Surgical Treatment for Intractable Epilepsy Caused by Cavernous Angioma in the Temporal Lobe of the Dominant Hemisphere

Three Case Reports

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Abstract

The surgical treatment modality for intractable epilepsy with cavernous angioma in the dominant hemisphere is still unclear. Three patients with medically intractable seizures associated with cavernous angioma in the dominant hemispheric temporal lobe underwent tailored resection based on magnetic resonance (MR) imaging, single photon emission computed tomography (SPECT), electroencephalography monitoring (from scalp and sphenoidal electrodes), and neuropsychologic assessment. Epileptogenic zones were located in the area surrounding the angioma in all patients and mesial temporal dysfunction in two patients. The adjacent cortex and gliotic tissues containing hemosiderin were resected, in conjunction with either total or partial resection of the nidus. Intraoperative electrocorticography (ECoG) was then performed. Additional resection of the mesial temporal structures or multiple subpial transection was performed as indicated by the ECoG findings. All three patients have been seizure free and showed no language or cognitive deterioration for 30, 18, and 14 postoperative months, respectively, while receiving tapered antiepileptic medication. Tailored resection based on electrophysiological data, MR imaging, SPECT, and intraoperative ECoG is effective for the treatment of medically intractable seizure associated with cavernous angioma in the temporal lobe of the dominant hemisphere.

Key words: surgical treatment, intractable epilepsy, cavernous angioma, tailored resection

Introduction

Cavernous angiomas cause epileptic seizures in nearly 50% of all cases, and tend to be intractable to medication in cases of mesial temporal or cortical lesions. Epileptic seizures are believed to result from the gliotic reaction to the deposition of hemosiderin and other blood products brought about by microhemorrhage from the lesion. Magnetic resonance (MR) imaging accurately depicts such lesions and thus increases the chances for successful surgical treatment outcome in patients. However, the surgical treatment methodology, especially related to the extent of brain resection, continues to be a subject of considerable debate. For example, whether standard temporal lobectomy is justified for the treatment of chronic seizure with cavernous angioma in the temporal lobe.

We surgically treated three patients with medically intractable epilepsy caused by cavernous angioma in the temporal lobe of the dominant hemisphere, using tailored resection based on electrophysiological data, modern imaging modalities, and intraoperative electrocorticography (ECoG).

Case Reports

Case 1: A 26-year-old right-handed male, working as a sales clerk in a grocery store, had suffered from complex partial seizures (1-2 times per month) and secondarily generalized tonic-clonic seizures (3-5 times per month) for 7 years and had gradually de-
Fig. 1  Case 1. Preoperative coronal magnetic resonance (MR) image (left) revealing a heterogeneously enhanced small lesion (arrow) in the fusiform gyrus surrounded by a low intensity area. Fluid-attenuated inversion recovery image (center) showing a hyperintense area (arrow) in the head of the hippocampus medial to the lesion. Single photon emission computed tomography scan (right) revealing a low perfusion area (arrow) in the left mesial temporal lobe.

Fig. 2  Case 1. Intraoperative electrocorticograms (center, right) recorded from a grid array placed on the lateral temporal surface and a flexible multicontact electrode (arrows) inserted into the inferior horn (left). No seizure activity was recorded from the grid array. Rhythmic spikes and slow waves were seen (center) in the No. 3 electrode placed on the head of the hippocampus. The No. 1 and No. 2 electrodes were placed on the body of the hippocampus. Only small spikes were recorded from the electrode inserted into the inferior horn (right) after hippocampectomy.

veloped memory disturbance. Medication with carbamazepine and zonisamide had failed to control the seizures. Scalp electroencephalography (EEG) showed interictal spikes in the left temporal lobe. Prolonged video-EEG monitoring showed ictal onsets, developing into a generalized tonic-clonic seizure, in the left anterior temporal and sphenoidal leads. Neuropsychological testing revealed severely compromised cognitive function, with a full scale intelligent quotient (IQ) of 57 according to the Wechsler Adult Intelligence Scale-Revised (WAIS-R). MR imaging depicted a small cavernous angioma surrounded by an area of hemosiderin deposition in the left fusiform (lateral occipitotemporal) gyrus (Fig. 1 left). Fluid-attenuated inversion recovery (FLAIR) imaging showed the left hippocampus as higher intensity compared to the contralateral region (Fig. 1 center). Interictal single photon emission computed tomography (SPECT) revealed low perfusion areas in the fusiform gyrus and the mesial temporal structures (Fig. 1 right). Wada's amytal test showed left-sided dominance of the patient's lan-
guage and verbal memory functions.

An area of the left anterolateral temporal lobe, 3 cm from the tip, including the cavernous angioma and the surrounding area containing hemosiderin, was resected through a frontotemporal craniotomy. ECoG was then performed using a flexible electrode inserted into the inferior horn and a grid array placed on the lateral surface of the temporal lobe under general anesthesia with 2.5% sevoflurane inhalation (Fig. 2 left). Rhythmic spikes and slow waves were recorded from the electrode on the head of the hippocampus (Fig. 2 center). The anteromedial temporal structure including the head of hippocampus was then removed. ECoG recorded from the electrode inserted into the inferior horn after the mesial temporal resection showed only slow spikes without slow waves (Fig. 2 right).

