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Intraoperative Radiation Therapy as an Adjunctive Therapy for Huge and Highly Vascular Parasagittal Meningiomas

This case presents a 34-year-old man who had a huge parasagittal meningioma. Initial treatment consisted of preoperative external carotid artery embolization and partial tumor resection. During the resection, we found that the tumor invaded the adjacent calvarium, and due to massive hemorrhage, total removal of the tumor was impossible. The patient was treated with intraoperative radiation therapy (IORT) (25 Gy via 16 MeV) as an adjunctive therapy. Eight months after IORT, we were able to remove the tumor completely without surgical difficulties. IORT can be considered an useful adjunctive therapy for the superficially located, huge, and highly vascular meningioma.

Key Words: *Vascular Neoplasms; Meningioma; Radiotherapy, Computer-Assisted*

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INTRODUCTION

Meningiomas are common tumors and account for 19% of intracranial and 25% of intraspinal neoplasm (1, 2). They are generally benign, well circumscribed, and slow growing. Some meningiomas cannot be removed totally, due to inaccessible anatomical location and/or invasive characteristics; some have a recurrent nature, recurring in different locations and requiring repeated surgical removal.

There are frequent instances of incomplete surgical resection with the subsequent need for additional therapy. Adjuvant therapy usually consists of fractionated external beam radiation (3), or focused radiation, either percutaneous (4) or interstitial (5), and all of which have demonstrated efficacy. A relatively small number of patients who are not candidates for focused irradiation and/or who failed conventional radiation therapy and require other adjuvant treatment remains. The advantage of intraoperative radiation therapy (IORT) is that the physician is able to directly visualize the tumor volume, as well as areas at risk, and is able to exclude normal structures from the radiation field. It is also possible to shield normal tissues underneath the tumor volume or to adjust the electron energy to spare normal structures located beneath the tumor mass. For these reasons it is possible to give the tumor a very high dose while minimizing the dose to normal tissue (6).

The purpose of this report is to raise the awareness of IORT as means to reducing tumor volume and vascularity in patients with a huge hemorrhagic parasagittal meningioma as well as a potential therapeutic option in meningiomas that prove to be difficult for surgical removal due to vascularity and mass size.

CASE REPORT

A 34-year-old man, who was admitted to the local hospital with several episodes of generalized seizures, was treated with medication since March, 1992. On December 2, 1993, the patient was referred to our institution with a diagnosis of possible meningiomas. At the time of referral, brain computerized tomography (CT) revealed a huge highly enhancing mass at the vertex area with surrounding edema. There was no history of radiation therapy for the tumor previously.

Examination

Additional clinical history elicited on admission included recurrent focal onset generalized seizure, occurring ap-

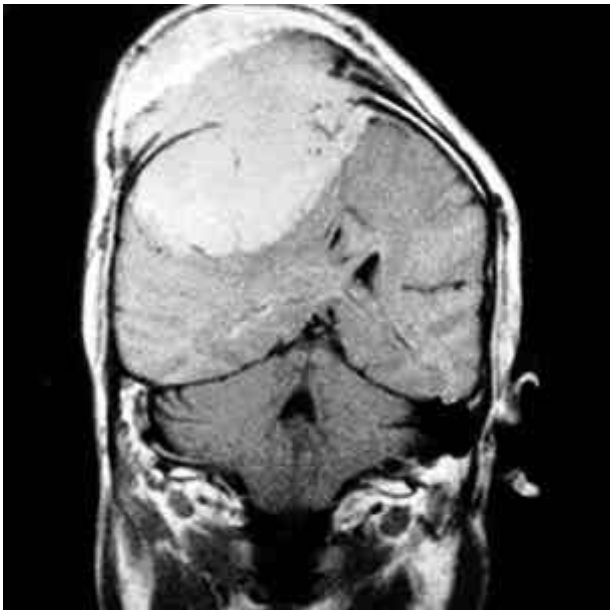

Fig. 1. Preoperative Gd-DTPA enhanced T1W1 of MRI shows a huge homogenously enhancing parasagittal convexity mass invading the cerebral parenchyma and scalp soft tissue. Destroyed cranial vault is noted.

proximately 6 times in spite of anticonvulsant medication. He was alert and well-oriented. There was no papilledema. Left-sided hemiparesis was worse in the arm than in the leg and his deep tendon reflexes were not increased on the left, with no pathological reflex. Magnetic resonance imaging (MRI) scan demonstrated well enhancing huge mass (10×8×6 cm) on right frontoparietal parasagittal convexity with surrounding edema. Extensive calvarial thickening and destruction were noted (Fig. 1).

