

# Clinical Analysis of Microsurgery for Brainstem Cavernous Malformations: Surgical Indications, Optimal Approaches, and Clinical Outcomes

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## ● ABSTRACT

**Objective :** This study aimed to analyze patients who underwent microsurgery for brainstem cavernous malformations (BCMs) and to investigate the effectiveness and the limitations of surgical resection of BCMs. **Methods :** We retrospectively analyzed the clinical data of patients who underwent surgical resections for BCMs between 1989 and 2010. We investigated the age distribution, preoperative hemorrhagic rates, initial clinical presentations, locations of the lesions, and preoperative and postoperative Karnofsky Performance Scale (KPS) scores. We also analyzed surgical indications, the timing of surgery, and surgical approaches. **Results :** All 15 patients underwent microsurgery for BCMs; 13 underwent total resection of their lesions, but 2 underwent incomplete resections and consequently experienced postoperative recurrent hemorrhage. We observed 11 patients through a complete follow-up, for a mean of 53.1 months (range 1-131 months) after diagnosis (nine patients > 24 months follow-up). During the follow-up periods, 3 patients were lost to follow-up, and one patient expired, due to aspiration pneumonia, 31 months postoperatively. The mean preoperative KPS score was 50, and the mean postoperative KPS score was 67. During the complete follow-up period, 3 patients recovered completely (KPS scores of 90-100) and 7 patients (63.6%) showed improvement in KPS scores. **Conclusions :** Surgeons should consider microsurgery for BCMs the treatment of choice for patients who suffer from progressive neurological decline. Successful resection of BCMs depends on an optimal surgical approach, appropriate timing of surgery, and well-informed surgical techniques. The aim of surgery must be total resection of the lesions without any deteriorative neurological morbidity. (*Kor J Cerebrovascular Surgery* 12(3):169-176, 2010)

**KEY WORDS :** Brainstem · Cavernous malformation · Cavernoma · Microsurgery · Surgical approach

## Introduction

Cavernous malformations (CMs) account for 5% to 15% of all central nervous system (CNS) vascular malformations. Brainstem cavernous malformations (BCMs) are rare, and 9% to 35% of all CMs are located in the brainstem.<sup>5)6)9)11)16)</sup> Because of their eloquent location, BCMs can result in hemorrhages, progressive neurological deficits, and fatal

outcomes, such as death.<sup>4)14)</sup> Due to their precarious location and potentially devastating clinical course, BCMs are particularly challenging for neurosurgeons.<sup>7)</sup> With the improvements in neuroimaging and microsurgical techniques, surgeons no longer consider BCMs inoperable.<sup>19)</sup> However, most BCMs have limited surgical indications and a considerable rate of surgical morbidity.

Surgeons should consider treating BCMs via surgical resection, given an appropriate clinical scenario. Patients who have had recurrent hemorrhages or who are experiencing progressive neurological decline should have the option of surgery. It is also reasonable to consider observation for patients with previous hemorrhagic episodes and acceptable neurological deficits.<sup>7)</sup> BCMs have a propensity for hemorrhage and re-hemorrhage. The incidence of hemorrhage and re-hemorrhage for BCMs is

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20-fold higher than that of supratentorial cavernous malformations is.<sup>2)(8)(17)</sup> Therefore, a BCM requires a prudent surgical decision.

We performed this retrospective clinical analysis on 15 patients that our hospital treated operatively for BCMs, between 1989 and 2010. We describe the immediate and long-term surgical outcomes, complications, and surgical indications, including locations of lesions, surgical approaches, and surgery time.

## Materials and Methods

### 1. Patients and clinical characteristics

We retrospectively analyzed clinical data of 15 patients who underwent microsurgical treatment for BCMs at our institution between August 1989 and March 2010. Table 1 summarizes the patients' clinical characteristics. All patients presented with at least one hemorrhagic episode at the time of their admission. Clinical presentations of all patients included hemiparesis, hemihypesthesia, ataxia, dizziness, nausea, vomiting, diplopia, dysphagia, signs of increased intracranial pressure (ICP), and cranial nerve (CN) palsies. In particular, we investigated the CN palsies in numerical order, from the third to the ninth CN. The clinical presentations differed according to the lesions' locations (Table 2). The anatomical locations of the lesions were defined via magnetic resonance imaging (MRI) and classified as follows: midbrain, pons-midbrain, pons, pons-medulla, and medulla oblongata.

