CLINICAL CASE REPORT

Hyperbaric oxygen therapy in the treatment of malign edema complication after arteriovenous malformation radiosurgery

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ABSTRACT

A 16-year-old female patient with headache was admitted to our hospital. Radiological examination showed a Spetzler-Martin Grade III arteriovenous malformation (AVM) located at the left frontal lobe. Volume-staged stereotactic radiosurgery (SRS) treatment performed in two fractions at three-month intervals and post-procedural period were uneventful. Eight months later the patient was admitted to our hospital with headache, vomiting, right-sided facial palsy and right upper extremity paresthesia. Radiological examination demonstrated severe vasogenic edema in the left centrum semiovale and temporal region. Due to severe and steroid-resistant malign edema, hyperbaric oxygen (HBO_2) therapy was performed as an alternative treatment option. Neurological symptoms resolved completely after HBO_2. Radiological examination demonstrated serious improvement of brain edema and mass effect.

INTRODUCTION

Cerebral arteriovenous malformation (AVM) is a congenital vascular anomaly that consists of a vessel tangle, resulting in and causes direct blood flow from arterial input to the venous system without an intervening capillary network to decrease the pressure. The most important risk is the rupture of the AVM, which has 10% mortality and 30%-50% morbidity from each bleed [1]

Microsurgical resection, endovascular occlusion, stereotactic radiosurgery (SRS), or combinations of these therapies are the main treatment options for these lesions. The morbidity and mortality risk of microsurgical treatment is higher especially for deep AVMs and/or AVMs in eloquent areas. For these types of AVMs gamma knife radiosurgery may be the most appropriate treatment option.

Although SRS allows giving an appropriate dose to a confined target area and reduces the undesired effects of radiation on normal brain parenchyma, big lesions have an increased risk of radiation injury due to high radiation doses. Early toxic effect of radiation due to SRS is rare: Seizure is the most common finding. Radiation-induced brain edema is a late onset SRS complication which is due to white matter injury (WMI) and radiologically defined as hyperintensity around target tissue on T2-weighted and FLAİR magnetic resonance imagining (MRI) [2-4].

Radiation-induced brain edema is a well-known complication after SRS for AVM. However, it is difficult to estimate which AVM patients who are treated with SRS will manifest with brain edema. Cohen-Inbar, et al. showed that 22.9% of patients whose AVMs were treated with SRS have symptomatic radiation-induced adverse effects. [5]. Most symptomatic radiation-induced brain edema can be resolved by medical treatment. Medical treatment options are steroids, anticoagulation, barbiturates and hypothermia. Surgical decompression remains a treatment option for severe and medically refractive brain edema after SRS. Hyperbaric oxygen therapy is an alternative treatment option for this type of malign brain edema complications of SRS [6].

KEYWORDS: arteriovenous malformation; brain edema, gamma knife radiosurgery; hyperbaric oxygen therapy; brain edema; neurosurgery

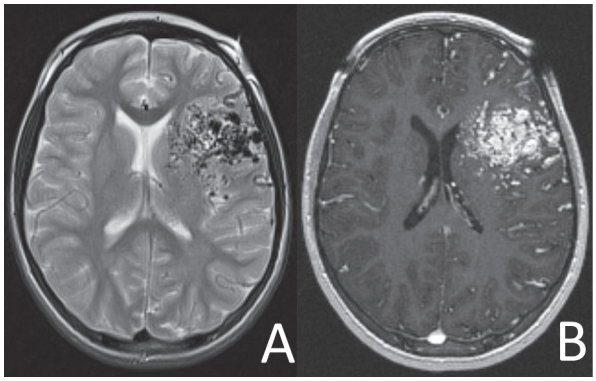

FIGURE 1: (**A**) T2-weighted axial and (**B**) T1-weighted axial contrast enhancing images of the MRI show a vascular lesion located at left frontal lobe which is compatible with AVM.

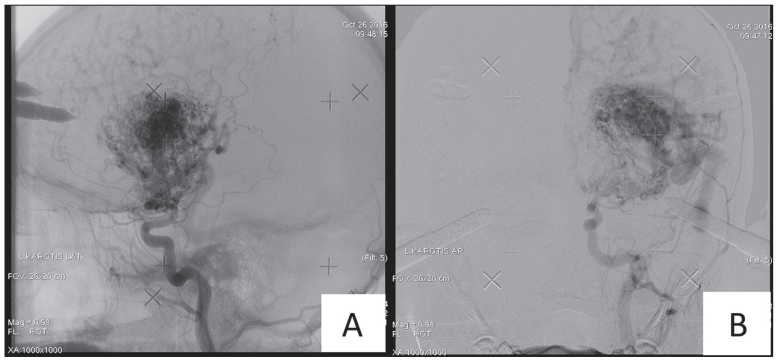

FIGURE 2: Angiography performed before SRS. (**A**) Lateral and (**B**) anteroposterior images show an AVM. Nidusis 3.5 cm in diameter. Lesion has deep venous drainage. AVM feeds from left anterior cerebral, middle cerebral and lenticulostriate arteries. Venous drainage is toward superior sagittal and transverse sinuses.

