Surgical approaches to brainstem cavernous malformations

Adib A. Abla, M.D., Jay D. Turner, M.D., Ph.D., Alim P. Mitha, M.D., M.Sc., Gregory Lekovic, M.D., Ph.D., J.D., and Robert F. Spetzler, M.D.

Division of Neurological Surgery, Barrow Neurological Institute, St. Joseph’s Hospital and Medical Center, Phoenix, Arizona

Brainstem cavernous malformations (CMs) are low-flow vascular lesions in eloquent locations. Their presentation is often marked with symptomatic hemorrhages that appear to occur more frequently than hemorrhage from supratentorial cavernomas. Brainstem CMs can be removed using 1 of the 5 standard skull-base approaches: retrosigmoid, suboccipital (with or without telovelar approach), supracerebellar infratentorial, orbitozygomatic, and far lateral.

Patients being referred to a tertiary institution often have lesions that are aggressive with respect to bleeding rates. Nonetheless, the indications for surgery, in the authors’ opinion, are the same for all lesions: those that are symptomatic, those that cause mass effect, or those that abut a pial surface. Patients often have relapsing and remitting courses of symptoms, with each hemorrhage causing a progressive and stepwise decline. Many patients experience new postoperative deficits, most of which are transient and resolve fully. Despite the risks associated with operating in this highly eloquent tissue, most patients have had favorable outcomes in the authors’ experience. Surgical treatment of brainstem CMs protects patients from the potentially devastating effects of rehemorrhage, and the authors believe that the benefits of intervention outweigh the risks in patients with the appropriate indications.

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Key Words • hemorrhage • cavernous malformation • surgical approach

Cavernous malformations are low-flow vascular lesions thought to be related to capillary telangiectasias and developmental venous anomalies. They are found throughout the CNS, with a minority of these lesions occurring in the brainstem. Cavernous malformations were once considered to be congenital lesions; however, it is now well established that these lesions also form de novo. Cavernous malformations located in the brainstem are particularly difficult to treat, given their location in eloquent tissue. Brainstem CMs can be found anywhere within the brainstem, but most commonly occur in the pons.

It has been reported that infratentorial CMs are more dangerous than their supratentorial counterparts. In terms of bleeding propensity, one series showed that the rates of hemorrhage in infratentorial lesions were 30 times greater in prospectively followed patients. Resection of brainstem CMs is associated with a significant risk of morbidity due to their highly eloquent location. However, complete removal can cure the patient of the often devastating symptoms associated with recurrent hemorrhages and hemosiderin deposition in the brainstem. In 1928 Walter Dandy reported the first case of a brainstem CM, which was surgically removed from the pontomedullary region in a 21-year-old patient. In the years since, our understanding of brainstem CMs has continued to evolve. Our knowledge is derived from a variety of publications that have reported on the pathophysiological characteristics of brainstem CMs, the natural history of the disease, and surgical approaches and outcomes.

We review the natural history of brainstem CMs, prior reports of surgically treated lesions, and the surgical technique and philosophy of the senior author (R.F.S.), and offer recommendations on surgical approach based on lesion location. We also include preliminary data on the clinical presentation, lesion location, and surgical approaches used, from the largest series ever reported in both children and adults.

Natural History and Annual Rates of Hemorrhage

It is difficult to have confidence in the various estimates of bleeding rates in patients with a brainstem CM due to 2 primary confounding factors. First, to determine accurate rates, the denominator of “time” must be well established. Although it was once assumed that all CMs...
were congenital, it is now understood that these lesions can also form de novo (resulting from irradiation, for example). However, due to an inability to diagnose the onset of de novo lesions, most retrospective studies that have reported hemorrhage rates have assumed that all lesions have been present since birth. Without accounting for de novo lesions, these studies probably underestimate true bleeding rates.

