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Clinical Article

Treatment of Brainstem Cavernous Malformation : Treatment Indication, Technical Consideration, and Results

Sang-Bok Lee, M.D., Jung-Il Lee, M.D., Jong-Soo Kim, M.D., Seung-Chyul Hong, M.D., Kwan Park, M.D.

Department of Neurosurgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Objective : The goal of this study is to provide the clinical data of patients with brainstem cavernous hemangiomas after treatment with microsurgery or radiosurgery after conducting a retrospective analysis of 21 patients at one institution.

Methods : Twenty one patients with brainstem cavernous hemangiomas were treated at the authors' institution between 1995 and 2004 and clinical analysis was performed by retrospective review of medical records and neuroimaging examinations. Thirteen patients underwent microsurgical resection and radiosurgery was performed as an initial treatment in 9 patients.

Results : Radical excision was achieved in 12 among 13 patients and transitory neurological deterioration or new neurological deficit developed during the immediate postoperative period in 7 (54%). The final outcomes at 5 - 70 months after surgery were improved in 11 patients (85%) and worsened in 2 patients (15%) compared with the preoperative state. Radiosurgery was performed in 9 patients. During the follow up period from 5 to 70 months there was neurological improvement in 3 patients, no significant change in 3 and deterioration in 3 patients. Two patients developed rebleeding at 5 months, 60 months respectively after radiosurgery.

Conclusion : Microsurgery for symptomatic cavernous hemangioma of brainstem can be performed with acceptable morbidity. Fatal complication is rare with careful selection of the optimal operative approach in well selected patients. Radiosurgery is an effective alternative for the lesions which are not accessible by surgical approach, however, there is still a possibility of rebleeding over a long period after radiosurgical treatment and microsurgery should be considered as a treatment with priority for the majority of cases.

KEY WORDS : Cavernous hemangioma · Brainstem · Microsurgery · Radiosurgery.

Introduction

Cavernous hamangiomas are rare lesions that account for 5 to 13% of all intracranial vascular malformation. Approximately 18 to 35% of intracranial cavernous malformations are located in the brainstem[14]. Because of their critical location, bleeding or growth of the lesion can result in serious neurological deficits. In general, it is thought that the surgical treatment of brainstem lesions is accompanied with a relatively high risk of morbidity and mortality and these lesions tend to be treated conservatively. Recently however, encouraging surgical results after the surgical resection of brainstem cavernous hemangioma were reported and microsurgery was recommended for the resection of symptomatic lesion[18]. Although achievement of satisfactory results after surgical intervention without significant postoperative morbidity is not always possible due to the critical location, the brainstem cavernous hemangioma reaching an accessible pial surface can be excised with a low rate of surgical morbidity[10].

We performed an analysis of treatment outcome in 21 consecutive patients with brainstem cavernous hemangioma to describe the immediate and long-term clinical outcomes, complications, and selection criteria of different treatment options including microsurgery and radiosurgery.

• Received : May 25, 2004 • Accepted : August 10, 2004
• Address for reprints : Jung-Il Lee, M.D., Department of Neurosurgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, 50 Ilwon-dong, Gangnam-gu, Seoul 135-710, Korea
Tel : 02)3410-3499, 3494 Fax : 02)3410-0048
E-mail : jilee@smc.samsung.co.kr

Materials and Methods

Patient population

Twenty one consecutive patients with cavernous hamangioma of the brainstem were treated in our institution between January 1995, and March 2004. Clinical characteristics of the patients

Table 1. Patients with cavernous hemangioma of the brainstem : Clinical findings and treatment

