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CASE REPORT

A case of multiple radiation-induced gliomas 24 years after radiation therapy against pituitary adenoma

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Key Clinical Message

We treated a case in which multiple astrocytomas of varying grades developed in the irradiation field 24 years after radiation therapy. Differentiation from radiation necrosis based on presurgical diagnostic imaging was difficult; therefore, we feel it is essential to aggressively pursue histological diagnoses to select the optimal treatment method.

Keywords

autopsy, multiple radiation-induced gliomas, pituitary adenoma, temozolomide.

Introduction

Although meningiomas and sarcomas are often reported after irradiation, very few reports of gliomas developing after radiation therapy exist [1–7]. We experienced a case in which multiple astrocytomas developed 24 years after radiation therapy for pituitary adenoma. A site that had appeared to be radiation necrosis during presurgical diagnostic imaging was actually a high-grade astrocytoma. Herein, we share our findings together with a discussion of the relevant literature.

Case History

Our patient was a 52-year-old woman. At age 26, she had presented with a chief complaint of abnormalities in her visual field and was diagnosed with pituitary adenoma. She was treated with a combination of surgery and radiation therapy (Fig. 1). However, 24 years after irradiation, a lesion was observed on the brainstem at another institution, and she was kept under observation. Thereafter, the lesion gradually grew, various symptoms such as ataxia and articulatory disorders began to appear, and an additional lesion presented in the left medial temporal lobe. FDG-PET showed abnormal uptake in the brainstem, but no accumulation was observed at the left temporal lobe site (Figs. 2 and 3). Two years later, the patient was referred to our hospital, and MR spectroscopy showed that neither lesion showed signs of lactate or lipid increases, while signs of high accumulation in both lesions were evident on TI-SPECT (Figs. 2 and 3). The brainstem lesion was believed to be a glioma, while the left temporal lobe lesion was thought to represent radiation necrosis. Family members refused to agree to further radiation treatment, so the patient was treated with temozolomide. However, symptoms failed to respond and the patient passed away 3 months after starting treatment. Autopsy findings confirmed that the brainstem lesion was a diffuse astrocytoma, while the left temporal lobe lesion was a high-grade astrocytoma that contained some necrotic tissue. The MIB-1 index was 2.7% in the brainstem and 9.1% in the left temporal lobe, whereas MGMT was slightly positive in the brainstem (Figs. 4 and 5).

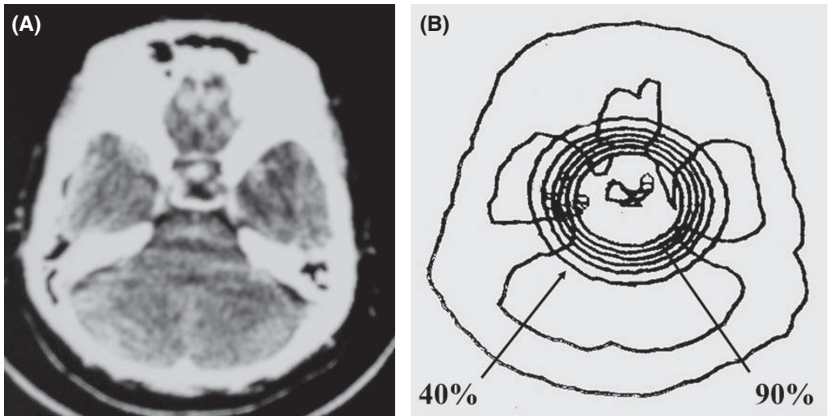

Figure 1. Preirradiation CT (A) and the irradiation field (B).