MRI scans were obtained for all patients. Surgeons did not perform cerebral angiographies when MRI showed patients with typical features of cavernous malformations. Angiography generally reveals no definite abnormal vascular structures, except coexisting venous anomalies. The typical MRI findings were "popcorn" or "mulberry" lesions from previous, recurrent hemorrhages.<sup>19)</sup> In each case, we measured the maximal diameter of the lesion on the preoperative MRI and also evaluated whether the lesion reached the pial surface of the brainstem or not. We defined lesions that reached the pial surface as "exophytic." Lesions that were not visible upon initial exposure we termed "intrinsic."<sup>8)</sup> We recorded intra-operative findings based on the operative reports. Each patient had received a diagnosis of cavernous malformation by means of a postoperative

histopathologic examination.

Patients were observed for a mean period of 53.1 months (range 1-131 months) after their diagnosis (nine patients > 24 months' follow-up). During the follow-up period, three patients were lost to the follow-up; also, one patient expired, due to aspiration pneumonia, 31 months postoperatively. Eleven patients completed follow-up and received evaluations comprising neurological examinations and postoperative imaging studies at the outpatient department or telephone interviews.

### 2. Surgical approaches

In each case, we had selected the surgical approaches based on the CMs' locations and the nearest site at which the hemorrhages presented to the pial or ependymal surfaces. We had also considered the location of the safe entry zone into each patient's brainstem for the optimal surgical approaches and had performed a midline suboccipital approach for any lesion located in the dorsal pontine or medulla oblongata, also using this approach, when appropriate, to explore the lesion through the fourth ventricle floor. When we approached the CM through the floor of the fourth ventricle, we accessed the lesion through either the upper-facial triangle or the lower-facial triangle, to minimize dissection and retraction of brainstem tissue.<sup>1)(13)(19)</sup> For lesions involving the inferior portion of the middle cerebellar peduncle, we resected them via a telovelar approach (which is the same as a transcerebello-medullary fissure approach).<sup>7)</sup> We resected cavernous malformations involving the midbrain's tectum or lateral surface through the occipital transtentorial approach. Patients with lesions in the anterolateral surface of the pons or the lateral surface of the midbrain underwent surgeries using a subtemporal approach or a transpetrosal approach. For infants, we used the transcortical transforaminal approach for any midbrain lesion presenting as postoperative recurrent hemorrhage. Table 1 and Table 3 summarize the surgical approaches we used in our series.

The aim of these surgeries was total resection of the CMs while minimizing damage to the brainstem. During each surgery, we first opened the hematoma wall and then removed the hematoma. Usually we dissected the hematoma together with the malformed vessel. A yellowish hemosiderin-stained layer around the hematoma is a helpful

**Table 1.** Summary of patients with brainstem cavernous malformations: clinical characteristics, postoperative outcomes, surgical approaches, and complications.

