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CASE REPORT

Unusual Case of Radiation-Induced Cavernous Malformation after Gamma Knife Radiosurgery for Meningioma

Chang Ki Jang, MD, Minsoo Kim, MD, Na Young Jung, MD, Young Goo Kim, MD, Won Seok Chang, MD, Hyun Ho Jung, MD, PhD, Jin Woo Chang, MD, PhD, Yong Gou Park, MD, PhD

Department of Neurosurgery, Yonsei Gamma Knife Center, Yonsei University College of Medicine, Seoul, Korea

We report an unusual case of delayed bleeding, highly suspected to be a radiation-induced cavernous malformation after gamma knife radiosurgery for meningioma. A 59-year-old woman underwent gamma knife radiosurgery with a marginal dose of 15 Gy with the 50% isodose line for parasagittal meningioma. After 5 years, magnetic resonance imaging (MRI) showed a marked decrease in the volume of the meningioma. The patient gradually developed right side weakness 7 years after the gamma knife radiosurgery. We performed another MRI scan and it showed a new hemorrhage compatible with cavernous malformation at the site of irradiation. Her weakness was conservatively treated and improved after about a month.

KEY WORDS: Radiation-induced cavernous malformation · Gamma knife radiosurgery · Meningioma · MRI.

INTRODUCTION

Gamma Knife Radiosurgery (GKRS) has been widely used for meningioma as a therapeutic or palliative treatment.[3)13)18)] No serious complications are usually reported, but in some cases, toxicity has been observed resulting in peritumoral edema, hemorrhage, delayed radiation necrosis and irradiation-related arteriopathy with stroke, or cranial nerve dysfunction.[1)15)] Unusual complications such as radiation-related tumors have also been recently reported.[9)] However, cavernous malformation (CM) after GKRS for meningioma has not been reported so far. We present a case of radiation-induced CM after GKRS for meningioma.

CASE REPORT

A 59-year-old woman visited the department of neurosurgery because of persistent headache, and was evaluated using magnetic resonance imaging (MRI). T1-weighted (T1WI) MRI showed a round homogeneously enhancing mass in the right frontal area, compatible with parasagittal meningioma (Fig. 1). Due to the small size, the maximal length of 2cm, and an incidental finding, we recommended GKRS to control the tumor. With the 50% isodose line, a marginal dose of 15Gy was prescribed using GKRS (Lek-Sell, type B) (Fig. 2). No subjective or definite neurological symptoms were noted during the 11 years of follow-up. An annual MRI was performed, and the tumor showed gradual shrinkage (Fig. 3). At 12 years after GKRS, the patient experienced progressive right side weakness. She visited our department and the MRI conducted at that time revealed an obvious new hemorrhagic lesion at the primary site of meningioma. The new lesion showed a heterogeneous round mass, 5cm in maximum size, surrounded by a rim of hemosiderin that appeared as hypointense on T2WI (Fig. 4). This finding was compatible with radiation-induced CM. Conservative management was initiated and her symptoms gradually improved.

Address for correspondence: Hyun Ho Jung, MD, PhD
Department of Neurosurgery, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea
Tel: +82-2-2228-2165, Fax: +82-2-393-9979
E-mail: JUNGHH@yuhs.ac

DISCUSSION

Over the past two decades, radiosurgery has been an alternative to surgery. However, radiation-induced complications, such as peritumoral imaging changes on follow-up MRI and transient cranial nerve dysfunction have been reported. Chang et al. reported that patients treated with GKRS for meningiomas experienced peritumorous imaging changes and cranial nerve dysfunction at a rate of 23.6% and 1.4%, respectively.[1)] Cavernous malformation after GKRS has not been previously reported.

