





### Applied Radiation and Isotopes

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# Nine-year interval recurrence after treatment of boron neutron capture therapy in a patient with glioblastoma: A case report



Toshiyuki Okazaki<sup>\*</sup>, Teruyoshi Kageji, Yoshifumi Mizobuchi, Takeshi Miyamoto, Shinji Nagahiro

Department of Neurosurgery, Institute of Health Biosciences, The University of Tokushima Graduate School, Tokushima 770-8503, Japan

#### HIGHLIGHTS

• A patients with glioblastoma mutliforme could be alive more than 9 years after BNCT.

• BNCT may be effective for the local control of GBM.

• The following TMZ and conventional radiation may be effective for prevention of CSF dissemination.

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#### ABSTRACT

Boron neutron capture therapy (BNCT) has been reported to be effective in the patients with glioblastoma multiforme (GBM). Median survival time (MST) of GBM patients treated with BNCT is approximately two years. GBM patients surviving 2 or 3 years are considered long-term survivors. In general, most recurrences are local and dissemination is rare. We report an unusual patient with three recurrences; the first and the second recurrences were local, and the third recurrence was dissemination nine years after BNCT.

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#### 1. Background

Glioblastoma multiforme (GBM) is the most common and aggressive primary malignant brain tumor (Adamson et al., 2009; Kanu et al., 2009). The estimated median survival time (MST) of GBM patients is about 12–16 months, despite multimodal treatment; survival of more than 2 years remains approximately 26%, even in patients treated with TMZ and conventional radio-therapy (Erpolat et al., 2009; Stupp et al., 2005). Local recurrence is common and cerebral CSF dissemination is only 8% (126/1491) (Parsa et al., 2005). Boron-10 nuclei preferentially capture slows 'thermal' neutrons, and after capture, they promptly undergo a 10B (n, alpha) 7Li reaction. The ionization tracks of energetic- and heavy-lithium and helium ions resulting from this reaction are only about one cell in diameter. Because of their high linear energy transfer, the relative biological effectiveness of these ions for controlling tumor growth is high (Diaz et al., 2000). Boron neutron

kageji@clin.med.tokushima-u.ac.jp (T. Kageji),

capture therapy (BNCT) is an interesting modality for the selective irradiation of tissues that harbor infiltrating glioma cells; MST of patients treated with BNCT has been reported to be 14.2, 19.5, 23.5, and 25.7 months (Henriksson et al., 2008; Kageji et al., 2011a; Kawabata et al., 2009; Yamamoto et al., 2009). We report a GBM patient who survived more than nine years after BNCT. The combined use of conventional irradiation and TMZ effectively addressed significant CSF dissemination at recurrence temporarily.

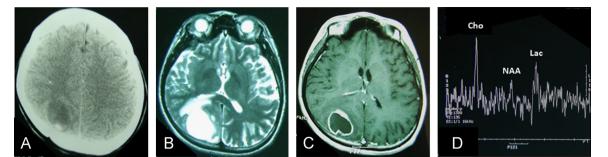
#### 2. Case presentation

A 22-year-old previously healthy woman was admitted to our department complaining of headache and vomiting. She had no family history of brain tumors. At time of admission, she manifested no remarkable neurological deficits. CT scan of the brain revealed a predominantly hypodense and a partially hyperdense lesion in the right parieto-occipital lobe (Fig. 1A). Magnetic resonance imaging (MRI) of the brain revealed a  $4 \times 3 \times 3$  cm mass in the right parieto-occipital lobe and peritumoral edema. The mass was predominantly hyperintense on T2-weighted MRI, suggesting that its largest portion was a cyst (Fig. 1B). On Gd-DTPA-enhanced images, the mass showed heterogeneous ring enhancement (Fig. 1C). MR spectroscopy lactate and choline were

