The incidence of cerebral cavernous malformation (CM) is 0.15 to 0.56 per 100,000 population. Hasegawa et al. [1] reported the incidence of CM is known to correspond to 0.1% to 4.0% of the population. Cerebral CM has been reported to constitute 8% to 15% of all cerebrovascular lesions. Tomlinson et al. [2] reported the incidence of all vascular malformations in the central nervous system accounts for about 5% to 15%. In 1991, Del Curing et al. [3] reported that the incidence of CM in the brain was 0.39%. In 1991, Robinson et al. [4] reported 0.47%. In 2012, Al-Shahi et al. [5] reported a CM incidence of 0.56%. In 2009, Morris et al. [6] reported that the incidence of CM was 0.16%. Up to one-third of CM patients have CMs associated developmental venous anomalies [7].

**Definition and clinical presentation**

Cerebral CM is a type of an abnormally large collection of “low-flow” vascular channels without brain parenchyma intervening between the sinusoidal vessels; these occult lesions on transfemoral catheter angiograms were formerly known as “cryptic” vascular lesions. In this review, we briefly describe the overall characteristics of cerebral CMs and summarize radiosurgical methods and results of radiosurgery as treatment for CMs. The incidence, definition, and natural history of cerebral CMs are described. The principal issues of CMs are recurrent bleeding and seizures. These issues are compared to the radiosurgical interventions for CMs. The rebleeding rates of CMs after radiosurgery is difficult to compare directly with untreated lesions because treated lesions are innately more vulnerable to rebleeding. Seizure outcomes after radiosurgery are also not easily estimated because of the various lesion locations; nevertheless, radiosurgery is an important treatment option for CMs in eloquent areas. Stereotactic radiosurgery (SRS) for CM has been effectively and widely used in recent years. Advances in magnetic resonance imaging and radiosurgery, as well as better studies of this condition’s natural history, are increasingly supporting the role of SRS as a complementary tool in CM treatment. More research is needed.
that are “occult” lesions on transfemoral catheter angiograms, formerly known as “cryptic” vascular lesions [8,9]. It has a characteristic structure with a grape-shaped racemose construction. Histologically, CMs are composed of a “mulberry-like” cluster of hyalinized dilated thin-walled capillaries, with surrounding hemosiderin. Caverns, blood-filled sinusoidial locules, are characterized by the lack of mural elements of mature vessel wall architecture and mature blood-brain-barrier [10]. Intraluminal thrombosis, recanalization, recurrent thrombosis and resolving hematoma are pathophysiological specificity. It is difficult to distinguish intracerebral resolving hematoma from CM. Cerebral CM causes various and distinct symptoms among patients, such as cerebral hemorrhages (30–40%), epileptic seizures (40–70%), and headaches (10–30%). Asymptomatic patients are also frequently found up to 20% to 50%. These estimates are largely based on autopsy and magnetic resonance imaging (MRI) studies, as 70% to 95% of lesions remain asymptomatic [10–13]. The patient’s symptoms are consistent with the lesion location, and supratentorial CMs are often found incidentally after seizures. Although seizures are the most common symptom of CMs, the initial symptoms are often caused by acute bleeding, and the symptoms vary depending on the location of the lesion. When CM bleeds in eloquent area, focal neurological deficits occur depending on the degree of bleeding and destruction of the brain parenchyma. Subcortical CM may present with hemorrhage accompanied by headache or seizure symptoms. Flemming et al. [14] reported that 37% of CM patients presented with seizures, 36% with hemorrhage, 23% with headaches, 22% with focal neurological deficits, and 10% were asymptomatic. Seizure presentation was most prevalent among supratentorial CMs, while focal neurological deficits were common in patients with infratentorial CMs. Overall, 19% of patients harbored multiple intracranial CMs, and 9% had radiographically apparent associated developmental venous anomalies. Sage et al. [11] reported a result of 2,000 consecutive brain MRI examination, and identified 0.9% of patients with CM lesions. Their presenting symptoms were seizures (48%), progressive neurologic deficits (17%), and acute hemorrhage (17%). Brainstem CM causes very typical focal neurological deficits. Symptomatic, multiple hemorrhagic CM of the brainstem often suffers from clinical difficulties because surgical resection with acceptable risk cannot be performed [15].

