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Short communication

Successful treatment of radiation-induced brain necrosis by hyperbaric oxygen therapy

Kiyotaka Kohshi[a,b,*], Hajime Imada[c], Satoshi Nomoto[c], Raizoh Yamaguchi[d], Haruhiko Abe[e], Haruaki Yamamoto[f]

[a] *Department of Neurosurgery, School of Medicine, University of Occupational and Environmental Health, 1-1 Iseigaoka, Yahatanishi-ku, Kitakyushu 807-8555, Japan*

[b] *Division of Hyperbaric Medicine, University Hospital of Occupational and Environmental Health, 1-1 Iseigaoka, Yahatanishi-ku, Kitakyushu 807-8555, Japan*

[c] *Department of Radiology, School of Medicine, University of Occupational and Environmental Health, 1-1 Iseigaoka, Yahatanishi-ku, Kitakyushu 807-8555, Japan*

[d] *Department of Urology, School of Medicine, University of Occupational and Environmental Health, 1-1 Iseigaoka, Yahatanishi-ku, Kitakyushu 807-8555, Japan*

[e] *Department of Internal Medicine, School of Medicine, University of Occupational and Environmental Health, 1-1 Iseigaoka, Yahatanishi-ku, Kitakyushu 807-8555, Japan*

[f] *Department of Neurosurgery and Division of Gamma Knife Center, Fukuoka Wajiro Hospital, 2-11-17 Wajirogaoka, Higashi-ku, Fukuoka 811-0213, Japan*

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Abstract

We describe a 68-year-old man who underwent hyperbaric oxygen (HBO) therapy to manage radiation necrosis of the brain, which developed after two treatments with stereotactic radiosurgery (SRS) to the same lesion. The necrosis was subsequently treated with steroids alone for 2 months; however, he progressed clinically and radiographically. Improvement again was noted with the reinstitution of HBO therapy. This case suggests that HBO therapy is an important therapeutic option in the treatment of brain radiation necrosis caused by SRS.

Keywords: Radiation necrosis; Radiosurgery; Hyperbaric oxygenation; Complication

1. Introduction

Stereotactic radiosurgery (SRS) has become an important therapeutic approach for the treatment of vascular malformations, benign and malignant tumors, and functional brain diseases. However, radiation necrosis of the brain is a feared complication of this therapy. Classic treatment for patients with radiation necrosis is to control cerebral edema with steroids or to resect avascular necrotic debris if symptoms persist despite of steroid therapy. Although the pathogenetic mechanisms are not well understood, radiation causes a progressive obliterative endarteritis of the small blood vessels, resulting in cellular hypoxia [1,2]. One promising new therapeutic intervention for cerebral radiation injury is hyperbaric oxygen (HBO) therapy [3–5], which has proven effectiveness in the management of this problem in other sites [2]. Here, we describe the successful treatment of a case of radiation necrosis after SRS with HBO therapy.

2. Case report

A 68-year-old man was referred to our institution 9 years after resection of a renal cell carcinoma and a metastatic lung tumor. Eight years following the resections, he complained of dizziness and a slight occipital headache, but he was neurologically intact. Computerized tomographic (CT) scans and magnetic resonance images (MRIs) showed a homogeneously enhanced mass lesion in the left cerebellar hemisphere. Based on the neuroradiological findings, the

* Corresponding author. Department of Neurosurgery, School of Medicine, University of Occupational and Environmental Health, 1-1 Iseigaoka, Yahatanishi-ku, Kitakyushu 807-8555, Japan. Tel.: +81-93-603-1611; fax: +81-93-691-4200.

E-mail address: k-kohshi@clnc.uoeh-u.ac.jp (K. Kohshi).

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lesion was diagnosed as metastatic brain tumor from the primary cancer. CT scans were used to plan the radiation dose for SRS. Stereotactic radiation treatment was administered with an X-Knife radiosurgery system. A dose of 29 Gy was administered to the 100% isocenter point and 26 Gy was delivered to the 80% isodose volume. The volume within the 26 Gy isodose curve was 2.7 cm^3.

The MRI performed at the 3-month follow-up examination showed that the area of contrast enhancement was significantly smaller than at the time of SRS. Nine months after treatment, however, a MRI revealed progressive contrast enhancement in the treated area. The enhanced region was felt to represent recurrent tumor as ^{201}Tl-SPECT scan revealed high uptake in the enhanced region. A repeat MRI exhibited further increase in the area of enhancement to a volume of 4.1 cm^3. Thus, a second SRS (maximum dose: 42 Gy, 80% isodose: 38 Gy) was performed 15 months after the first SRS. For 3 months after the treatment, the enhanced area showed a slight regression in size with a central necrosis.

