Resection of supratentorial lobar cavernous malformations in children

Clinical article

BRADLEY A. GROSS, M.D., EDWARD R. SMITH, M.D., LILIANA GOUMNEROVA, M.D., MARK R. PROCTOR, M.D., JOSEPH R. MADSSEN, M.D., AND R. MICHAEL SCOTT, M.D.

Department of Neurosurgery, Boston Children's Hospital, Harvard Medical School, Boston, Massachusetts

Object. The authors present a series of children with supratentorial lobar cavernous malformations (CMs). Current imaging and operative techniques along with long-term follow-up were incorporated to characterize the response to surgical treatment in this pediatric population.

Methods. The senior author’s operative experience was reviewed retrospectively along with a review of the Boston Children’s Hospital database from 1997 to 2011 for children with supratentorial lobar CMs. Lobar CM was defined as having a supratentorial location but not involving the thalamus/hypothalamus or basal ganglia. Baseline patient demographics, pertinent radiographic findings, operative outcomes, and long-term results were evaluated and compared between patients managed operatively and those who were managed nonoperatively.

Results. Of 238 CMs identified, 181 (76%) were lobar. Compared with patients managed with observation only, those selected for surgery were older (p = 0.03), more likely to have symptomatic lesions (p < 0.001), and had larger lesions (p < 0.001). Of the 83 CMs selected for surgery, 98% were completely resected. Over a total of 384.5 patient-years of follow-up after surgery (mean 4.6 years; median 2.7 years; range 0.1–22.3 years), there were no subsequent hemorrhages in any patient undergoing complete resection; 1 of the 2 incompletely resected lesions rebled during the follow-up period. Radiographically, there was 1 recurrence (1.2%) in a child with multiple CMs; there were no recurrences of completely resected single lesions. Of the 48 patients who presented with seizures (acute or chronic), 46 (96%) were seizure free at follow-up. The permanent neurological complication rate of surgery was 5%; these complications were limited to those patients whose lesions were in eloquent locations.

Conclusions. Pediatric patients with symptomatic supratentorial lobar CMs are ideal candidates for surgery, for which there are high complete resection rates, rewarding long-term seizure outcomes, and low operative morbidity. Observation may be warranted in smaller asymptomatic lesions located within eloquent cortex.

key words • cavernous malformation • cavernoma • lobar • pediatric • children • surgery • seizure • epilepsy

Cavernous malformations (CMs) are blood vessel malformations of the brain composed of sinusoidal vessels lined by a single layer of endothelium usually without interdigitated brain tissue. They are typically well circumscribed but may be intimately associated with other vascular anomalies of the brain, including developmental venous anomalies (DVAs) and venous or capillary telangiectasias. Cavernous malformations usually present because of seizures, headaches, or neurological deficits due to hemorrhage or focal mass effect, and they frequently come to neurosurgical attention for evaluation of surgical excision.1,18,28,30

We undertook this study to review data obtained in a large cohort of children with lobar CMs, comparing those selected for surgery with those managed nonoperatively. After comparing demographics and angiographic features between groups, we evaluated long-term outcomes and complications for each management, particularly in terms of freedom from seizures and late hemorrhage.

Methods

Population and Inclusion Criteria

With the approval of the Boston Children’s Hospital Institutional Review Board, we undertook a retrospective review of departmental and hospital databases to find all...
patients less than 22 years of age, surgically and nonsurgically treated, who were diagnosed with cerebral CMs from 1997 through 2011. We required that all lesions be at least 4 mm in size and visible on T2-weighted MRI. We added a retrospective analysis of the senior author’s operative experience with these lesions spanning 4 decades. This combined search identified 183 children with 238 CMs. Of the 238 CMs, 181 (76%) were supratentorial lobar lesions, which we defined as located above the tentorium but not involving the thalamus/hypothalamus or basal ganglia.

Data Collection and Analysis
We reviewed these patients’ hospital and office charts to determine the following information: patient age at presentation, sex, modality of presentation, family history of CMs, history of cranial radiation therapy, CM size and location, associated DVAs, CM treatment modality (resection or observation), initial results, and long-term neurological follow-up. We performed statistical analysis (STATA 12.0) of categorical variables using the Fisher exact test and of mean values (patient age and CM size) with a 2-tailed t-test.

Surgical Technique
Surgical technique was as previously described, with the usage of intraoperative frameless stereotaxy in all cases since 2003. Intraoperative MRI has been used for select cases since 2005, and intraoperative ultrasound has been employed almost universally since 2005. Following craniotomy, the CM was identified (on the surface or after a small corticectomy), and its margins were identified and dissected from adjacent normal brain tissue with microdissectors and bipolar cautery under the operating microscope, frequently employing suction for traction on the lesion. The lesion was grasped and manipulated with microforceps as its feeders were coagulated and divided to deliver it from the operative bed. Care was taken to preserve any DVA, if present. No effort was made in any patient to resect hemosiderin-laden tissue around the lesion proper.