Lesion locations in the brain
CMs are usually located in the supratentorial area from less than 1 mm to several centimeters in diameter. About two-thirds of all CMs were in the cerebral hemispheres (66%). CMs 10% to 20% are located in the deep brain including basal ganglia or thalamus (8%). The brainstem has been reported to account for 8.5% to 35% of all CMs [16,17]. The most common location in the brainstem is the pons (62%) followed by midbrain (14%), midbrain and cerebospinal junction (12%), and medulla (5%). All CMs 10% to 23% are present in the posterior fossa including cerebellum (6%) and others (2.5%) [3,4,18].

When studying CM patients referred to a radiosurgery center, the lesion site seems to have more frequent deep, eloquent, and high-risk patients compared to known epidemiologic studies. According to Kondziolka et al. [19], a prospective observation of patients referred between 1987 and 1993, the malformation was located in the brainstem 35%, the basal ganglia/thalamus 17%, and a hemispheric area 48%.

Characteristic appearances on magnetic resonance imaging
The widespread use of MRI has not only increased the frequency of CM diagnosis, but has also advanced the understanding of natural history and epidemiology [7,20–25]. Because CM is low-pressure and low-flow vascular malformations, single or multiple lumen formations in the vessels are observed on MRI [26]. Bleeding in CM is caused by leakage of blood from a vein either intrallesional or perilesional. “slow ooze” or “cluster of bleeding sites” are configured and can cause defects in the blood brain barrier [21,27]. Hemorrhagic cavernous anomalies show a characteristic “popcorn” or “berry” appearance with a low signal rim due to hemosiderosis on MRI images. T1-weighted image (T1WI) and T2-weighted image (T2WI) are useful for accurately detailing the dimensions and characteristics of a CM. Time-dependent signal phase 2 of blood components, low-intensity borders around high signal intensity, small fluid levels, and internal septum may be visible. In case of acute bleeding, edema around the lesion may appear. Gradient echo (GRE) and susceptibility-weighted imaging (SWI) showed higher sensitivity and superiority to distinguish old and new blood products when discriminating multiple cerebral CMs. However, the size of the lesion is exaggerated due to “blooming artifact” in the presence of hemosiderin. Differential diagnosis on MRI is broad and includes hemorrhagic metastasis, epidermal cysts, meningioma, schwannoma, melanoma, diffuse cerebral microhemorrhage, cerebral amyloid angiopathy, and chronic hypertensive angiopathy. CMs can be grouped into four types based on MRI appearances using the Zabramski classification [18].

Mutations of cerebral cavernous malformation
CM are single or multiple, familial or sporadic, and congenital or de novo. The pathogenesis of CM is not yet fully understood. CMs are sporadic in common. Multiple CM has a high probabili
ty of familial CM with an autosomal dominant inheritance pattern. Epigenetic or environmental exposure, radiation exposure may contribute to make gene function loss. The disease-related mutation was identified into one of the CCM1, CCM2, and CCM3 genes. The rate of these mutations is relatively low. The underlying molecular mechanism has remained largely elusive [20,28]. Pathogenic variants of CCM1 (KRIT1), CCM2 or CCM3 (PDCD10) can be identified in 87% to 98% of the CM family [29].

**Natural annual hemorrhage rate**

The overall annual rates of rupture varied from 0.25% to 2.3% [30,31]. In some reports the bleeding rates have been estimated at 0.7% to 1.1% lesions/yr [4,18,23] and 1.6% to 3.1% patients/yr [14,16,19,32,33], in other reports an annual bleeding rate of 0.6% to 11% [4,17-19,30,34-36]. Whether pregnancy is associated with an increased risk of rupture in occult vascular abnormalities is sparse and conflicting [4,17,37,38].

