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Cerebral Radiation Necrosis with Accumulation of Thallium 201 on Single-Photon Emission CT

Yoshihiko Yoshii, Takashi Moritake, Kensuke Suzuki, Keishi Fujita, Tadao Nose, and Motohiro Satou

Summary: A patient who had previously undergone resection of a malignant glioma followed by radiation therapy was found to have a focus of a high accumulation of thallous chloride Tl 201 on single-photon emission CT scans, suggesting recurrent tumor. Resection of this area was performed and the specimen showed radiation necrosis, including such reactive changes as reactive astrocytes and lymphocytes in the necrotic tissue. This case illustrates a diagnostic pitfall in the use of ^{201}Tl single-photon emission CT for distinguishing radiation necrosis from recurrent tumor in patients treated for malignant glioma.

Index terms: Radiation, necrosis; Single-photon emission computed tomography

Planar imaging with thallous chloride Tl 201 (thallium-201) was shown to have some potential for the *in vivo* characterization of brain tumors (1), and many authors have reported that ^{201}Tl single-photon emission computed tomography (SPECT) is effective for use in determining the malignant viability of intracerebral tumors (2–9). We describe a patient in whom SPECT scans showed a high accumulation of thallium-201 after resection of a malignant glioma and radiation therapy. The focus of high activity was resected and found to be an area of radiation necrosis.

Case Report

A 50-year-old woman had headache, vomiting, and left-sided weakness of the lower extremities. A neurologic examination showed signs of increased intracranial pressure, disorientation, memory disturbance, and slight left-sided hemiparesis. CT and magnetic resonance (MR) studies of the brain on admission showed a large, ring-shaped, enhancing mass in the right frontal lobe (Fig 1A). The patient underwent a right frontal lobectomy with gross total removal of the tumor. The pathologic diagnosis was aplastic ganglioglioma.

Radiation therapy was instituted, with fractionated doses of 1.8 Gy to a total dose of 66.6 Gy, over a 5-week period. During radiation therapy, the patient received local chemotherapy to the postoperative cavity via an Ommaya reservoir with 2 mg of methotrexate twice weekly for 5 consecutive weeks, for a total of 20 mg. In addition, a single 120-mg dose of ACNU was given intravenously halfway through the radiotherapy. An MR examination performed 14 weeks after tumor resection showed no recurrence of tumor at the lobectomy site.

The patient did well for 1 year, when she was readmitted to our hospital because of progressive gait disturbance, urinary incontinence, and mild alteration in mental status. CT and MR studies showed no recurrence in the area of previous surgery, but both scans showed marked ventricular enlargement and a subcutaneous hematoma on the right side of the forehead, sustained during a fall (Fig 1B). A cisternogram with ^{111}In -DTPA showed reflux of tracer at 24 hours and an accumulation of tracer at 48 hours after injection. In light of this result, normal pressure hydrocephalus was diagnosed. A ventricular-peritoneal shunt was placed, and the patient was discharged 9 weeks later, with some improvement in gait disturbance and urinary incontinence, but no improvement in mental status. A CT scan at discharge showed a mild decrease in ventricular size.

The patient was readmitted 4 months later with severe mental impairment, urinary incontinence, imbalance, gait disturbance, and mild right-sided hemiparesis. CT and MR studies at this time showed a new enhancing mass with edema in the left frontal region adjacent to the shunt tube with no abnormal findings in the corpus callosum (Fig 1C). Again noted was a chronic subdural hematoma in the left frontal region. There was no evidence of recurrence of the tumor in the right frontal surgical bed.

A ^{201}Tl SPECT scan (Headtome Set 050; Shimadzu Co, Japan) revealed high uptake in the new lesion immediately and 3 hours after injection. The thallium-201 indexes (5) were 2.5 and 2.0 in the early and delayed scans, respectively, and the retention index was 18.4% (Fig 1D). Those values were consistent with viable malignant tumor. Of interest, a review of the isodose curves showed the