Radiation-induced CM is a very rare complication of

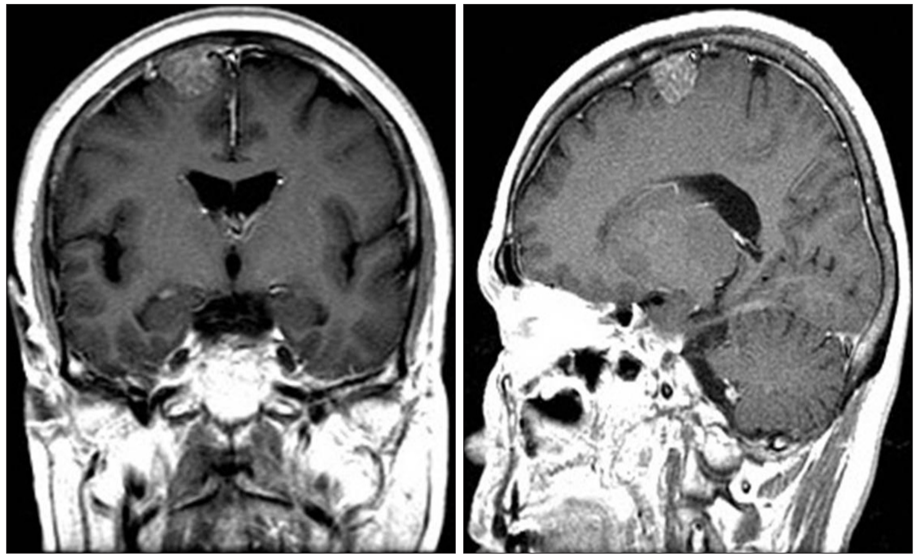

Fig. 1. Coronal/Sagittal T1 weighted magnetic resonance image with gadolinium obtained in Feb 2003 (pre-gamma knife radiosurgery) showing no evidence of cavernous malformation. The findings from the image suggested parasagittal meningioma.

