Case report

Epileptogenic temporal cavernous malformations: Operative strategies and postoperative seizure outcomes

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ABSTRACT

Operative treatment of epileptogenic cavernous malformations (CM) continues under debate. Most studies focus on surgery for supratentorial CM in general. For temporal lobe CM, surgical decision-making concerns in particular whether to perform lesionectomy alone or the additional excision of mesial temporal structures. The purpose of this case series was to evaluate operative strategies used to treat epileptogenic temporal CM and to report resultant postoperative seizure outcomes.

Twelve consecutive cases of patients with medically intractable epilepsy who underwent operation for temporal CM between 1996 and 2006 were retrospectively reviewed. When the temporal CM directly invaded the hippocampus or amygdala, the affected structures were resected in addition to the lesion; when the CM was located in the superficial temporal cortex, and there was no radiographic evidence of hippocampal sclerosis, lesionectomy alone was done; with CM located between the superficial temporal cortex and the mesial temporal region, other factors were considered in decision-making, such as lesion proximity to the deep mesiotemporal structures and preoperative epilepsy duration.

For six of the twelve patients, extended lesionectomy (EL) alone was done; for the other six, tailored anteromedial temporal resection with hippocampectomy and/or amygdalection was performed in addition to EL. Postoperatively, 11 patients – all with preoperative VEM demonstrating electroclinical seizure patterns concordant with lesion location – were seizure-free. We conclude that epileptogenic temporal CM are surgically remediable, when approached with the above operative strategies and presurgical VEM. On the basis of these postoperative seizure control results, we recommend consideration of concurrent resection of mesial temporal structures with EL for certain temporal CM.

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1. Introduction

The management of cavernous malformations (CM) causing seizures continues to be the subject of vigorous debate. Cerebral CM are angiographically occult vascular lesions found in approximately 0.5% of the population according to autopsy and imaging studies. They are often epileptogenic when supratentorial.1–4

Cerebral CM consist of abnormal, enlarged blood-filled vascular channels with hyalinized walls, without interposed brain parenchyma. They have a clinically significant prospective hemorrhage rate of approximately 3% per patient/year after diagnosis.5,6 Chronic often undetected microhemorrhages of these lesions result in iron deposition in adjacent brain tissue in the form of hemosiderin, and the iron in this perilesional hemosiderin is thought to play a major role in their epileptogenicity.7–11 Seizures are in fact the most common initial presentation of supratentorial CM, and patients with seizures due to CM often go on to develop epilepsy that is medically intractable.3,5,6,12–17

A consensus about treatment options for epileptogenic CM is arising from recent investigations. Most studies focus on the outcomes of surgery for supratentorial CM in general, and these analyses have provided evidence that for appropriately selected
epileptic patients with CM, surgery provides better seizure control than medical treatment.17,18 In addition, multiple studies have demonstrated benefit of extended lesionectomy for epileptogenic CMs, as compared to restricted lesionectomy, with respect to postoperative seizure control.11,19–21 However, few studies address the details of operative approach for CM according to their specific anatomic location.22,23 Questions regarding optimal surgical approach for epileptogenic CM located in the temporal lobe are still unanswered.

Surgical decision-making for individual cases of epileptogenic temporal CM is challenging. The aim of this study was to examine the presurgical evaluation, operative strategies, and seizure control outcomes in a consecutive series of surgically treated patients with medically intractable epilepsy and temporal lobe CM, to make explicit all factors considered in decision-making for optimal operative management. For CM located in the temporal lobe, operative planning concerns whether these lesions should be treated with lesionectomy alone or with the additional excision of mesiotemporal structures. For this reason we examined in particular the factors weighed in decisions whether to resect the hippocampus and/or amygdala concurrently with the temporal CM.

We used a specific surgical strategy algorithm for decision-making in the operative treatment of temporal CM. In general, in temporal CM cases in which anteromedial temporal resection is not originally performed with the lesionectomy, if the patient still has seizures postoperatively, a second operation is often performed to resect the deep mesiotemporal structures. We used a specific surgical strategy algorithm to achieve good postoperative seizure control, obviating the need for re-operation.