No.	Sex	Age	Chief complains	No. of hemorrhage	Location	Op. approach	Intrinsic / Exophytic	Preop. KPS	Postop. KPS	Time of surgery	Complications	F/U (months)
1	F	47	Lt. hemiparesis	3	Medulla	Suboccipital	Intrinsic	40		15	none †	loss
2	F	36	Rt. hemiparesis	1	Pons	Subtemporal	Intrinsic	60		16	none †	loss
3	F	51	Lt. hemiparesis, diplopia, Lt. facial weakness, IICP* Sx	1	Pons, Midbrain	Suboccipital	Intrinsic	30		4	none †	loss
4	F	5	Lt. hemiparesis, diplopia, IICP* Sx	3	Midbrain	Supracerebellar	Intrinsic	20	90	26	none †	131
5	M	35	IICP* Sx	3	Medulla	Suboccipital	Intrinsic	30	90	4	none †	99
6	F	41	Lt. hemiparesis, diplopia	1	Pons, Midbrain	Suboccipital	Exophytic	30	80	51	Rt. Facial palsy	77
7	F	35	Lt. hemiparesis, diplopia, IICP* Sx	1	Pons	Suboccipital	Intrinsic	30	80	19	Rt. Facial palsy	76
8	M	48	Diplopia, Lt. facial weakness	2	Pons	Transpetrosal	ntinsic	40	30	14	Dysphagia, quadriparesis, Respiratory difficulty (tracheostomy)	40
9	F	58	Diplopia	1	Midbrain	Occipital transtentorial	ntinsic	80	50	1 yr	Recurrent hemorrhages ‡ Lt. 3rd CN palsy, Rt. hemiparesis	35
10	F	38	Rt. hemiparesis, diplopia, Rt. facial weakness, dysphagia	2	Pons, Midbrain	Suboccipital	Exophytic	30	50	11	none †	1
11	M	3	Rt. hemiparesis, diplopia, IICP* Sx	2	Midbrain	Occipital transtentorial	Intrinsic	40		0	Recurrent hemorrhages§ Rt. 3rd CN palsy, hydrocephalus, dyskinetic involuntary movement	Expired
12	M	29	Diplopia, Rt. facial weakness	2	Pons, Medulla	Suboccipital	Exophytic	80	90	35	none †	11
13	M	67	Rt hemiparesis, diplopia, Lt. facial weakness	2	Pons	Suboccipital	Intrinsic	60	40	16	Dysphagia, quadriparesis, resp.difficulty (tracheostomy)	38
14	M	48	Diplopia, Lt. facial weakness	2	Pons, Medulla	Suboccipital	Exophytic	60	70	12	Hemihypesthesia, decreased tongue sense, Postop. ED**	51
15	M	46	Both hand numbness & pain	1	Medulla	Suboccipital	Exophytic	90	70	31	Quadriparesis voiding difficulty	25

Rt., Right; Lt., Left; No, Numbers; Op., Operative; Preop., Preoperative; Postop., Postoperative; KPS, Karnofsky Performance Scale; F/U, Follow-up

\* IICP = Increased intracranial pressure

† No change or transient aggravation of preexisting neurological deficit

‡ The patient suffered recurrent hemorrhages twice postoperatively, because of subtotal resection.

§The patient suffered recurrent hemorrhages three times postoperatively, because of subtotal resection.

\*\*Immediate postoperative epidural hematoma

guide for surgical resection.<sup>19)</sup> We used neuronavigation for identifying the location of the hematoma and repeated electrophysiological stimulation of the resection bed and floor of the fourth ventricle to confirm preservation of

brainstem nuclei.<sup>14)</sup> We usually carried out intraoperative monitoring of somatosensory evoked potentials, brainstem auditory evoked potentials, and facial electromyography (EMG) in these cases.

**Table 2.** Clinical presentations according to the brainstem cavernous malformations' locations

Signs & symptoms	Midbrain (3)	Pons– Midbrain (3)	Pons (4)	Pons– Medulla (2)	Medulla (3)
Hemiparesis	2	3	3		1
Hemihyesthesia		2	1		
Ataxia	1		1	1	
Dizziness		2	1	2	1
Nausea / vomiting		2	1	1	1
Diplopia	3	3	3		
Hand numbness					1
CN 3 palsy	3	2			
CN 4 palsy					
CN 5 palsy			2		
CN 6 palsy		3	3	2	
CN 7 palsy		2	2	2	
CN 8 palsy		1	1		
CN 9 palsy		2			
Dysphagia		2			
IICP* symptoms	2	1	1		1

\*\*IICP = Increased intracranial pressure

**Table 3.** Summary of the surgical approaches for brainstem cavernous malformations (15 patients, 18 operations, including re-operations for recurrent hemorrhages)

