Radiation-Induced Astrocytoma With Rapid Malignant Transformation
—Case Report—

Fuminari KOMATSU,1 Hiroshi KAWAGUCHI,1 Hitoshi TSUGU,1 Shinya OSHIRO,1 Mika KOMATSU,1 Takeo FUKUSHIMA,1 Kazuki NABESHIMA,2 and Tooru INOUE1

Departments of 1Neurosurgery and 2Pathology, Faculty of Medicine, Fukuoka University, Fukuoka

Abstract

A 23-year-old man was admitted with a rare case of radiation-induced astrocytoma manifesting as 3-month history of unstable gait. He had received 50 Gy of irradiation therapy for a germ cell tumor in the right basal ganglia 13 years earlier. Magnetic resonance (MR) imaging on admission showed a non-enhanced mass lesion in the right cerebellar hemisphere with expansion to the vermis. The histological diagnosis of the stereotaxic biopsy specimen was grade II astrocytoma. Two months later, he developed drowsiness, and MR imaging demonstrated that the tumor had enlarged and was enhanced after gadolinium injection. The clinical diagnosis was high-grade glioma resulting from malignant transformation. The tumor had compressed the mesencephalic aqueduct, leading to obstructive hydrocephalus. Endoscopic third ventriculostomy was performed to improve the cerebrospinal fluid circulation. He underwent chemotherapy with temozolomide postoperatively, but died 8 months after the initial diagnosis of astrocytoma. The clinical course of radiation-induced astrocytoma is not benign. The potential for malignant transformation necessitates careful postoperative follow up for patients with this tumor.

Key words: radiation-induced glioma, astrocytoma, malignant transformation, endoscopic third ventriculostomy, temozolomide

Introduction

Cranial irradiation is widely used as a therapeutic tool for treating various lesions, particularly neoplasms. Radiation therapy is usually well tolerated, but occasionally induces clinically significant long-term toxicity, such as secondary neoplasm and radiation necrosis.10) So far, more than 140 cases of radiation-induced glioma have been reported, mainly in cases of high-grade glioma, with a few of low-grade glioma.10) Review of the reported cases of radiation-induced glioma found that patients with radiation-induced glioma are younger than those with primary glioma, and radiation-induced gliomas may occur in all cerebral locations, including the posterior fossa, and usually have a malignant histotype.10) The clinical features of radiation-induced, high-grade glioma are now clearer, but those of radiation-induced, low-grade glioma remain obscure. We describe a case of radiation-induced astrocytoma, and discuss the clinical features of radiation-induced astrocytoma.

Case Report

A 23-year-old male first developed left hemiparesis at the age of 10 years, and computed tomography (CT) demonstrated a mass lesion in the right basal ganglia. Stereotaxic biopsy was carried out, and the diagnosis was germ cell tumor. Postoperatively, he underwent a total of 50 Gy of ir-
Fig. 1 A–C: Magnetic resonance images on admission revealing a lesion, appearing as low intensity on T₁-weighted imaging (A, arrow) and high intensity on T₂-weighted imaging (B, arrow), in the right cerebellum extending to the vermis and the right middle cerebellar peduncle, with no enhancement after gadolinium injection (C, arrow). D, E: Proton magnetic resonance spectroscopy scan of the lesion showing increased choline (Cho)/N-acetylaspartate (NAA) and Cho/creatine (Cr) ratios, with no lipid or lactate.

Fig. 2 Photomicrographs of the stereotaxic biopsy specimen (A: hematoxylin and eosin staining, original magnification × 100) showing an astrocytic tumor with low cellularity, without mitosis, necrosis, microvascular proliferation, or palisading figures, with MIB-1 index of 50% (B: immunohistological staining for MIB-1, original magnification × 100). The histological diagnosis was diffuse grade II astrocytoma.

Fig. 3 A, B: T₁-weighted magnetic resonance images, taken 2 months after the diagnosis of astrocytoma, showing that the cerebellar tumor has enlarged, with enhancement after gadolinium injection (arrows). C, D: Proton magnetic resonance spectroscopy scan of the tumor revealing the presence of lipid (L), compared with 2 months earlier. Cho: choline, Cr: creatine, NAA: N-acetylaspartate.

radiation encompassing the tumor bed and the whole ventricle. Chemotherapy was combined using carboplatin and VP-16 with irradiation, resulting in complete remission. CT showed complete disappearance of the tumor, and he made a good recovery, although slight left hemiparesis remained. Thirteen years later, he complained of a 3-month history of unstable gait and was referred to our hospital.