Second, the various reports on the natural history of brainstem CMs have an inherent selection bias. Surgical series are primarily based on a selected cohort of patients who have presented as a result of a symptomatic hemorrhage, and who have been referred to tertiary care centers for consideration of surgical treatment. Patients who have experienced silent hemorrhages are not considered in these studies. It is also likely that patients with large, highly symptomatic, and/or recurrent hemorrhages are part of a higher-risk subpopulation. At our institution, for example, a retrospective hemorrhage rate from 260 adult patients (assuming brainstem CMs were present since birth) was calculated to be 4.6%, and the rate of rehemorrhage was greater than 30%. Most of our patients (97%) had a history of hemorrhage, and 146 patients (56%) had a history of repeat hemorrhages before surgery, a fact that probably reflects both our referral and selection biases. We suspect that the true hemorrhage rate for patients with a brainstem CM in the general population is likely to be significantly lower. We have previously reported a 5% annual rate of hemorrhage for all patients from the same institution. In another large surgical series of 137 patients who were surgically treated, an approximately 6% hemorrhage rate per year was reported. Our data show that a prior rupture increases the annual hemorrhage rates during the observational period carried forward from that time point, as compared with the hemorrhage rate for the initial event.

Conversely, observational studies probably represent less aggressive brainstem CMs and underestimate hemorrhage rates. Brainstem CMs that have resulted in devastating presentations and cannot be observed are excluded from the analysis. Several attempts have been made to evaluate prospectively the natural histories of untreated lesions. Kondziolka et al. found an annual bleeding rate of 0.6% in patients without a prior rupture, and of 4.5% in those who had prior hemorrhages. Of 122 patients, 43 harbored cavernomas in the brainstem. The bleeding rates were similar to supratentorial lesions. In a prospective group of 68 patients with CMs (20% infratentorial), Moriarity et al. found a rehemorrhage rate of 3.1% per patient-year. In female patients, the prospectively recorded rate was 4.2%. Prior ruptures did not correlate with a higher annual bleeding rate during observation. In a prospective study of patients with familial CMs, Zabramski et al. found a 6.5% annual hemorrhage rate per patient-year.

### Indications for Surgical Treatment of Brainstem CMs

Not every patient with a brainstem CM who is referred to us will be offered surgery. Significant morbidity is potentially associated with the treatment of these lesions, even at a high-volume center. In appropriately selected patients, however, surgery is warranted given that surgical outcomes can be favorable when balanced against observation, which often leads to further morbidity in patients with more aggressive lesions.

The risks of surgery need to be balanced against the natural history of the disease. As stated, the natural history of CMs is controversial. Although we presume that cavernomas are histologically the same in all locations, brainstem CMs manifest and behave differently from supratentorial lesions: hemorrhages are far less likely to be subclinical and are more likely to be accompanied by more severe symptoms.

Dates of initial presentation, dates of hemorrhage, and interval between hemorrhages were determined for all patients who presented to our institution. We defined a history of hemorrhage as follows: 1) intra- or extradural blood products on MR imaging, and 2) an acute onset of focal neurological deficit. We did not include patients with progressive symptoms without hemosiderin staining on their radiographs (or vice versa) as having definitive hemorrhage. Surgery was offered to patients with either acute extralesional hemorrhage, an exophytic (that is, pial surface–abutting) lesion, repeat hemorrhages and clinical deterioration, or mass effect caused by hemorrhages.

Those with mild symptoms and/or deep-seated CMs were observed until further bleeding episodes made the lesions more amenable to intervention (that is, the pial surface could be reached via the hemorrhagic cavity). Over the years, based on the large experience of the senior author, more lesions that did not abut a pial surface have been removed. Across time, morbidity has been minimized by improvements in surgical navigation, surgical instruments, and surgical technique, and by the reduced use of more invasive approaches, including transcochlear approaches or full OZ craniotomies. Lesions that do not place eloquent tissue at risk when traversing a pial surface are removed with the help of intraoperative navigation, which facilitates resection of lesions that do not leave hemosiderin staining on the cortical surface.

It is important to note that because the cumulative lifetime risk of bleeding is higher in patients with a longer life expectancy, it may be appropriate to have a lower threshold for surgical intervention in children. The prevention of rehemorrhage is likely to have a greater impact in the pediatric population than in adults, and this fact should be considered during treatment planning.