Both internal carotid angiograms showed mass and heterogenous tumor staining with pial feeders, which was more prominent on the right side. Part of superior sagittal sinus was encased by the tumor (Fig. 2). Both external carotid angiograms revealed multiple feeding branches to tumor, mainly from superficial temporal, middle meningeal, and occipital artery. Each feeder was embolized effectively via superselective catheters (Tracker 10, Target therapeutics, U.S.A.) with polyvinyl alcohol (PVA) particles (Contour, Interventional Therapeutics Corporation, CA, U.S.A.) contrast media mixture (150-250 u, 250-355 u, 355-500 u) (Fig. 3).

First operation

During surgery at 24 hr after embolization, removal of the tumor as well as invaded skull, was achieved but total removal of the tumor inside the skull was not feasible due to a massive hemorrhage during debulking. The tumor mass was decreased after operation (10×6×6 cm) (Fig. 4).

Pathological examination

Histological examination of the tumor revealed a typical meningotheliomatous meningioma with hemorrhagic necrosis. There was thrombotic occlusion of the adjacent blood vessels (Fig. 5).

First postoperative course

The patient was found to have no new neurological

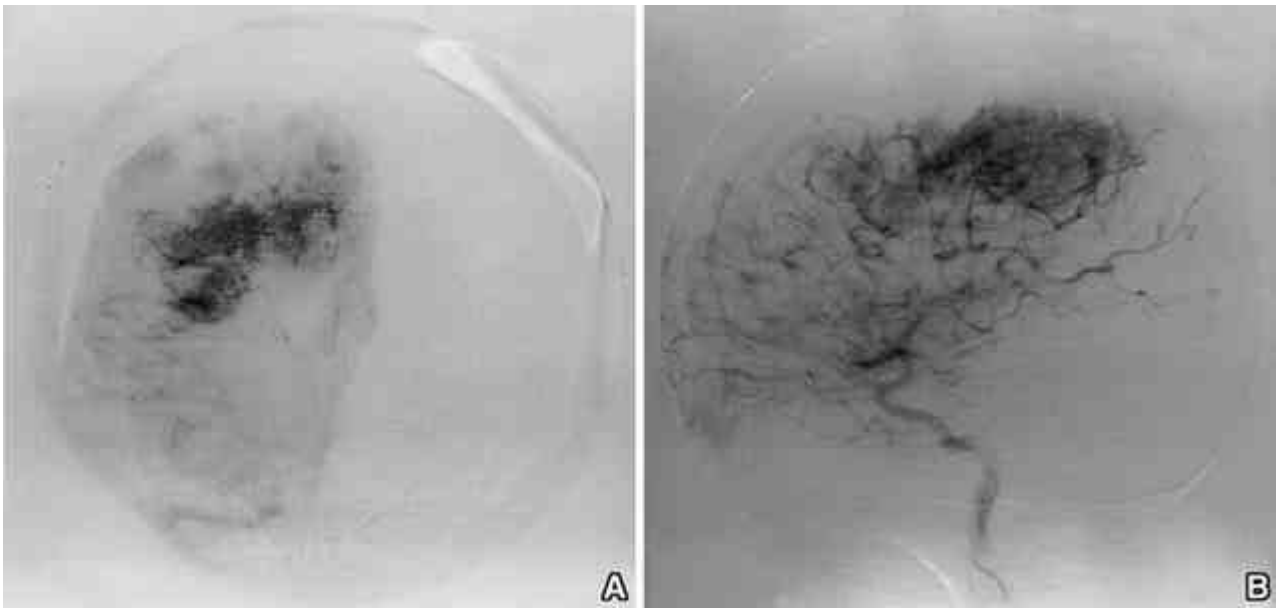

Fig. 2. Internal carotid angiogram (A-P and lateral view) shows extensive tumor staining of pial feeders on tumor periphery.