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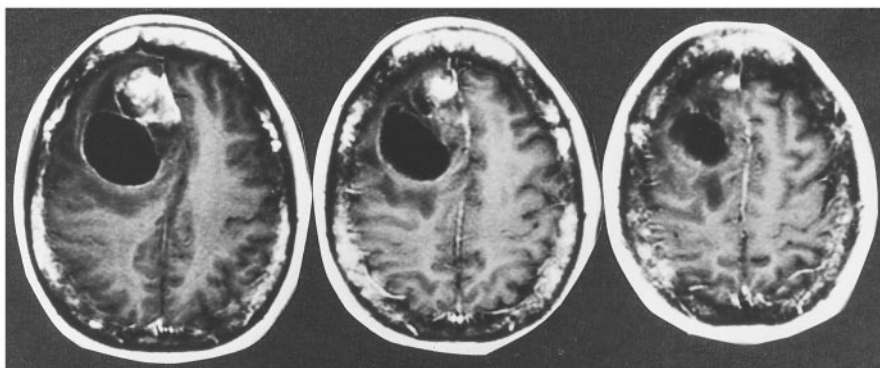
Fig 1. A 53-year-old woman with increased intracranial pressure, memory disturbance, and right hemiparesis.

A, Contrast-enhanced T1-weighted (380/11 [repetition time/echo time]) MR images show a ring-enhancing lesion in the right frontal lobe. The enhancement is inhomogeneous and there appear to be several cystic regions within the lesion.

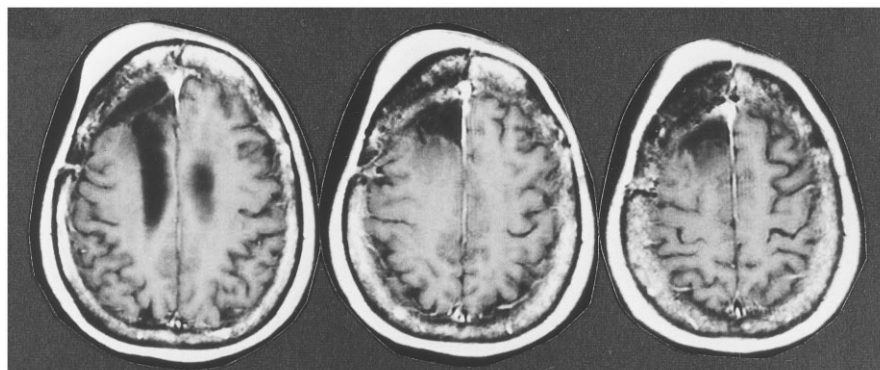
B, Contrast-enhanced T1-weighted (437/13) MR images, obtained 8 months after resection of the primary tumor, show mild ventricular enlargement and no evidence of recurrent tumor in the surgical bed.

C, Axial (left) and coronal (right) contrast-enhanced T1-weighted (380/11) MR images 13 months after resection of the primary tumor show a new enhancing mass in the left frontal region. The new lesion is adjacent to the shunt tube (arrows). There is no evidence of recurrence in the right frontal surgical bed. A chronic subdural hematoma can be seen over the left frontal cerebral convexity, but there is no enhancement in the corpus callosum on the coronal view.

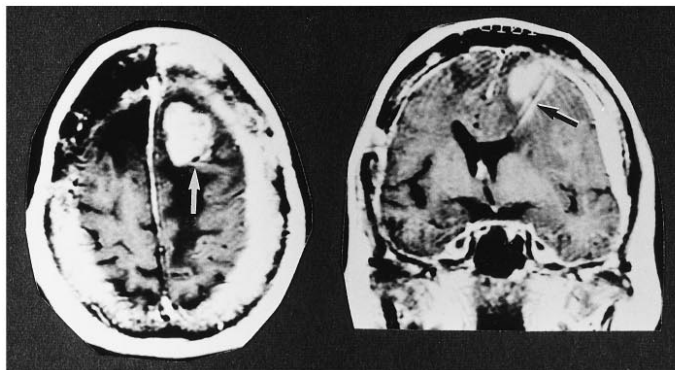
D, Early (left) and delayed (right) ^{201}Tl SPECT scans of the brain 13 months after surgery show intense tracer accumulation in the left frontal region (arrows).



