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Cyst formation after linac-based radiosurgery for arteriovenous malformation: Examination of predictive factors using magnetic resonance imaging

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ABSTRACT

Objective: Cyst formation is a well-known complication following radiosurgery for arteriovenous malformations (AVMs). In this retrospective study, the authors studied predictors for AVMs using magnetic resonance imaging (MRI) to assess the mechanism of cyst formation after linac-based radiosurgery (LBRS).
Methods: From April 1993 to April 2008, LBRS was performed on 109 patients with cerebral AVMs at our institution. Six patients (5.5%) were diagnosed with cyst formation after LBRS, and 5 of them underwent regular MRI follow-up every 3–4 months for 2 years post-LBRS, and every 6–12 months thereafter.
Results: Time from initial LBRS until cyst formation ranged from 8 months to 10.5 years. MRI showed contrast changes at the irradiated site and its periphery within a period of 4 months to 7 years after the initial LBRS. Moreover, the emergence of a high-intensity area (HIA) was observed on T2-weighted MRI (T2W-MRI) during the same period when changes were found on contrast-enhanced imaging. The emergence of a low-intensity area on T2W-MRI was observed prior to cyst formation or expansion, which was believed to be due to a subclinical hemorrhage near the irradiated region in all patients. Histological examination of the cyst nodule revealed hemosiderin deposits and microbleeding.
Conclusions: Future cyst formation was suggested by the emergence of subclinical hemorrhage (microbleeding) in an irradiated field after gadolinium-enhanced MRI showed contrast changes and T2W-MRI showed a HIA around the irradiated field. MRI follow-up should be conducted on a regular basis in such patients, even after a complete occlusion has been diagnosed.

1. Introduction

Radiosurgery is an established management option for intracranial arteriovenous malformation (AVM), and results in an approximately 70% complete obliteration of the lesion 2–3 years following treatment. However, adverse events including bleeding and late onset radiation injury have been observed when observation periods are extended past 2–3 years. In particular, cyst formation, late-onset bleeding, and other adverse events have been reported. One of the most frequent and clinically important of these events is delayed cyst formation near the target area [1–6].

The aim of this study was to analyze magnetic resonance (MR) images before the appearance of cyst after linac-based radiosurgery (LBRS) in AVM and to determine the mechanism of cyst formation.

2. Materials and methods

From April 1993 to April 2008, LBRS was performed on 109 patients with cerebral AVM at our institution. Continuous MRI was performed in 100 of these patients, and 9 patients were followed-up at other institutions. Interviews with these patients regarding cyst formation was conducted over telephone. Six patients (5.5%) were diagnosed with cyst formation following radiosurgery. One case was excluded because MRI follow-up had been performed at another hospital. The 5 remaining patients (3 men, 2 women), who had undergone regular MRI follow-up at our institution, were included in this study. In all cases, MRIs were evaluated every 3–4 months for 2 years following LBRS and every 6–12 months thereafter. One patient had a history of previous intracerebral hemorrhage due to a ruptured AVM (Table 1). Three of the 5 patients

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Table 1
Summary of the clinical and treatment data in patients with cyst formation.

Case no.	Age/sex	Initial presentation	Location	Prior treatment	Presenting symptoms at the time of cyst treatment	LBRS	Nidus volume (cc)	Marginal dose (Gy)	Maximum dose (Gy)	Complete obliteration (years)
1	11/male	Headache	Lt. parietal	None	Hemiparesis	Initial	5	15	26.3	Yes (7.5)
						2nd	1.6	15	18.8	
2	22/female	Bleeding	Lt. frontal	Excision	Headache	Initial	1.25	18	22.5	Yes (2)
3	43/female	Seizure	Rt. frontal	None	Hemiparesis	Initial	13.56	12	26.1	Yes (6)
						2nd	9.39	12	33	
4	21/male	Headache	Lt. temporal	None	Hemianopsia	Initial	10.75	12	23.3	Yes (9.5)
						2nd	8.02	12	15	
						3rd	5.45	15	18.8	
5	65/male	Hemianopsia	Lt. occipital	None	Hemianopsia	Initial	11.4	15	28.9	Yes (3)

were subjected to additional LBRS as a treatment for a remaining nidus. The mechanisms and predictive factors of cyst formation were examined using serial MRI findings from early stages until cyst formation, with a particular focus on: (1) the contrast effect on the nidus and its periphery; (2) the edematous changes around the nidus; and (3) any bleeding inside the nidus and the cysts. Two patients subjected to cyst extraction were also included in the pathological study.