Number	Age/Sex	Location	Clinical presentation	No. of hemorrhage	Treatment	Complication
1	25/M	pons	Rt.hemiparesis, dysarthria	1	midline suboccipital approach	none*
2	42/F	midbrain	Lt. paresthesia	2	LINAC RS, subtemporal approach	hemorrhage
3	58/F	pons	Rt. hemiparesis	1	midline suboccipital approach	none*
4	53/F	pons	Rt. hemiparesis, dysarthria, dysphagia	1	midline suboccipital approach	hydrocephalus
5	35/F	pons	Lt. hemiparesis, diplopia	1	midline suboccipital approach	none*
6	52/M	midbrain	altered mentality, Rt. hemiparesis, dysarthria	1	subtemporal approach	ICH
7	25/ F	pons	Rt. hemiparesis	2	midline suboccipital approach	none*
8	34/ F	midbrain	Lt. facial hypesthesia	2	subtemporal approach	none*
9	65/M	pons	Rt. hemiparesis,dysarthria	1	midline suboccipital approach	dyspahgia, Lt.facial palsy,
10	58/F	pons	dizziness, diplopia	1	midline suboccipital approach	none*
11	34/F	pons	Rt. hemiparesis	1	midline suboccipital approach	diplopia, Rt.hemiparesis
12	42/M	pons	Rt.hemiparesis, dysarthria	2	midline suboccipital approach	none*
13	55/M	pons	dizziness, diplopia facial palsy	1	midline suboccipital approach	none*
14	70/F	pons	Rt. hemiparesis	2	LINAC RS	none*
15	64/F	pons	deadache,dizziness	1	GKS	none*
16	23/F	pons	diplopia	2	GKS	none*
17	52/F	pons	diplopia	1	GKS	none*
18	62/F	pons	Rt. hemiparesis	2	GKS	none*
19	42/F	pons	dizziness	1	GKS	none*
20	60/F	midbrain	diziness	1	GKS	none*
21	34/F	midbrain	headache, Lt.parestehsia	2	GKS	dysarthria, Lt.paresthesia

LINAC RS : Linear accelerator radiosurgery GKS : Gamma Knife radiosurgery * : no change or transient aggravation of preexisting neurologic deficit

are summarized in table 1. These cases were retrospectively analyzed. The data were obtained by review of medical records, radiologic imaging during admission periods and out-patients-department visits. There were 5 male and 16 female patients who ranged in age from 23 to 70 years (mean age 46.9). All patients presented with clinical and radiological signs of one or multiple brainstem hemorrhages. Diagnostic workup included multiplanar MR studies in all cases. Angiography was not performed when MRI appearance was characteristic for the cavernous hemangioma. Patients were observed for a mean of 8.2 months (range 5-70months) after diagnosis. Surgical outcomes compared with the patients' preoperative status or incidence of bleeding were investigated.

Of the 21 patients, 13 patients underwent microsurgical operation. Nine patients underwent linear accelerator (LINAC) or Gamma Knife radiosurgery (GKS) and one of them experienced rebleeding 60months after radiosurgery and underwent subsequent operation.

Surgical approach and intraoperative monitoring

The surgical approach in each case was chosen according to the nearest site of cavernous hemangioma presentation to the pial or ependymal surface. For 10 cases with cavernous hemangioma in the midline medulla or pons that is close to the fourth ventricle floor, a midline subocccipital approach was used for exploration of the lesion through the fourth ventricle floor. Suboccipital craniotomy was performed at the prone position, reaching the foramen magnum. The cerebellar tonsils were retracted and the inferior midline vermis was sectioned to facilitate exposure. Functional mapping of the cranial nerve motor nuclei was performed using stimulating electrode to localize facial folliculi and to determine the safety area for incision. For 3 cases presented with the lateral or anterior surfaces of the midbrain, the lesion was exposed via a subtemporal approach.

Intraoperative monitoring of somatosensory evoked potentials, brainstem auditory evoked potentials and bilateral facial EMG were performed in all surgical cases. Electrophysiological mapping of the brainstem VII cranial nerve motor nuclei, using a tiny stimulating electrode (Fig. 1A, B), permits more precise planning of safe incision through the floor of the fourth ventricle. Whenever possible, a midline incision of the floor of the fourth ventricle was avoided, because this approach could cause bilateral internuclear opthalmoplegia. Continuous monitoring of sensory pathways and facial EMG allowed early detection of excessive retraction or manipulation of critical structures.

