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Differential diagnosis in patients with ring-like thallium-201 uptake in brain SPECT

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This study was performed to investigate lesions with ring-like thallium-201 (^{201}Tl) uptake and to determine whether SPECT provides any information in differential diagnosis. ***Methods:*** A total of 244 ^{201}Tl SPECT images were reviewed. In each study, early (15 min postinjection) and late (3 hr) brain SPECT images were obtained with 111 MBq of ^{201}Tl. The early uptake ratio (ER; lesion to normal brain average count ratio) and the late uptake ratio (LR) and the L/E ratio (ratio of LR to ER) were calculated. ***Results:*** Ring-like uptake was observed in pre-therapeutic 26 SPECT images, including ten glioblastoma multiformes (ER, 3.45 ± 0.64; LR, 2.74 ± 0.54; L/E ratio 0.80 ± 0.13), five meningiomas (6.48 ± 2.34; 4.41 ± 1.41; 0.72 ± 0.19), four metastatic lung cancers (3.47 ± 1.23; 2.40 ± 0.98; 0.70 ± 0.14), four brain abscesses (2.48 ± 1.06; 1.59 ± 0.30; 0.78 ± 0.15), one invasive lesion of squamous cell carcinoma from the ethmoid sinus (1.54; 1.52; 0.99), one medulloblastoma (3.53; 3.52; 1.00) and one hematoma (3.32; 2.36; 0.71). The ER of meningioma was significantly higher than those of glioblastoma multiforme ($p < 0.0005$), metastatic lung cancer ($p < 0.005$) and brain abscess ($p < 0.0005$). There were no significant differences among these three entities. The LR of meningioma was significantly higher than those of glioblastoma multiforme ($p < 0.005$), metastatic lung cancer ($p < 0.005$) and brain abscess ($p < 0.0001$). The LR of brain abscess was significantly lower than that of glioblastoma multiforme ($p < 0.05$). The L/E ratio could not differentiate these four entities. ***Conclusion:*** High ER and high LR in a lesion with ring-like uptake is likely an indicator of meningioma. The LR of brain abscess was significantly lower than that of glioblastoma multiforme, but ^{201}Tl SPECT has still difficulty in differentiating abscess from brain tumor.

Key words: thallium-201, SPECT, glioblastoma multiforme, meningioma, brain abscess

INTRODUCTION

IMAGING METHODS such as magnetic resonance imaging (MRI) and X-ray computerized tomography (CT) can accurately localize intracranial lesions, but cannot always determine the characteristics of lesions, which are required to decide the treatment strategy.

Thallium-201 chloride (^{201}Tl) is a potassium analogue with significant affinity with sodium and potassium activated adenosine triphosphatase (Na^+-K^+ ATPase) pump activity.[1] ^{201}Tl uptake in intracranical lesions depends on regional blood flow, destruction of the blood-brain barrier, tissue viability, cell activity and cell density.[2] Since Ancri et al. first introduced ^{201}Tl scintigraphy for the assessment of brain tumors,[3] there have been a number of related reports; recent studies have demonstrated a potential