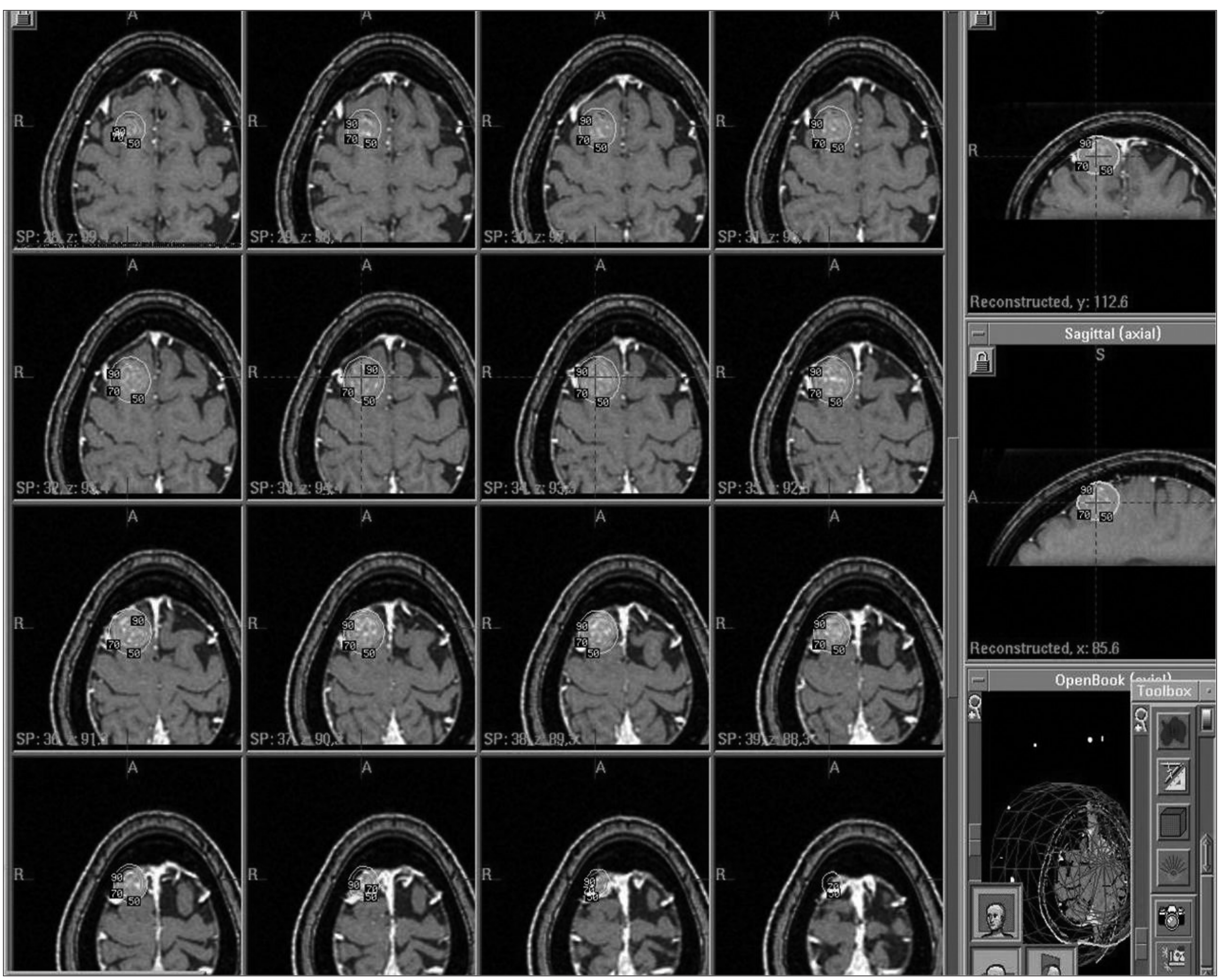

Fig. 2. Axial T1 magnetic resonance image in March 2003 (gamma knife radiosurgery planning MRI) wih the 50% isodose line, a marginal dose of 15Gy.

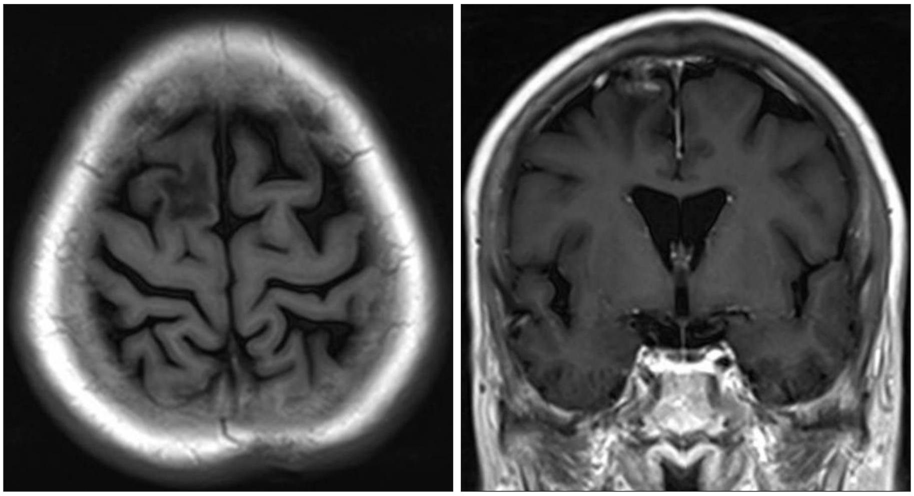

Fig. 3. Axial/coronal T1-weighted magnetic resonance image with gadolinium obtained in Dec 2008 (66 months post gamma knife radiosurgery) showing that the parasagittal meningioma had almost disappeared.