Postoperatively, the patient was treated with 400 mg/day of zonisamide. He has had no epileptic seizures in the 14 months since surgery. Deterioration of recent memory transiently occurred for several days after the surgery. He has suffered from no language or cognitive problems since then and has returned to his former job.

**Case 2:** A congenital deaf-mute, 17-year-old, right-handed high school boy had suffered for 3 years from 8-16 episodes of complex partial seizures per month, with occasional secondary generalization. He had been treated with phenytoin, zonisamide, and carbamazepine, with blood concentrations above the minimal effective levels, including a toxic level of 32.8 μg/ml phenytoin. Intercital scalp and sphenoidal electrode EEG showed intermittent and focal spike discharges bilaterally in the temporal leads. The ictal discharges originated in the left temporal lobe. Whether the ictal onset was localized to the mesial or lateral temporal structures could not be determined. T2-weighted MR imaging demonstrated a cavernous angioma surrounded by a low intensity area in the white matter deep in the left middle and inferior temporal gyri (Fig. 3 left). Even FLAIR imaging did not show any abnormalities in the medial temporal structures. SPECT detected a small area of low perfusion in the lateral side of the left temporal lobe. Intraoperative ECoG, recorded through strip electrodes inserted under the temporal lobe so that the most distal electrode recorded from the parahippocampal gyrus and the grid array was placed on the temporal surface, showed spike discharges only on the lateral temporal cortex.

The cavernous angioma was resected together with the surrounding gliotic tissue containing hemosiderin. ECoG after the lesionectomy showed persistent independent spike activities in the surrounding cortices, possibly including a part of the verbal cognitive center. Multiple subpial transections were performed in these cortices (Fig. 3 right). ECoG after the transections showed remarkable subsidence of spike activity.

In the early stages following the surgery, the patient had two spells of automatism. The patient has now been seizure free for 30 months. He has received tapered doses of antiepileptics and has shown no neurological deterioration resulting from the surgery.

**Case 3:** A 61-year-old right-handed unemployed male had suffered for more than 20 years from complex partial seizures, which occasionally developed into generalized seizures. The seizures occurred 2-8 times per month despite medication with valproate, zonisamide, and carbamazepine. The blood concentrations of these drugs exceeded the

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**Fig. 3** Case 2. T2-weighted magnetic resonance image (left) showing a small nidus (arrow) deep in the middle and inferior temporal gyri surrounded by a hypointense area. Intraoperative photograph (right) showing the resected area (asterisk) in the temporal cortex (T). Parallel stripes surrounding the defect show scratches made by multiple subpial transection. F: frontal lobe.
Fig. 4 Case 3. Preoperative computed tomography scan (left) showing a calcified mass in the uncus of the left temporal lobe. Coronal T1-weighted magnetic resonance image (center) showing a low intensity area (arrow) in the amygdala adjacent to the lesion. Single photon emission computed tomography scan (right) revealing low perfusion in the mesial temporal lobe (arrow).

minimum effective levels. Interictal EEG recorded from scalp and sphenoidal electrodes showed sporadic spikes in the left temporal lobe. Ictal onset was localized to the left sphenoidal lead. Computed tomography revealed a calcified mass in the left mesial temporal region (Fig. 4 left). MR imaging revealed that the cavernous angioma was lodged in the uncus. T1- and T2-weighted MR imaging showed the adjacent amygdala as hypointense (Fig. 4 center), suggestive of hemosiderin deposition, and the atrophic hippocampus. SPECT showed hypoperfusion in the mesial temporal region (Fig. 4 right). Although mild dementia had already developed (WAIS-R full scale IQ of 60), a burn injury during a recent seizure prompted the patient and his family to request surgical intervention. A Wada's amytal test was not performed because of his compromised memory for remembering verbal tasks.

The gliotic amygdala and surrounding tissue containing hemosiderin were resected through a transylvian approach (Fig. 5 left). The lateral aspect of the cavernous angioma was also partially resected. Total excision was not attempted because of the firmness of the nidus and the strong adherence to the pia mater and anterior choroidal artery. ECoG recorded from a flexible electrode inserted into the inferior horn showed intermittent spike discharges under 2.5% sevoflurane general anesthesia. Resection of the hippocampus (Fig. 5 right), 2 cm from its tip, resulted in cessation of the spike discharges.

No changes were observed in the patient's language or cognitive function postoperatively. He has been seizure free for 18 months under medication with tapered doses of antiepileptics.