**RADIOSURGERY FOR CEREBRAL CAVERNOUS MALFORMATIONS**

**Hemorrhage rate before and after radiosurgery**

Stereotactic radiosurgery (SRS) may reduce the rebleeding rate of CMs. Prior hemorrhage and female are risk factors for bleeding, while CM size and multiplicity did not affect hemorrhage rates. Although not impacting the hemorrhage rate itself, deep location was a risk factor for increased clinical aggressiveness [36]. The risk of recurrent intracranial hemorrhage or focal neurological deficits due to CM is greater than the risk of first bleeding. Women have a greater risk of bleeding than men, which decreases over 5 years [39]. Pollock et al. [40] reported good results of SRS. The rebleeding rate in the first 2 years after SRS was 8.8%, and the bleeding rate after 2 years was 2.9%. After a latency period of about 2 years, the rebleeding rate was reduced. In 2016, Gross et al. [41] reviewed CM in children, which differed from studies in adults. Patients who presented initially with symptomatic hemorrhage were at higher risk for future hemorrhage, and hemorrhage risk decreased with time. Male sex, and multiplicity of CMs also increased the risk of hemorrhage [14]. The median time from first to second hemorrhage was 8 months. Kondziolka et al. [19] reported that the location of intracerebral hemorrhage in CM patients was deep-seated in 52% and lobar in 48% of cases and there was no statistic difference in the rate of bleeds between brain locations. Patients’ sex or the presence of seizures, headaches, or solitary versus multiple lesions were not significant predictors of later hemorrhage. They reported that the annual hemorrhage rate before Gamma knife radiosurgery (GKS) was 5.9% to 56.5% depending on the calculation method. The hemorrhage rate decreased to 8.8% during the first 2 years after GKS procedure and to 1.1% after 2 years. Considering that the patients subject to radiosurgery had an average of 2.3 multiple bleeding before the GKS procedure, it was reported that radiosurgery would have a significant effect on the reduction of the bleeding rate.

Karlsson et al. [22] reported that the annual posttreatment hemorrhage rate was 8% in 22 patients who underwent GKS, but was 11% during the first 4 years after the procedure, and decreased to 6% after 4 years. Although there was no correlation between the occurrence of rebleeding and the location of the lesion, rebleeding occurred in six of 13 cases with central lesions and three of nine with lesions located at the periphery. Rebleeding occurred in three of 11 patients with high dose applied and five of 11 patients with low dose. Although there was no statistical significance, there was an estimated correlation between the radiation dose and the occurrence of bleeding. Hasegawa et al. [1] observed that after radiosurgery was performed on a total of 82 patients, the bleeding rate before surgery was 33.9%. The bleeding rate was 0.76%. It was concluded that the risk of bleeding was significantly reduced from 2 years after radiosurgery. The initial presentation of symptomatic bleeding is 8% to 37% of all CM patients [42,43]. After the first bleeding, the AHR increases to 4% and reaches 34% in patients with a history of CM and multiple bleeding [14,19,32,34,44,45]. Furthermore, the bleeding risk in patients with brainstem CM is estimated to be 34% after the first case of bleeding [32]. Asymptomatic CMs are known to have a low annual risk of bleeding, in the range of 0.25% to 0.6% per year [22,32]. The annual risk of new symptomatic hemorrhage with new neurological deficits and evidence of acute bleeding on MRI was 0.6%. The annual rebleeding rate after a single hemorrhage was 4.5%. However, the annual rebleeding rate increased dramatically to 32% per year after patients with CM had suffered two or more past bleedings. Hemorrhage in CM can occur either intracerebral or exophytic. The occurrence of clinical symptoms after bleeding is associated with anatomic location [32]. Developmental venous anomaly (DVA) coexists in 2.1% to 36% of patients with CMs and it is considered a risk factor of increased hemorrhage [8,46].