Results
Background and Demographics for Surgically Treated CMs
Of the 181 supratentorial lobar CMs identified, 83 (46%) were selected for resection, and 98 (54%) were observed without operation (Table 1). The mean patient age in the surgical cohort was 11.8 years (median 12.1 years; range 0.7–22 years) and 57% were male. Fourteen percent of children had a family history of CM, and 8% had undergone prior cranial radiation therapy (6 children for acute lymphocytic leukemia and 1 for medulloblastoma). The majority (75%) presented with symptomatic hemorrhagic lesions, 58% had experienced at least 1 seizure, 40% had headaches, and 12% had focal neurological deficits. Four (5%) were asymptomatic, undergoing surgery due to either an increase in CM size or strong family preference. Lesions were predominantly (52%) in the frontal lobe; 25% were temporal, 18% parietal, and 5% occipital. Thirty percent of lesions were in eloquent cortex (motor, sensory, speech, or calcarine cortex). Mean lesion size was 2.2 cm, and 13% had a radiographically apparent DVA seen on post-Gd T1-weighted MRI.

Surgical Treatment
Overall, 81 (98%) of 83 CMs were completely resected. In 1 case, a hemorrhagic CM confirmed by intraoperative motor stimulation to be entirely embedded in the motor cortex without a safe corridor of access was left in place (Fig. 1). After 15 years of follow-up, the patient has not had a recurrent event and remains off medications. Remarkably, the lesion appears on follow-up MRI to have spontaneously thrombosed. In another case, the CM was associated with an extensive venous telangiectasia that precluded complete resection (Fig. 2).

Follow-Up, Complications, and Long-Term Outcome After Surgery
The mean postoperative follow-up period was 4.6 years (median 2.7 years; range 0.1–22.3 years) for the full cohort, representing a total of 384.5 patient-years of follow-up. There were no hemorrhages in any cases following a complete resection. One of the 2 incompletely resected lesions bled 7.5 years postoperatively; this lesion was associated with an extensive venous telangiectasia (Fig. 2). At the 9-year follow-up, the patient had an improving left upper-extremity paresis and medically controlled seizures.

Radiographically, there was 1 recurrence (1.2%) in a child with multiple CMs; there were no recurrences in completely resected single lesions. This recurrence represents an unusual case of a child with von Willebrand disease who also developed multiple other de novo lesions (Fig. 3).

Symptomatically, 46 (96%) of 48 children were seizure-free at the last follow-up. Seizure outcomes are further summarized in Table 2. The operative permanent complication rate was 5%, with complications occurring only in patients with eloquent lesions (16% vs 0%, respectively, of noneloquent CM). Complication rates did not significantly differ for lesions associated with a DVA (p = 0.45), in patients with a family history of CM (p = 1.0), or in those with radiation-induced lesions (p = 1.0).

Only 1 child (1.2%) developed a delayed de novo seizure condition after resection of a temporal CM, now controlled with antiepileptic medications. Six children developed new or worsening neurological deficits after surgery: 5 with frontal lesions had new or worsening hemiparesis, and 1 with an occipital lesion had a new visual field deficit. The deficits were permanent in 3 cases (all hemiparesis). Including the 1 child with de novo seizures, the permanent complication rate was 5% (4 of 83 patients).

Comparative Analysis to Nonoperative Cases
Compared with patients managed with observation only, patients selected for surgery were older (mean age 11.8 vs 9.8 years, respectively, p = 0.03), were more likely to have symptomatic lesions (p < 0.0001), and had larger lesions (mean lesion size 2.2 vs 1.0 cm, respectively, p

Lobar cavernous malformations

Although 20 patients in the nonoperative cohort had medically controlled seizures, of 75 patients in the nonoperative group who had not initially presented with seizures, 5 patients developed new seizures (7%); in the operative cohort, of 35 patients who did not have seizures preoperatively, only 1 (3%) developed new seizures after surgery. Over a total of 561.2 patient-years of follow-up for 98 cases of nonoperative CM, 5 hemorrhages occurred, corresponding to an overall hemorrhage rate of 0.9% per lesion-year. This rate was 0.5% per lesion-year for asymptomatic CM, 2.3% per lesion-year for CM associated with seizures, and 3.0% per lesion-year for hemorrhagic CM. Over a total of 360.8 patient-years of follow-up for 78 cases of completely resected CM, no hemorrhages occurred.

