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Electrocorticography-Guided Surgical Treatment of Solitary Supratentorial Cavernous Malformations with Secondary Epilepsy

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Objective To evaluate the efficacy of electrocorticographic (ECoG) monitoring and the application of different surgical approaches in the surgical treatment of solitary supratentorial cavernous malformations with secondary epilepsy.

Methods This study enrolled a consecutive series of 36 patients with solitary supratentorial cavernous malformations and secondary epilepsy who underwent surgery with intraoperative ECoG monitoring in the Department of Neurosurgery between January 2004 and January 2008. The patients were composed of 15 males and 21 females, aged between 8 and 52 years (mean age 27.3 ± 2.8 years) at the time of surgery. Epilepsy history, the type of epilepsy at the presentation, lesion location, the incidence of residual epileptiform discharges, and postoperative outcomes were evaluated.

Results Histopathological examination indicated cavernous malformations and hippocampal sclerosis in 36 and 5 cases, respectively. Neuronal degeneration, glial cell proliferation, and neurofibrillary tangles were found in all the resected cerebral tissues of extended lesionectomy of residual epileptic foci. Lesionectomy, anterior temporal lobectomy, anterior temporal lobectomy plus cortical thermocoagulation, extended lesionectomy, extended lesionectomy plus cortical thermocoagulation were performed in 4, 4, 1, 14, and 13 cases, respectively. Residual epileptiform discharges were captured in 9 out of the 14 patients who had additional cortical thermocoagulation. According to Engle class for postoperative outcomes, 27 cases were class I (75.00%), 5 were class II (13.89%), 2 were class III (5.56%), and 2 were class IV (5.56%), thus the total effective rate (class I+class II) was 88.89%. Neither of epilepsy history, the type of epilepsy, and the location of cavernous malformation was significantly related to outcomes ($P > 0.05$). A significant relationship was found between the incidence of residual epileptiform discharges and outcomes ($P = 0.041$).

Conclusions Intraoperative ECoG monitoring, the application of different surgical approaches, and the resection of residual epileptic foci could produce good result in the surgical treatment of supratentorial cavernous malformation with secondary epilepsy. Postoperative residual epileptiform discharges could be a useful predictor for evaluating the outcomes.

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CAVERNOUS malformations, or cavernous hemangioma, is a benign vascular lesion without neuronal elements, in which seizures and hemorrhage are the main clinical manifestations. The microsurgical resection of cavernous malformations could effectively treat intractable epilepsy and prevent repetitive hemorrhage. In this article, we reviewed the application of electrocorticographic (ECoG) monitoring and different surgical approaches in the treatment of solitary supratentorial cavernous malformations with secondary epilepsy, and analyzed postoperative outcomes, aiming to evaluate the efficacy of ECoG guidance and to form an optimal surgical plan for this clinical condition.

PATIENTS AND METHODS

Patient selection

Patients were selected from January 2004 to January 2008 in the Department of Neurosurgery of Guizhou Provincial People's Hospital. Inclusion criteria are: (1) patients with solitary supratentorial cavernous malformations and were regularly administered with antiepileptic drugs for 2 years before operation; (2) epilepsy control was not satisfied; (3) having complete medical records, including electroencephalography (EEG), 24-hour video EEG (VEEG), three-dimensional EEG, intraoperative ECoG records and magnetic resonance imaging (MRI) records, regular outpatient follow-up chart, and a follow-up time of over 2 years. Antiepileptic drugs were routinely administered postoperatively.

Surgical procedures

All the procedures were performed under general anesthesia. A large scalp incision and a bone flap were made based on the preoperative localization of the epilepsy foci and primary lesions. ECoG monitoring was performed in all the patients to locate the epileptic foci before the resection of the primary lesion. Resection of epileptic foci, cortical thermocoagulation, and anterior temporal lobectomy were conducted according to the clinical manifestations of seizure. The location of the lesion and epileptiform discharges were detected by intraoperative ECoG monitoring after the resection of the primary lesion.