CASE REPORT

A 16-year-old female patient complained of continuous headache. It was especially problematic on the left side and had occurred over a one-year period. Neurological examination was normal. MRI revealed a Spetzler-Martin Grade III AVM located at the left frontal lobe. Angiographic examination was performed. It showed that the nidus was 3.5 cm in diameter, and the AVM had deep venous drainage. The AVM was feeding from the left anterior cerebral, middle cerebral and lenticulostriate arteries, and venous drainage was toward the superior sagittal and transverse sinuses (Figures 1, 2). Treatment options, their success rate, and possible complications were explained to the patient and her parents. It was decided that the lesion would be treated by volume-staged SRS in two fractions.

Our treatment methodology was previously described [7]. Briefly, after placement of the stereotactic head frame, MRI and angiography were performed as part of the treatment plan. The treatment plan was arranged by a neurosurgeon, a radiation oncologist and a medical physicist. SRS treatment was performed by using a Leksell Gamma Knife® Perfexion™ procedure at Gazi University Gamma Knife Center. In stage I of the radiosurgery, 12.2 cm^3 of volume was treated with a marginal dose of 18 Gy (minimum 1.7 Gy – maximum 36.6 Gy) and in stage II 13.9 cm^3 of volume was treated with a marginal dose of 18 Gy (minimum 15.1 Gy – maximum 36.6 Gy). Post procedural period was uneventful, without any symptom or complication after both sessions of SRS. The patient was treated with a prophylactic oral steroid (dexamethasone; 4 mg every six hours tapered in one week) for brain

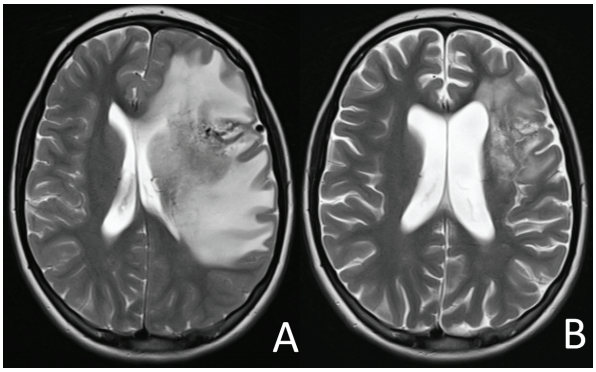

FIGURE 3: (**A**) Pre-HBO_2 T2-weighted axial MRI indicates massive brain edema which is causing midline shift. (**B**) After three months of 10 sessions HBO_2 therapy a dramatic reduction in edema on T2-weighted axial MRI is shown.

edema and non-steroidal anti-inflammatory medication (paracetamol 500 mg every eight hours) for pain control.

There was no symptom or complaint after the second session of SR. However, after eight-months the patient presented with headache, vomiting, right-sided facial palsy and right upper extremity paresthesia. Neurological examination showed House-Brackmann Grade II facial palsy on the right side. A computerized tomography (CT) of the head demonstrated severe vasogenic edema in the left centrum semiovale and temporal region. Malign edema was causing an 8 mm midline shift as well (Figure 3A). Medical treatment for edema was started with intravenous steroid (dexamethasone 6 mg every four hours). Although headache and vomiting symptoms were relieved after medical treatment, facial palsy and radiological malign edema findings persisted. Due to these persistent neurological symptoms HBO_2 therapy was agreed upon by the neurosurgeon, radiation oncologist and hyperbaric medicine specialist.

The patient was treated in a multiplace hyperbaric chamber with daily two-hour HBO_2 sessions at 2.4 atmospheres absolute, which continued for 10 days. During the 10th session of HBO_2 the patient had a new-onset generalized tonic clonic seizure, so treatment was terminated. Neurological symptoms had totally resolved after HBO_2 therapy. An MRI scan performed three months after the treatment demonstrated serious improvement of brain edema and mass effect (Figures 3B, 4).

DISCUSSION

Although SRS is an effective treatment option for AVM, it contains several complication risks. Acute onset toxic effect of radiation is rare after SRS treatment, late onset radiation-induced brain edema is a more common complication of SRS.