**Seizure rate before and after radiosurgery**

Seizures are the most common symptom. Seizures occur in approximately 30% to 50% of symptomatic cerebral CMs [39]. After radiosurgery for CMs with seizure, factors affecting the treatment outcome are the duration of symptoms, radiation dose, and location of the lesion. The most important prognostic factor is the
location of the lesion. Men are more prone to seizures than women [3,4,8,18,19,30,47]. CM lesions were single in 80% of patients and multiple in 20%. Patients 4.3% who did not initially present with seizures developed seizure in the follow-up period [19]. Age less than 40 was the only significant factor predisposing to seizure disability. Lesion size, multiplicity, and other factors did not influence clinical disability [48]. Seizures of CMs are associated with hemosiderin deposition, calcification, and recurrent microbleeds. Patients 47% to 60% can be controlled with antiepileptic drugs (AEDs). Patients 20% to 40% develop drug-resistant epilepsy, which requires surgical intervention [3,4,8,18,19,47]. Patients with CM-related epilepsy who undergo surgical resection achieve postoperative seizure freedom in 75% of cases (Table 1) [49]. Lindquist et al. [50] reported that there seems to be no direct relationship between complete occlusion of the lesion and the anti-convulsant effect, since there are cases where seizures can be controlled even before complete occlusion of the nidus occurs. Régis et al. [51] reported microsurgical resection can provide efficient treatment of drug-resistant associated epilepsy. However, seizure control can be reached when a good electroclinical correlation exists between CM location and epileptogenic zone. GKS can be proposed for the treatment of epilepsy when the CM is located in a highly functional area. CMs located in the Rolandic region cause simple partial motor seizures. Although the lesion and the epileptogenic zone are relatively identical in this region, complex partial seizures usually occur when the lesion is located in the mesiotemporal region. The mesiotemporal site was associated with a higher risk of failure. Because the epileptogenic zone of complex partial seizures extends beyond the lesion, radiosurgery is less effective than simple partial seizures. On their result, 26 out of 49 patients (53%) were seizure-free (Engel’s Class I), including 24 in Class IA (49%) and two patients with occasional auras (Class IB, 4%). A highly significant decrease in the number of seizures was achieved in 10 patients (Class IIB, 20%). The remaining 13 patients (26%) showed little or no improvement. Zhang and Chitlur [52] reported that in 28 patients with convulsions, the frequency and intensity of convulsions decreased in four out of seven patients who showed bleeding and convulsions after radiosurgery. Eighteen patients who showed only convulsive symptoms showed improvement of symptoms. They found that the seizure symptoms improved in the case of brain edema after radiosurgery, but the seizure worsened again after the brain edema findings disappeared. Moore et al. [36] reported long term result of incidentally discovered CMs. There were 1,311 patient-years of follow-up among the 107 patients (49.5% male; mean age at diagnosis 52 years) eligible for this study, the definitive prospective bleed rate was 0.08% per patient-year. No new seizures developed in any of the patients during the follow-up period. In 2018, Nagy et al. [53] reported that the rate of improvement in epilepsy was 84.9% after radiosurgery in patients with at least one seizure prior to treatment, not depending on the presence of hemorrhage or the time interval between presentation and treatment. Favorable outcome

Table 1. Reported seizure and hemorrhage risk

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Lesions (n)</th>
<th>Follow-up duration (mean, yr)</th>
<th>Seizure risk</th>
<th>Hemorrhage risk (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Porter et al. [17]</td>
<td>1999</td>
<td>103</td>
<td>13</td>
<td>Overall annual event rate of 4.2%. 4.3%</td>
<td>5% per lesion/yr</td>
</tr>
<tr>
<td>Kondziolka et al. [19]</td>
<td>1995</td>
<td>122</td>
<td>2.8</td>
<td>Overall 2.63 per person-yr With first hemorrhage, 4.5 Without hemorrhage, 0.6</td>
<td></td>
</tr>
<tr>
<td>Nagy et al. [53]</td>
<td>2018</td>
<td>109</td>
<td>7 (1–21)</td>
<td>The rate of improvement in epilepsy was 84.9% after radiosurgery in patients with at least one seizure prior to treatment</td>
<td>AHR 0.4% per lesion Rebleed rate in the single-bleed group decreased from 1.8% within the first 2 years after radiosurgery to 0.7%</td>
</tr>
<tr>
<td>Flemming et al. [14]</td>
<td>2012</td>
<td>292</td>
<td>10 (between 1989 and 1999)</td>
<td>Incidentally diagnosed, 0.33</td>
<td>With first hemorrhage, 6.19 Without hemorrhage, 2.18</td>
</tr>
<tr>
<td>Li et al. [45]</td>
<td>2014</td>
<td>331</td>
<td>6.5</td>
<td>With first hemorrhage, 12–15 Without hemorrhage, 8.7</td>
<td></td>
</tr>
<tr>
<td>Moore et al. [36]</td>
<td>2014</td>
<td>107</td>
<td>12.3</td>
<td>Overall 0.08% per person-yr</td>
<td>1.1% per lesion-yr</td>
</tr>
<tr>
<td>Zabramski et al. [18]</td>
<td>1994</td>
<td>128</td>
<td>2.2</td>
<td>2.5% per lesion-yr</td>
<td></td>
</tr>
<tr>
<td>Labauge et al. [35]</td>
<td>2000</td>
<td>40</td>
<td>3.2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