Single or combined surgical approaches were performed in the patients. (1) Lesionectomy (excision of the cavernous malformation only) was performed according to immediate intraoperative ECoG monitoring which indicated no epileptiform discharges after the resection of the lesion. (2) Anterior temporal lobectomy was performed in patients with cavernous malformation and hippocampal sclerosis in the homolateral temporal lobe, presenting the clinical

manifestation of generalized or partial seizures with secondary generalization. The findings of VEEG indicated typical temporal epilepsy. (3) Extended lesionectomy of residual epileptic foci was performed according to immediate intraoperative ECoG monitoring which indicated epileptiform discharges in the nonfunctional cortex adjacent to the lesion. (4) Cortical thermocoagulation of residual epileptic foci was performed according to the ECoG monitoring findings that indicated the existence of epileptiform discharges in the functional cortex adjacent to the lesion. The resected cavernous malformation, hippocampus, and the nonfunctional cortex were examined for histopathological anomalies.

Statistical analysis

Data analysis was performed using SPSS 16.0 software (SPSS Inc., Chicago, IL, USA). Intergroup comparisons were analyzed using Student's *t* test. $P < 0.05$ was considered to indicate statistically significant difference.

RESULTS

General information

Thirty-six patients with solitary supratentorial cavernous malformations and secondary epilepsy were included in this study. The diagnoses of all the patients were confirmed by clinical manifestations, preoperative EEG, intraoperative ECoG, neuroimaging, and histopathological examination. The included patients were composed of 15 males and 21 females, aged between 8 and 52 years (mean age 27.3 ± 2.8 years) at the time of surgery. The type of preoperative epileptic seizures was simple partial attacks in 10 patients, complex partial attacks in 9, and primary generalized or partial seizures with secondary generalization in 17. The history of epilepsy was < 4 years in 16 cases (mean 2.7 ± 0.7 years), and ≥ 4 years in the other 20 cases (mean 6.3 ± 1.8 years).

EEG, 24-hour VEEG, and MRI findings

Regular EEG, 24-hour VEEG, and MRI were performed in all the patients. Preoperative EEG indicated mild abnormality in 9 cases, moderate abnormality in 5 cases, severe abnormality in 3 cases, and no abnormality in 19 cases. The findings of 24-hour VEEG on the location of the epileptic foci conformed with the lesions revealed by MRI in 30 patients. The ictal phase was captured in 6 patients. Six patients underwent additional prolonged VEEG to reconfirm the epileptic focus caused by hippocampal sclerosis. Prolonged VEEG indicated that the epileptic focus was closely associated with the cavernous malformations. MRI

findings revealed solitary cavernous malformations in all the patients. Low-signal hemosiderin rim was found at the peripheral area (0.3-0.5 cm) of the cavernous malformations on T2 weighted image. Twelve cases involving the extratemporal lobes were found, including 7 involving the frontal lobe, 3 the parietal lobe, and 2 the occipital lobe, respectively. Of these, 5 patients had homolateral hippocampal sclerosis. Of the 24 cases involving the temporal lobe, 3 had contralateral hippocampal sclerosis.

Surgical information

Lesionectomy was performed in 4 cases, anterior temporal lobectomy in 4, anterior temporal lobectomy plus cortical thermocoagulation in 1, extended lesionectomy in 14, and extended lesionectomy plus cortical thermocoagulation in 13.

ECoG monitoring findings

Epileptiform discharges were detected before the resection of the primary lesion in all the 36 patients. The epileptic wave was located at 0.5-3.0 cm in the peripheral areas of the cavernous malformations in 32 patients in immediate postoperative ECoG monitoring. Residual epileptiform discharges were captured in 9 out of the 14 patients who underwent additional cortical thermocoagulation. However,

the frequency of epileptiform discharges decreased in varying degrees, as shown in Figure 1.

Histopathological findings

Thirty-six cases of cavernous malformations and 5 cases of hippocampal sclerosis were found. Neuronal degeneration, glial cell proliferation, and neurofibrillary tangles were found in all resected cerebral tissues of the extended lesionectomy of the residual epileptic foci (Fig. 1H, I).