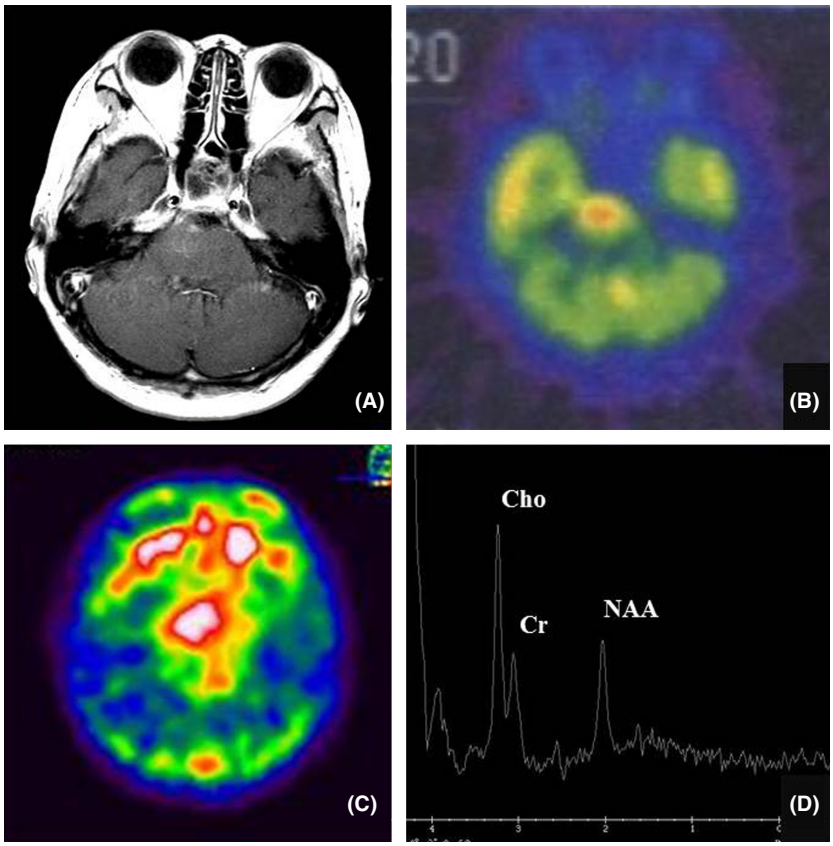

Figure 2. The brainstem was the contrast in MRI (A), FDG-PET showed abnormal uptake (B), TI-SPECT showed signs of uptake in the early phase (C), and MR spectroscopy showed no signs of lactate or lipid increases (D).

Discussion

Very few reports of gliomas occurring secondary to radiation therapy exist (fewer than 100 cases to date) [1–8]. Among these, those that occurred as a result of radiation treatment for pituitary adenoma were the second most common, following those that occurred following radiation treatment for acute lymphoid leukemia [1, 9]. Since the introduction of the gamma-knife, pituitary adenomas are less frequently treated with radiation therapy, and we expect reports of tumors that develop after irradiation of pituitary adenoma to decrease in the future. Although

