De novo cavernous malformation after radiosurgery for cerebellar arteriovenous malformation: A case report

Sang Heum Kim MD, Tae Gon Kim MD, Min Ho Kong MD

Department of Neuroradiology and Department of Neurosurgery, CHA Bundang Medical Center, CHA University, School of Medicine, Seongnam-si, Republic of Korea; Department of Neurosurgery, Seoul Medical Center, Seoul, Republic of Korea

Abstract

Stereotactic radiosurgery, including gamma knife radiosurgery (GKS), can in rare cases result in de novo cavernous malformations (CMs). Here, we present a case of de novo CM induced by GKS following treatment of a cerebellar arteriovenous malformation (AVM). A 48-year-old woman was diagnosed with left unilateral Moyamoya disease. Conventional cerebral angiography also revealed an AVM in the left cerebellum. The patient underwent GKS using a 50% isodose of 15 Gy at the margin of the left cerebellar AVM. Magnetic resonance imaging (MRI) taken 3 years after GKS revealed small chronic hemorrhages with perilesional edema in the left cerebellum. Five years later, the lesions became aggravated, but were asymptomatic. Eight years following GKS, the patient was admitted complaining of headache and dizziness. Brain MRI revealed a 1.3cm hemosiderin deposit with an inner hyperintense nodular portion that was enhanced in the left cerebellum. An open craniotomy was performed and the mass was removed, from which pathological findings were compatible with those for CM. The patient recovered to the prehemorrhagic state. This case shows that De novo CMs can rarely develop after radiosurgery. Most CMs have been reported to develop following radiosurgery for brain tumors. As shown in this patient, CMs can also develop after radiosurgery for cerebellar AVM in adults.

Keywords: De novo cavernous malformation, Radiation therapy, Radiosurgery, Arteriovenous malformation

INTRODUCTION

Cavernous malformations (CMs) sometimes cause symptomatic hemorrhages or neurological deficits and the incidence is reported as approximately 0.1–1.0%. They are generally known as congenital lesions, but radiation is known as a causative factor of de novo CM since 1994. Most of these cases are pediatric patients who received radiation therapy for brain tumors. Stereotactic radiosurgery, including gamma knife radiosurgery (GKS), can also result in de novo CM, although it is relatively very rare and has been reported in only 5 cases. These cases were associated with radiosurgery to treat CMs, cerebral arteriovenous malformation (AVM) or brain tumors. Here, we present a rare case of de novo CM induced by GKS for the treatment of a cerebellar AVM in an adult.

CASE REPORT

In 2005, a 48-year-old woman was diagnosed with spontaneous intracerebral hemorrhage in the left fronto-parietal region that resulted from Moyamoya disease. Conventional cerebral angiography revealed unilateral Moyamoya disease involving only left side (Figure 1A) and an AVM in the left cerebellum (Figure 1B). The patient was managed conservatively and was not considered for revascularization surgery because brain single positron emission computed tomography with diamox showed no impaired vascular reservoir. Two months later, the patient underwent GKS using a 50% isodosage of 15 Gy at the margin of the left cerebellar AVM and she was discharged with right hemiparesis. MRC motor power grading of III to IV minus. Seven months later, the patient has a second bout of intracerebral bleeding in the left basal ganglia, which was managed by stereotactic catheter insertion into the hematomas. Three months after the second hemorrhage, she was discharged to another rehabilitation hospital with motor aphasia and right-sided motor weakness of grade III. In 2009, 3 years after the GKS, the patient...
underwent an MRI that revealed small chronic hemorrhages with perilesional edema in the left cerebellum (Figure 2A). In 2011, 5 years after GKS, a repeat MRI revealed an aggravated chronic hemorrhages with perilesional edema in the left cerebellum (Figure 2B). The lesion was still asymptomatic. Eight years after GKS (2014) the patient was admitted complaining of headache and dizziness for 2 months. On neurological examination, there was quadriparesis of motor power grade III. A brain CT scan revealed a cystic mass lesion with a fluid-fluid level in the left cerebellum, which was the same site as the previously noted chronic hemorrhages (Figure 2C). The size of the mass was approximately 4.5 × 3.5 cm and caused upward herniation with mild midline shifting. Brain MRI revealed a 1.3 cm sized hemosiderin deposit and inner hyperintense nodular portion with enhancement in the posteroinferior aspect of the cystic lesion (Figure 2E, 2F). There was no remarkable hydrocephalus or infarct. Conventional cerebral angiography did not reveal residual AVM or other vascular anomalies in the left cerebellum (Figure 2D). She was treated with an open craniotomy and en bloc removal of the mass and hematoma (Figure 3A, 3B). The surface of the mass was noted to be red and gray in color. Postoperative brain CT and MRI revealed no residual enhancing lesion and relief of the compression to the 4th ventricle (Figure 2G, 2H). Pathological evaluation of the mass showed the aggregation of dilated, thin walled vessels, with hemorrhage and surrounding brain parenchyma showing ectatic small vessels that was suggestive of CM (Figure 3C). The patient recovered to the prehemorrhagic state and was discharged uneventfully 10 days after the surgery.