At 5 months after the last treatment, he complained of worsening dizziness and developed slight ataxia in the left lower limb. MRI demonstrated a cystic enhanced region with surrounding edema in the previously treated area (Fig. 1A). Since he had a medical history of diabetes mellitus that required pharmacological treatment, he was subsequently managed with a low dose of steroid medication (betamethasone 2 mg/day). He coincidentally underwent HBO therapy (60 sessions at 2.5 atmospheres absolute, for 60 min) five times per week using a multiplace chamber. He reported improvement in his clinical status a few weeks after the beginning of the combined treatment. Due to a slight regression of the enhanced region and surrounding edema 3 months after the therapy (Fig. 1B), he received only steroid medication (using betamethasone at the same dose). Unfortunately, a follow-up MRI 2 months after the completion of HBO therapy showed a thick wall of the enhanced area with surrounding brain edema accompanied with a worsening of clinical symptoms, such as dizziness and ataxic gait (Fig. 1C). Therefore, we adjunctively started HBO therapy again for 2.5 months (50 sessions). His neurological symptoms improved 11 months after the second SRS and the enhanced wall of the mass lesion regressed gradually (Fig. 1D). At 22 months after the end of such treatment, the patient has no worsening of either neurological conditions or MRI findings. He was able to walk unassisted.