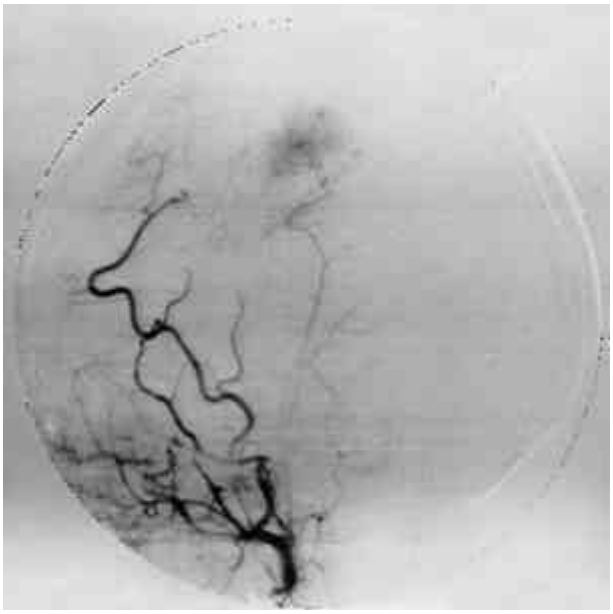

Fig. 3. After selective embolization of external carotid arterial feeders with appropriate PVA particles, lateral view of ECA angiogram shows occlusion of feeders and small portion of residual tumor staining.

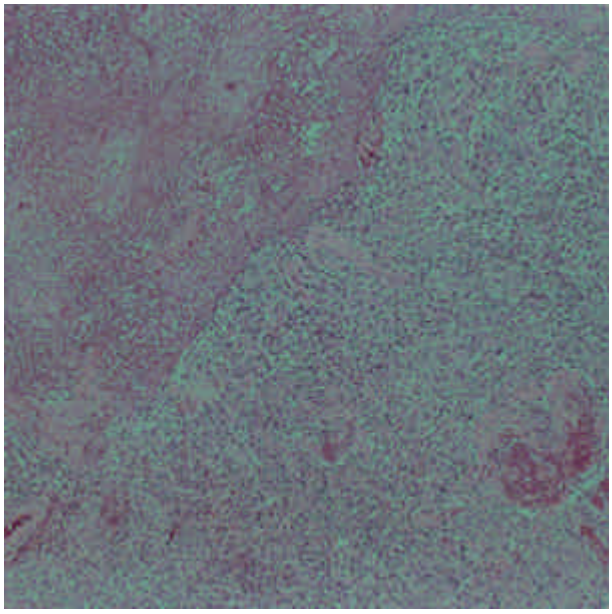

Fig. 5. Postembolization state: Tumor shows hemorrhagic necrosis. There is thrombotic occlusion of the adjacent blood vessels. Meningioma cells are still prominent (H&E, ×40).

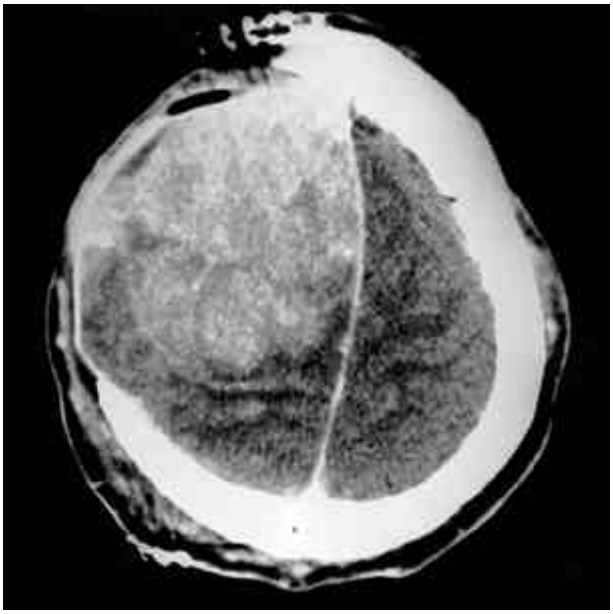

Fig. 4. Enhanced axial CT, taken after first surgery before IORT, showed homogenously enhancing residual tumor.