Discussion

Surgical excision of a lesion more or less improves control of seizures due to cavernous angioma.1,2,4,7,8,10 Sporadic seizures are easily controlled by simple lesionectomy2,10 in patients with good concordance between the site of the lesion and electroclinical data, regardless of whether excision of the hemosiderin ring has been performed.6 However, simple lesionectomy fails to improve seizure control in a substantial number of patients with chronic and medically intractable seizures.2,4,7 and the rates of

Neurol Med Chir (Tokyo) 40, August, 2000
Control of Epilepsy Caused by Cavernous Angioma

seizure-free cases following simple lesionectomy are very low. Only 13 of 29 patients remained seizure free at the final follow-up of a group of patients with chronic seizures. No improvements in seizure control were achieved in four cases, attributed to contralateral hippocampal atrophy, multiplicity of angiomas, or incomplete excision of the angioma. Poor seizure outcome after lesionectomy correlates with long seizure history, increase in seizure frequency, and female sex.

Patients with cavernous angioma can be classified into three categories according to seizure control. Patients with well-controlled seizures are not considered as candidates for lesion excision. Patients with epilepsy that was difficult to control, but not truly intractable or disabling, might be offered the option of lesion excision. Patients with truly intractable seizures are advised to undergo preoperative electrophysiological evaluation. Resection of mesial temporal structures in the dominant hemisphere can be considered if the patient's temporal lobe is dysfunctional. Careful preoperative localization of the epileptogenicity and/or greater extent of resection achieve an approximately 90% seizure-free rate at the final follow-up.

ECOG can be used for intraoperative tailoring of temporal lobe resection. The degree of residual spike recorded by intraoperative ECoG is well correlated with postoperative seizure control. Intraoperative ECoG under 2.5% sevoflurane general anesthesia can detect the interictal spikes and indicate the epileptogenic zone. In all three cases, ECoG was recorded after the lesionectomy from the hippocampus through strip or flexible electrodes. In Cases 1 and 3, we removed the mesial temporal structures judged to be epileptogenic based on ECoG. These medial temporal structures were also judged to be dysfunctional based on preoperative neuropsychological testing, MR imaging, and SPECT findings. The patients refused the option of two-stage resection, secondary mesial temporal resection following failure of seizure control after the lesionectomy, because of the high incidence of disabling seizures. The patients' language and cognitive functions were not disturbed by resection. In both cases, secondary epileptogenicity appeared to result from long-standing temporal lobe epilepsy originally caused by microhemorrhage and hemosiderin deposition in the cortices surrounding the angioma.

Hippocampal sclerosis coexisting with extrahippocampal lesions has been referred to as "dual pathology." Such "dual pathology" occurs in 17% of patients with temporal epilepsy who had extrahippocampal lesions. Pathology of the resected hippocampus was not obtained in our series, because we elected to do piece-by-piece removal using suction for the sake of safety as these patients were undergoing surgery. However, preoperative SPECT and MR imaging suggested the development of organic changes in the hippocampi. Hippocampal sclerosis develops as the consequence of chronic seizures caused by mass lesions in the temporal lobe. The total number of seizures is correlated with secondary epileptogenicity. However, the relationship between severity of hippocampal cell loss and seizure duration, secondary generalization, or number of seizures has not been corroborated.

A common pathogenic mechanism during embryogenesis or early development may explain the occurrence of "dual pathology." No matter what kind of pathomechanism may be proposed, formation of secondary foci, regardless of whether they are contiguous or distant from the lesion, will reduce the effectiveness of simple lesionectomy in subduing the seizures.

Magnetic source imaging, which was not available in our institution when these patients were treated, would have allowed more accurate detection of the mesial temporal epileptogenicity associated with the temporal lobe cavernous angioma prior to surgery.

Identification of essential speech areas and epileptogenic zones occasionally requires preoperative mapping studies using subdural grid array implantation for a lateral temporal lesion, as in Case 2. However, as the patient's deafness precluded the chance of obtaining an adequate assessment of the required extent of brain resection from the study, we did not perform the procedure. Independent spike activity was observed posterosuperior to the lesion but spike activity from the parahippocampal gyrus was absent, so we did not adopt anterior temporal lobectomy but performed multiple subpial transection, which caused the spike activity to subside. This technique is widely accepted as an alternative to resection of the eloquent cortex. In particular, the rate of seizure-free outcome is high when performed in conjunction with cortical resection, as in our patient.

The nidus of the angioma per se is obviously non-epileptogenic. In Case 3, calcification and thick adherence to the arteries in the ambient cistern inhibited safe excision of the angioma. We avoided this risk because of the patient's age (61 years) and degree of dementia. Excision of the surrounding gliotic tissue including the amygdala and head of the hippocampus resulted in effective control of seizures. The incidence of new seizures caused by cavernous angioma is very low at 2.4%/year, so the

Neurin Med Chir (Tokyo) 40, August, 2000
patient is likely to remain free from subsequent sei-

Our patients were all followed up for far longer
than the 6 months considered to be a good indicator
of long-term seizure outcome.20 We conclude that
tailored resection, based on electroclinical data,
neuropsychological testing, MR imaging, SPECT,
and ECoG, can achieve maximal control of medi-
cally intractable seizures associated with cavernous
angioma in the temporal lobe of the dominant
hemisphere.

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