2. Methods

2.1. Subjects

Twelve consecutive patients (seven men and five women) with medically intractable epilepsy who underwent operative treatment for temporal CM between 1996 and 2006 were identified in the epilepsy surgery databases of UCLA Medical Center. Inclusion criteria consisted of: medically intractable epilepsy, temporal lesion with radiographic appearance consistent with CM, video scalp EEG monitoring (VEM) evaluation, pathologically confirmed diagnosis of the resected temporal lesion as CM, and minimum postoperative follow-up of 12 months. Patients with more than one supratentorial CM were included (cases 5 and 6). Medically intractable epilepsy was defined as failure of pharmacologic seizure control with adequate trials of at least two first-line antiepileptic drugs (AEDs).24–26

2.2. Data analyzed

Data retrospectively analyzed consisted of age at first seizure and at operation; seizure type and frequency; AED history; neurologic disease other than epilepsy; pre- and postoperative neurologic examination; preoperative MRI findings including number, location, and size (maximum diameter) of CM, as well as radiographic evidence of hippocampal sclerosis; VEM data; FDG-PET; neurocognitive testing; Wada test results when done; intraoperative findings; pathologic specimens; and postoperative seizure control outcomes. Institutional Review Board approval for the study was obtained (UCLA IRB G09-04-094-01).

2.3. Preoperative evaluation

The preoperative evaluation in the 12 cases included: MRI, scalp VEM, FDG-PET, and neurocognitive testing. One patient underwent interictal MEG (case 6). When deemed necessary, Wada test was performed in the cases in which hippocampal resection was considered in combination with lesionectomy. (Wada test was done in four of the five hippocampal-resection cases: done in cases 4, 8, 9, 11, not done in case 12.) One patient underwent preoperative fMRI to assess language (case 2).

2.3.1. Preoperative MRI

Preoperative MRI scans obtained in all patients via 1.5 T scanner included axial T1-weighted images, axial and coronal T2-weighted images, and axial gradient-echo T2-weighted images. Through 2003, MRI included T1-weighted spoiled gradient-echo (SPGR) sequences and after 2003, T1-weighted magnetization-prepared rapid gradient-echo (MPRAGE) sequences. In patients who did not undergo digital-subtraction cerebral angiogram (DSA) as part of a Wada test, axial and coronal T1-weighted sequences were acquired after gadolinium injection for enhanced MR sequences to assess for developmental venous anomaly (DVA).

2.3.2. Preoperative VEM

Preoperative VEM scalp recordings were obtained in all 12 patients, with a minimum of three clinically stereotypical seizures separated by at least 8 h recorded. Preoperative or intraoperative invasive recordings were recorded in three patients: extraoperative recording from subdural grid and strip electrodes in one patient (case 2) and intraoperative electrocorticography (ECoG) in two patients (cases 1 and 2).

2.4. Surgical procedures

All operations were performed by one surgeon (I.F.) and consisted of extended lesionectomy either alone or combined with tailored anteromedial temporal resection (AMTR). Extended lesionectomy is defined here as microsurgical resection of the cavernous malformation and perilesional tissue with abnormal appearance on direct intraoperative visualization.11 The tailored AMTR operations differed in whether both or part of the hippocampus and/or amygdala were microsurgically resected. (See Section 3 and Table 1.) These tailored procedures always involved resection of anterior temporal neocortex (antero middle temporal gyrus and inferior temporal gyrus) of 3–3.5 cm in the dominant hemisphere and 3.5–4 cm in the non-dominant hemisphere, as well as the anterior 1 cm of the superior temporal gyrus (STG). (The term ‘tailored’ is defined here as ‘fitted’ to the diagnostic data, including ictal EEG findings from scalp VEM, and is not meant to imply the use of invasive EEG recording. Intraoperative ECoG was used only in select cases when deemed useful by the epileptologist and surgeon.) Developmental venous anomalies (DVAs) associated with CM were not resected.

2.4.1. Algorithm of surgical strategy for epileptogenic temporal CM

1. Selection of patients for operation was based on electroclinical congruence of scalp VEM ictal EEG with the location of CM on MRI.

2. In patients with multiple supratentorial CM, ictal EEG findings were used to identify a single epileptogenic CM to be resected.

3. If the temporal CM directly invaded the hippocampus or amygdala, the involved structure was resected in addition to the lesion.