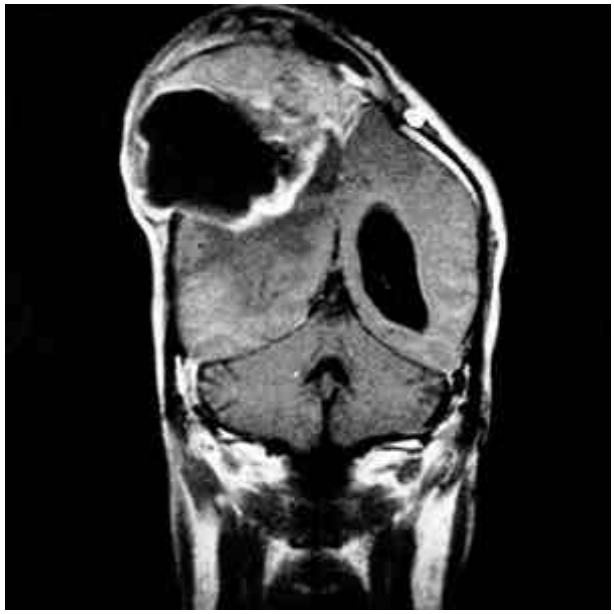

Fig. 6. MRI Gd-DTPA enhanced T1W1, taken on post-IORT before second surgery, reveals considerable size reduction of mass and extensive necrotic cavity within the mass. Enhancing residual mass and surrounding edema still noted.

deficits postoperatively but developed skin necrosis around scalp flap, so external irradiation could not be considered as a safe treatment. Therefore, at debridement of the skin, the decision to treat the patient with IORT was made. The tumor was suitable for IORT because it located superficially and was expected to be reduced its vascularity by IORT.

IORT as a second operation

About 8 weeks after first operation, IORT was done as adjunctive measures. After exposing the previous oper-