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Table 1 List of patients

No.	age	sex	size (cm)	ER	LR	L/E ratio	diagnosis
1	71	M	7.0	3.50	2.64	0.75	glioblastoma multiforme
2	62	F	3.0	3.02	2.98	0.99	glioblastoma multiforme
3	62	M	5.0	2.13	1.58	0.74	glioblastoma multiforme
4	74	F	5.0	3.44	2.72	0.79	glioblastoma multiforme
5	65	M	6.0	3.49	2.02	0.58	glioblastoma multiforme
6	63	M	5.0	3.11	2.93	0.94	glioblastoma multiforme
7	75	M	4.5	3.32	3.18	0.96	glioblastoma multiforme
8	72	F	4.5	4.18	3.18	0.76	glioblastoma multiforme
9	63	F	5.5	4.14	2.91	0.70	glioblastoma multiforme
10	63	F	5.5	4.20	3.27	0.78	glioblastoma multiforme
11	46	M	7.0	9.97	6.03	0.60	malignant meningioma
12	59	M	7.0	7.33	4.16	0.57	malignant meningioma (meningothelial type)
13	33	M	5.0	6.08	3.76	0.62	meningioma (psammomatous type)
14	65	F	4.0	5.28	5.56	1.05	meningioma (transitional to fibrous type)
15	39	F	5.0	3.75	2.54	0.68	cystic meningioma
16	71	F	6.0	2.89	2.39	0.83	metastatic lung cancer (adenocarcinoma)
17	57	M	3.0	4.92	3.76	0.76	metastatic lung cancer (SCC)
18	68	M	4.0	2.10	1.48	0.70	metastatic lung cancer (large cell carcinoma)
19	71	M	5.0	3.93	1.96	0.50	metastatic lung cancer (small cell carcinoma)
20	62	M	4.5	2.28	1.56	0.68	brain abscess
21	44	F	3.0	1.63	1.23	0.75	brain abscess
22	63	M	5.0	4.02	1.61	0.68	brain abscess
23	66	M	3.0	1.97	1.96	1.00	brain abscess
24	65	F	4.0	1.54	1.52	0.99	intracranial invasion from SCC of the ethmoid sinus
25	10	M	4.0	3.53	3.52	1.00	medulloblastoma of cerebellum
26	69	F	4.5	3.32	2.36	0.71	hematoma

ER; early uptake ratio, LR; late uptake ratio, L/E ratio; ratio of LR to ER, SCC; squamous cell carcinoma

role of ^{201}Tl brain single photon emission computed tomography (SPECT) in patients with viable lesions, especially in the assessment of high-grade and low-grade gliomas. ^{201}Tl SPECT may also differentiate a recurrent mass from scarring or radiation necrosis.[3–7] Furthermore, ^{201}Tl uptake likely correlates with the proliferative activity of brain tumors and the prognosis of patients with gliomas.[8]

Brain abscess is usually found as a lesion with ring enhancement on MRI and CT. Brain tumors often show a similar enhanced pattern, which may make differential diagnosis of abscesses and tumors difficult. Abscesses need antibiotic treatment and discrimination of abscesses from other tumorous lesions is required by the neurosurgeon: glucocorticoids should not be used in patients with abscesses, though it is preoperatively used in those with brain tumors.

Martinez et al. suggest a note of caution in the interpretation of ^{201}Tl brain images in the differential diagnosis of an intracranial expanding mass.[9] The aim of this retrospective study is to determine whether SPECT provides any information in the differential diagnosis of lesions with ring ^{201}Tl uptake, especially in the discrimination of brain abscesses from other tumorous lesions.

SUBJECTS AND METHODS

A total of 244 ^{201}Tl SPECT performed between January 1991 and December 2001 were reviewed. In each study, early (15 min postinjection) and late (3 hr) brain SPECT images were obtained with 111 MBq of ^{201}Tl by using a single-head rotating gamma camera (GCA-901A, Toshiba Co., Tokyo) equipped with a low-energy, high-resolution collimator, interfaced with a computer (GMS 550-U, Toshiba Co., Tokyo). The images were acquired in a 64×64 pixel matrix with 60 anglar steps over 360 degree at 30 seconds per step. The data were reconstructed with a Butterworth prefilter and backprojection with a Ramp filter. Transverse, coronal and sagittal sections were reconstructed without attenuation correction or scatter correction. The slice thickness was 4 mm. The full-width at half-maximum (FWHM) of the system was 13.8 mm at the center of rotation when the rotation radius was set to 13 cm. Setting regions of interest were performed as follows: for ring uptake, two circles along with the outer and the inner rim were drawn and subtractions of the counts and the pixels were performed, and for semiring uptake crescent-shaped regions of interest were drawn. The normal brain regions of interest were drawn over the contralateral site on the same slice. The early uptake ratio (ER: lesion to normal brain average count ratio in early

Table 2 Comparison of early uptake ratio, late uptake ratio and ratio of late uptake ratio to early uptake ratio in glioblastoma multiformes, meningiomas, metastatic lung cancer and brain abscesses