2.1. Radiosurgery technique

Radiosurgery was performed using the 10-MeV X-ray beam of a linear accelerator (Clinac 2100C, Varian, U.S.A.). A convergent beam irradiation (CBI) system (F.L. Fischer, Germany) was used as the stereotactic radiosurgery system. Radiosurgery procedures were planned with the STP 3D-planning system (F.L. Fischer, Germany). Additional irradiation was considered if total obliteration was not observed 3 years after treatment and no changes were observed in MRI or MR angiography images (Table 1).

3. Results

Serial MR images taken 4 months to 7 years after the initial LBRS showed changes in contrast at the irradiated site and its periphery. T2-weighted MRI (T2W-MRI) also showed the emergence of a high intensity area (HIA) during approximately the same time as the observed changes in contrast-enhanced imaging. In cases 1, 3, 4 and 5, T2W-MRI showed the emergence of a low intensity area (LIA) following the appearance of changes in contrast and edematous state in the surrounding cerebral parenchyma. Case 2 had already showed a hematoma cavity around the nidus at the time of the LBRS. The observation of the LIA led us to question whether subclinical microbleeding was present near the irradiated area. Time of cyst formation ranged from 8 months to 10.5 years after the initial LBRS. Moreover, the time between the observed changes on imaging until cyst formation was 4.5–5.5 years. Case 2, who had shown a hematoma cavity since the time of LBRS, the cyst increased in size along with the appearance of contrast changes. However, the same patient also showed findings that led us to suspect a subclinical hemorrhage. Case 3 and 5, the cysts continued to increase in size. The nodules detected on Gadolinium (Gd)-enhanced MR images were therefore extracted, and the cysts were opened surgically 11.5 years after the initial treatment for both patients, and at 1 year and 3.5 years after cyst formation, respectively. However, in cases 3 and 5 underwent cyst extraction, the HIA surrounding the cysts detected on T2W-MRI persisted after surgery. Case 2 with early cyst formation, the administration of adrenocortical hormones resulted in a reduction in size of the cysts. However, for the 2 other patients, 2 years and 2.5 years have passed, respectively, since the formation of the cysts, but no change in cyst size has been found, and observations are continuing.

3.1. Relationship between cyst formation and complete occlusion of an AVM nidus

In the 2 patients for whom occlusion was confirmed based on a single LBRS irradiation procedure, the cerebral angiography at 2 and 3 years led to the diagnosis of complete occlusion. In 1 patient who showed cyst formation soon after treatment, cyst formation was also found before complete occlusion of the AVM niduses. For 3 of the 5 patients, nidus occlusion was incomplete, and thus additional irradiation was performed during LBRS. These 3 patients (2 patients irradiated twice, 1 patient irradiated 3 times) were diagnosed with complete occlusion at 1.2, 1.7, and 3.5 years, respectively, on the basis of cerebral angiography findings. For these 3 patients, the time from the last irradiation until cyst formation was 4.2, 3.3, and 5 years, respectively, with cyst formation occurring after complete occlusion of AVM niduses.

3.2. Appearance of abnormal findings on MR images after LBRS

In the 100 cases of AVM in which continuous MRI follow-up were possible, the appearance of an HIA on T2W-MRI was 22% (22 cases), while the appearance of contrast effects on Gd-enhanced MRI was 15% (15 cases). Meanwhile, the appearance of LIAs thought to be due to subclinical bleeding on T2W-MRI was 6% (6 cases); in 5 of these patients, the LIAs were related to cyst formation, and the remaining patient is currently undergoing follow-up.

3.3. Illustrative cases

3.3.1. Case 1

An 11-year-old boy presented with a headache. MRI revealed a left parietal lobe AVM. LBRS was conducted using a marginal dose of 15 Gy for the treatment of AVM, with a volume of 5.0 cm^3. No complete occlusion of AVM was found. At 6.3 years after the initial treatment, LBRS was performed using an additional 15 Gy irradiation dose for the treatment of a residual AVM measuring 1.6 cm^3 in volume. Seven years later (8 months after the additional irradiation), MRI findings showed a contrast enhancement in the region corresponding to the AVM. This contrast change was considered associated with nidus occlusion after treatment; therefore, follow-up was continued. The complete occlusion of niduses was confirmed by cerebral angiography at 7.5 years (1.2 years after additional irradiation). Thereafter, the contrast-enhanced region continued to increase gradually in size and reached a maximum size 8.5 years later (2.2 years after additional treatment). The central region was an LIA and presented with an irregularly shaped contrast effect (Fig. 1, upper). Concurrent to this, the patient developed