**DISCUSSION**

Radiation therapy is a very useful tool, specifically for brain tumors. The adverse effects of radiation...
Figure 2. Brain imaging scans taken serially after gamma knife surgery (GKS). An MRI in Year 3 after GKS revealed small chronic hemorrhages with perilesional edema in left cerebellum (A), which had worsened in Year 5 (B). A brain CT scan taken in Year 8 revealed a cystic mass lesion with a fluid-fluid level (C), but angiography did not reveal vascular anomalies (D). A brain MRI in Year 8 revealed a 1.3 cm hemosiderin deposit and inner hyperintense nodular portion with enhancement in the postero-inferior aspect (E-T2, F-T1 with contrast) and postoperative brain MRI revealed no residual enhancing lesion (G-T2, H-T1 with contrast).

Figure 3. Gross findings of the lesion in the operative field and pathological findings. The surface of the mass was noted to be red and gray in color (A) and en bloc removal of the mass and hematoma was performed. (B) Pathological evaluation of the mass showed the aggregation of dilated, thin walled vessels, with hemorrhage and surrounding brain parenchyma showing ectatic small vessels that was suggestive of cavernous malformation (C).
therapy are well known and are classified into three categories by time to lesion development. Acute effects include acute encephalopathy, which develops within the first 2 weeks after radiation therapy. Subacute effects include subacute encephalopathy and transient myelopathy, which develop 1–4 months after radiation therapy. Late effects include delayed cerebral radiation necrosis, necrotic myelopathy, cerebral vasculopathy, and radiation-induced brain tumors, which develop 4 months to 4 years or more after radiation. Recently stereotactic radiosurgery has been popularized for various intracranial lesions such as brain tumors, vascular malformations (mainly in patients with AVM and selectively in patients with the CM), and some neuralgias. Although the radiation dose of radiosurgery to adjacent normal brain tissue is relatively lower than that of conventional radiotherapy, complications after radiosurgery have been reported.

One of the rare late complications for radiation therapy is induction of de novo CM. Gaensler et al. first reported the association between radiation therapy and CM in 20 patients with MR imaging. Since then, many others (over 80 cases in the literature) have reported de novo CM after radiation therapy. In most of those 80 cases, conventional radiotherapy was used for cerebral vascular lesions in pediatric patients. The pediatric brain is thought to be more vulnerable to radiation injury, but some cases have also showed CM development following radiation in adults. The mechanisms of CM development after radiation therapy are not clear, but some explanations have been suggested. First, cryptic CM may have existed before radiation therapy, but are not detected because they are radiographically occult and could be detected on MRI only after radiation exposure. Second, radiation therapy can result in vessel wall necrosis, vasogenic edema, increased capillary permeability, and vessel wall changes including hyalinization, fibrosis, and mineralization. Changes of this sort might predispose the development of CM over a long period of time. Third, the ionizing effect of the radiation energy can make vascular and connective tissue changes in the stroma. In our patient, T2-weighted MRI did not reveal any CM like lesion in the left cerebellum in the initial MRI, and the follow-up MRI revealed small chronic hemorrhages with perilesional edema (Figure 2A), which had worsened (Figure 2B). The area in which the CM developed 8 years after GKS was the exact same spot that the GKS was performed for the AVM in the left cerebellum. Thus, this support that our patient is a de novo CM after radiosurgery.

De novo CM formation after radiosurgery is a very rare complication. In the literature, only 5 cases have been reported previously in adults (Table 1). Pozzati et al. reported a 25-year-old female patient in whom multiple CM developed 5 years after GKS for CM and was surgically removed. Pozzati et al. attributed the multiple CM to genetic factor rather than to radiosurgery. Iwai et al. reported a 40-year-old male patient in whom CM developed 2 years after two applications of GKS. In the patient, the CM was surgically removed and the symptoms, such as seizures, had abated. Motegi et al. reported a 50-year-old male patient in whom CM developed 2 years after linear accelerator radiosurgery for AVM. The CM was surgically removed and the patient was discharged without any neurological deficit. Sasagawa et al. reported a 45-year-old male patient in whom CM developed 10 years after GKS for an acoustic schwannoma. The patient was managed conservatively and gait disturbance resolved spontaneously. Park et al. reported a 25-year-old female patient in whom CM developed 3 years after GKS for a pineocytoma. It was managed conservatively, but rebleeding occurred 4 years after GKS. The CM was treated with another GKS and the patient had no more recurrent hemorrhages.