Follow-up outcomes

Follow-up in 4-8 years showed 27 cases classified under Engle class I (75.00%), 5 cases under class II (13.89%), 2 cases under class III (5.56%), and 2 cases under class IV (5.56%). Thirty-two cases were seizure free, thus the total effective rate was 88.89%. A low-maintenance dosage was administered in 3 cases after antiepileptic drug withdrawal. The initial dosage was repeated or adjusted to other antiepileptic drugs in 1 case for recurrent seizures, thereby decreasing the frequency of seizure.

No significant relationship was found between epileptic history, the type of epilepsy at the presentation, location of the cavernous malformation, and outcomes (all $P>0.05$). A significant relationship was observed between residual epileptiform discharges and outcomes ($P=0.041$) (Table 1).

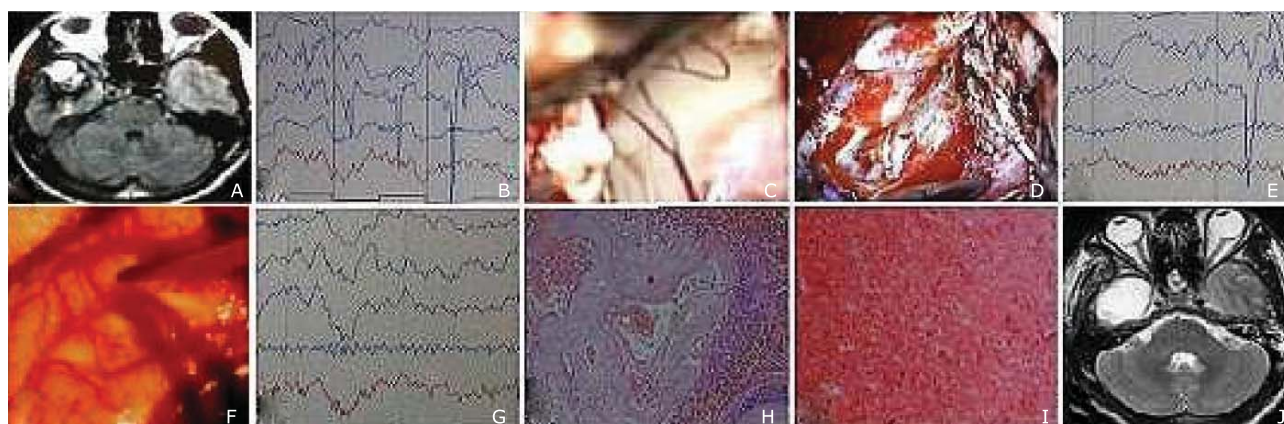


Figure 1. A 51-year-old man presented with solitary supratentorial cavernous malformation and homolateral hippocampal sclerosis in the right temporal lobe. Antiepileptic drugs did not satisfactorily control epilepsy and secondary generalized epilepsy for 6 years. Eletrocorticography (ECoG)-guided anterior temporal lobectomy was performed with good outcome.

A. T1-weighted MRI showed cavernous malformation and homolateral hippocampal sclerosis in the right temporal lobe.

B. Epileptiform discharges were recorded before the resection of the anterior temporal lobe.

C. Intraoperative image of the top of the hippocampus.

D. Intraoperative image after the resection of the temporal lobe.

E. Epileptiform discharges were recorded, and the location of the epileptic focus was reconfirmed by intraoperative ECoG monitoring.

F. Cortical thermocoagulation of residual epileptic foci was performed according to the ECoG monitoring findings, which indicated the existence of epileptiform discharges in the motor cortex.

G. No epileptiform discharges were detected by ECoG monitoring immediately after cortical thermocoagulation was performed.

