Tracer Accumulation in Radiation Necrosis of the Brain After Thallium-201 SPECT and [^{11}C]Methionine PET

—Case Report—

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Abstract

A 69-year-old woman was treated by local irradiation for a malignant lymphoma of the left parotid gland. Three years after the radiation therapy, magnetic resonance imaging revealed heterogeneously enhanced masses in the left temporal lobe and left cerebellum. Thallium-201 chloride single photon emission computed tomography (Tl-SPECT) revealed high uptake and [^{11}C]methionine positron emission tomography (Met-PET) revealed moderate uptake in both masses. Stereotactic biopsy was performed. The histological diagnosis was radiation necrosis. She was treated with steroids. Neurosurgeons should be aware of the difficulty in differentiating tumor recurrence from radiation necrosis even with Tl-SPECT and Met-PET, and the importance of obtaining a histological diagnosis for radiation necrosis.

Key words: radiotherapy, radiation necrosis, single photon emission computed tomography, positron emission tomography, biopsy

Introduction

Differential diagnosis between tumor recurrence and radiation necrosis is extremely difficult after treatment of intracranial lesions by radiation therapy.¹⁾ However, this differential diagnosis is very important in treating patients who have received radiation therapy. Recently, thallium-201 chloride single photon emission computed tomography (Tl-SPECT) and [^{11}C]methionine and [^{18}F]fluorodeoxyglucose positron emission tomography (Met-PET, FDG-PET) have been used to differentiate tumor recurrence from radiation necrosis, because Tl accumulates in malignant tumors and PET agents accumulate in hypermetabolic lesions such as recurrent tumors, but not at the sites of hypometabolic radiation necrosis.^{3-5,7)} We report a case in which tracers accumulated in the lesions of radiation necrosis using both Tl-SPECT and Met-PET.

Case Report

A 69-year-old woman with malignant lymphoma (mucosa-associated lymphoid tissue type) of the left parotid gland underwent resection of the tumor and radiation therapy (40 Gy) in October 1994. The patient complained of a floating sensation and hearing disturbance beginning in August 1997. Magnetic resonance (MR) imaging revealed two heterogeneously enhanced masses in the left temporal lobe and left cerebellum (Fig. 1). Intracranial metastasis or recurrence of malignant lymphoma was suspected. She underwent whole brain irradiation (46 Gy) at the hospital, but there was no response.

The patient was referred to our hospital for gamma knife radiosurgery. However, we considered the possibility of radiation necrosis from the clinical course and radiological findings. Tl-SPECT and Met-PET were performed to exclude radiation necrosis. Tl-SPECT revealed moderate uptake on the early scans and high uptake on the delayed scan (Fig. 2), and Met-PET also revealed moderate uptake in both tumors (Fig. 3). Stereotactic biopsy was performed for the temporal mass, and the histological

Fig. 1 T₁-weighted magnetic resonance images with gadolinium revealing heterogeneously enhanced lesions in the left cerebellar hemisphere (arrow) (A) and the left temporal lobe with perifocal edema (arrow) (B).

Fig. 3 [¹¹C]methionine positron emission tomography scans demonstrating hypermetabolic areas corresponding to the enhanced lesions on the magnetic resonance images (arrow) (A: left cerebellum, B: left temporal lobe).

Fig. 2 Delayed thallium-201 chloride single photon emission computed tomography scans demonstrating intense accumulation corresponding to the enhanced lesions on the magnetic resonance images (arrow) (A: left cerebellum, B: left temporal lobe).

Fig. 4 Photomicrograph showing hyalinized thickening of the blood vessels and reactive glia. HE stain, ×100.

diagnosis was radiation necrosis (Fig. 4). Steroid hormone was administered and the patient was then observed.

She developed tetraparesis in September 1998. MR imaging revealed a heterogeneously enhanced lesion at C-1 to C-3 of the spinal cord with diffuse edema (Fig. 5). Based on the clinical course and MR imaging findings, the diagnosis of these lesions was also radiation necrosis. Treatment with steroid hormone was continued, and no change was noted in her condition during the follow-up period.

Discussion

Clinically, radiation injury can be classified into acute reaction, early delayed reaction, or late

delayed reaction. Acute reaction occurs during radiation therapy, whereas early delayed reaction occurs a few weeks to several months after irradiation, probably due to temporary demyelination and vascular damage. Late delayed reaction occurs several months to years after irradiation. Radiation necrosis is considered to be a late reaction due to vascular changes.⁸⁾ The incidence of radiation necrosis of the brain after radiation therapy differs depending on the radiation dose, and is reported as 0.04% to 5%.⁸⁾

TL-SPECT is useful for the diagnosis of malignant tumor and differential diagnosis between radiation necrosis and tumor recurrence.^{2,4)} The sensitivity and specificity of TL-SPECT for detection of tumor recurrence are 94% and 63%, respectively.²⁾ Three of 32 patients with radiation necrosis (9%) showed

Fig. 5 T₁-weighted magnetic resonance image with gadolinium of the cervical cord demonstrating an irregular enhanced lesion at C-1 to C-3 with perifocal edema.

false-positive results for radiation necrosis.²⁾ Uptake of Tl has also been observed in cases of radiation necrosis.¹²⁾

FDG-PET is useful for the diagnosis of malignant glioma and radiation necrosis.^{3,5)} This technique can distinguish radiation necrosis from tumor recurrence in 84% of cases.¹¹⁾ However, among eight cases of histologically proven radiation necrosis obtained with FDG-PET, hypermetabolic lesions were found in seven cases, and hypometabolic in only one. Therefore, the capacity for differentiation between tumor recurrence and radiation necrosis is limited with FDG-PET.⁶⁾ Met-PET is also useful for differentiation of tumor recurrence from radiation necrosis.⁹⁾ However, uptake of both Tl and Met occurred in one case of radiation necrosis after treatment of malignant glioma.¹⁰⁾

The mechanism of uptake of radiopharmacological agents at sites of radiation necrosis is as follows. The primary damage occurs in endothelial cells of the small- to medium-sized arteries. Occlusion of these arteries leads to progressive ischemic necrosis and blood-brain barrier disruption, and may also result in leakage of the radiopharmaceuticals into neutrophils and thus induce high uptake in such cells in proportion to their activity.^{7,10)} In addition to

the vascular pathology, modifications of transport mechanisms, such as those associated with epileptic activity, reactive gliosis, or inflammatory changes, may also influence the uptake of radiopharmaceuticals in non-neoplastic lesions.¹²⁾

The differential diagnosis of tumor recurrence and radiation necrosis is sometimes difficult even with Tl-SPECT and Met-PET. Histological confirmation of the lesion is important to differentiate recurrence from radiation necrosis. Stereotactic biopsy is very useful, as it is minimally invasive and highly accurate.¹⁾ Diagnosis of radiation necrosis by stereotactic biopsy has been criticized because of the possibility of an inadequate or inrepresentative sample. In our case, there was no recurrence of lesions during the follow-up period, and we confirmed the presence of radiation necrosis.

Neurosurgeons should be aware of the difficulty of differentiating tumor recurrence from radiation necrosis even with Tl-SPECT and Met-PET, and the importance of establishing the histological diagnosis for radiation necrosis.

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