Radiation-induced brain edema is due to WMI and radiologically defined as hyperintensity around target tissue on T2-weighted and FLAİR magnetic resonance imagining. Different studies have shown that radiological findings of radiation-induced changes have been associated with a larger treatment dose than 12 Gy. Flickinger, et al. reported rates of 42.4% radiological findings and 10% neurological findings after SRS was associated with more than 12-Gy treatment volumes of 56.5 cm^3 [8]. Another study showed an incidence of delayed onset or progressive brain edema of 10% (four of 40 cases) after SRS for cranial metastases [9]. White matter injury and brain edema complication after SRS were observed more frequently for AVMs than for cranial metastases [2, 3].

Late-onset radionecrosis may contribute to chronic inflammatory reaction and induce cerebral edema. Corticosteroids are classical treatment options for cerebral edema in prophylaxis and for refractory cases as well. Also, new investigations are studying anticoagulation, growth factors and stem cells for treatment and prevention of radiation-induced neurotoxicity [10].

Different studies have described radiation-induced brain edema complication in 3% to 45% of patients after SRS for AVMs [11-14]. A permanent deficit has been de-

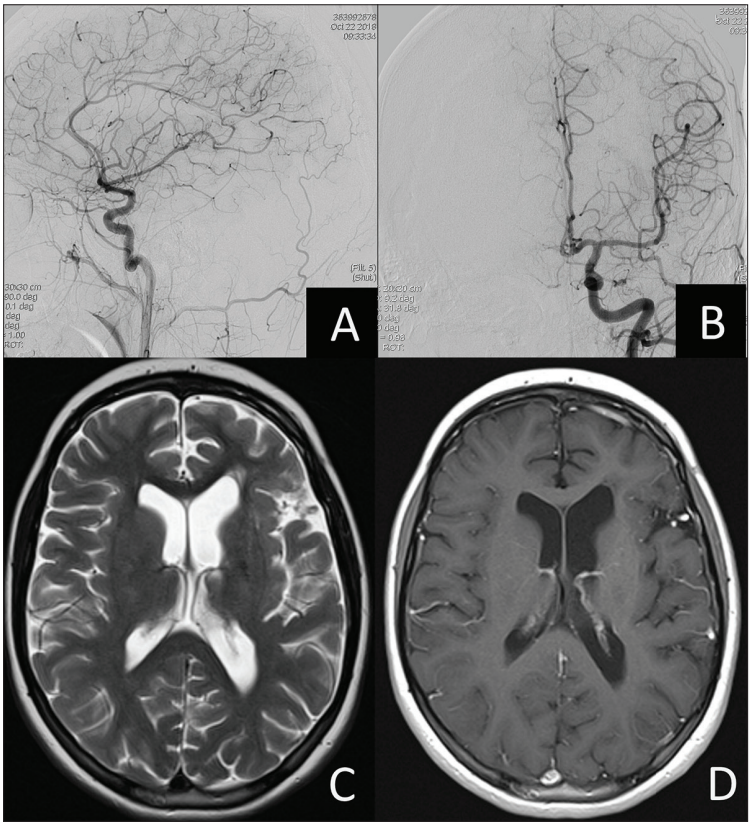

FIGURE 4: Last radiological follow-up has been performed after 48 months. **(A)** Lateral and **(B)** anteroposterior angiographic images indicate complete obliteration of the AVM. **(C)** T2-weighted axial and **(D)** T1-weighted axial contrast enhancing MRI images indicates complete resolution of edema.

scribed in 2% to 5%. Major etiological factors of edema include vasogenic edema and metabolic suppression. High radiation doses are usually the cause for this complication. Some studies are suggesting that obstruction of the draining vein is the underlying mechanism of SRS-induced edema [6].

HBO_2 therapy is a functional treatment for SRS-induced brain edema. Increasing tissue oxygenation by HBO_2 can induce cellular and vascular regeneration. HBO_2 creates oxygen level differences between radiated and non-irradiated tissue. This gradient causes a stimulus for fibroblast and capillary angiogenesis. HBO_2 can cause a decrease of lactate level in cerebrospinal fluid (CSF). This effect of HBO_2 can restore anaerobic condition of neurons [6].

HBO_2 has been used for bone and soft-tissue radionecrosis of the head and neck region [15]. HBO_2 promotes neovascularization at hypoperfused tissue. Neovascularization may cause improvement of functionality in radiation-induced damaged tissue. The main results of HBO_2 are to decrease cerebral edema, provide normal water content to the brain parenchyma, decrease severity of brain infarction, provide blood-brain barrier integrity, maintain antioxidant defenses, decrease the proliferation of foam cells and macrophages, and block astrocyte and macrophage release of neurotoxic factors. These changes cause improvement of neuronal integrity and patient outcome for patients with radiation-induced SRS [16].

Another potential treatment mechanism of HBO_2 is cerebral vasoconstriction. Cerebral vasoconstriction results in decreased cerebral blood flow. HBO_2 can also decrease vascular permeability, which in turn can decrease cerebral edema after SRS. HBO_2 may be a potential treatment option for SRS-induced brain edema with these mechanisms [6].