AHR: annual hemorrhage rate.

https://doi.org/10.52662/jksfn.2022.00255
occurred in 81% of patients whose seizures were not controlled with antiepileptic medication prior to SRS. A better effect will be obtained if the target includes not only the lesion but also the surrounding epileptogenic zone.

Radiation-induced complications

The incidence of radiation-induced complications after radiosurgery for CMs is reported to be 9% to 59%. This result is higher compared to radiosurgery complications for cerebral arteriovenous malformations (AVMs) [26,48]. Overall radiation-induced morbidity ranged from 2.5% to 59%, with higher complication rates in patients with brainstem lesion locations. Researchers applying mean radiation doses of 15–16.2 Gy to the tumor margin saw both low radiation-induced complication rates (0–9.1%) and adequate hemorrhage control (0.8–5.2% > 2 years after treatment), whereas mean doses of 16.5 Gy or more were associated with higher total radiation-induced morbidity rates (> 17%). Although the use of SRS remains controversial, patients with angiographically occult vascular malformations located in surgically inaccessible areas of the brain may benefit from such treatment [54].

Gross et al. [55] reported that CMs of the basal ganglia and thalamus present a unique therapeutic challenge to the neurosurgeon given their unclear natural history, the risk of surgical treatment, and the unproven efficacy of radiosurgical therapy. Given the compounded risks of radiation-induced injury and post-radiosurgical rebleeding, radiosurgery at modest dosimetry (12–14 Gy marginal doses) is only an option for patients with surgically inaccessible, aggressive lesions.

MANAGEMENT OF CAVERNOUS MALFORMATION

Microsurgical resection

Total microsurgical resection is a definitive treatment for cerebral CMs. However, the decision to operate remains challenging as postoperative morbidity may approach or exceed the complications of the untreated disease [56]. The goal of surgery is a minimal and complete removal of the lesion. Surgery may be reserved for symptomatic growth, hemorrhage, or focal neurological deficits. If it is proper to establish a corridor for a neurosurgical operative approach, surgical removal may be recommended for ruptured subcortical CM. For non-eloquent and supratentorial lesions, microsurgical excision can be curative [57]. In symptomatic hemorrhage and in cases of medically refractory epilepsy, early surgery is favored [9,49,58].

In 1994, Tomlinson et al. [2] explained that microsurgical excision is a satisfactory method of treatment. The reason is as follows. Histologically cavernous lesions are the commonest form of occult vascular malformation and possess a capillary component. A purely compact or cavernous architectural pattern is uncommon, most lesions showing a partially racemose architecture. Clinical growth of CMs may have its basis in intraluminal thrombosis and subsequent recanalization.

Up to 82% of patients with brainstem lesions involve the corticospinal and other major fiber tracts [59]. Aggressive intervention in the brainstem is reserved for patients who have suffered a single disabling bleed, or with long life expectancy which may pose a higher cumulative risk for future hemorrhage [9,60,61]. With the utilization of image guidance, appropriate patient and approach selection, and detailed knowledge of the intrinsic brainstem anatomy, these lesions can be resected [62]. When the intractable seizures focus is localized non-eloquent areas, we should remove hemosiderin-laden gliotic lesion. Large lesions can be partially excised, and small lesions can be excised en-bloc [63]. CM associated developmental venous anomalies should be spared during microsurgical resection. More research is needed to provide good evidence to define the relative roles of microsurgery, SRS, and conservative treatment in the management of CM.