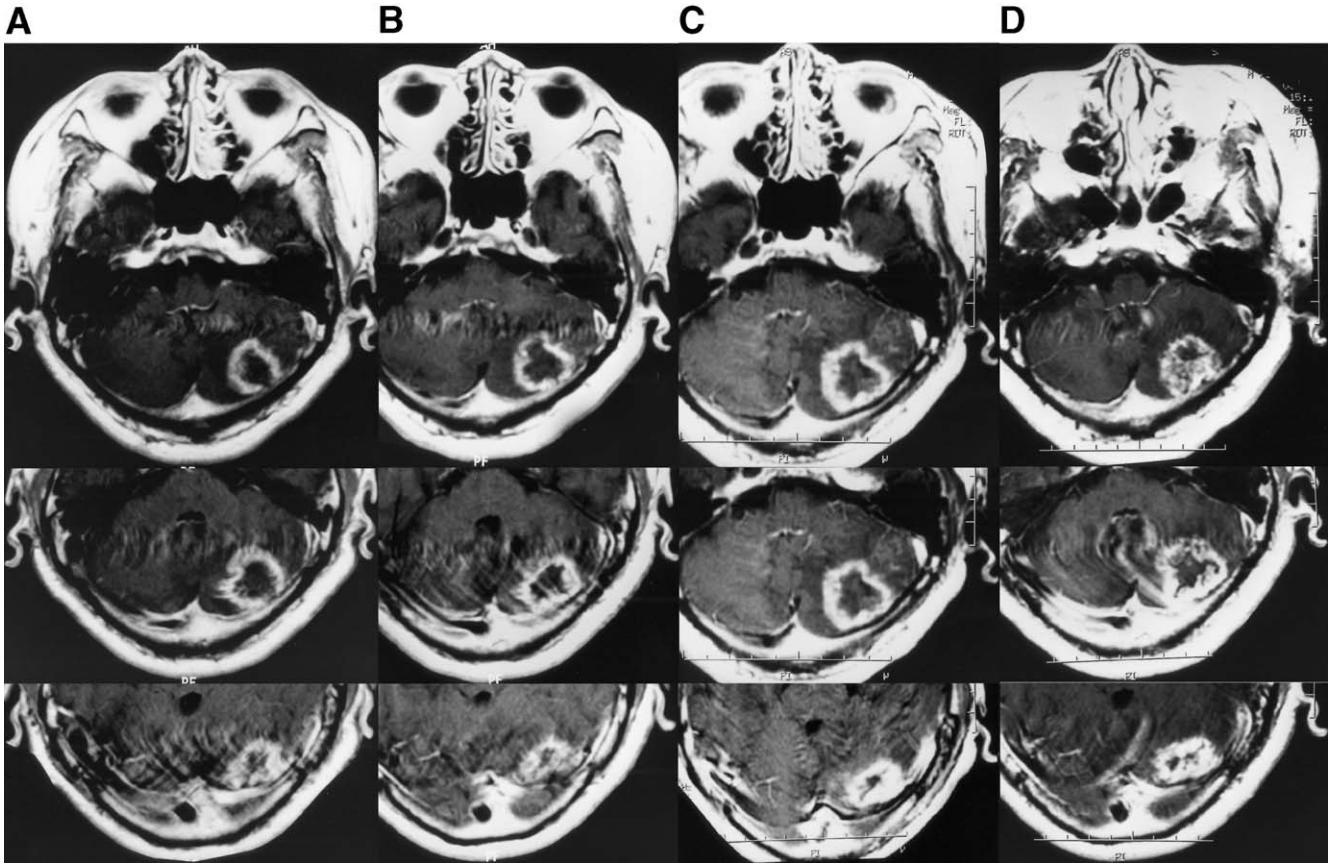

Fig. 1. Contrast-enhanced magnetic resonance images of radiation necrosis obtained before HBO (A), after the first series of HBO (60 sessions for 3 months) (B), at 2 months after completion of HBO (C) and at 6 months after the second series of HBO (50 sessions for 2.5 months) (D).

3. Discussion

This case demonstrates the clinical usefulness of HBO therapy for radiation necrosis of the brain. He showed improvement in both clinical symptoms and MRI findings after HBO therapy, despite failure of steroid therapy alone at the given dose. However, we cannot determine that HBO therapy alone is effective for radiation necrosis because he received steroid treatment simultaneously.

A number of risk factors have been identified for radiation injury of the brain after SRS. As generally expected, two important factors are treatment volume and radiation dose. Clearly, the risks associated with SRS can be minimized if the dose is kept relatively low and the treatment volume is small. Moreover, a more powerful predictor of radiation necrosis is repeated radiosurgical treatment to the same region. Chin et al. [6] reviewed in a gamma knife treated series that 4 of 17 patients with radiation necrosis underwent two or more radiosurgical treatments but only 1 of 226 cases without necrosis did a repeated treatment. Their results indicate that four out of all five patients treated with repeated SRS had radiation necrosis. Physicians should use extreme caution in exposing the same brain lesion to more than two SRS treatments.

Until now, available regimens for medical management of radiation necrosis have proved relatively ineffective. Traditional therapies have been attempted to reduce brain edema with steroids, nonsteroidal anti-inflammatory drugs and anticoagulants [4]. Steroid medications sometimes improve symptoms, but do not slow progression of this condition. Resection of avascular necrotic debris is frequently beneficial for patients who develop mass effects, but is unlikely to be of use in patients with surgically inaccessible lesions. Recently, effects of HBO therapy have been investigated for brain radiation necrosis after SRS [3–5]. Chuba et al. [3] reported that 10 young patients who failed steroid therapy for this condition received HBO treatment and all of them demonstrated initially stable or improved symptoms and/or imaging findings. All patients were medicated with steroids during and after HBO therapy. Likewise, Tandon et al. [4], who treated a patient of severe radiation necrosis, managed its progression by steroid and anticoagulant treatments combined with HBO therapy. Their reported case had a gradual clinical improvement after the initiation of HBO therapy. The above two reports indicate that HBO therapy would be proposed as an adjunctive treatment for radiation necrosis. In contrast, Leber et al. [5] documented two patients with arteriovenous malformations whose radiation necrosis responded well to HBO therapy without steroid treatment; one lesion disappeared and the other was reduced significantly in size after 40 sessions of HBO therapy. In our patient who had an improvement of clinical symptoms and a regression of radiation necrosis after HBO therapy, this condition progressed several months after the finish of therapy. The clinical course in our patient and others suggest that HBO therapy is an important option for the treatments of radiation necrosis, especially at the early progressive stage of this condition.

Histological characteristic of this complication is coagulation necrosis with thickened vessel walls, thrombosed vessels, vascular proliferation and microhemorrhages [7,8]. These findings are similar to those in soft tissues including skin, bladder and intestine [1,2]. The pathogenic mechanism of brain radiation necrosis is probably primary vascular, with necrosis and glial loss secondary ischemia. This condition in other sites has been treated by HBO therapy with good results for many years [2]. The beneficial effect of HBO therapy has been explained by the induction of neovascularization leading to an increased local oxygen tension [2,3,5]. More recently, a study using a non-irradiated surgical wound model indicated that HBO exposure enhances vascular endothelial growth factor (VEGF) production and that HBO is an even greater stimulus for VEGF than hypoxia [9]. It has therefore been proposed that HBO promotes angiogenesis in radiation-injured tissue by increasing the levels of VEGF. However, further investigations are needed to define the precise nature of the mechanisms.

In conclusion, we describe a patient that underwent HBO therapy and steroid treatment to manage brain radiation necrosis after repeated SRS. He clinically failed steroid treatment alone, but had an improvement in clinical and imaging studies after the resumption of HBO therapy. This case suggests that HBO therapy is an effective, non-invasive modality for the treatment of radiation-induced brain necrosis.

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