Discussion

Cerebral CMs are clusters of dilated sinusoidal vessels lined by endothelium without intervening neural parenchyma. They are the most common cerebral angiographically occult vascular malformation, with an estimated prevalence ranging from 0.4% to 0.6% across both adult and pediatric populations. The most common location for intracranial CMs is lobar, defined as supratentorial but not involving the thalamus/hypothalamus or basal ganglia. These lesions can serve as a source of neurological morbidity as a result of seizures and/or hemorrhage. It has been repeatedly demonstrated that hemorrhagic CMs are more likely to rebleed, adding further neurological morbidity with time.

Although the management of CMs in eloquent or deep locations, such as the basal ganglia or brainstem, accounts for some of the most intriguing reports in the literature, it is important to segregate their re-
sults from those of managing lobar CM in order to more clearly delineate the morbidity and long-term outcomes in the more common lobar lesions. Surgical management of lobar CMs has been described, although the preponderance of the data comes from adult patients. Some excellent pediatric series have been reported, although larger cohorts that include current operative techniques, recent imaging technologies, and lengthy follow-up are more limited in number. This report presents a large surgical cohort of children exclusively with lobar supratentorial CM, focusing on surgical results and complications as well as long-term outcomes.

Descriptions of operative treatment of cerebral CMs in children have existed for decades, with the earliest surgical series reported by Pozzati et al. in 1980. As noted then, the relatively safe access to supratentorial lobar lesions marks them as appealing surgical targets, with resection predicated on reducing seizure frequency and 

**Fig. 2.** A and B: Axial T2-weighted and T1-weighted post-Gd MR images. C: Axial MR image of a complex right frontal CM in association with an extensive venous telangiectasia. This 3-year-old male presented with seizures from this CM. Partial resection was performed; however, the lesion rebled after surgery.

**Fig. 3.** A: Axial T2-weighted MR image. This 2-year-old child with von Willebrand disease had undergone partial resection of a left frontal CM at an outside institution. The lesion was then resected. B: Postoperative axial T2-weighted MR image. C: Axial T2-weighted MR image at 6-year follow-up. Black arrow designates recurrent lesion, which was first seen at 1.5-year follow-up. D: Axial T2-weighted MR image at 6-year follow-up. Black arrow indicates recurrent lesion. E: Axial T2-weighted MR image at 6-year follow-up. Black arrow designates 2 de novo lesions.
Lobar cavernous malformations

Table 2: Seizure outcomes stratified by Engel class

<table>
<thead>
<tr>
<th>Engel Class</th>
<th>Description</th>
<th>Seizure Cohort (n = 48)</th>
<th>Entire Cohort (n = 83)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>seizure free</td>
<td>46 (96%)</td>
<td>80 (96%)</td>
</tr>
<tr>
<td>II</td>
<td>rare seizures</td>
<td>2 (4%)</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>III</td>
<td>improvement in seizure frequency</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>IV</td>
<td>no improvement/worsening in seizures</td>
<td>0</td>
<td>1 (1%)</td>
</tr>
</tbody>
</table>

Eliminating future hemorrhages and resultant neurological deficits. However, a small risk of complications exists with any cranial surgery, and there is ongoing debate regarding how best to find equipoise between the risk of observation and the risk of surgery in this population.2,5,12

Our series serves to reinforce the findings from larger adult series and smaller pediatric series that suggest that operative management of lobar CMs can be achieved with a high rate of complete resection. Extracting patient data from previous reports (9 series with 189 patients) demonstrates consistent, exceedingly high complete resection rates for these lesions (99% overall) (Table 3).2,5,10,12,13,15,19,27 Improved intraoperative navigation, intraoperative ultrasound, and now intraoperative MRI are key components to achieving this statistic. Our 2 cases of incomplete resection represent exceptional cases—one with a lesion entirely embedded in motor cortex without a safe corridor of access (Fig. 1) and another in association with a complex venous telangiectasia (Fig. 2). These cases underscore the need for careful assessment of operability and risk, including the potential role for functional MRI and diffusion tensor imaging, coupled with intraoperative neurophysiological monitoring for select cases. In particular, subcortical lesions contained within eloquent cortex or intimately associated with critical vascular structures may be less amenable to complete resection.

Surgical treatment of lobar CMs has a low complication rate, with new permanent neurological complications at approximately 4% across pediatric series (Table 3).2,5,12 Of particular note is the marked increased risk for complications (not unexpectedly) for lesions in eloquent cortex. Only 2 patients (1%) across all reviewed series had worsening seizures after treatment, while 94% of patients were seizure free at follow-up. In our own cohort, 96% of patients presenting with seizures were seizure free at follow-up, although none of our patients had intractable seizures prior to surgery. Nevertheless, this high rate of symptom resolution, coupled with low morbidity, supports the role of resection in this cohort.