Nimjee et al. analyzed 76 patients with de novo formation of CM after radiation and reported the mean radiation dose as 60.45 Gy. In the 5 cases of CM developed after radiosurgery, the radiation doses were from 12 to 25 Gy. In the present case, the radiation dose was relatively low at 15 Gy. This suggests that the dose of radiation might not be the only factor in the development of CM. CM development is rarer after radiosurgery than after conventional radiation therapy. Most CMs that develop after radiation and radiosurgery are related to the radiation of a variety of brain tumors, such as medulloblastoma, glioma, and ependymoma. Pozzati’s and Motegi’s cases are unusual where CM developed after radiosurgery for cerebral vascular lesions. Our case provide another example where CM developed after GKS for AVM.

In conclusion, radiation therapy or radiosurgery has been a very useful tool to treat multiple, inoperable, or remnant brain tumors after surgical removal. In rare cases, de novo CM after radiation therapy can develop in pediatric and some adult patients. De novo CM after radiosurgery can also develop, but they are rare. Most CMs develop
Table 1: Summary of reported cases of radiosurgery-induced cavernous malformations

<table>
<thead>
<tr>
<th>Authors, year</th>
<th>Age(years)/Sex</th>
<th>CM location</th>
<th>Symptom</th>
<th>Presentation</th>
<th>Treatment</th>
<th>Latency (years)</th>
<th>Primary lesion</th>
<th>Primary pathology</th>
<th>Previous treatment</th>
<th>Marginal radiation dose(Gy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pozzati et al., 1996</td>
<td>20/F</td>
<td>Right frontal lobe (adjacent)</td>
<td>Headache</td>
<td>Hemorrhages</td>
<td>Surgery</td>
<td>5</td>
<td>Right caudate nucleus</td>
<td>CM</td>
<td>GKS</td>
<td>25</td>
</tr>
<tr>
<td>Iwai et al., 2007</td>
<td>40/M</td>
<td>Left temporal lobe</td>
<td>Headache</td>
<td>Seizures</td>
<td>Surgery</td>
<td>2</td>
<td>Left temporal lobe</td>
<td>Metastatic brain tumor</td>
<td>GKS</td>
<td>23</td>
</tr>
<tr>
<td>Motegi et al., 2008</td>
<td>50/M</td>
<td>Right frontal lobe</td>
<td>Headache</td>
<td>Seizures</td>
<td>Surgery</td>
<td>2</td>
<td>Right caudate nucleus</td>
<td>AVM</td>
<td>LINAC</td>
<td>12.5</td>
</tr>
<tr>
<td>Sasagawa et al., 2008</td>
<td>45/M</td>
<td>Lower pons (adjacent)</td>
<td>Gait disturbance</td>
<td>Hemorrhages</td>
<td>Observation</td>
<td>10</td>
<td>Left cerebello-pontine angle</td>
<td>Vestibular schwannoma</td>
<td>GKS</td>
<td>12</td>
</tr>
<tr>
<td>Park et al., 2011</td>
<td>25/F</td>
<td>Midbrain (adjacent)</td>
<td>Facial palsy</td>
<td>Hemorrhages</td>
<td>GKS</td>
<td>3</td>
<td>Pineal</td>
<td>Pineocytoma</td>
<td>GKS</td>
<td>14.5</td>
</tr>
<tr>
<td>Present study</td>
<td>56/F</td>
<td>Left cerebellum</td>
<td>Dizziness</td>
<td>Hemorrhages</td>
<td>Surgery</td>
<td>8</td>
<td>Left cerebellum</td>
<td>AVM</td>
<td>GKS</td>
<td>15</td>
</tr>
</tbody>
</table>

CM, cavernous malformation; AVM, arteriovenous malformation; Gy, gray; GKS, gamma knife radiosurgery; LINAC, linear accelerator
following radiosurgery for brain tumors, but CM can also develop after radiosurgery for cerebellar AVM in adults, as in the present case.

DISCLOSURE
Conflict of interest: None

REFERENCES