4. If the temporal CM was located in the superficial temporal neocortex far from the hippocampus and amygdala, and there was no radiographic evidence of hippocampal sclerosis, extended lesionectomy alone was done.
The clinical data includes age at seizure onset, age at operation, epilepsy duration prior to operation. The diagnostic data includes MRI findings (location and diameter of lesions), EEG findings (interictal and ictal), FDG-PET findings (interictal hypometabolism), and whether neurocognitive test and Wada test were done. The operative and outcome data includes type of operation, postoperative seizure outcomes (Engel classes), and longest duration follow-up (months) in 12 patients with epileptogenic temporal CM.

5. If the temporal CM was located between the temporal neocortex and the deep mesiotemporal structures, other factors were considered in the decision whether or not to resect the hippocampus and amygdala, such as proximity of the CM to the mesial temporal region, preoperative duration of epilepsy, and effects of prior treatment modalities.

6. All surgical decisions were constrained by functional data, including neurocognitive, Wada, and fMRI findings, and tempered by direct operative visualization.

7. DVAs associated with CM were not resected.

2.5. Outcome evaluation

Postoperative seizure control outcomes were assessed at clinic visits or with follow-up clinical telephone calls, using Engel's classification as follows: "class IA, completely seizure-free since surgery; class IB, nondisabling simple partial seizures only since surgery; class IC, some disabling seizures after surgery, but free of disabling seizures for at least two years; class ID, generalized convulsion with AED withdrawal only; class II, rare disabling seizures; class III, worthwhile improvement; class IV, no worthwhile improvement". The standard postoperative AED protocol consisted of continuation of patients' preoperative AED regimen for a minimum of two years postoperatively.

3. Results

3.1. Demographic and presurgical evaluation results

The mean age of subjects at seizure onset was 23 (range: 6–40 years old). The mean age at operation was 41 (range: 21–54 years old). The mean preoperative epilepsy duration was 17.5 years (range: 4–48 years). Table 1 shows these data for all patients and all pertinent diagnostic data, including MRI findings (location and diameter of lesions), EEG findings (interictal and ictal), FDG-PET findings (interictal hypometabolism), and whether neurocognitive and Wada tests were done.

3.2. Operative and postoperative results

Table 1 shows for all patients: type of operation, postoperative seizure outcomes based on the Engel classification, and longest duration follow-up.

3.2.1. Morbidity and mortality

There were no operative or perioperative morbidities or mortality.

3.2.2. Types of operation

For six of the twelve patients, extended lesionectomy alone was done, with sparing of the mesial temporal structures (cases 1, 2, 3, 5, 6, 10). Of these six lesionectomy cases, three were right-sided and three were left-sided. For the other six patients, tailored variations of AMTR with resection of the hippocampus and/or amygdala were performed, in combination with extended lesionectomy (cases 4, 7, 8, 9, 11, 12). Of these six cases, four were right-sided and two were left-sided. In five of these six cases, the hippocampus was resected (four right-sided and one left-sided). In one of these six cases, partial resection of the amygdala was done in addition to extended lesionectomy, with sparing of the hippocampus (case 7). The CM was completely resected in 11 of the 12 cases. Partial extended lesionectomy of the CM was necessary in one case due to a DVA encasing the patient's left hippocampal CM (case 8). In this case the DVA was not resected, as per standard of care, to avoid the risk of interrupting venous drainage of normal brain tissue.

### Table 1

<table>
<thead>
<tr>
<th>Pt</th>
<th>Ages + duration (Onset/op yrs)</th>
<th>MRI: temp CM loc (Size: diameter in cm)</th>
<th>EEG</th>
<th>PET</th>
<th>Ncog/Wada</th>
<th>Operation</th>
<th>Outcome (months)</th>
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<tr>
<td>1</td>
<td>14/49 + 35</td>
<td>R Posterior inf temp (1.1)</td>
<td>F8, S2</td>
<td>F8, S2</td>
<td>No hyp</td>
<td>NA/+</td>
<td>R EL (120)</td>
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<tr>
<td>2</td>
<td>14/44 + 30</td>
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<td>L cent temp</td>
<td>Ips hyp</td>
<td>+/-</td>
<td>L EL  (108)</td>
</tr>
<tr>
<td>3</td>
<td>17/37 + 20</td>
<td>L Fusiform gyrus (1.5)</td>
<td>T1, T3 + T2, T4</td>
<td>None</td>
<td>Ips hyp</td>
<td>+/-</td>
<td>L EL  (64)</td>
</tr>
<tr>
<td>4</td>
<td>26/53 + 26</td>
<td>R Hipp head (1.7)</td>
<td>F8, S2, F8, S2</td>
<td>Ips hyp</td>
<td>+/-</td>
<td>R Hippocampectomy + EL</td>
<td>ID (12)</td>
</tr>
</tbody>
</table>