### Note on Offering Patients Radiation Treatment for Lesions That are not Amenable to Surgery

There are reports of the use of radiation therapy, including proton beam therapy, to treat CMs that are unsuitable for surgery. We believe that this treatment requires further validation. Our preference has not been to recommend radiation treatment for brainstem CMs. Although a cause and effect relationship has not been established, in a patient at our institution, a previously irradiated brainstem CM later degenerated into an arteriovenous malformation at the same location. The significance of this finding requires further study.
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Common Presentations

Symptomatology tends to correspond with the deficits that would be predicted by lesions in various parts of the brainstem (Table 1). Cranial nerves are affected depending on the site of hemorrhage. Those in the midbrain are more likely to affect CNs III and IV as well as motor fibers of the cerebral peduncles. Pontine lesions are more likely to be associated with palsy of CNs V, VI, and VII. Medullary lesions often manifest with hic-coughs, swallowing difficulty, or vocal cord paralysis. In our experience, the combined presentation of a brainstem hemorrhage and the acute onset of any of those common deficits, which first gradually remit but later relapse, can predict the finding of a brainstem CM, even in the absence of MR imaging.

A Relapsing and Remitting Course

Most patients whom we evaluate have a history of rupture and have been referred from other institutions. Many neurological deficits caused by hemorrhage ultimately resolve over time. This clinical improvement is probably due to the resorption of blood products within the cavity, and supports the theory that the blood products displace rather than invade the surrounding tissue. Additional hemorrhages will create a new stepwise deterioration in baseline neurological status. When patients undergo surgery, the procedure often creates symptoms that were present during previous events. As many as half of patients have temporary deficits, but these deficits also tend to resolve in many of them. In patients with permanent “new” deficits, these are frequently similar to prior deficits that may have improved before treatment. We believe that this relapsing and remitting course can be halted by resection of the brainstem CM in most patients. Our preoperative consultation informs patients of the possibility of new deficits, and that surgery will often mimic an additional bleeding event, with the hope that no further events will occur. Patients who have had the best outcomes have had extended follow-up of 10 years or longer, with gradual improvement in new or prior deficits in the absence of recurrent hemorrhages in almost 90% of all those treated.

Surgical Techniques and Philosophy

We routinely monitor somatosensory evoked potentials and motor evoked potentials, but we do not routinely map the motor fibers or floor of the fourth ventricle, nor do we use diffusion tensor imaging modalities. When a CM is resected, a small cortical opening is made, and the fibers of the brainstem are stretched. The lesion is removed piecemeal to limit the cortical opening. The use of a CO₂ laser can help break up, vaporize, or cut the cavernoma within the brainstem, and has been helpful in select cases. Even in the case of more deeply seated lesions, in our opinion, a minimal access approach renders these surgeries better tolerated.

We have found the use of intraoperative image guidance to be indispensable in these procedures. The image guidance aids in transtentorial approaches when the tentorium is sectioned for further access to thalamic lesions originating in the brainstem, as well as to deep-seated lesions that do not exhibit a telling hemosiderin stain at the cortical entry point. Without image guidance, we do not believe that the cortical opening can proceed safely when lesions are hidden from the surface of the brainstem.

We have found that a developmental venous anomaly is inherently associated with each brainstem CM. Such venous anomalies are benign but abnormal constellations of veins draining normal brain tissue. Our observations do not support removal of a developmental venous anomaly to prevent recurrence or regrowth. Because the anomaly may indeed be essential to the venous drainage of the surrounding brainstem, its removal is unnecessary and can pose an unnecessary risk of venous infarction.

Although the corridors involved in the surgical removal of brainstem CMs are often long, we do not advocate the use of retraction, to minimize potential retraction injuries. Our preference is to perform retraction with the use of the 2 instruments in hand, the dissection instrument or the suction instrument, which is moved as the lesion is removed or the surgical focus moves farther from the retractor. This process avoids placing further stretch on normal brain tissue. We have begun to find that using lighted instruments, a bipolar device, or a microsuction device can help with illumination when the microscope’s focused area of view and the light source are sufficiently divergent, as tends to occur at high magnification. We do not attempt to resect hemosiderin-laden brain surrounding a brainstem CM, but we do attempt to remove as much of the CM as can be performed safely.

In the evolution of the surgical treatment of brainstem CMs, we have largely abandoned more invasive approaches, including anterior petrosectomy, transcocochlear, and full OZ craniotomy in favor of the following most-used approaches in the removal of brainstem CM: the retrosigmoid, suboccipital with or without telovelar, and lateral SCIT craniotomies (Table 2). With these 3 “workhorse” approaches as well as with the far-lateral and a miniature/modified OZ approach, a lesion in any part of the brainstem is accessible. The specific approach is selected on a case-by-case basis, according to the anatomical location of the lesion. The 2-point method was used as an objective means to choose the surgical approach. One point is placed in the center of the lesion, and a second point is placed either where the lesion comes closest to a pial surface or at the safest entry point into the brainstem.