Of the 9 patients who underwent radiosurgery, LINAC radiosurgery was done in 2 patients with the marginal doses of 13 and 15Gy, prescribed to 80% of maximal doses, respectively. Seven patients underwent GKS with the mean marginal dose of 14.5Gy (13-15Gy) prescribed to the 50% of isodoses contour.

Clinical grading

Patients were graded clinically according to the Modified Rankin scale (MRS)[19]. 0- no symptoms at all, 1- no significant disability despite symptoms : able to carry out usual duties and activities, 2-slight disability : unable to carry out all previous activities. Able to look after own affairs without assistance, 3- moderate disability : requiring some help, but able to walk without assistance, 4; moderately severe disability : unable to walk without assistance, and unable to attend to own bodily needs without assistance, 5- severe disability : bedridden, incontinent, and requiring constant nursing care and attention (Table 2).

Results

Clinical grading

All 21 patients presented with hemorrhage at the time of admission. In 13 patients one episode of hemorrhage had occurred, in 8 patients hemorrhage had occurred twice before treatment.

Location of the lesion was pons in 16 cases and midbrain in 5 cases. Multiple lesions were presented in 2 patients. All patients had motor and sensory symptoms due to previous symptomatic hemorrhage. At the time of initial presentation hemipaersis were presented in 11 patients (84%), cranial nerve deficit in 9 patients (69%), face or body sensory disturbance in 5 patients (38%), dizziness/vertigo in 5 patients (38%), mental change in 1 patient (8%). Cranial nerve symptoms were dysarthria, diplopia, facial nerve palsy and dysphagia. At presentation 2 patients were MRS grade 5, 2 were grade 4, 5 were grade 3, 7 were grade 2 and 5 were grade 1.

Outcomes of treatment

Microsurgery for cavernous hemangioma

Thirteen patients underwent microsurgical operation. For 10 cases with cavernous hemangioma in the medulla or pons that is close to the fourth ventricle floor, a midline subocccipital approach was used, operating through a floor of the fourth ventricle (Fig. 2). For 3 cases cavernous hemangioma, presenting to the lateral or anterior surfaces of the midbrain, was exposed via a subtemporal approach (Fig. 3).

Removal of the lesion was attempted in 13 patients. Total

Fig. 1. A and B : Photographs demonstrating both intraoperative stimulation of the fourth ventricle floor. Facial colliculus identified by the monopolar stimulator.

thirteen patients who underwent microsurgery. One patient underwent surgery after several years postictus and total removal could not be accomplished because of gliosis and fibrous pseudocapsule which were not easily dissected from the surrounding normal tissue. The immediate postoperative outcomes compared with the preoperative state were better in

Table 2. Clinical grade of 15 patients before and after treatment (microsurgery or radiosurgery)

Grade (MRS*)	No. of patients	
	Preop. (1month)	Last follow up (5 ~ 70months)
0	0	0
1	5	7
2	7	5
3	5	5
4	2	3
5	2	1

* Modified Rankin Score(MRS) 0– no symptom at all, 1–no significant disability despite symptoms : able to carry out usual duties & activities, 2– slight disability : unable to carry out all previous activities. Able to look after own affairs with out assistance, 3– moderate disability : requiring some help, but able to walk without assistance, 4– moderately severe disability : unable to walk without assistance, and unable to attend to own bodily needs without assistance, 5– severe disability : bedridden, incontinent, and requiring constant nursing care and attention

6 patients (46%), unchanged or only minor transient neurologic deterioration were detected in 5 patients (39%) and significant neurological deterioration developed in two patients (15%). One experienced dysarthria, facial palsy, oculomotor palsy and hypesthesia following removal of a pontine cavernous hemangioma. The other experienced diplopia and aggravated right side hemiparesis following removal of a pontine cavernous hemangioma. The final neurological outcomes at the last follow up revealed improvement in 11 patients and persistently worsened status in 2 patients. Repeated hemorrhage occurred in none of them.