+Other findings on MRI

1. If the temporal CM was located between the temporal neocortex and the deep mesiotemporal structures, other factors were considered in the decision whether or not to resect the hippocampus and amygdala, such as proximity of the CM to the mesial temporal region, preoperative duration of epilepsy, and effects of prior treatment modalities.

2. All surgical decisions were constrained by functional data, including neurocognitive, Wada, and fMRI findings, and tempered by direct operative visualization.

3. DVAs associated with CM were not resected.

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3.2.3. Location of lesion and types of operation

In the six patients who underwent extended lesionectomy alone, the epileptogenic CM did not have a mesial temporal location. It was located in the temporal neocortex in five (cases 2, 3, 5, 6, 10) and in the central temporal lobe white matter between the neocortical temporal and mesial temporal regions in one case (case 1). For the six patients who underwent tailored AMTR variants in addition to extended lesionectomy, the CM directly involved the amygdala or hippocampus in three cases (cases 4, 7, 8), was located between the lateral temporal neocortex and the mesial temporal region in one case (case 9), and was in a mesial temporal location in very close proximity to the amygdala and hippocampus in two cases (case 11, in the right PHG; case 12, mesial to the right hippocampal head).

3.2.4. Wada test and type of operation

For the two patients with left temporal CM who had poor verbal memory scores after the left-sided injection in the Wada test, extended lesionectomy alone was done (cases 2 and 3). For one of the six cases in which hippocampal resection was planned, Wada test was not done for logistical reasons (case 12): The patient had high seizure frequency (three to four seizures per day) and a non-dominant hemisphere lesion, with CM located mesial to the right hippocampal head. Given the distance at which the patient lived from tertiary medical care, pursuit of Wada test would have further delayed an already-delayed operation. The patient underwent right AMTR with microsurgical resection of the hippocampus and amygdala combined with extended lesionectomy.

3.2.5. Postoperative follow-up and seizure outcomes

The mean postoperative follow-up period for the 12 patients was 50 months (range: 12–120 months). Eleven patients – all with preoperative VEM demonstrating electroclinical seizure patterns congruent with the location of the subsequently resected lesion – were seizure-free (Engel class I). One patient (case 3) had no postoperative improvement in epilepsy status (Engel class IV) (follow-up 64 months). This patient had interictal EEG findings suggestive of bilateral independent temporal epileptogenic zones and ictal VEM recordings that were non-localizing and non-lateralizing; her operation was performed with palliative intent.

Two patients had more than one supratentorial CM. Both patients were seizure-free after resection of one CM only, i.e. after resection of the temporal CM that had been identified by VEM as epileptogenic (cases 5 and 6). In case 5, scalp VEM indicated that the patient’s right temporal CM – rather than the right parietal CM – was epileptogenic. The patient’s continued postoperative seizure freedom after extended lesionectomy of the right temporal CM alone confirmed the VEM results regarding epileptogenicity (follow-up 70 months). In case 6, scalp VEM showed the patient’s left temporal CM to be epileptogenic, rather than the right frontal or two left parietal CM. Similarly, the patient’s continued postoperative seizure freedom after extended lesionectomy of the left temporal CM alone was confirmatory of the VEM findings (follow-up 55 months).

3.3. Pathologic results

For all 12 patients, the resected temporal lesion was identified as a CM by gross and histopathologic examination. In the five cases in which the hippocampus was resected, the hippocampal specimens were analyzed pathologically. Two hippocampi (cases 4 and 9) showed granule cell dispersion in the dentate gyrus, a finding generally restricted to TLE patients and found in 40% of hippocampal sclerosis cases.28–30 One of these two patients had radiographic evidence of hippocampal sclerosis predictive of these hippocampal pathologic findings (case 4). One hippocampal specimen – from a patient whose temporal CM involved the body of the hippocampus – showed deformation grossly and vascular calcinosis histologically (case 8). Two hippocampal specimens consisted of material insufficient for histopathologic analysis (cases 11 and 12).