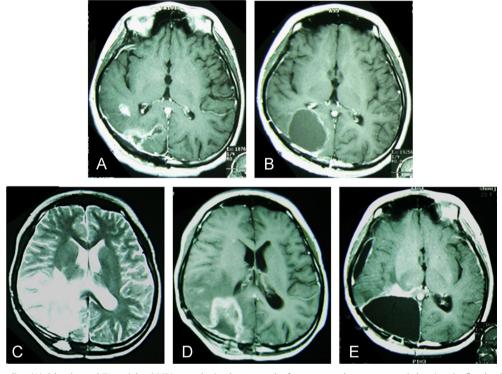
<sup>\*</sup> Corresponding author. Tel.: +81 88 633 7149; fax: +81 88 632 9464. *E-mail addresses:* tokazaki1978@sirius.ocn.ne.jp (T. Okazaki),

mizo@yj8.so-net.ne.jp (Y. Mizobuchi), takeshi\_edit@yahoo.co.jp (T. Miyamoto), snagahi@clin.med.tokushima-u.ac.jp (S. Nagahiro).

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**Fig. 1.** Initial CT and MRI images. (A) CT scan revealing a hypodense lesion in the right parieto-occipital area. (B) Axial T2-weighted image showing a predominantly hyperintense lesion and peritumoral edema. (C) Axial T1-weighted image obtained after Gd-DTPA administration revealing a ring-enhanced lesion in the right parieto-occipital area. (D) MR spectroscopy indicating high-grade glioma; lactate (Lac) and choline (Cho) were elevated and *N*-acetylaspartate (NAA) was decreased.



**Fig. 2.** Follow-up MRI studies. (A) Gd-enhanced T1-weighted MRI scan obtained one month after gross total tumor removal showing the first local recurrence in the right temporal lobe. (B) Gd-enhanced T1-weighted MRI performed two months after BNCT showing the disappearance of the enhanced lesion. The cyst formation was attributed to radiation necrosis. ((C) and (D)) T2-weighted and Gd-enhanced T1-weighted MRI performed 5 months after BNCT showing that edema due to radiation necrosis. (E) Gd-enhanced T1-weighted MRI performed one year after initial diagnosis showing a second tumor recurrence at the margin of the removal cavity.

elevated and *N*-acetylaspartate was decreased (Fig. 1D); a diagnosis of high-grade glioma was made. The patient underwent gross total tumor removal surgery. The pathological diagnosis was GBM. We were unable to analyze MGMT methylation of the removed tumor tissue.

At one month follow-up, Gd-MRI revealed tumor recurrence in the right temporal lobe at a distance from the primary lesion (Fig. 2A). Following BNCT consisting of intravenous delivery of 100 mg/kg sodium borocaptate (BSH), she manifested homonymous hemianopia and hemiparesis on the left side, but was able to pursue daily living activities almost independently. At twomonth follow-up, a Gd-MRI scan showed that the enhanced lesion had completely disappeared; the cystic formation was attributed to radiation necrosis (Fig. 2B). To prevent further recurrence, she underwent nine monthly sessions of standard chemotherapy with ACNU (100 mg), VCR (1.0 mg), and interferon-beta (300<sup>6</sup> IU) delivered intravenously.

Six months following BNCT, the patient experienced headache and vomiting due to elevation of intracranial pressure. Gd-MRI

showed enhancement of a lesion surrounding the cavity produced at initial surgery; a T2-weighted MRI scan revealed severe edema thought to be attributable to radiation necrosis surrounding the cavity (Fig. 2C and D). Due to brain herniation as a result of edema, she underwent a second emergent resection procedure. Histopathological study identified necrosis but no tumor cells in the tissue.

One year after BNCT, Gd-MRI demonstrated a homogeneously enhanced lesion (Fig. 2E). We were unable to determine whether the lesion was the result of a radiation necrosis or a second recurrence at the margin of the removal cavity, and performed stereotactic radiosurgery (SRS). Her condition was stable, except for the above symptoms; she was followed at 3-month intervals without any additional therapy. Follow-up MRI scans revealed no evidence of recurrence. During the 7-year and 9-month intervals following SRS, Gd-MRI showed a cystic formation in the right temporal lobe due to radiation necrosis; there was no mass sign (Fig. 3A–C). However, 9 years after initial diagnosis, she again suffered severe headaches and vomiting. Gd-MRI showed acute Download English Version:

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