On admission, neurological examination showed truncal and right limb ataxia, in addition to the previous left hemiparesis. Germ cell tumor marker levels were normal. Magnetic resonance (MR) imaging revealed a non-enhanced area in the right cerebellum extending to the vermis and the right middle cerebellar peduncle, which was located within the previously irradiated area (Fig. 1A–C). No evidence of recurrence of germ cell tumor in the right basal ganglia was found. Proton MR spectroscopy (¹H-MRS) of the lesion indicated increased ratios of choline to N-acetylaspartate and choline to creatine, with no lipid or lactate (Fig. 1D, E). Stereotaxic biopsy was performed, and the diagnosis was grade II astrocytoma (Fig. 2A). The MIB-1 index was 50% (Fig. 2B). The patient was discharged and followed up at the outpatient service.

Two months later, he was re-admitted because of drowsiness and vomiting. MR imaging demonstrated that the cerebellar tumor had enlarged and was enhanced after gadolinium injection (Fig. 3A, B). ¹H-MRS of the tumor revealed the presence of lipid, compared with 2 months earlier (Fig. 3C, D). The clinical diagnosis was high-grade glioma resulting from malignant transformation. The tumor had compressed the mesencephalic aqueduct, leading to obstructive hydrocephalus. Endoscopic third ventriculostomy was performed to improve the cerebrospinal fluid circulation. Postoperatively, the patient regained consciousness and underwent a total of five courses of chemotherapy with temozolomide. The tumor responded moderately to temozolomide administration. The patient died of tumor progression 8 months after the initial diagnosis of astrocytoma.

Discussion

The present case was diagnosed as diffuse astrocytoma grade II, although the MIB-1 index was too high for a low grade astrocytoma. The World Health Organization Clas-
sification of Tumours of the Central Nervous System (fourth edition) grading of astrocytic tumors is based on the findings of hematoxylin and eosin staining and not on the MIB-1 index.9 The histological diagnosis in the present case was consistent with the neuroimaging findings. On the other hand, the developmental process of malignant glioma was observed on MR imaging at an early stage in three previous cases.8,9,14 In these cases, the tumors appeared as non-enhanced lesions on T1-weighted imaging in the early stage, and then grew rapidly and were enhanced by gadolinium on T1-weighted imaging in a few months. The clinical course of our case resembles the reported cases, but a histological specimen was obtained only in our case before the tumor became enhanced on T1-weighted imaging. Although the histological diagnosis was diffuse astrocytoma at the biopsy, and the neuroimaging findings were consistent with low grade astrocytoma, the growth potential of the tumor might have been similar to that of malignant glioma at the initial stage before the transition, because the MIB-1 index showed high proliferative activity.

The detailed features of radiation-induced low-grade glioma have not been described. Twelve cases of radiation-induced grade II astrocytoma are summarized in Table 1.1,3,5,7,10–13 The mean age was 25.7 years, and the male/female ratio was 7:5. The reason for first irradiation included acute lymphocytic leukemia (n = 5), tinea capitis (n = 3), germ cell tumor (n = 1), medulloblastoma (n = 1), meningioma (n = 1), and chronic ear infection (n = 1). The mean dosage of the first irradiation was 25.3 Gy (4 to 50 Gy). The mean latency time for the development of radiation-induced astrocytoma was 14.6 years. The symptoms included seizures (n = 4), motor weakness (n = 4), headache (n = 3), and vomiting (n = 3). The tumors were located in the posterior fossa in three cases.7,11 Malignant transformation was confirmed within 3 years in two cases.31 The patient backgrounds and therapeutic strategies differed in each case, but four of six patients (excluding six unknown cases) survived for less than 36 months.3,7 The course of radiation-induced astrocytoma tends to be dismal, even with an initial histological diagnosis of astrocytoma.

Specific radiographic or histological features for differentiating between radiation-induced gliomas and de novo gliomas have not been identified. However, unique molecular characteristics were described in five cases of radiation-induced glioblastomas in children and young adults, compared with child glioblastomas.8 The gene amplification of tumor cells expressed a homogeneous pattern in radiation-induced glioblastomas, compared with the great heterogeneity of de novo glioblastomas, indicating a common tumorigenic origin and pathway for radiation-induced glioblastomas. In addition, the clinical course of radiation-induced glioblastomas was more aggressive than that of de novo glioblastomas.8 The previous experience does not include radiation-induced astrocytoma, so further molecular biological investigations may demonstrate molecular differences between radiation-induced astrocytoma and de novo astrocytoma.

The present case demonstrates that the clinical course of radiation-induced astrocytoma is not benign. The potential for rapid malignant transformation and tumor recurrence necessitates careful postoperative follow up for patients with this tumor.

## References

1) Albert RE, Omran AR, Brauer EW, Dove DC, Cohen NC,
8) Ono K, Tohma Y, Yoshida M, Takamori M: [A case of glioblastoma multiforme which indicated the early stage on brain MRI]. No To Shinkei 52: 325–329, 2000 (Japanese)

Address reprint requests to: Fuminari Komatsu, MD, Department of Neurosurgery, Faculty of Medicine, Fukuoka University, 7–45–1 Nanakuma, Jonan–ku, Fukuoka 814–0180, Japan. e-mail: fkomatsu@fukuoka-u.ac.jp