Surgical approaches	Total	Locations of the lesions				
		Midbrain	Pons–midbrain	Pons	Pons–medulla	Medulla
Midline Suboccipital	10		3	2	2	3
Telovelar app.	5		1	2	2	
Transvermian app.	2		2			
Others	3					3
Subtemporal	1			1		
Transpetrosal	1			1		
Occipital	4	4				
transtentorial †						
Supracerebellar	1	1				
infratentorial						
Transcortical	1					
transforaminal ‡						

† Including two re-operations

‡ Including one re-operation

### 3. Clinical outcomes

To evaluate clinical outcomes, we used Karnofsky Performance Scale (KPS) scores. Preoperative KPS scores ranged from 20 to 90. The final 11 patients completed follow-up (9 patients > 24 months follow-up), and we obtained follow-up data by means of telephone interviews and/or outpatient clinic visits. Patients were asked if they were “the same”, “better”, or “worse,” compared to their preoperative statuses. We used the KPS score to provide an objective measurement of the patients’ preoperative and postoperative neurological statuses. We defined “poor outcome” as a KPS score lower than 60 on last follow-up, which was more than 1 month after surgery or initial evaluation. We also investigated their complications, including any newly-developed postoperative neurological deficit, recurrent hemorrhagic rates, and surgery-related complications, such as postoperative epidural hematoma.

We summarized the clinical outcomes using the following parameters: surgical approach according to the location of the lesion, timing of surgery, KPS score, surgery related complications, recurrent hemorrhagic rates, and whether the patient underwent a total resection or not. Table 1 summarizes these parameters.

## Results

### 1. Patient characteristics and clinical presentations

All 15 patients received microsurgery for evacuation of a hematoma and extirpation of a CM. There were 7 males and 8 females, and the mean age was 39.1 years (range, 3-67 years old). Most patients had presented with a hemorrhage at the time of admission; 6 patients had experienced 1 hemorrhage episode, while 9 patients had experienced 2 or more before surgery. There were 5 patients (33%) with exophytic lesions, and the rest had intrinsic lesions. We found multiple lesions in 2 patients (13.3%).

We categorized the patients according to the location(s) of their CM(s) as follows: midbrain, pons-midbrain, pons, pons-medulla, and medulla oblongata. There were 3 patients with lesions in the midbrain (20%), 3 with lesions in the pons-midbrain (20%), 4 lesions in the pons (26.7%), 2, in the pons-medulla (13.3%), and 3 in the medulla oblongata (20%). Most patients (87%) presented with sudden-onset symptoms. At the time of their initial presentation, we

observed hemiparesis in 9 patients (60%), diplopia in 11 patients (73.3%), facial weakness in 6 (40%), and increased ICP Symptoms in 5 (33.3%). Only 1 patient had numbness and pain in both hands. The clinical presentations differed according to the locations of the lesions (Table 2). Hemiparesis and diplopia were the most common presentations, occurring in all groups. All patients in the midbrain group suffered diplopia, defined as oculomotor nerve palsy. Most lesions involving the pons had various CN palsies; 8 patients with pons lesions (pons-midbrain, pons, and pons-medulla) presented with sixth CN palsy, and 6 with lesions in any of these pons categories presented with seventh CN palsy. Also, 2 of the 3 patients with a lesion in the midbrain presented with symptoms of increased ICP.

### 2. Surgical approaches

All 15 patients underwent microsurgery. For the 10 patients with CMs in a medulla or a pons category, we used a midline suboccipital approach. However, we used the telovelar approach for 5 such patients, because their lesions were close to the fourth ventricle floor. For 2 patients with huge hematomas in the pons-midbrain, we used the transvermian approach. For 2 patients whose CMs presented on the lateral or anterolateral surface of the midbrain, we used the occipital transtentorial approach. However, both patients had re-operations for postoperative recurrent hemorrhage. Of the 2 surgically treated for recurrent hemorrhage, 1 underwent surgeries using the same approach (occipital transtentorial) twice postoperatively, and the other underwent the transcortical transforaminal approach for a lesion on the anterolateral surface of the midbrain. One patient with a lesion in the posterior midbrain underwent surgery using the supracerebellar-infratentorial approach, 1 patient with the lesion on the anterolateral surface of the pons underwent surgery using the subtemporal approach, and one patient with the lesion in the lateral surface of the pons underwent surgery using the posterior transpetrosal approach.