Gamma knife radiosurgery

Location is the most important factor that determines the natural history of CM [63]. The eloquent and deep area CM have the high risk of increased morbidity after repeated bleeding. Supratentorial CM lesions have relatively lower annual bleed rate and lower risk of neurologic deficits. Goals of GKS are to reduce the risk of rebleeding, reduce neurologic deficits, and reduce the risk of adverse radiation effects. GKS has been effectively performed for ruptured and deep-seated CMs in the cerebral hemispheres, as well as basal ganglia regions such as the thalamus, caudate nucleus, pallor and inner capsule, or the brainstem and cerebellum. In CM patients with a history of multiple bleeding, the annual rebleeding rate was 32% before SRS treatment, but decreased to 1.5% within 2 years after SRS treatment. They found overall hemorrhage rates of 2.0% to 6.4%, overall post-radiosurgery hemorrhage rates of 1.6% to 8%, and stratified post-radiosurgery hemorrhage rates of 7.3% to 22.4% in the period immediately to 2 years after treatment; these latter rates declined to 0.8% to 5.2% > 2 years after treatment [54,61,64]. To reduce the rebleeding rate, the following GKS indications are recommended: 1) Clinically significant one or more bleeding; 2) Typical CM confirmed on MRI; 3) Excludes actual AVM or DVA; 4) If multiple CM is present, only symptomatic hemorrhagic CM; 5) When the patient cannot accept the expected risk during surgical removal. GKS is...
considered when new symptoms develop in patients without neurological deficits or in patients with disabilities [35]. CM lesion regression may occur on post GKS follow-up MRI. The disappearance of the lesion after radiosurgery for CM may not be confirmed by imaging. After CM radiosurgery, regular MRI follow-up and long-term evaluation are recommended for possible side effects. Though it is very difficult to accurately define the radiosurgical target of CM, in general, the target is defined as the area seen as a mixed signal located inside the ring, which is seen as low signal intensity due to hemosiderin around the lesion on MRI. The general dose planning method is to exclude the hemosiderin ring and the bleeding site around the lesion because it contains adjacent brain tissue [17,19]. Patet et al. [24] reported that radiation-induced cavernous malformation (RICM) is a delayed complication induced by childhood irradiation. Its natural history is largely unknown and its incidence may be underestimated as RICMs tend to develop several years following radiation. No clear consensus exists regarding the long-term follow-up or treatment. Authors reported that RICM patients received radiation therapy with an average dose of 50.0 Gy, and the average age was 7.3 years, with a boy dominance rate of 54%. On average 9.2 years after brain irradiation, approximately 2.6 RICMs were detected per child in the frontal (35%) and temporal (34%) lobes away from the primary lesion. Asymptomatic (67%) or bleeding (21%) was present. All but two children had good clinical results. The authors suggested follow-up for at least 15 years after radiation therapy in children. When RICM treatment is asymptomatic, lesions can be observed. In addition to radiosurgery, CM management strategies include close and meticulous follow-up, AED therapy, and minimally invasive microsurgery. Decision making for clinical treatment is not always straightforward. A nuanced approach, controlled by experience and good judgment, is critical to achieving good clinical outcomes. Conservative management and observation are therefore favored for all patients with solitary CM who are asymptomatic [9].