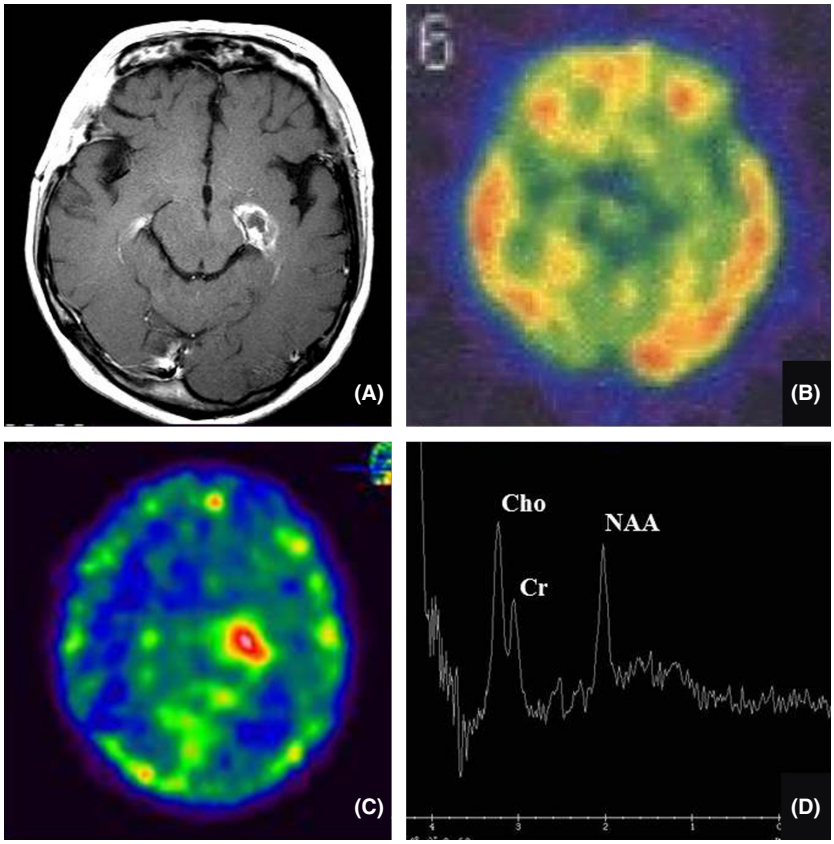

Figure 3. The left medial temporal lobe was the contrast in MRI (A), FDG-PET showed no abnormal uptake (B), TI-SPECT showed signs of uptake in the early phase (C), and MR spectroscopy showed no signs of lactate or lipid increases (D).

the time from irradiation to the onset of a secondary tumor ranges widely from several years to as many as 20 years, the secondary tumor must satisfy the four criteria of Huang et al. (based on the radiation-induced bone sarcoma diagnostic criteria of Cahan et al. [10]): (i) the brain tumor must appear after a longer period of time than it had already been present at the time of irradiation; (ii) it must occur within the irradiation field; (iii) it must be a different histological type than the tumor that was present at the time of irradiation; and (iv) it was not caused by a genetic disorder, such as neurofibromatosis or nodular sclerosis [6]. Salvati et al. published a summary of 76 cases of radiation-induced gliomas, and found that they tended to be more aggressive than other gliomas and appeared in younger patients (mean age at irradiation, 21.9 years). However, these investigators reported that no correlation was found between the radiation dose and latency period, or between the age of radiation therapy and the latency period [9]. The present case was characterized by the onset of multiple astrocytomas of varying grades that appeared 24 years after radiation therapy. It is difficult to distinguish between gliomas caused by irradiation and radiation necrosis, but Kato et al. reported that MR spectroscopy was useful in the diagnosis, whereas Tamura et al. have shown that FDG-PET can be useful [1, 5]. Ito et al. reported a case in which no FDG uptake was observed, even though the MIB-1 index was highly elevated at 30%. Marked edema of the surrounding area was noted, and they suggested that a partial volume effect with necrosis of the interior could lead to false-negative results [11]. In the present patient, the left temporal lobe fell into this category. In addition, since the grades of both lesions differed, diagnosis was difficult by FDG-PET, TI-SPECT, and MR spectroscopy, which likely made differential diagnosis impossible.

We have yet to reach a consensus on how best to treat radiation-induced gliomas; while radiation therapy and chemotherapy are sometimes used, surgery alone may also be employed [1, 3, 4, 7, 8]. Dritschilo et al. summarized 32 cases that received radiation therapy on multiple occasions and presented data showing that if three or more years passed between treatments, retreatment with radiation is safe, although signs of radiation