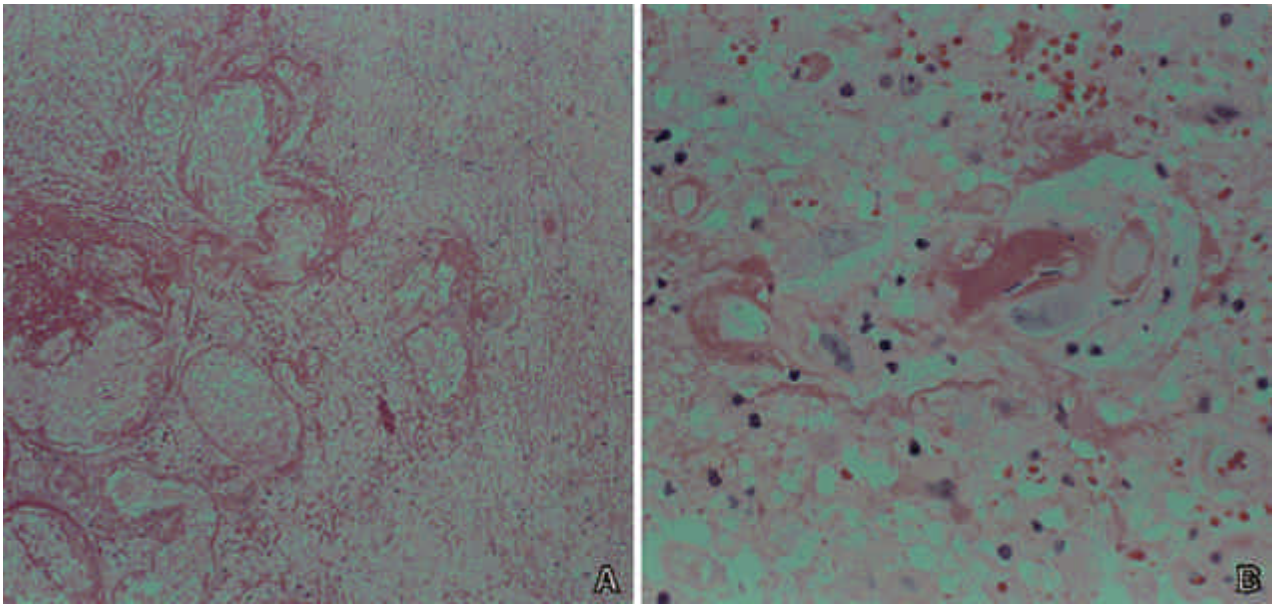

Fig. 7. (A) Postirradiation state: Tumor cells are entirely necrotic and blood vessels are degenerated and dilated (H&E, ×40). (B) There are a few viable blood vessels, but endothelial cells show enlarged nuclei in the large cytoplasm. It may be a radiation induced changes (H&E, ×400).

ation flap, yellow fluid gushed out of artificial dura and a hypervascular reddish tumor mass was revealed after removal of artificial dura. The tumor was exposed widely and IORT was performed using 16 MeV electron beam, using a nine centimeter circular cone. IORT field covered the whole tumor mass and excluded adjacent normal brain. A total dose of 25 Gy was given at 90% isodose line.

Post-IORT course

The post-IORT course was unremarkable until the patient noticed the left extremity weakness and the reattack of intermittent seizure despite anticonvulsant medication at 8 months after the treatment. An MRI taken 8 months after IORT revealed the multiloculated cystic changes of the residual tumor (10×3×5 cm), with irregular peripheral enhancing rim (Fig. 6).

Third operation

The third operation was performed on September 29, 1994. The artificial dura was opened. The artificial dura was densely adhesed to the residual tumor at its margin. A plane was made between the tumor and surrounding gliotic brain. A cyst containing yellowish fluid along the tumor surface, facilitating the dissection. The tumor was firm and very less vascular in comparison with the first operation. A gross total resection was achieved without difficulty. The excised tumor was firm and gray to dark red.

Pathological examination of third operation

Tumor cells were entirely necrotic and blood vessels were degenerated and dilatated (Fig. 7).

Third postoperative course

The patient awoke with a marked increase in weakness in the left lower extremity and rapidly react to command.

Neurologically, he was lethargic but easily arousable. He followed the commands but showed a severe expressive aphasia.

Postoperatively, he recovered some ability to move left extremities and gradually his speech improved. On MRI of the brain taken 1 month postoperatively, marked reduction of mass was noted, with residual peripheral enhancing areas (Fig. 8).

Two months after third operation, his mental status was apathic and very slow reaction to command. Hydrocephalus was treated with ventriculo-peritoneal (V-P) shunt around 10th week after third operation. Since the V-P shunt, his neurological condition has continued to improve. He has been treated continuously with dilantine and phenobarbital.

DISCUSSION

Radiotherapy has been used in the treatment of various forms of brain tumors, especially for malignant glioma,

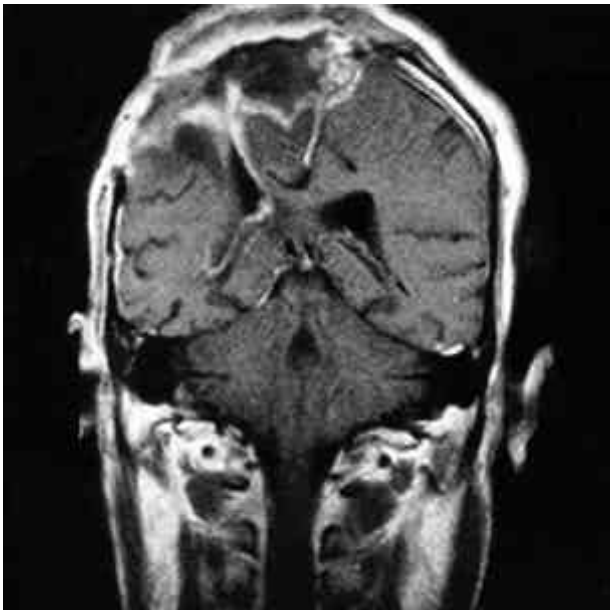

Fig. 8. Gd-DTPA enhanced T1W1 MRI, post-IORT followed by third surgery, reveals a marked reduction of mass in volume as compared with pre-IORT and surgery state. Small portion of residual peripheral enhancing lesion and gliotic reaction is noted.