One of the important aspects of our series is the relatively long-term follow-up in a pediatric population (total of 384.5 patient-years of follow-up; mean 4.6 years). Radiographic cure rates for completely resected lesions were excellent, with only 1 recurrence (1.2%) found in a child who ultimately went on to develop multiple lesions, demonstrating a likely underlying genetic propensity to grow new CMs. Clinically, perioperative morbidity commonly resolves and symptom relief is substantial and durable.

Risk Stratification and Case Selection

Attempts to risk-stratify cerebral CMs in grading schemes analogous to those utilized for arteriovenous malformations have been recently attempted;22 however, the inclusion of lesions in all locations creates a focus on the challenge of ganglionic, thalamic, and brainstem lesions. These CMs have a significantly greater associated surgical risk,16,17,30 and including results of their treatment among supratentorial lobar lesions potentially dilutes the accuracy of predicting outcomes for specific locations. As we demonstrate, a focus on supratentorial lobar lesions, generally ideal surgical targets, reveals exceedingly high resection and seizure control rates with very low morbidity. However, our series also underscores the importance of caution when considering lesions in eloquent cortex for resection.

Table 3: Compendium of extracted data from surgical series of pediatric CM detailing supratentorial lobar lesions

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>No. of Cases</th>
<th>Full Resection</th>
<th>Permanent Complications</th>
<th>Seizure Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acciari et al., 2009</td>
<td>35</td>
<td>35/35</td>
<td>3/35</td>
<td>29</td>
</tr>
<tr>
<td>Alexiou et al., 2009</td>
<td>14</td>
<td>14/14</td>
<td>0/14</td>
<td>11</td>
</tr>
<tr>
<td>Buckingham et al., 1989</td>
<td>7</td>
<td>0/7</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Consales et al., 2010</td>
<td>18</td>
<td>18/18</td>
<td>0/18</td>
<td>18</td>
</tr>
<tr>
<td>Di Rocco et al., 1996</td>
<td>17</td>
<td>17/17</td>
<td>0/17</td>
<td>17</td>
</tr>
<tr>
<td>Fortuna et al., 1989</td>
<td>5</td>
<td>5/5</td>
<td>0/5</td>
<td>5</td>
</tr>
<tr>
<td>Herter et al., 1988</td>
<td>5</td>
<td>0/5</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Pozzati et al., 1980</td>
<td>5</td>
<td>1/5</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>current series</td>
<td>83</td>
<td>81/83</td>
<td>4/83</td>
<td>80</td>
</tr>
<tr>
<td>pooled (%)</td>
<td>189</td>
<td>170/172 (99)</td>
<td>8/189 (4)</td>
<td>177 (94)</td>
</tr>
</tbody>
</table>
Summary

Our series supports the literature advocating a role for the resection of lobar CMs in children. The high rate of complete resection, low frequencies of recurrence, and small number of complications reported in other series is further corroborated by our experience. The long follow-up in our pediatric population suggests that the beneficial effects of surgery are durable, information hopefully of use to clinicians treating affected children. Factors such as lesion size, hemorrhage at presentation, and specific location in the hemispheres are intuitively based patient treatment selection factors that are born out by this series. The quantification of their effect in this patient population will improve the ability of the neurosurgeon to make an informed therapeutic decision in the pediatric patient with a lobar CM.

Conclusions

The resection of symptomatic supratentorial lobar CMs is a safe and effective procedure with high complete resection rates, rewarding long-term seizure outcomes, and low complication rates. Asymptomatic lesions or those in eloquent cortex may be better candidates for observation, although individualized assessment of risks and benefits remains critical. Following complete excision of lobar CMs in the pediatric patient, there appears to be both excellent symptom relief and durable radiographic cure rates.

Disclosures

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

Author contributions to the study and manuscript preparation include the following: Conception and design: Scott, Gross. Acquisition of data: Scott, Gross, Goumnerova. Analysis and interpretation of data: all authors. Drafting the article: Gross, Smith, Scott. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Scott. Statistical analysis: Gross. Administrative/technical/material support: Scott, Smith, Goumnerova, Proctor, Madsen. Study supervision: Scott.

References


B. A. Gross et al.
Lobar cavernous malformations


Manuscript submitted March 14, 2013. Accepted July 1, 2013. Please include this information when citing this paper: published online August 23, 2013; DOI: 10.3171/2013.7.PEDS13126. Address correspondence to: R. Michael Scott, M.D., Department of Neurological Surgery, Boston Children’s Hospital, 300 Longwood Ave., Boston, MA 02115. email: michael.scott@childrens.harvard.edu.