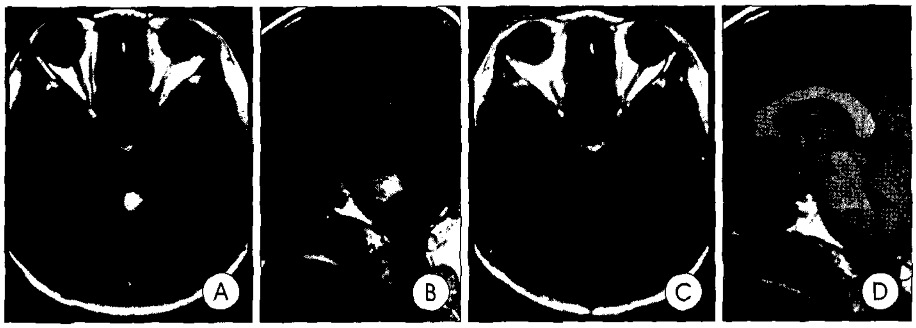

Fig. 2. Case 11. A 33-year-old woman presented with right sided weakness and headache. Preoperative T1-weighted axial (A) and sagittal (B) magnetic resonace images reveal a pontine cavernous hemangioma. The patient underwent a midline suboccipital approach to remove the cavernous hemangioma and experienced significant improvement in her preoperative symptoms. Postoperative images (C, D) indicate complete resection of the lesion.

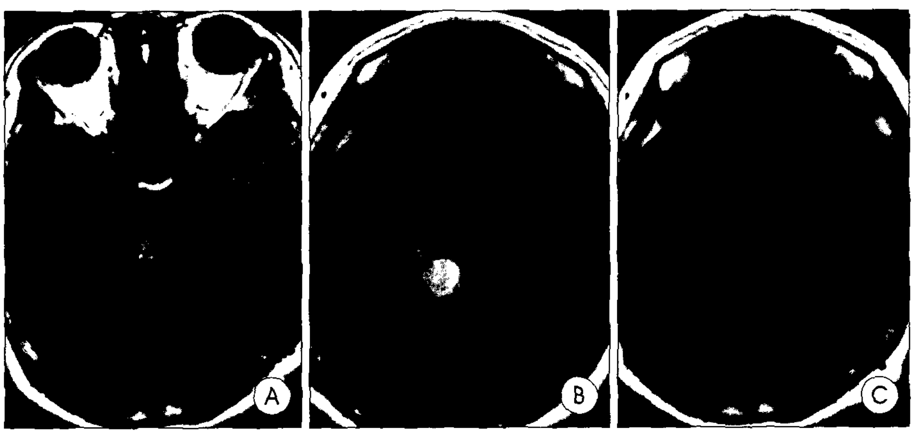

Fig. 3. Case 2. A 42-year-old woman developed left paresthesia as a result of hemorrhage from a right midbrain cavernous hemangioma (A). She underwent linear accelerator radiosurgery. At 60 months after radiosurgery, she experiences rebleeding (B). She underwent surgery via a right subtemporal approach to the lateral midbrain. Postoperative magnetic resonance image (C) reveals complete resection of the lesion.

Radiosurgery for cavernous hemangioma

Nine patients were treated with stereotactic radiosurgery as an initial treatment. Seven patients underwent GKS, 2 patients were treated with LINAC. All of them were female patients with a mean age of 50.7years (range 23-70years). Five patients had multiple episodes of hemorrhages and 4 patients had one.