### 3. Clinical outcomes

We could give the complete follow-up to 11 of the 15 patients. The mean follow-up period was 53.1 months (range 1-131 months) after diagnosis (9 patients > 24 months follow-up). There were 3 patients lost to follow-up, and 1

patient expired, due to aspiration pneumonia, 31 months postoperatively. The expired patient's condition remained the same compared to his preoperative condition (KPS score of 40). The mean preoperative KPS score was 50, and the mean postoperative KPS score was 67. During the complete follow-up period, 3 patients recovered completely (KPS scores of 90-100) and resumed daily activities, while 2 patients could perform normal activities with effort (KPS scores of 80). Another 2 patients could care for themselves but were unable to return to work (KPS scores of 70). Mostly, the patients' neurological statuses were better than before surgery. Of the 11 patients (63.6%) with complete follow-up, 7 had higher KPS scores, while 4 patients ultimately had poor postoperative scores. Of these 4, 2 needed considerable assistance (KPS scores of 50), another patient required special medical care (KPS score of 40) and the remaining 1 was severely disabled (KPS score of 30). The last 2 patients (KPS scores of 30-40) were hospitalized at a rehabilitation center.

Thirteen of 15 patients successfully underwent total resection of CMs, while 2 patients underwent partial resections of their lesions and suffered postoperative recurrent hemorrhages. Both of them had lesions in the midbrain and underwent surgeries that used the occipital transtentorial approach. One of the 2 suffered recurrent hemorrhage 20 months postoperative and underwent re-operation via the transcortical transforaminal approach. The other patient underwent re-operation twice, via the occipital transtentorial approach both times. Both of these patients

finally underwent total resection of CMs and suffered no more recurrent hemorrhages postoperatively (Fig. 1-B, C).

We observed various postoperative complications. One patient with deteriorated mentality underwent re-operation for postoperative epidural hematoma and immediately experienced an improvement in symptoms. At 1 month after surgery, all 15 patients underwent follow-up examinations to determine their postoperative statuses. Seven of them had no newly developed complications or aggravations of the preexisting neurological deficits. Six patients suffered newly-appearing incomplete CN palsies or aggravation of their previous symptoms. At present, 4 of them have experienced improved symptoms. However, the other 2 have suffered from quadriparesis, respiration difficulties, and severe dysphagia. These severely disabled patients underwent tracheostomies and needed gastric tubes for feeding.

## Discussion

Cavernous malformations are uncommon congenital vascular anomalies of the brain. Their characteristics include having sinusoidal vascular spaces in-between one another, with no intervening brain parenchyma, and occurrence in any part of the central nervous system.<sup>14)</sup> CMs have a significant risk of intracranial hemorrhages. In particular, a brainstem cavernous malformation can present with progressive neurological decline and result in neurological mortality and morbidity. Each CM has a different hemorrhagic rate,



**Fig. 1.** A 58-year-old female with a brainstem cavernous malformation underwent subtotal resection of cavernous malformations and suffered recurrent hemorrhages twice postoperatively. (A) Preoperative T2 weighted MR image shows a chronic hemorrhagic cyst in the midbrain. (B) Axial non-contrast CT scan shows a postoperative recurrent hemorrhage. (C) Postoperative T2 FLAIR image shows total resection of the cavernous malformation. The patient suffered no more recurrent hemorrhage postoperatively.

depending on its intracranial location. BCMs have a 20-times greater hemorrhage and re-hemorrhage rate than do supratentorial lesions.<sup>2)(8)(17)</sup> Wang et al. reported that the BCMs' annual bleeding rate was 6%, higher than that of CMs in other intracranial locations.<sup>19)</sup> Generally, the estimated risk of hemorrhage from BCM is about 0.7% to 6.0% per year, per lesion. The recurrent hemorrhagic rate is about 5% to 30% per year per lesion.<sup>3)(8)(10)(17)(19)</sup> The risk of recurrent hemorrhage is higher for the familial type, infratentorial lesions, deep lesions, and lesions with previous hemorrhage.<sup>2)(11)(12)(17)</sup> In our study, 9 of 15 patients (60%) suffered hemorrhagic episodes 2 or more times before their surgeries.