### TABLE 1: Most common presenting deficits in 260 adult patients with brainstem CMs

<table>
<thead>
<tr>
<th>Deficit</th>
<th>% of Patients w/ Deficit</th>
</tr>
</thead>
<tbody>
<tr>
<td>CN</td>
<td>63</td>
</tr>
<tr>
<td>sensory</td>
<td>53</td>
</tr>
<tr>
<td>headache</td>
<td>39</td>
</tr>
<tr>
<td>motor deficit of extremity</td>
<td>37</td>
</tr>
<tr>
<td>diplopia</td>
<td>33</td>
</tr>
<tr>
<td>ataxia</td>
<td>29</td>
</tr>
<tr>
<td>vertigo</td>
<td>25</td>
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</table>
Connecting these 2 points, a line is drawn and extended to the skull; this method guides the selection of the most appropriate craniotomy.

When necessary, it is possible to combine the approaches; for example, a combined far-lateral/retrosigmoid approach for anterolateral lesions at the pontomedullary junction, or a combined supracerebellar/retrosigmoid approach when a lesion sits farther superiorly and lateral in the MCP than can reasonably be accessed with a telovelar approach. Recently, we have incorporated more uses for the SCIT approach than we previously had anticipated. Such cases include resection of pontomesencephalic lesions, laterally located lesions of the cerebral peduncle, and supratentorial lesions such as those located in the midbrain and thalamus, which can be resected by a SCIT approach with the added step of opening the tentorial junction, or a combined supracerebellar/retrosigmoid approach for anterolateral lesions at the pontomedullary junction, or a combined supracerebellar/retrosigmoid approach when a lesion sits farther superiorly and lateral in the MCP than can reasonably be accessed with a telovelar approach. Recently, we have incorporated more uses for the SCIT approach than we previously had anticipated. Such cases include resection of pontomesencephalic lesions, laterally located lesions of the cerebral peduncle, and supratentorial lesions such as those located in the midbrain and thalamus, which can be resected by a SCIT approach with the added step of opening the tentorial edge to increase working room.

**Correlating Lesion Location With Approach**

Although we have moved away from more invasive approaches, we still believe that exposure and adequate visualization are the most important goals in these surgeries. We advocate increased bone removal, within reason, to limit brain retraction and to enhance visibility. Most lesions are located in the pons (Table 3), which requires several approaches to address adequately all lesions in this location (Table 2 and Fig. 1). In the case of a brainstem CM of the cerebellopontine angle, the 2-point method might suggest a lateral trajectory such as a transpetrosal approach, which would have been our approach early in the experience at our institution. However, a sufficiently lateral trajectory can be achieved with mild cerebellar retraction and a retrosigmoid approach. Anterolateral lesions in the pons and midbrain also may require modifications to the suggested approach when the 2-point method is used. We avoid entry into the cerebral peduncle to resect a CM by entering lateral to the peduncle from an OZ approach to reach a brainstem CM situated more anteriorly in the midbrain, unless it sits between the peduncles, at which point the 2-point method is valid in suggesting an interpeduncular OZ approach. If a lesion is situated in the posterothalamic pons, we use either a retrosigmoid approach for more inferior lesions, ideally making a cortical entry between fibers of CNs V and VII (Fig. 2), or a lateral SCIT approach for more superior lesions in the posterolateral pontomesencephalic junction and midbrain/thalamus. The suboccipital approach is useful for cavernomas in the floor of the fourth ventricle or posterior medulla. We add the telovelar variation to the suboccipital approach for inferioromedial MCP lesions (Fig. 1). Cavernomas laterally situated in the MCP can be accessed via retrosigmoid or lateral SCIT approaches. Lateral or anterolateral lesions of the medulla necessitate a far-lateral approach.