and its effectiveness is now widely recognized (7, 8). The usual dose of external beam irradiation, 1.8-2 Gy per day in five fraction per week for a total 50-60 Gy, is not always enough to sterilize the gross or macroscopic tumor of considerable size. The amount of radiation which can be given is limited by the tolerance of the surrounding brain. Radiation can lead to vasculopathy. Some authors suggest that the degree of radiation-induced angiopathy is dependent on total radiation dose, treatment intervals, dose per treatment, age of irradiated vessels, and the relative radiosensitivity of the tissues (9-11). Information on the effect of radiation on the human brain is sparse, particularly regarding single-session high doses of radiation administered to small target volumes. Data on brain tissue reactions to single-dose irradiation in animals were summarized by van der Kogel (12), who concluded that the vasculature, glial cells and cells of the subependymal plate are the tissue components of the brain mainly affected by exposure to ionizing radiation. In animals, whole-brain radiation doses around 20 Gy produce radiation injury secondary to the vascular damage within 1 to 2 years, whereas 40 Gy or more is required to cause direct demyelination and white matter necrosis within 1 year (12).

Pathological specimen after IORT in our case showed the degenerated blood vessels which may be related to the reduction of the tumor size and vascularity. And this histological changes contributed to easy surgical excision of vascular memingioma after IORT. Arterial medial degeneration is hypothesized to be a secondary effect of occlusive vasculopathy within the vasa vasorum, which is primarily injured by the radiation (13).

In vitro studies indicate that inflammatory cytokines such as interleukin-1a, tumor necrosis factor-a, and interleukin-6 may be stimulated soon after treatment with ionizing radiation, suggesting a potential radioprotective role (14). The extensive and prolonged release of cytokines into the local microenvironment from activated macrophages, however long after the initial radiation therapy, may stimulate astrocyte proliferation, endothelial cell proliferation and blood-brain barrier disruption. These factors may contribute to gliosis, vascular injury and tissue necrosis that develop after radiation damage to the CNS (15).

IORT still has several problems that need answers. Firstly, the optimum dose has not yet been defined. The maximum tolerated dose is considered to be 25 Gy with an electron beam energy. The second problem is the selection of the electron beam energy, which will decide the depth of delivered radiation. Controversy still rages on the role of radiation therapy in the management of meningiomas. The study by Sheline (16) suggested that radiation therapy at the minimum increased the recurrence-free interval sufficiently to be of clinical significance in cases of incompletely resected meningiomas. Fukui et al. (17) indicated that irradiation is useful in tumors of the hemangiopericytic type as an adjunct to surgery or for palliation in advanced stages. Waga et al. (18) were unable to establish whether prophylactic radiation therapy was effective in preventing repeated recurrence in benign meningiomas. Yamashita et al. (19) concluded that irradiation of recurrent meningiomas is of litte value, although it might be beneficial occasionally. Practically most neurosurgeons are agree with the idea of Carella et al. (20) that radiation therapy has an established role in the treatment of incompletely excised, recurrent, or malignant meningiomas. If the conventional radiation therapy is not feasible due to skin infection like our case, IORT can be considered as an adjunctive treatment for residual meningioma.

Whether radiotherapy significantly influences the prevention of meningioma recurrence still remains open to question. And, preoperative radiotherapy, presumably for highly vascular tumors, and radiation therapy as the primary treatment, have few proponents (20).

To the best of our knowledge, IORT has never been used as an adjuvant therapy for the treatment of meningioma. Based on our limited expererience, IORT can be applied to huge, vascular meningioma, pre or postoperatively as an adjuvant therapy.

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