The mean follow-up period was 15.2 months (range, 5-70months). None showed neurological change during the immediate postoperative state. Compared with the preoperative state, the neurological states were improved in 3 patients, unchanged in 3 patients and worsened in 3 patients at the last follow up. Among the worsened patients, one patient who was treated with LINAC experienced rebleeding at 60 months after radiosurgery and underwent subsequent operation. A second patient had neurological deterioration accompanied by increase in size and edema on MRI, suggestive of new bleeding, at 5 months after GKS (Fig. 4). Preoperative symptoms were worsened after GKS in another patient, but follow-up imaging at 2 months showed no interval changes.

Serial MRI scans were obtained between 5 months and 70 months. Follow up MRI scan revealed decrease of the lesion size in 3 patients, no interval changes in 3, rebleeding in 2 and aggravated perilesional edema in 1.

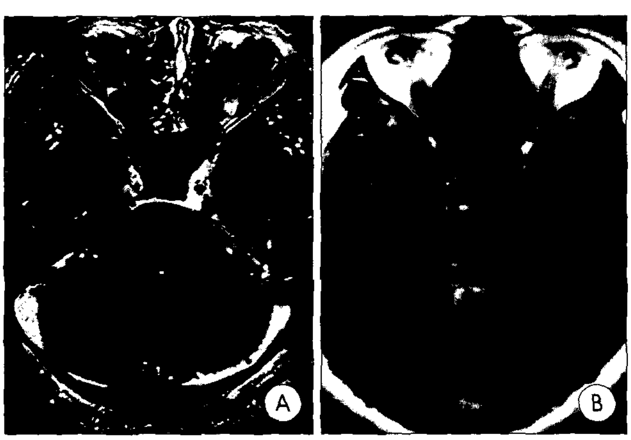

Fig. 4. Case 21. A 34-year-old woman developed headache and left side paresthesia. Axial magnetic resonance(MR) image (A) shows a cavernous hemangioma in the right side of upper pons. She underwent gamma knife radiosurgery. At 5 months after radiosurgery, she experiences aggravation of neurologic symptoms. Axial T1-weighted MR image (B) shows an increase in the size of the lesion suggesting rebleeding or swelling possibly related with radiation effect.

Discussion

Natural history of cavernous hamangioma

Cavernous hemangiomas are uncommon lesions composed of large sinusoidal vascular spaces and account for 5~10% of all cerebrovascular malfomations[7]. Brainstem cavernous hemangioma accounts for fewer than 20% of intracerebral cavernous hemangioma and are mostly found in the pons in approximately 57% of the cases, followed by the midbrain (14%), pontomedullary junction(12%), and medulla (5%)[13].

The natural history of untreated cavernous hamangioma in the brainstem is variable and incompletely described. However, several studies indicated a clinical bleeding rate of 0.25% to 29%/yr and that the neurological morbidity and mortality rates associated with bleeding can be significant [3,7,9,12].

Brainstem cavernous hemangioma may bleed and cause devastating neurological deficits because of their precarious location[17]. There are some data suggesting that brainstem cavernous hemangioma with clinical hemorrhage (especially two clinical bleeding episode) may exhibit a higher rate of rebleeding. Neurosurgeons should be more aggressive in the surgical treatment of patients suffering from symptomatic hemorrhages.

Indication of surgery

The indications for microsurgery have been repeatedly stated[2,20]. Most authors recommended surgery for symptomatic accessible lesions. Brainstem and deep lesions are usually considered accessible if they reach a pial surface. The decision of whether to undertake surgery in patients harboring brainstem cavernous hemangioma is mainly based on the number of previous hemorrhagic events, neurological status, and the precise location of the lesion with regard to the fourth ventricle or cerebrospinal fluid cisterns. Patients who suffer multiple hemorrhages and in whom the lesion is located close to the floor of the fourth ventricle or cistern should undergo surgery after the last hemorrhagic episode as soon as neurological recovery or stabilization has been achieved. In patients with clinically asymptomatic brainstem cavernous hemanangioma but with MR imaging-documented bleeding, the indication for surgery will depend on the location of the lesion. Surgery is advised especially in young patients in whom there is radiological documentation of bleeding and cavernous hemangioma bulging into the fourth ventricle. In cases of incidentally discovered cavernous hemangiomas located within the brainstem without any close contact with the surface, surgery is not recommended, instead a conservative approach (expectant observation) is preferred because of the surgery-related risks and possible postoperative morbidity.