Dose plan and irradiation in Gamma knife radiosurgery

SRS was carried out using a Gamma Knife Model (Elekta AB, Stockholm, Sweden). Under the scalp local anesthetic injection, the procedure began with application of a model G Leksell stereotactic frame (Elekta Instruments) to the patient’s head. After attachment of a fiducial system to the frame, all patients underwent MRI. A high-definition computed tomography scan was additionally taken as needed. Stereotactic MRI, including contrast-enhanced T1WI, T2WI, three-dimensional (3D) Time-Of-Flight magnetic resonance angiography, 3D-GRE, was important to explain CM. To investigate and follow-up, SWI or GRE is requested. MRIs were exported to the Gamma-Plan (Elekta AB) to perform a dose-plan. The radiosurgery target margin is the mixed signal change area within the T2-defined hemosiderin rim surrounding the CM (Fig. 1). The dose plan was established in a single or multiple isocenter considering the conformity and selectivity of the target. Acute or subacute hemorrhage was excluded from the dose planning, because iron breakdown products may be a radiation sensitizer. To deliver a highly conformal dose to the CM, multiple small isocenters were used. The CM in the anterior part of the brain stem requires careful dose planning considering the ventral corticospinal tract. Care should be taken not to include DVA observed near the lesion. The radiation dose tends to decrease compared to the initial stage. Karlsson et al. [22] initially prescribed a radiation dose of 20 Gy by applying GKS for AVM, but reduced it to 18 Gy due to radiation-induced complications. After that, a marginal dose of 15 Gy was applied. Pollock et al. [40] 18 Gy, Kondziolka et al. [65], and Liscak et al. [66] applied a marginal dose of 16 Gy and tried to reduce ARE. Azimi et al. [67], and Park and Hwang [68] prescribed a low marginal dose of 13 Gy on average (Table 2) [19,22,29,40,66-72]. In 2019, Lunsford et al. [32] wrote that the median radiation dose to the CM margin was 13 Gy to reduce hemorrhagic risk and radiation-induced complications. The maximal radiation doses varied between 20 and 34 Gy, and the marginal doses varied between 10 and 17 Gy. The median marginal dose was 13 Gy in the medulla oblongata, 13 Gy in the pons, and 13.5 Gy in the midbrain. The 50% isodose line was used for the margin. After SRS, methylprednisolone injection used to be recommended and were discharged from the hospital within a day. For advanced GKS management and research on CM, the following factors should be considered. Active discussion and sufficient preparation are required to establish a comparative study of the control group. The classification of perioperative bleeding, the natural history of CM, the consistency of the CM patient group should be included with multidisciplinary treatment plan.

CONCLUSION

SRS for cerebral CMs has been effectively and widely used recently. Advances in MRI and radiosurgery, as well as better studies of natural history, are evidence. Complementing microsurgery and conservative treatment, SRS is an important treatment option. The application of GKS to CM has evolved from experimental attempts to treat aggressive inoperable lesions. If symptomatic cerebral CM is present in deep, eloquent areas, the use of SRS for CMs located in the brainstem, thalamus, basal ganglia, or inner capsule should be considered. Because the cumulative morbidity
Fig. 1. Gamma knife radiosurgery for a brainstem cavernous malformation with developmental venous anomaly. Radiation dose planning for a cavernous malformation (CM) in the ponto-mesencephalic region of the brainstem. We used the fast spoiled gradient echo method of three-dimensional magnetic resonance imaging. The CM was treated with a radiation dose of 13 Gy at the 50% prescription isodose line within the hemosiderin rim as a key for modern CM radiosurgery. The bilateral cerebellar developmental venous anomalies associated with this lesion are also visible on axial T1-weighted (A) and T2-weighted (B) images.
of recurrent bleeding is acknowledged and, on the other hand, the risk of radiation-induced side effects is low, immediately after the first bleeding, the patient is willing to treat after recovery and resolution of the hematoma. We acknowledge that SRS in the treatment of CM remains controversial. SRS requires more high-level medical researches.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES


https://doi.org/10.52662/jksfn.2022.00255
39. Taslimi S, Modabbernia A, Amin-Hanjani S, Barker FG 2nd,
Radiosurgery for cerebral cavernous malformations


61. Gross BA, Batjer HH, Awad IA, Bendok BR, Du R. Brainstem cavernous malformations: 1390 surgical cases from the literature. World Neurosurg 2013;80:89-93


63. Ellis JA, Barrow DL. Supratentorial cavernous malformations. Handb Clin Neurol 2017;143:283-9


68. Park SH, Hwang SK. Gamma knife radiosurgery for symptomatic brainstem intra-axial cavernous malformations. World Neurosurg 2013;80:e261-6