4. Results: illustrative case

Case 9 is described to provide an example of factors involved in the decision to resect the mesiotemporal structures concomitant with extended lesionectomy.

Fig. 1. MRI brain scan of case 9, preoperative, showing right temporal pole CM. (A) MR brain coronal T2 image. (B) MR brain axial T2 image.
4.1. Case 9

4.1.1. Extended lesionectomy combined with AMTR, microsurgical resection of hippocampus and amygdala

This 54-year-old right-handed man presented with pharmaco-logically refractory complex partial seizures, onset at age six years. As a business owner, he found that his chronic seizure disorder limited the expansion of his company and prevented independent travel. Neurologic examination showed no gross or focal deficits. MRI revealed a 1.1 cm lesion radiographically consistent with CM in the right temporal pole, anterior to the parahippocampal gyrus. (See Fig. 1.) MRI also showed the right hippocampus to be slightly smaller than the left, but there was no focal signal abnormality suggestive of hippocampal sclerosis. Epilepsy evaluation included [i] scalp VEM revealing electrographic seizure onset in the right mesial temporal region, [ii] interictal FDG-PET showing moderate right temporal hypometabolism, and [iii] neuropsychologic test findings consistent with subtle right and left mesial temporal dysfunction, suggestive of 'crowding' of functions into the left mesial temporal region. Wada test with right-sided injection showed left hemispheric dominance for language and a good memory score (87%). Given (a) all data congruent for right temporal epileptogenic zone in the region of the CM, (b) the proximity of the epileptogenic lesion to the amygdala/hippocampal head, as well as (c) the patient's lengthy epilepsy duration (48 years), decision was made to offer the patient right AMTR (including microsurgical resection of the hippocampus and amygdala) with extended lesionectomy, as most likely to improve the patient's seizure control. Operative findings included: the right temporal pole CM itself, surrounded by abnormal tissue with yellow discoloration, affecting the head of the hippocampus and partially the amygdala. The abnormal hemosiderin staining extended to the entorhinal cortex, the anterior border of the hippocampus, and the amygdala, as well as the parahippocampal region. Histopathology confirmed the lesion as a CM (see Fig. 2); the hippocampal specimen showed granule cell dispersion. The patient's postoperative seizure outcome was Engel class IB (no seizures and one déjà vu aura) at 25 months follow-up, on his continued two AED regimen. Functionally, he has continued to work successfully as the owner of his own business and is now driving and traveling independently.

4.1.2. Decision to resect mesiotemporal structures based on multiple factors in case 9

This case illustrates the fact that: when CM do not directly involve the hippocampus and amygdala, decision-making about whether to resect these mesial temporal structures concurrently with extended lesionectomy is based on multiple factors, such as lesion location and preoperative epilepsy duration here.

5. Discussion

We report 12 cases of surgically treated epileptogenic temporal CM with details of their presurgical evaluation, operative treatment, and postoperative seizure control outcomes, to address still open questions about optimal operative strategy for these...
lesions. Moran et al. laid out these questions in their 1999 report combining a literature review with their own case series of epileptogenic supratentorial CM. Their series included 11 patients with temporal CM treated with lesionectomy, with postoperative seizure outcomes classified as Engel class I in six, class II in one, class III in one, and class IV in three cases. Only one of those 11 patients underwent AMTR/amygdalohippocampectomy, done subsequent to the initial lesionectomy due to lack of postoperative improvement in seizure control. That is, this patient required a second operation consisting of AMTR/amygdalohippocampectomy, which then resulted in worthwhile improvement in seizure control (Engel class III). Another CM case series included 12 temporal CM treated initially with lesionectomy and – similar to Moran’s series – described one patient with no improvement in postoperative seizure control who later underwent AMTR/amygdalohippocampectomy with subsequent seizure freedom (in that series, case #13). In discussing the postoperative seizure control outcomes both in the literature and in their own series, Moran and colleagues stated: “It was only possible to analyze the outcome of lesionectomy, as there are very few reported cases in which other colleagues stated: ‘It was only possible to analyze the outcome of lesionectomy, as there are very few reported cases in which other forms of surgery, particularly temporal lobectomy, were employed. The increasing recognition of dual pathology … however, makes this an area in need of further investigation.”