**Postoperative Imaging**

Magnetic resonance imaging is performed in all patients while they are hospitalized on postoperative Day 1. Patients undergo repeat imaging each year for the first 2 to 3 years, and then every 2 to 4 years thereafter. Patients who develop symptoms between MR imaging follow-up examinations undergo imaging sooner. In patients with MR imaging studies that suggest residual or recurrent growth of a residual lesion, images are obtained as often as annually. We routinely obtain imaging while the patients are hospitalized, although the immediate postoperative milieu of the surgical cavity can make it difficult to discern residual brainstem CM from hemostatic agents. We have considered obtaining MR imaging 2 weeks after surgery, but it becomes difficult to implement because many patients have already left the state or the country to return home by then. An enlarging surgical cavity or evidence of rehemorrhage probably represents an incompletely resected lesion that has grown and/or rebled. If we suspect residual lesion on the immediate postoperative MR imaging study, we return patients to surgery to remove additional cavernoma during the same hospitalization to maximize protection from future events. However, we do not advocate an overly aggressive resection or one that involves removal of hemosiderin-laden tissue. Rather, if postoperative surgical products in the resection cavity (such as hemostatic agents or blood) cannot be distinguished from CMs, we obtain subsequent imaging sooner than the first annual MR imaging session.

<table>
<thead>
<tr>
<th>TABLE 2: Surgical approaches in 300 patients with brainstem CMs</th>
<th>TABLE 3: Location of lesion in 300 patients with brainstem CMs</th>
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</thead>
<tbody>
<tr>
<td><strong>Approach</strong></td>
<td><strong>No. (%)</strong></td>
</tr>
<tr>
<td></td>
<td>Adults</td>
</tr>
<tr>
<td>suboccipital (w/ or w/o telovelar)</td>
<td>74 (28.5)</td>
</tr>
<tr>
<td>retrosigmoid</td>
<td>57 (21.9)</td>
</tr>
<tr>
<td>lat SCIT</td>
<td>53 (20.4)</td>
</tr>
<tr>
<td>far lat</td>
<td>33 (12.7)</td>
</tr>
<tr>
<td>OZ</td>
<td>18 (6.9)</td>
</tr>
<tr>
<td>retrolabyrinthine</td>
<td>6 (2.3)</td>
</tr>
<tr>
<td>subtemporal/anterior petrosectomy</td>
<td>6 (2.3)</td>
</tr>
<tr>
<td>other</td>
<td>13 (5.0)</td>
</tr>
<tr>
<td>total</td>
<td>260</td>
</tr>
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</table>

* Includes cervicomedullary lesions.
† Includes lesions involving the floor of the fourth ventricle and/or MCP.
‡ Includes mesencephalic lesions extending into the thalamus.
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Forthcoming Reports

We are currently in the process of reporting our series of 300 surgically treated patients (260 adults and 40 children) with brainstem CMs with regard to preoperative hemorrhage rates, rates of postoperative hemorrhage and/or regrowth of cavernomas, rate of new postoperative deficits, and clinical outcomes.

Conclusions

Brainstem CMs warrant resection in patients with symptomatic lesions that are surgically accessible. Those that reach or are near a pial surface can be removed using standard skull base techniques (Table 3), and as suggested, by using the 2-point method. Asymptomatic patients or those with considerable brainstem tissue that would need to be transgressed to resect a brainstem CM should be observed. Future hemorrhagic events in observed patients may provide a more accessible corridor to the cavernoma for resection.

In most patients, surgical treatment of brainstem CMs is associated with new neurological deficits, most of which resolve by the last follow-up. Given the high rates of rehemorrhage in patients who have not had surgery, and the improved quality of life due to a reduced relaps-
ing and remitting clinical course with repeat hemorrhages, a relatively low rate of rebleeding from recurrence/residual lesion, and excellent postoperative neurological outcomes, resection is indicated in symptomatic patients with accessible lesions. Patients with new deficits experience symptoms similar to those that appeared with prior hemorrhages, and often make a significant recovery over time while attaining increased protection from future bleeding events.

Disclosure

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: Abla, Spetzler. Acquisition of data: Abla, Turner, Mitha, Lekovic. Analysis and interpretation of data: Abla, Turner, Mitha, Lekovic. Drafting the article: Abla, Turner. Critically revising the article: all authors. Reviewed final version of the manuscript and approved it for submission: all authors. Statistical analysis: Abla, Turner. Administrative/technical/material support: Spetzler, Turner, Mitha, Lekovic. Study supervision: Spetzler, Mitha.

References


Address correspondence to: Robert F. Spetzler, M.D., c/o Neuroscience Publications, Barrow Neurological Institute, 350 West Thomas Road, Phoenix, Arizona 85013. email: neuropub@chw.edu.