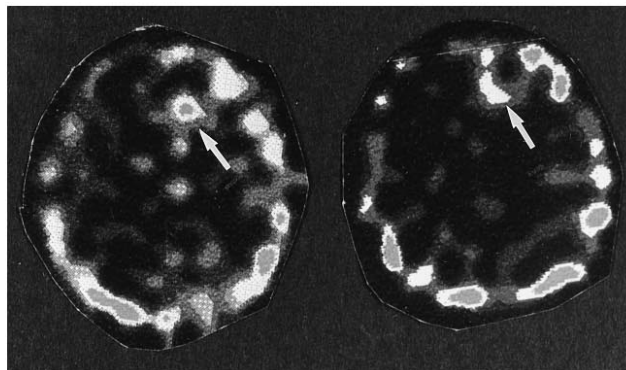
A



B



C



D

mass to be within the 90% irradiated (60 Gy) area. Without evidence of contiguous tumor spread on CT or MR studies, the new lesion was thought to represent spread of tumor through the cerebrospinal fluid with extension along the shunt tract.

A second operation was performed for total resection of the new left frontal mass. Surgical exploration revealed slight edemas and yellowish discoloration of the left frontal lobe. The arachnoid membrane was intact and the subarachnoid space was not infiltrated with tumor cells. The mass was firm and nonhemorrhagic, and could not be aspirated. Histologic examination of the specimen revealed coagulative necrosis of the cerebral parenchyma

and reactive gliosis with the typical perivascular lymphocytic infiltration of radiation necrosis. There was fibrinoid necrosis of vessels with thickened, hyalinized walls. In addition, there were abundant reactive astrocytes and lymphocytes within or adjacent to the necrotic tissue. Approximately 9% of those cells were positively stained by the MIB-1 method (10). The pathologic diagnosis was radiation necrosis without evidence of neoplasm. At the time of discharge, the patient was again able to walk slowly without assistance, her urinary incontinence had improved moderately, and her attention span had improved slightly, but her major cognitive functions showed no improvement.

Discussion

Delayed radiation necrosis appears as a mass lesion several months to years after radiation therapy. There is evidence to suggest that the administration of methotrexate via intrathecal injection increases the risk of cerebral radiation necrosis. Radiation necrosis is often impossible to differentiate from tumor recurrence either clinically or by CT or MR imaging, particularly if located in the area of the previous surgery (11–13). Positron emission tomography with fludeoxyglucose F 18 and carbon-11 putrescin have been reported to differentiate malignant gliomas from radiation necrosis in the brain. However this technology is of limited availability (14–16).

Many investigators suggest that ^{201}Tl SPECT scans of brain tumors more accurately reflect viable tumor burden than do CT, MR, or other radionuclide studies (1–9). In our previous ^{201}Tl SPECT studies (5), the thallium-201 index of radiation necrosis was between 1.0 and 1.2 (mean, $1.1 \pm \text{SD } 0.1$) in early scans, and $1.1 (\pm \text{SD } 0)$ on delayed scans. On the other hand, the thallium-201 index of viable malignant gliomas was between 1.2 and 7.0 (mean, $2.6 \pm \text{SD } 1.3$) on early scans and from 1.8 to 6.4 (mean, $2.3 \pm \text{SD } 1.5$) on delayed scans with a retention index ranging from -42.6% to 32.2% (mean, $-0.3 \pm \text{SD } 27.2$). Other investigators have shown that quantitative ^{201}Tl SPECT is effective for diagnosing the viability and malignancy of human gliomas and cerebral radiation necrosis (3, 5, 6, 8, 17, 18). Some authors have reported minimal accumulation of thallium-201 in a few patients with cerebral radiation necrosis (6, 17).

Because alterations of the capillary structures in delayed radiation necrosis appear to be sufficient to produce necrosis (19–21), regional blood flow in the setting of disruption of the blood-brain barrier result in minimal uptake of thallium-201 (22). In addition, reactive changes such as the presence of reactive astrocytes and lymphocytes, may cause accumulation of thallium-201 due to the Na^+/K^+ adenosine triphosphatase on the cell membrane (23, 24) in cells adjacent to viable tumor cells. Although ^{201}Tl SPECT appears to offer a reliable method of distinguishing radiation necrosis from recurrent tumor in patients treated for malignant glioma, the findings in this patient demonstrate a diag-

nostic pitfall in the use of this imaging technique.

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