The existing literature has primarily focused on postoperative seizure control outcomes, usually of lesionectomy, with omission of the details of surgical approach. The majority of studies reporting temporal CM grouped them with CM in other supratentorial locations and considered a heterogeneous population of patients – that is, patients with medically intractable epilepsy and patients who have only had a few seizures which then self-resolved or were well-controlled with AED monotherapy. In their excellent large multicenter study, Baumann et al. focused on postoperative outcomes and did not address surgical decision-making regarding which temporal CM might appropriately be treated by lesionectomy alone and which by additional resection of the mesial temporal structures. Given that the focus of their study was not operative decision-making, they generalized about surgical approach in their temporal CM cases, stating that amygdalohippocampectomy was performed in most patients with mesiotemporal CM.

One other study has focused on the presurgical evaluation and operative treatment of temporal lobe CM. In Paolini et al.’s series of eight patients with drug-resistant TLE and solitary temporal CM, two patients underwent lesionectomy alone and six underwent variations of temporal lobectomy in addition to lesionectomy. They reported excellent postoperative seizure outcomes for all eight cases (Engel class I), with relatively short follow-up in two cases (follow-up range: 2–46 months). They did not focus on explaining how the decision was made to resect the mesiotemporal structures in their four cases of temporal neocortical CM. Our case series addresses this still unanswered question about the details of surgical decision-making for epileptogenic temporal cavernous malformations.

Eleven of the twelve cases reported in our series had excellent postoperative seizure control outcomes (Engel class I) after one operation only. The pertinent question concerns what strategy led to improved postoperative seizure control in these 11 cases, and what led to failure of seizure reduction in one case in this series. To answer this question, the surgical decision-making in these 12 cases is discussed here.

5.1. Surgical decision-making

For planning the optimal operative strategy for epileptogenic temporal CM, scalp VEM and structural MRI were the two most important factors. First, scalp VEM recording of ictal EEG was necessary to establish electroclinical congruence with the anatomic location of the temporal CM seen on MRI, to localize a focal epileptogenic zone. Second, the CM location on MRI was a heavily weighted factor in decision-making about whether to resect the mesiotemporal structures in addition to the lesion. When ictal EEG and CM location on structural MRI were concordant, and other data (FDG-PET, neurocognitive testing) were not contradictory, it was the specific anatomic location of the CM within the temporal lobe on structural MRI that carried the most weight in the decision to perform extended lesionectomy alone versus extended lesionectomy combined with AMTR.

5.2. Scalp VEM ictal EEG

The importance of scalp VEM in the preoperative evaluation of these epileptic patients’ supratentorial CM is consistent with other studies’ results. In our case series, concordance of scalp VEM ictal EEG findings with structural MRI was crucial to the selection of patients for operative treatment, for good postoperative seizure control. For 11 cases in our series – all the lesionectomy cases and all cases of lesionectomy combined with AMTR in which scalp VEM ictal EEG findings were congruent with the radiographic lesion – the patients were seizure-free postoperatively (Engel class I). In the one lesionectomy case in which the ictal EEG was not focally congruent with the radiographic lesion location, postoperative seizure control was not improved (case 3, Engel class IV).

5.3. Role of ictal EEG in cases of multiple supratentorial CM

In the two epileptic patients with more than one supratentorial CM in this series, use of scalp VEM data identified a single epileptogenic CM (cases 5 and 6). In one case, interictal magnetoencephalography used as an adjunctive study confirmed the ictal EEG findings (case 6). This identification permitted lesionectomy of one CM only in these two cases, with resultant postoperative seizure freedom for both patients. Given that the minimal resection possible is always a surgical goal, this use of VEM benefits patients with multiple supratentorial CM undergoing operative treatment for seizure control.

5.4. Anatomic relationship of temporal CM to the mesiotemporal structures

Actual anatomic encroachment on mesiotemporal structures by the CM was the most important factor in the decision to resect them with the lesion. After involvement of the deep mesiotemporal structures by the CM shown on MRI was confirmed by direct operative inspection, these structures were then either completely or partially resected, with constraint from functional data (cases 4, 7, 8). This functional constraint was provided by neurocognitive, Wada, or fMRI findings and tempered by direct operative visualization.

