior temporal lobectomy, which includes the additional resection of temporal neocortex, can produce more serious cognitive impairment [32]. Even a lesionectomy can produce memory impairment in some patients with language-dominant hemispheric CMs, extended resection in the same patients might lead to more serious damage in memory function.

4.5. Surgical strategy for CMs in the temporal neocortex

Our study showed that the seizure outcomes in patients treated by lesionectomy or extended resection were excellent. Pathological studies of resected hippocampal specimens revealed that neuron loss was limited to CA4 even in patients whose intracranial EEG recordings revealed a seizure onset at mesial temporal structures.

Extended resection was performed during the early period in our institute. Later on, considering that lesionectomy is usually sufficient for seizure relief, lesionectomy gradually became the first choice. Several authors reported that ECoG-guided extended resection may improve postoperative seizure outcome [14,15,21]. Von der Brelie et al. [21] reported that patients with the most drug-resistant epilepsy (66 cases; 87%) underwent extended resections. They suggested that outcome can be good if more extensive resections are used and if noninvasive and/or invasive presurgical epileptologic workup is used. They speculated that the frequent use of invasive evaluation techniques is most likely to produce good outcomes, although, statistically, invasive monitoring did not improve outcome in the groups with more longstanding types of epilepsy [21]. For clarifying the usefulness of intracranial EEG for deciding whether to resect mesial structures, further studies are necessary. Complication of intracranial EEG cannot be ignored. It potentially has 9.2% of clinically relevant complications [33], and the indication should be carefully considered.

A high-resolution MRI can help to determine whether or not to resect the mesial temporal lobe structure, if it is available [34,35]. The patients with intractable epilepsy who have dual pathology (CM + hippocampal sclerosis) may obtain better postoperative seizure outcomes by extended resection.

Neuropsychological data were not investigated in the previous studies [15,21]. Since our data indicated verbal memory deterioration in two of 5 patients with language-dominant hemispheric CMs, the risks for deterioration in memory function if the mesial temporal structures are removed should be considered in each individual patient.

In addition to memory dysfunction, symptomatic visual field defects (VFD) were seen in 37 of 389 patients (9.5%), and persistent neurologic deficits were seen in 2 of 389 patients (0.5%) in a large series of mesial temporal lobe surgery [36]. In our series, contralateral upper quadrantanopia occurred in all of the patients who underwent extended resection. Therefore, in patients with intractable epilepsy associated with CM in the lateral temporal cortex, lesionectomy, including resection of the hemosiderin-positive rim, should be the first choice for surgical treatment. Use of invasive monitoring or intraoperative ECoG is not mandatory. When the initial operation fails to control the seizures, subsequent mesial temporal resection may be a choice.

5. Limitations

The main limitation of our study is the sample size, which was small because we included only patients with intractable seizures who harbored neocortical temporal CM and who met strict inclusion criteria. Another limitation is that the choice of surgical procedures mainly reflects our surgical strategy at the time. Although the number of patients is small, the sample is clinically very homogenous. Therefore, we believe that the comparison between the patients with lesionectomy and those with extended resection is still meaningful.

6. Conclusion

We assessed the clinical data of 18 patients with intractable epilepsy who had undergone surgery to remove a CM in the temporal neocortex. We also evaluated chronic intracranial EEG recordings and the pathology of the resected hippocampal specimens. Excellent seizure outcomes were obtained even in patients who underwent lesionectomy alone. Therefore, we suggest that the basic surgical strategy for intractable epilepsy due to CM in the temporal neocortex should be lesionectomy alone, especially in patients whose lesion is located in the language-dominant hemisphere. Our suggestion must be validated by prospective studies on larger cohorts.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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