WMI is more frequent after SRS for AVMs and more benign lesions [17] than metastatic brain tumors. Therefore, prophylactic HBO_2 could be an option before or after SRS for AVMs [17].

CONCLUSION

Radionecrosis and brain edema are well-known complications after stereotactic radiosurgery. This complication is more frequent after treatment of arteriovenous malformation and benign tumors. Medical treatment is sufficient for most symptomatic radiation-induced brain edema, but in refractory cases hyperbaric oxygen therapy is an alternative treatment option for malign brain edema complications of SRS.

Conflict of interest statement
The authors have declared that no conflict of interest exists with this submission.

REFERENCES

1. Fleetwood IG, Steinberg GK. Arteriovenous malformations. Lancet. 2002;359(9309):863-873.

2. Guo WY, Nordell B, Karlsson B, Soderman M, Lindqvist M, Ericson K, et al. Target delineation in radiosurgery for cerebral arteriovenous malformations. Assessment of the value of stereotaxic MR imaging and MR angiography. Acta radiologica. 1993;34(5):457-463.

3. Flickinger JC, Lunsford LD, Kondziolka D, Maitz AH, Epstein AH, Simons SR, et al. Radiosurgery and brain tolerance: an analysis of neurodiagnostic imaging changes after gamma knife radiosurgery for arteriovenous malformations. Int J Radiat Oncol Biol Phys. 1992;23(1):19-26.

4. Chin LS, Lazio BE, Biggins T, Amin P. Acute complications following gamma knife radiosurgery are rare. Surg Neurol. 2000;53(5):498-502.

5. Cohen-Inbar O, Lee CC, Xu Z, Schlesinger D, Sheehan JP. A quantitative analysis of adverse radiation effects following Gamma Knife radiosurgery for arteriovenous malformations. J Neurosurg. 2015;123(4):945-953.

6. Wanebo JE, Kidd GA, King MC, Chung TS. Hyperbaric oxygen therapy for treatment of adverse radiation effects after stereotactic radiosurgery of arteriovenous malformations: case report and review of literature. Surg Neurol.2009;72(2):162-167; discussion 7-8.

7. Borcek AO, Emmez H, Akkan KM, Ocal O, Kurt G, Aykol S, et al. Gamma Knife radiosurgery for arteriovenous malformations in pediatric patients. Childs Nerv Syst. 2014;30(9):1485-1492.

8. Flickinger JC, Kondziolka D, Maitz AH, Lunsford LD. Analysis of neurological sequelae from radiosurgery of arteriovenous malformations: how location affects outcome. Int J Radiat Oncol Biol Phys. 1998;40(2):273-278.

9. Mehta MP, Rozental JM, Levin AB, Mackie TR, Kubsad SS, Gehring MA, et al. Defining the role of radiosurgery in the management of brain metastases. Int J Radiat Oncol Biol Phys. 1992;24(4):619-625.

10. Belka C, Budach W, Kortmann RD, Bamberg M. Radiation induced CNS toxicity--molecular and cellular mechanisms. Br J Cancer. 2001;85(9):1233-1239.

11. Cohen-Inbar O, Starke RM, Lee CC, Kano H, Huang P, Kondziolka D, et al. Stereotactic radiosurgery for brainstem arteriovenous malformations: a multicenter study. Neurosurgery. 2017;81(6):910-20.

12. Lo EH, Fabrikant JI. Delayed biologic reactions to stereotactic charged-particle radiosurgery in the human brain. Stereotact Funct Neurosurg. 1991;56(4):197-212.

13. Flickinger JC, Kondziolka D, Lunsford LD, Pollock BE, Yamamoto M, Gorman DA, et al. A multi-institutional analysis of complication outcomes after arteriovenous malformation radiosurgery. International journal of radiation oncology, biology, physics. 1999;44(1):67-74.

14. Aoki Y, Nakagawa K, Tago M, Terahara A, Kurita H, Sasaki Y. Clinical evaluation of gamma knife radiosurgery for intracranial arteriovenous malformation. Radiation medicine. 1996;14(5): 265-268.

15. Lynn M, Friedman WA. Hyperbaric oxygen in the treatment of a radiosurgical complication: technical case report. Neurosurgery. 2007;60(3):E579.

16. Kuffler DP. Hyperbaric oxygen therapy: can it prevent irradiation-induced necrosis? Exp Neurol. 2012;235(2):517-527.

17. Ohguri T, Imada H, Kohshi K, Kakeda S, Ohnari N, Morioka T, et al. Effect of prophylactic hyperbaric oxygen treatment for radiation-induced brain injury after stereotactic radiosurgery of brain metastases. Int J Radiat Oncol Biol Phys. 2007;67(1): 248-255.