In all cases in this series in which the epileptogenic CM and the surrounding hemosiderin-stained brain tissue were confined to the temporal neocortex, the mesial temporal structures were not resected; extended lesionectomy alone was done (cases 2, 3, 5, 6, 10). In cases where the CM did not actually invade the mesiotemporal structures and also was not located in the superficial temporal neocortex, but rather lay between the two regions, the decision regarding whether or not to take the hippocampus or amygdala was not obvious (cases 1, 9, 11, 12). In such cases the relative proximity of the CM to the mesiotemporal structures shown by MRI, clinical history such as prior treatment modalities and preoperative epilepsy duration, as well as direct operative visualization of hemosiderin staining all were important factors in the surgical decision-making. In the one case in this series in which the epileptogenic temporal CM was located in the central white matter of the temporal lobe
between neocortex and allocortex, the mesiotemporal structures were not resected; lesionectomy alone was done (case 1). In the three cases in this series in which the CM was in close proximity to the mesiotemporal structures but not actually invading them, both the hippocampus and amygdala were resected, in addition to the lesion (cases 9, 11, 12). In case 9, the CM was located in the right temporal pole near the parahippocampal gyrus. In addition to this limbic proximity, the patient's long duration of epilepsy (48 years) also played a role in the decision to resect the deep mesiotemporal structures in addition to extended lesionectomy. In case 11, the patient had undergone stereotactic radiosurgery directed at the right parahippocampal CM by other practitioners four years prior to surgical evaluation; concern about possible radiation injury to the mesial temporal region influenced the decision to resect the hippocampus and amygdala along with the CM.

5.5. Role of functional data

The operative strategy in case 7 provides an example of surgical decision-making based on anatomic involvement of the mesiotemporal structures by the temporal CM with constraint by functional data. In this case MRI showed the patient's 2.3 cm CM to be located in the left temporal pole, extending to involve the left entorhinal cortex, parahippocampal gyrus, fusiform gyrus, and encroaching upon the amygdala. Direct visualization intraoperatively revealed that the CM actually invaded the left amygdala but did not touch the hippocampus. In addition, the hippocampus showed no abnormal yellowish stain, indicating absence of hemosiderin deposition. Given neurocognitive findings of excellent verbal memory, upon which the patient's profession depended, as well as direct operative visualization revealing no gross hippocampal abnormality, the hippocampus was spared, while the amygdala was partially resected in the region of CM involvement, concurrently with extended lesionectomy.

For temporal CM that did not directly invade the deep mesiotemporal structures, functional data such as predicted verbal memory deficits on Wada testing also played a role in surgical decision-making. For the two patients with CM located in the left fusiform gyrus, Wada test results showing very poor verbal memory deficit indicated a pertinent factor in the decision to resect the hippocampus and amygdala along with CM.

5.6. DVA associated with CM

Anatomic association of a developmental venous anomaly with CM factored into the surgical decision-making in one case in this series. DVAs, also called venous malformations, have not been shown to be epileptogenic and should not be resected. They consist of anomalous veins arrayed centripetally around a dilated venous trunk, surrounded by normal brain parenchyma for which they supply anomalous venous drainage. Resection of a DVA can suddenly obstruct the venous drainage of normal brain tissue, causing venous hypertension that may result in hemorrhage and/or infarction. While a DVA in a different location in the brain is not considered in CM operative planning (e.g. the right frontal DVA in case 10), direct encroachment of a DVA on a CM can prevent complete resection of the lesion. In the one case in this series in which a DVA encased the CM, partial lesionectomy of the CM was necessary to avoid resection of the DVA (case 8).

Reports in the literature regarding the percentage of CMs associated with DVAs vary widely, from 2.1% to 59.6%. This wide range in percentages is due to the different methods of data acquisition used in the various studies, with study design ranging from retrospective analysis of imaging studies, prospective MR and DSA, to direct operative inspection. DVAs can be missed on MRI and then visualized directly during operation. Alternatively, they can be suspected on MRI due to gadolinium enhancement and then found not to be present on direct operative visualization, as in case 9 in this series.