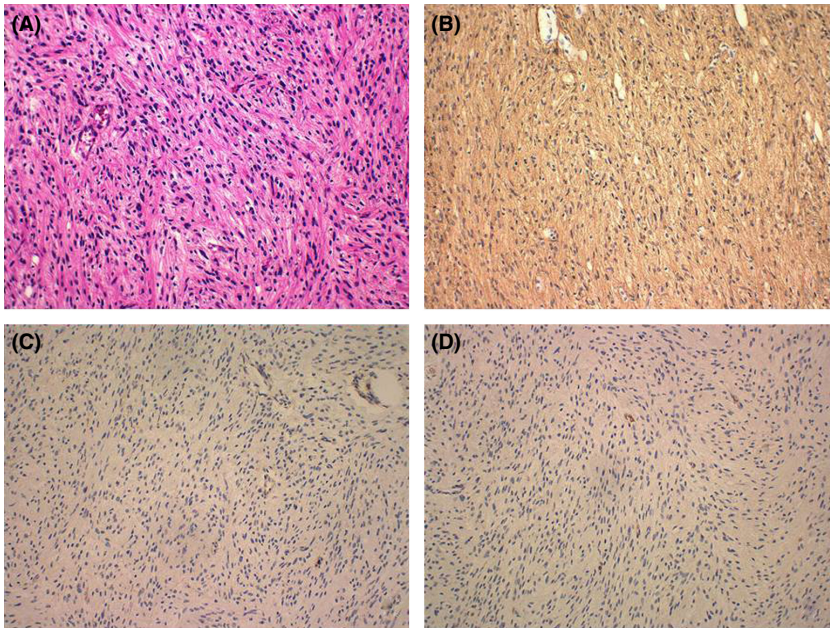

Figure 4. HE staining of the brainstem revealed a diffuse astrocytoma (A), GFAP positivity (B), an MIB-1 index of 2.7% (C), and MGMT positivity (D).

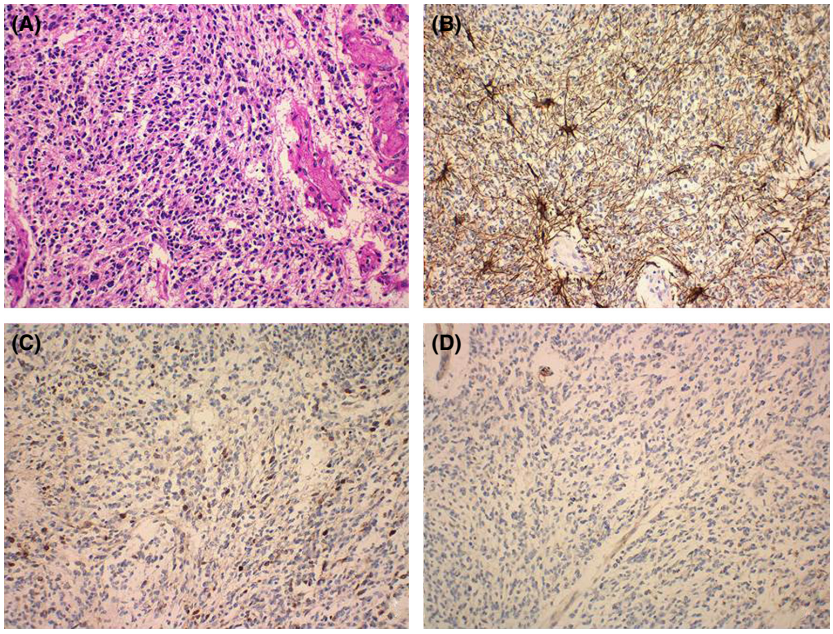

Figure 5. HE staining of the left medial temporal lobe revealed a high-grade astrocytoma (A), GFAP positivity (B), an MIB-1 index of 9.1% (C), and MGMT negativity (D).

necrosis were apparent in two of these cases upon autopsy [12]. Paulino et al. reported that patients who underwent reirradiation for radiation-induced gliomas have longer survival compared with those not receiving reirradiation [13]. Various medications, such as angiotensin converting enzyme inhibitors, statins, superoxide dismutase, and vascular endothelial growth factor (VEGF) inhibitors, have been suggested as effective prophylactic agents against radiation necrosis; however, no clinical studies have evaluated the preventative effects of these agents against the development of radiation-induced tumors [14]. In the present case, the left tem-

poral lobe lesion was diagnosed as radiation necrosis, so we were forced to be cautious about the reinitiation of radiation treatment; however, oral temozolomide alone was not effective. We feel that aggressive histological diagnosis is essential to determine the best treatment options in any given case.

Conflicts of Interest

None declared.

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