Differentiation of Malignant Glioma and Metastatic Brain Tumor by Thallium-201 Single Photon Emission Computed Tomography

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Abstract

The use of superdelayed thallium-201 single photon emission computed tomography (201Tl SPECT) for differentiating malignant gliomas from cerebral metastases was investigated in 23 patients (7 with meningioma, 6 with glioma, 7 with cerebral metastasis, 1 with each of neurinoma, abscess, and necrosis). 4 mCi of 201Tl was injected intravenously, and gamma camera scans were performed after 10 minutes and 4, 24, 72, and 96 hours (superdelayed scan). The mean thallium index of meningiomas was significantly higher than those of gliomas and cerebral metastases after 10 minutes, while the mean thallium indices of meningiomas and gliomas were significantly higher than those of cerebral metastases after 96 hours. The combination of early and superdelayed 201Tl SPECT may be useful in differentiating malignant gliomas from cerebral metastases.

Key words: thallium-201, single photon emission computed tomography, glioma, cerebral metastasis

Introduction

Malignant gliomas are sometimes difficult to differentiate from cerebral metastatic tumors on conventional computed tomography (CT) scans. The ideal radiopharmaceutical for tumor localization should be readily available and have a high affinity for neoplastic tissue relative to normal tissue.14,22) Seven gamma emitting-labeled tumor screening agents have been used to visualize tumors.8,10,17,19) The most promising agent for detecting brain tumors is thought to be thallium-201 (201Tl).1,2,6,14,18,22) 201Tl, a potassium analogue, reflects the regional blood flow,3,12) destruction of the blood-brain barrier, and Na⁺-K⁺ adenosine triphosphatase (ATPase) activity.3,9,11,13) 201Tl is apparently incorporated into viable tumor cells more rapidly than into normal brain cells.14,16) 201Tl can differentiate tumors from infections, infarctions, and necrosis,2-4,7,15,16,21) low- and high-grade gliomas,6,14,16,22) and identify residual astrocytomas after radiation therapy.3,4,7,15,16,21)

Various radionuclide agents have been used to detect cerebral metastases, including technetium-99m9) and 201Tl.1) However, the differentiation of cerebral metastases from gliomas by 201Tl single photon emission computed tomography (SPECT) has not been reported.

Here we describe a superdelayed 201Tl SPECT technique which can discriminate malignant gliomas from cerebral metastases.

Materials and Methods

We performed 201Tl SPECT, and CT or magnetic resonance (MR) imaging on 23 patients with brain tumors: seven patients with meningioma, six with malignant glioma, seven with cerebral metastasis, and three with neurinoma, abscess, and necrosis (1 each). All six gliomas were grade 3 or 4 according to the standard Kernohan and Sayre classification.11,21) The seven metastatic lesions originated in the lung in six cases and breast in one. The seven meningiomas were five fibrous and two meningothelial types.

Each patient was injected with 120 MBq (4 mCi)
of $^{201}$TI in physiological saline solution. SPECT scans were made 10 minutes and 4, 24, 72, and 96 hours (superdelayed scan) after injection using a STARCAM 400ACT (General Electric CGR, Kriens, Switzerland). Images were acquired with 64 angular steps over 360° at 60 sec/step, with an average of 30,000 cps/step. Each slice was 4 mm in thickness. A 64 x 64 matrix with a Hanning lamp filter (General Electric CGR) was used to reconstruct images in the transverse plane.

Operator-defined regions of interest (ROI) were drawn around the tumor based on CT or MR imaging findings. These same regions were used for comparison with follow-up scans. The ROI for nonaffected tissue was determined by creating a mirror image of the tumor ROI on the contralateral side. The thallium index, to allow comparison between serial scans, was calculated as follows:

$$\text{Thallium index} = \frac{(\text{tumor region counts} - \text{normal region counts})}{\text{normal region counts}}$$

The mean thallium indices of meningiomas, malignant gliomas, and cerebral metastases were compared with a one-tailed Student's t-test.

**Results**

$^{201}$TI SPECT and CT or MR imaging studies demonstrated abnormalities of apparently the same size and location in the brain of all patients (Figs. 1–3).

Table 1 shows the mean thallium index of meningiomas, gliomas, cerebral metastases, and other lesions. The mean thallium index 10 minutes after injection in meningiomas was significantly higher than that in gliomas ($p < 0.05$) and in cerebral metastases ($p < 0.05$). However, there was no significant difference in mean thallium index between gliomas and cerebral metastases. The mean thallium index of cerebral metastases at 96 hours after injection was significantly lower than those of meningiomas and gliomas ($p < 0.05$).