Most patients (87%) presented with sudden-onset symptoms and experienced various forms of CNS deficit. Manifestation of CN deficit was decided by the location of lesions. We reported that the lesion involving the pons had multiple CN deficits. With conservative treatment, the patient's neurological deficit usually improves, but BCMs are very likely to re-bleed, resulting in new or more pronounced neurological deficits. Wang et al. described this "relapsing and remitting" history and reported that patients' neurological deficits became more pronounced and permanent.<sup>19)</sup> Garrett et al. suggested considering surgical resection of the lesion, given the appropriate clinical scenario.<sup>7)</sup>

Most authors recommended surgery for symptomatic and accessible lesions. In this study, we considered surgery for patients with progressive neurological deficits or surgically accessible lesions. Wang et al. suggested considering surgery for BCMs if indications include any of the following: (1) progressive neurological deficits; (2) grave clinical presentations like coma and cardiac and respiratory instability; (3) overt acute or subacute hemorrhage on MRI, either inside or outside CMs, with a mass effect; or (4) either the CM or the hematoma reaches < 2mm from the pial surface.<sup>19)</sup> Many researchers, including Li et al., recommend surgery for lesions with recurrent hemorrhage.<sup>14)</sup> In the cases of asymptomatic lesions or obvious recent hemorrhagic lesions without access to the pial surface of the brainstem, Li et al. do not recommend surgery. In the current study, a chronic hemorrhagic cystic lesion on MRI, with clinically mild symptoms (KPS score of 80), was surgically accessible. However, the surgical outcome was poor, and the patient

suffered postoperative morbidity. We suggest treating patients with asymptomatic or mild neurological signs conservatively because of surgery-related risks and possible postoperative morbidity.

The most important factor in a successful postoperative outcome is the total resection of the lesion. Many authors emphasize the importance of total resection for CMs because residual CMs tend to experience recurrent hemorrhage, with considerable cumulative morbidity.<sup>18)</sup> In our series, 2 of 15 patients treated with microsurgery underwent subtotal resection of their lesions at the time of their first surgeries. Both patients suffered recurrent hemorrhage postoperatively and experienced morbidity as a result. We at first thought the recurrent hemorrhage was the result of an inappropriate surgical approach. We had used the occipital transtentorial approach on 1 of them. However, this approach was not proper, because the lesion was in the anterolateral surface of the midbrain. The inappropriate surgical approach limited the operative field, which hampered successful total resection of the lesion.

Many authors consider that the timing of surgery is an important factor for successful BCMs surgery. Unless patients had severe neurological deterioration or showed cardiorespiratory instability that requiring emergent evacuation, we preferred to treat patients with steroids and mannitol for a week or two intravenously, letting their edema subside, and then proceeded with their microsurgery. Most authors suggested this method for successfully performing total resection of a hematoma and minimizing the dissection and retraction of brainstem tissue. The hematoma may become well-organized with the passage of time. This may make it difficult to explore the margins of the cavity and separate cavernous malformation tissue from reactive gliotic tissue.<sup>14)</sup> In the case of a patient with a chronic hemorrhagic cyst, we had trouble in dissecting the lesion from the margin of cavernous malformations during the surgery (Fig. 1A). We performed the surgeries between 10 and 25 days after each patient's last hemorrhage (mean, 15 days). Most authors reported that patients who had surgery in the subacute hemorrhagic stage had better postoperative outcomes than did those who had surgery at a later stage.<sup>14)(15)</sup>

## Conclusion

BCMs can cause recurrent hemorrhage, progressive neurological deficits, and mortality. Surgeons should consider microsurgical resection the treatment of choice when a patient suffers progressive neurological decline. The success of surgery is dependent on an accurate surgical approach, the appropriate timing for surgery, and successful total resection of the lesion. In addition, surgeons must understand the complex anatomy of the brainstem and use a well-informed surgical approach for this eloquent region.

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