	ER	LR	L/E ratio
glioblastoma multiforme (n = 10)	3.45 ± 0.64	2.74 ± 0.54	0.80 ± 0.13
meningioma (n = 5)	6.48 ± 2.34*	4.41 ± 1.41†	0.72 ± 0.19
metastatic lung cancer (n = 4)	3.47 ± 1.23	2.40 ± 0.98	0.70 ± 0.14
brain abscess (n = 4)	2.48 ± 1.06	1.59 ± 0.30‡	0.78 ± 0.15

mean ± s.d.
ER; early uptake ratio, LR; late uptake ratio, L/E ratio; ratio of LR to ER
*Significant vs. glioblastoma multiforme ($p < 0.0005$), metastatic lung cancer ($p < 0.005$) and brain abscess ($p < 0.0005$)
† Significant vs. glioblastoma multiforme ($p < 0.005$), metastatic lung cancer ($p < 0.005$) and brain abscess ($p < 0.0001$)
‡ Significant vs. glioblastoma multiforme ($p < 0.05$)
Results in invasive lesion of squamous cell carcinoma from ethmoid sinus (ER 1.54; LR 1.52; L/E ratio 0.99), medulloblastoma (3.53; 3.52; 1.00) and hematoma (3.32; 2.36; 0.71) were not included in this table.

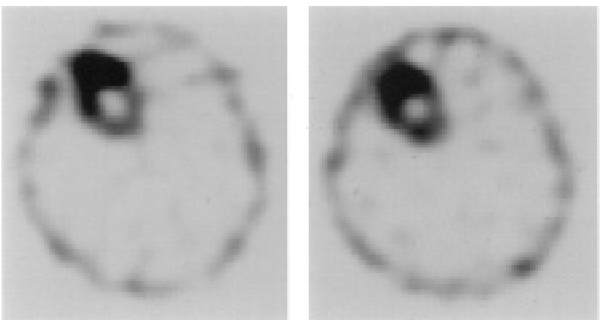

Fig. 1 Tl-201 early (*left image*) and late (*right*) brain SPECT in a 63-year-old woman with glioblastoma multiforme, 5.5 cm in diameter. The early uptake ratio (ER), the late uptake ratio (LR) and the ratio of LR to ER were 4.20, 3.27 and 0.78, respectively.

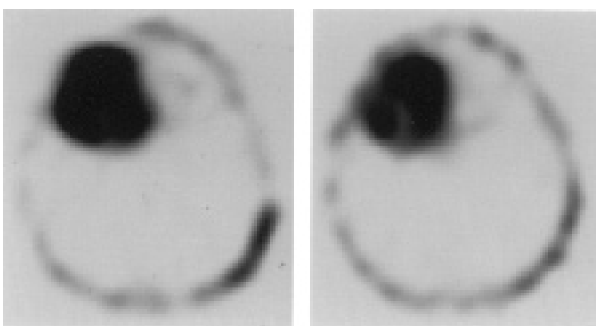

Fig. 2 Tl-201 early (*left image*) and late (*right*) brain SPECT in a 46-year-old man with malignant meningioma, 7.0 cm in diameter. The early uptake ratio (ER), the late uptake ratio (LR) and the ratio of LR to ER were 9.97, 6.03 and 0.60, respectively.

image) and the late uptake ratio (LR: lesion to normal brain average count ratio in late image) and the ratio of LR to ER (L/E ratio) were calculated.

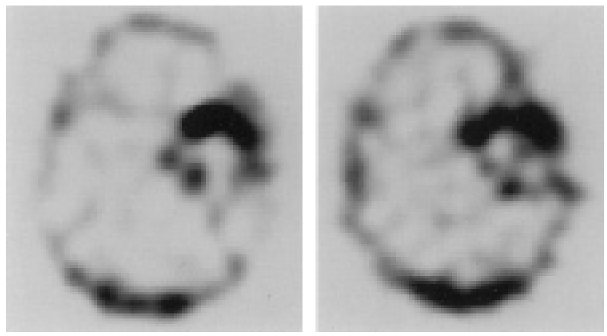

Fig. 3 Tl-201 early (*left image*) and late (*right*) brain SPECT in a 71-year-old woman with metastatic lesions from lung carcinoma, 6.0 cm in diameter. The early uptake ratio (ER), the late uptake ratio (LR) and the ratio of LR to ER were 2.89, 2.39 and 0.83, respectively.