Timing of surgery

Another factor that may influence the incidence of temporary morbidity is timing of surgery. Steinberg, et al.[18] advocated surgery 4weeks after ictus and Mathiesen, et al.[11] revealed a statistically significant difference between surgery in the subacute stage (between 10 and 20 days postictus) and late surgery. They recommended operation in the subacute stage because patients who underwent surgery improved to a condition on which surgery may cause a local deficit. In the subacute stage, there are less scarring of tissue and organization of the hematoma followed by encapsulation of the hematoma by fibroblast which make operation easy[5,11].

In our experience, we performed surgery between 10 and 25days postictus (mean 21days). During this period, the hematoma is easy to remove and the surrounding nervous tissues have had time to stabilize.

Clinical outcome and complication

Our data showing the finally worsened outcome in 2 patients agree with those of previous reports of a low risk (15% compare with 10%) of newly developed permanent deficit[15] from surgery. Most postoperative morbidity was related to transient aggravation of preexisting neurologic deficit and the long-term outcomes were gratifying. Transient neurological deterioration after surgery was reported in as many as 69% of the patients[11]. However, the risk of microsurgery is not really significant.

Some authors have issued warnings about incomplete surgery because residual cavernous hemangioma tends to bleed repeatedly, with considerable cumulative morbidity[16].

In our series, total removal of the lesion was done in 12 of 13 cases and there was postoperative rebleeding in none of them.

Role of radiosurgery

Radiosurgery has been established as an effective alternative option for the treatment of small arteriovenous malformations in eloquent areas or deep regions of the brain. Some controversy exists regarding the value of radiosurgery for cavernomas[4,6,8,9]. The radiosurgery group at Harvard university reported a decrease in the annual hemorrhage rate from 17.3% before radiosurgery to 4.5% after a latency period of 2 years after radiosurgery[1]. Similarly, Kondziolka et al.[9] observed that symptomatic hemorrhage rates for brainstem cavernous hemangioma were reduced from 8.8% during the first 2years after gamma knife radiosurgery to 1.1% thereafter. Meanwhile, Mathiesen et al.[11] reported that the incidence of hemorrhage from radiosurgically treated cavernomas was even higher than that documented in untreated incidental or untreated symptomatic cavernomas.

In our series, 2 patients experienced rebleeding at 5months and 60months respectively after radiosurgery. Radiosurgery maybe be useful and safe for carvenous angioma located in surgically inaccessible regions of the brain. But the role of radiosurgery is not clear and long term clinical follow-up is required, reserving radiosurgery for those lesions in surgically inaccessible or high risk regions. So, radiosurgery should not be the first treatment, as brainstem cavernous hemangioma, depending on their exact location, can be successfully removed.

Conclusion

Brainstem cavernous hemangioma can cause recurrent hemorrhages and significant neurological deterioration. Although brainstem location makes surgical intervention without significant postoperative morbidity difficult, our result suggests that the majority of symptomatic brainstem cavernous hemangioma can be successfully resected, with a long-term neurological morbidity rate of only 15 %. However, significant immediate postoperative morbidity must be anticipated. Neurosurgeons should consider microsurgery if patients experience clinically symptomatic hemorrhaging and cavernous hemangioma is presented to a pial or ventricular surface.

Radiosurgery may be useful for cavernous hemangioma in surgically inaccessible regions of the brainstem. But the value of radiosurgery for treatment of patients with cavernous hemangioma has not been well documented and long-term clinical follow-up is required.

Fatal complication is rare with appropriate surgical approach in well-selected patients and microsurgery should be considered as a treatment with priority for the majority of cases.

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