5.7. Epilepsy duration as a factor in surgical decision-making

Preoperative epilepsy duration played a role in the decision to resect the mesiotemporal structures in one patient (case 9). Though the literature does not show complete agreement on this issue, multiple case series have found an association of longer preoperative epilepsy duration with poorer postoperative outcome. Given these published reports, it has been accepted opinion that for patients with lengthy preoperative epilepsy duration and high seizure frequency, a more extensive resection than simple lesionectomy – that is, resection including the mesiotemporal structures – would more likely result in improved postoperative seizure control. Recently, however, a large multicenter study found the converse, i.e. no significant association between preoperative epilepsy duration and postoperative seizure control. This study concerned supratentorial CM in general, was specifically temporal CM, and did not detail the type of operation performed for each temporal CM. The lack of agreement in the literature on this point is not a reason to disregard epilepsy duration as a factor in surgical decision-making, since the question of impact of epilepsy duration on postoperative seizure control outcome remains open. Long epilepsy duration may result in hippocampal sclerosis. If this does occur, then long preoperative epilepsy duration may be a pertinent factor in the decision to resect the hippocampus concomitant with lesionectomy. This remains an area of speculation.

In our study, there appeared to be no relationship between preoperative epilepsy duration and postoperative seizure outcome. However, it is not clear what role that factor would have played if mesiotemporal structures had not been resected. The limited number of cases analyzed here constrains our ability to make any conclusion about the association of preoperative epilepsy duration with postoperative seizure control outcome.

5.8. Size of CM

Baumann et al.'s multicenter study found lesion diameter less than 1.5 cm to be a significant predictor for improved postoperative seizure control, though only in the first two years after operation. In our series, the size of the CM did not appear to have any association with postoperative seizure outcome, but again the limited number of cases does not permit definitive statement.

5.9. Dual pathology

Of the five cases that included hippocampal resection, three hippocampal specimens were analyzed; the three cases all had hippocampal histopathologic findings consistent with a designation of dual pathology (cases 4, 8, 9), that is, these cases had hippocampal abnormalities in addition to the temporal CM. This dual pathology can be viewed as 'hindsight' confirmation that the decision to resect the mesiotemporal structures was a correct one, just as these patients' excellent postoperative seizure control can likewise be viewed as evidence that a correct decision was made. However, it is obviously impossible to know what the postoperative seizure control outcome of a patient would have been if the mesiotemporal structures had not been resected.
5.10. Limitations of our study

The patients in our case series are a homogenous population with respect to two factors: all had medically intractable epilepsy and all had a temporal lobe CM demonstrated by scalp VEM to be epileptogenic. The homogeneity of the cases in our series gives weight to our conclusions in discussing the operative treatment of temporal lobe CM in patients with medically intractable epilepsy. However, our strict inclusion criteria did not allow the collection of large numbers of cases and for that reason did not permit assessment of statistical significance.

5.11. Evaluating our temporal CM surgical strategy algorithm

Our goal in following the surgical strategy algorithm for temporal CM detailed in the Methods Section was excellent postoperative seizure control, to obviate any need for re-operation. There has in fact been no need for re-operation in these cases. The only case in which Engel Class I postoperative seizure control was not obtained was constrained by functional data, that is, the mesiotemporal structures could not be resected given the Wada test results. In this one case, only EL was performed, and this was done with palliative rather than curative intent. (See Appendix B, for details of case 3).

6. Conclusions

Epileptogenic temporal CM are surgically remediable with appropriate patient selection and careful operative planning. When CM do not directly involve the hippocampus and amygdala, decision-making about whether to resect these mesial temporal structures concurrently with extended lesionectomy is based on multiple factors. Carefully planned operative strategy following the surgical algorithm described here typically leads to excellent postoperative seizure control in patients with ictal VEM findings concordant with CM location on structural MRI. The detailed data that we report regarding surgical decision-making and outcomes in 12 consecutive cases of epileptogenic temporal CM may be useful in the selection of patients for operation, planning the optimal surgical approach, and counseling patients with these lesions.

Conflicts of interest

The authors have no conflicts of interest to declare.

Institutional Review Board approval for this study was obtained (UCLA IRB C09-04-094-01).

Appendices A and B. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.seizure.2009.11.006.

References