The washout rates (tumor region counts - normal region counts at 96 hrs/tumor region counts - normal region counts at 10 min) were $0.11 \pm 0.04$

![Fig. 1](image)

A 76-year-old male with a sphenoid ridge meningioma. A: Postcontrast CT scan showing homogeneous enhancement in the right sphenoid ridge area. B-F: $^{201}$TI SPECT images at 10 minutes (B) and 4 (C), 24 (D), 72 (E), and 96 hours (F) revealing activity in the right frontotemporal region, which was still relatively high after 96 hours. The surgical specimen was a fibrous meningioma.

*Neurol Med Chir (Tokyo) 34, September, 1994*
(mean ± SE) in meningiomas, 0.19 ± 0.11 in gliomas, and 0.03 ± 0.06 in cerebral metastases. The washout rate in gliomas was slow and $^{201}$TI was present even after 96 hours (Fig. 2), but $^{201}$TI in cerebral metastases after 96 hours was almost washed out (Fig. 3).

There was no difference in thallium index between fibrous and meningothelial meningiomas. No difference in thallium index was identified among cerebral metastases from different primary origins.

### Table 1  Mean thallium index

<table>
<thead>
<tr>
<th></th>
<th>No. of cases</th>
<th>10 min</th>
<th>4 hrs</th>
<th>24 hrs</th>
<th>72 hrs</th>
<th>96 hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meningioma</td>
<td>7</td>
<td>9.0 ± 4.4</td>
<td>4.4 ± 1.2</td>
<td>1.4 ± 0.2</td>
<td>0.7 ± 0.2</td>
<td>0.5 ± 0.2</td>
</tr>
<tr>
<td>Glioma</td>
<td>6</td>
<td>2.9 ± 0.5*</td>
<td>2.2 ± 0.6</td>
<td>1.1 ± 0.3</td>
<td>0.4 ± 0.1</td>
<td>0.6 ± 0.1</td>
</tr>
<tr>
<td>Metastatic tumor</td>
<td>7</td>
<td>4.7 ± 0.9*</td>
<td>2.3 ± 0.5</td>
<td>0.7 ± 0.1*</td>
<td>0.2 ± 0.1**</td>
<td>0.1 ± 0.1*</td>
</tr>
<tr>
<td>Neurinoma</td>
<td>1</td>
<td>0.03</td>
<td>0.3</td>
<td>0.01</td>
<td>-0.2</td>
<td>-0.2</td>
</tr>
<tr>
<td>Abscess</td>
<td>1</td>
<td>0.2</td>
<td>NP</td>
<td>NP</td>
<td>NP</td>
<td>NP</td>
</tr>
<tr>
<td>Necrosis</td>
<td>1</td>
<td>1.1</td>
<td>0.9</td>
<td>0.8</td>
<td>NP</td>
<td>NP</td>
</tr>
</tbody>
</table>

Values are mean ± SE. *p < 0.05, **p < 0.01 vs. meningioma. *p < 0.05 vs. glioma. NP: not performed.

### Discussion

Our $^{201}$TI SPECT studies of various brain tumors agreed with previous results in that gliomas could be easily distinguished from meningiomas, but it was impossible to distinguish gliomas from cerebral metastases by early $^{201}$TI SPECT images. CT scanning or cerebral angiography can easily distinguish meningiomas from gliomas or cerebral metastases, but cannot differentiate between gliomas and cerebral metastases. We therefore tried to distinguish...
Fig. 3  A 73-year-old female with a metastatic tumor from pulmonary carcinoma. A: Postcontrast CT scan showing a ring-like enhancement in the right parietal lobe with perifocal edema. B–F: $^{201}$TI SPECT images at 10 minutes (B) and 4 hours (C) revealed high activity in the same region, which had disappeared after 96 hours (F). D: 24 hours, E: 72 hours. Histological studies demonstrated an undifferentiated adenocarcinoma.

gliomas from cerebral metastases by superdelayed scanning. Our results showed that the thallium indices on superdelayed images (96 hrs after injection of $^{201}$TI Cl) of five of six gliomas were higher than 0.4, while those of six of seven cerebral metastases were lower than 0.3. Therefore, superdelayed imaging could distinguish cerebral metastases from gliomas.

The mechanism causing the different washout rates of gliomas and cerebral metastases is still unknown. However, as cell growth is correlated with Na$^+$-K$^+$ ATPase activity, the slow washout in gliomas may be due to lower activity of Na$^+$-K$^+$ ATPase compared with metastatic brain tumors.

The $^{201}$TI SPECT findings in our series agreed well with the histological data. In all seven patients with cerebral metastases, early images showed regions of moderate $^{201}$TI uptake and superdelayed images showed low uptake compared with that of gliomas.

This preliminary study has not determined the limitations of the thallium index for distinguishing cerebral metastases from gliomas on superdelayed images. Also, the cerebral metastases originated from only two locations, so other types of metastasis should be investigated.

Acknowledgments

We would like to thank Isao Yamamoto, M.D., Department of Neurosurgery, Yokohama City University School of Medicine for reading the manuscript.

References

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Neurol Med Chir (Tokyo) 34, September, 1994


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