H, I. Cavernous malformation and hippocampal sclerosis were reconfirmed by pathological examination. (HE×200)

J. T1-weighted MRI after a 2-year follow-up.

Table 1. The relationship between clinical features and outcomes after surgical treatment for solitary supratentorial cavernous malformations (*n*)

Engle class	Epilepsy history		Type of epilepsy		Location of cavernous malformation		Residual epileptiform discharges	
	<4 years	≥4 years	Simple/complex partial	Primary/secondary generalized	Extratemporal lobes	Temporal lobe	Yes	No
I (<i>n</i> =27)	14	13	15	12	8	19	4	23
II (<i>n</i> =5)	1	4	1	4	2	3	2	3
III (<i>n</i> =2)	1	1	1	1	2	0	1	1
IV (<i>n</i> =2)	0	2	0	2	0	2	2	0
Effective cases	15	17	16	16	10	22	6	23
<i>P</i> value	0.394		0.333		0.465		0.041	

DISCUSSION

Cavernous malformation is a benign vascular lesion. The prevalence of cavernous malformation in the central nervous system in the general population is 0.02%-0.53%.^{1,2} The main clinical manifestations are seizures and hemorrhage.³ Epilepsy is the most common clinical sign in patients with intracranial cavernous malformations, with an incidence of 40%-70%, and is the leading cause of morbidity in these patients.⁴⁻⁶ The hemorrhage rate in cavernous malformation (supratentorial and infratentorial) is estimated between 0.25% and 1.3% a year.^{1,6,7} Cavernous malformations are easily localized and resected by microsurgery. It has been agreed that the surgical resection of cavernous malformation is effective in curing hemorrhage; however, different results have been reported for epilepsy.^{8,9} Baumann et al¹⁰ advised that surgical resection of cerebral cavernous malformations should be considered in all the patients with supratentorial cavernous malformations and concomitant epilepsy. The key point in treating secondary epilepsy in cerebral cavernous malformation is the simultaneous resection of the angioma and epileptic foci.

Cavernous malformation can be easily and accurately localized with current neuroimaging technology, especially with MRI. The typical T2-weighted image of cavernous malformations shows a reticulated core of mixed signals representing blood in various states of degradation, surrounded by a hypo-intense hemosiderin rim. T1-weighted image also shows a mixed signal core, but is less sensitive. Fluid attenuated inversion recovery and gradient spin echo sequences were applied to improve the imaging of perilesional hemosiderin. Studies generally attribute epileptic foci to the hemosiderin layer, ischemic cerebral cortex, and deteriorated gliosis.¹¹⁻¹³

The location of epileptic foci plays a crucial role in seizure-free outcomes. Epileptic foci can be accurately located and safely resected under ECoG monitoring. Ogiwara et al¹⁴ verified that intraoperative ECoG can improve the outcome of surgery for intractable epilepsy by localizing epileptic foci for resection. The range of the epileptiform discharge (0.5-3.0 cm) is larger than the low-signal hemosiderin rim (0.3-0.5 cm) on the T2-weighted image in the present study. This finding reconfirmed that the lesion detected in neuroimaging is not equivalent to epileptic foci.

Different surgical approaches were performed under ECoG-guidance to eliminate residual epileptic foci and prevent neural dysfunction. Lesionectomy was conducted when intraoperative ECoG findings indicated no epileptiform discharges after the resection of cavernous malformation. Anterior temporal lobectomy was chosen for cavernous malformation and homolateral hippocampal sclerosis, as supported by Okujava et al.¹⁵ Extended lesionectomy (the resection of residual epileptic foci, including the hemosiderin layer, neuronal degeneration, and glial hyperplasia) was performed when intraoperative ECoG monitoring indicated epileptiform discharges in the nonfunctional cortex adjacent to the lesion. Cortical thermocoagulation was performed to resect residual epileptic foci located in the functional cortex. Cortical thermocoagulation was performed in 14 patients. The residual epileptiform discharges disappeared and decreased in 5 and 9 patients, respectively.

Epilepsy history, the type of epilepsy during surgery, and lesion location were found not significantly related to outcomes (all $P>0.05$). A significant relationship was found between postoperative residual epileptiform discharges and outcomes ($P=0.041$), suggesting that postoperative residual epileptiform discharges could be a useful predictor in evaluating outcomes.

In conclusion, the application of different surgical approaches and the resection of residual epileptic foci including the hemosiderin layer according to the findings of intraoperative ECoG monitoring could produce favorable results in the surgical treatment of supratentorial cavernous malformations with secondary epilepsy. Postoperative residual epileptiform discharges can be a useful predictor for evaluating outcomes.

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