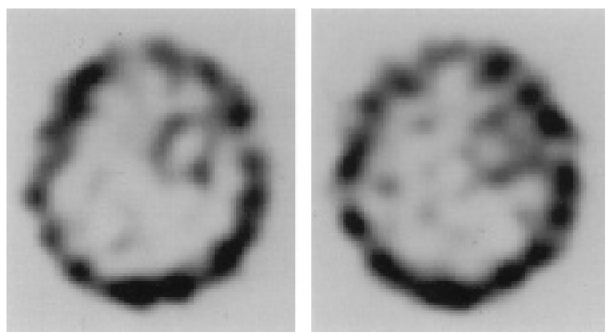

Fig. 4 Tl-201 early (*left image*) and late (*right*) brain SPECT in a 62-year-old man with brain abscess, 4.5 cm in diameter. The early uptake ratio (ER), the late uptake ratio (LR) and the ratio of LR to ER were 2.28, 1.56 and 0.68, respectively.

RESULTS

SPECT showed ring-like ^{201}Tl uptake in 26 pre-therapeutic patients (11 women and 15 men, age 59.9 ± 14.6), with ten glioblastoma multiformes, five meningiomas, four metastatic lung cancers, four brain abscesses, one invasion of squamous cell carcinoma originating in the ethmoid sinus, one medulloblastoma and one hematoma. The patients list and the comparison of ER, LR and L/E ratios (mean ± s.d.) are shown in Tables 1 and 2, respectively.

DISCUSSION

Among the brain lesions delineated as a ring-like uptake in ^{201}Tl SPECT, meningioma demonstrated higher ER and higher LR than other pathological entities. Furthermore, both ER and LR in malignant meningioma tended to be higher than those in benign meningioma although the number of subjects was limited. These results are concordant with a previous report.[10] Intense ^{201}Tl accumulation in meningioma has been attributed to the lack of a blood-brain barrier and voluminous intratumoral vascular bed[11]; this might be the mechanism of our results.

Several reports emphasized the role of ^{201}Tl scintigraphy in assessing the grade of gliomas.[3–7,12] The relationship between high accumulation levels of ^{201}Tl and high Na^+-K^+ ATPase activity in glioblastoma has been demonstrated,[11] but Kosuda et al. concluded that ^{201}Tl SPECT cannot effectively distinguish gliomas from other brain tumors in preoperative patients.[7] Kallen also investigated lesions with ring enhancement on CT and demonstrated that ^{201}Tl scintigraphy cannot always differentiate high-grade gliomas from low-grade ones or abscesses.[13] Similar negative results regarding this issue were found in the present study.

Differentiation of abscesses from tumors is essential in a pre-operative setting, because steroid, which is used to reduce brain edema in patients with tumors, should not be used in those with abscesses. The ER in abscess tended to be lower than glioblastoma multiforme and metastatic lung cancer and the LR was significantly lower than glioblastoma multiforme, but the differential diagnosis seems to be difficult due to an overlap of uptake ratios among these three entities. Reported results that demonstrated a wide range of the ER in abscesses would support this conclusion; ^{201}Tl uptake ratios were 1.0 by Kosuda et al.,[7] 1.6 (median in 4 patients) by Kallen et al.,[13] 2.2 by Sato et al.[14] and 2.2 by Krishna et al.[15] We suspect that a difference in ^{201}Tl uptake in an abscess may depend on its clinical phase such as duration from the onset of infection, size of lesions and FWHM of the images.

Previous reports have indicated the usefulness of time-sequential ^{201}Tl SPECT. Ueda et al.[16] claimed that the degree of ^{201}Tl retention would indicate the characteristics of tumors, such as tumor malignancy. Taki et al. demonstrated the importance of the L/E ratio cut-off level of 0.7 in the differentiation of benign/malignant tumors with the exception in meningioma and pituitary adenoma.[17] They also demonstrated a significantly lower L/E ratio in meningioma compared to those in glioblastoma and metastatic lesions which can be one of the clues to differential diagnosis, which was not proved in our study and we did not find this kind of usefulness of the L/E ratio in the present study. This might be due to the limited number of subjects, and further extended study is required in this regard.

CONCLUSION

High ER and high LR in a lesion with ring-like uptake is most likely an indicator of meningioma. The LR of brain abscess was significantly lower than that of glioblastoma multiforme, but ^{201}Tl SPECT still has difficulty in differentiating abscesses from brain tumors.

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