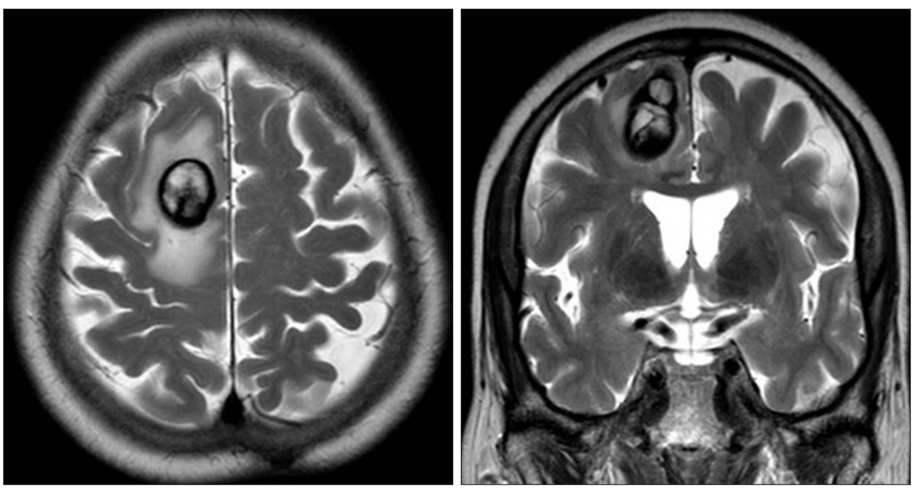

Fig. 4. Axial/coronal T1-weighted magnetic resonance image with gadolinium obtained in January 2015 (141 months post-gamma knife radiosurgery) showing a heterogeneous round mass with a maximal diameter of 5 cm, surrounded by a rim of hemosiderin that appeared as hypointense on T2WI.

GKRS.[5)12)14)] The first case report of radiation-induced cavernous malformation was of intracerebral hemorrhage from a vascular malformation in a patient who had undergone radiation therapy 8 years earlier for a nasopharyngeal squamous cell carcinoma, with a pathological description similar to CM.[17)]

In the previous case reports, two hypotheses have been proposed for the development of CM after radiation, one is de novo formation, and the other is that CM was already present at that site but not detected at the time of radiosurgery.[8)] Newly developed cavernous malformation after irradiation was mainly observed in pediatric patients,[10)] although it can also be observed in adults. Heckl et al. concluded that the younger the patient was at the time of radiation treatment, the more likely a hemorrhagic event was to occur subsequently.[4)] CM formation after irradiation in pediatric patients is likely due to their immature brains.

Generally, CM formation after GKRS is caused by a radiation-induced increase in vascular endothelial growth factor expression, which affects angiogenesis. Additionally, radiation can also damage DNA.[11)] Recently, Kim et al. hypothesized that radiation-induced hemorrhage could originate from radiation-induced cavity shrinkage at the target site of radiation.[2)16)] After shrinkage, the cavity would be filled with blood, and the subsequent spillage of fibrin would inhibit further extension of the hemorrhage. Finally, a stabilized hematoma would appear.

A high dose of radiation has been thought to be the cause of radiation-induced CM.[7)] In the previous studies reporting conventional radiation-induced CM, a relatively high dose (20−50Gy) was used to control tumor growth. Nimjee et al.[10)] analyzed 76 cases of radiation-induced CM that had been treated with conventional radiation therapy (mean radiation dose of 60.45Gy) for various types of brain tumors. Sagawa et al. reported a case of CM induced by GKRS for vestibular schwannoma (maximum dose 24Gy, marginal dose 12Gy). The area of CM had been exposed to approximately 7Gy, corresponding to 30% of the maximum dose delivered to the tumor center.[14] In our case, CM developed at the GKRS targeted site with the 50% isodose line, marginal dose of 15Gy. Healthy tissues adjacent to the GKRS target receive a lower dose of irradiation compared with the dose received in conventional radiation. We concluded that even low doses of radiation have the potential to induce secondary vascular malformation. In our case, CM developed at the radiation-targeted site with a relatively low dose.

Our case presented some limitations. First, although CM is easy to differentiate from other lesions due to the distinctive MRI pattern (a reticulated core of heterogeneous signal intensity with a dark peripheral rim of hemosiderin, giving a typical "popcorn" appearance), the diagnosis of radiation-induced CM was compatible consistent with MRI findings, but was not confirmed pathologically. The treatment for radiation-induced CM is not well established. Some authors suggest that it is usually asymptomatic and has a low risk of hemorrhage.[6] In our case, the neurologic symptoms were not progressive. We plan on following up our findings with a more comprehensive imaging study.

CONCLUSION

We report an unusual case of delayed bleeding, which was highly suspected to be radiation-induced CM after GKRS for meningioma.

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