

Thallium-201 scintigraphy of neuroblastoma: Different results for primary tumors and skeletal lesions

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Thallium-201 scintigraphy was performed in 8 children with neuroblastoma, and uptake by the tumors was evaluated in comparison with the results of ^{123}I -MIBG scintigraphy. No primary tumors or metastatic lymph nodes showed ^{201}Tl accumulation, but in 4 cases of bone marrow metastases accompanied by focal cortical invasion, the metastatic lesion was demonstrated more clearly on the early image than on the delayed image. In another case of bone metastases infiltrating cortical bone revealed by ^{123}I -MIBG scintigraphy and biopsy before treatment, ^{201}Tl scintigraphy performed after chemotherapy showed abnormal accumulation in the tibia, but the second ^{123}I -MIBG scintigraphy performed 1 week after the ^{201}Tl scintigraphy showed no abnormal uptake. ^{201}Tl does not appear to have good affinity for neuroblastoma, but it accumulates in metastatic skeletal lesions. A reactive hypermetabolic bone marrow, and/or inflammatory process and periosteal reaction due to the presence of metastatic foci may have induced the ^{201}Tl accumulation. It seems that ^{201}Tl is not useful for the diagnosis. Nevertheless, the discordance between ^{201}Tl uptake in primary tumors and skeletal lesions allows speculation on the mechanism of ^{201}Tl accumulation in skeletons.

Key words: ^{201}Tl scintigraphy, neuroblastoma, skeletal lesion

INTRODUCTION

NEUROBLASTOMA is a representative solid tumor in infants or children, and it is derived embryonically from the neural crest. It has high malignant potential, but the prognosis varies with cases. There are some neuroblastomas which show spontaneous regression without any treatment in the natural course; on the other hand some cases show very progressive features.¹ Many factors are known as the prognostic factor, and age and clinical stage at diagnosis are thought to be the most significant.² But cases of widespread disease do not always have a poor outcome.³

Meta-iodobenzylguanidine (MIBG) labeled with I-131

or I-123 is widely used for the diagnosis,⁴ staging,⁵ and the follow-up of neuroblastoma,⁶ and its utility has been demonstrated because of its high sensitivity and specificity. But according to our experience with more than 40 patients of ^{123}I -MIBG scintigraphy (a total of more than 200 studies), there seems no correlation between the avidity of the radiopharmaceutical for the tumor and its malignant potential.

Thallium-201 chloride (^{201}Tl) scintigraphy has recently become widely accepted for imaging malignant tumors, especially for the diagnosis or identification of the pathological type or grade of tumors of the lung, thyroid, bone, soft tissue, and brain.^{7–12}

We performed ^{201}Tl scintigraphy in 8 patients with neuroblastoma and discussed the findings retrospectively to evaluate the utility of ^{201}Tl from the prognostic viewpoint if possible. Our unexpected but interesting results are discussed.

MATERIALS AND METHODS

^{201}Tl scintigraphy was performed in 8 patients with known

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Table 1 Summary of the clinical data

Patient No.	Age	Sex	VMA	HVA	Origin	Histology ^{a)}	Distant lesion ^{b)}	Patient outcome
			($\mu\text{g}/\text{mg}/\text{Cre}$)					
1	2	m	17.8	19.8	lt. adrenal	RF	N.D.	free (5 years)
2	7	m	9.8	11.5	retroperitoneum	RC	N.D.	free (3 years)
3	0.7	m	30.6	32.8	rt. adrenal	RF	N.D.	free (0.5 years)
4	4	f	644	655	lt. adrenal	RF	B, BM	died
5	1.5	m	90.2	86.9	lt. adrenal	RF	B, BM	free (3 years)
6	2	f	97.8	180.2	rt. adrenal	GNBpd	B, BM	on chemotherapy
7	11	f	107	168	rt. adrenal	RF	B, BM	on chemotherapy
8*	5	m	9.5	12.3	lt. adrenal (resected)	RF	B	free (3 months)

^{a)} RF: neuroblastoma rosette-fibrillary type, RC: neuroblastoma round cell type, GNBpd: ganglioneuroblastoma poorly differentiated type

^{b)} N.D.: not detected, B: bone metastasi(e)s, BM: bone marrow metastasi(e)s

* The data when the recurrence was discovered

Table 2 Summary of the imaging data

1) Primary lesions

Patient No.	MIBG	Tl (10 min/4 hrs)
1	posi	neg/neg
2	posi	neg/neg
3	posi	neg/neg
4	posi	neg/neg
5	posi	neg/neg
6	posi	neg/neg
7	posi	neg/neg

posi: positive, neg: negative

D: diffuse accumulation

S: spot accumulation

NE: not examined

BM: bone marrow metastasi(e)s

B: bone metastasi(e)s

* The results of lumbar spines are mentioned

2) Metastatic lesions

Patient No.	site	MIBG	HMDP	diagnosis	Tl (10 min/4 hrs)
4	vertebrae	D	S	BM + B	D/unclear
	pelvis	D	S	BM + B	D/unclear
	both humeri	D	neg	BM	D/neg
	both femora	D	S	BM + B	D/neg
5	both tibias	S	neg	BM	S/neg
	rt. fibula	S	neg	BM	S/neg
	pelvis	S	neg	BM	S/neg
	both femora	S	neg	BM	S/neg
6	lt. tibia	D	D	BM + B	D/neg
	skull	D	S	BM + B	neg/neg
	vertebrae	D	S	BM + B	D/neg
	pelvis	D	S	BM + B	D/neg
7	both femora	D	S	BM + B	D/neg
	both humeri	D	S	BM + B	D/neg
	both tibias	S	neg	BM	S/neg
	skull	S	S	B	S/neg
8	vertebrae	D	S	BM + B	D/neg*
	pelvis	D	S	BM + B	D/neg
	scapula	S	neg	BM	neg/NE
	ribs	S	S	BM + B	S/NE
8	both humeri	S	neg	BM	S/NE
	both femora	S	neg	BM	S/NE
	lt. tibia (after therapy)	neg	NE	B	S/neg

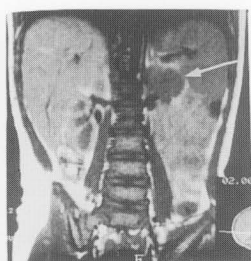
or suspected neuroblastoma, aged 0.7–11 years, 5 boys and 3 girls.

Seven patients had been admitted for the first time, and scintigraphy was performed for diagnosis and staging before treatment. In 3 of them the tumor was localized in the adrenal gland and no metastatic lesion was detected by any other examination, including ^{123}I -MIBG scintigraphy, bone scan, bone marrow aspiration or biopsy, or abdominal computed tomography (CT). The other 4 had bone marrow metastases with partial cortical bone invasion revealed by ^{123}I -MIBG scintigraphy, bone scan, bone

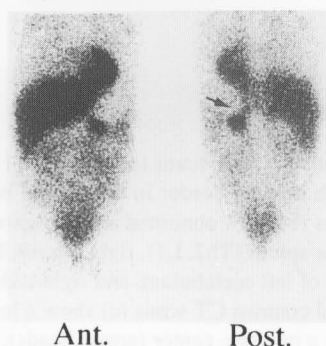
marrow aspiration, X-ray radiographs, and magnetic resonance imaging (MRI). Biopsy or operative section of the tumor prior to chemotherapy confirmed the diagnosis of neuroblastoma in these 7 patients.

The remaining patient (Patient 8) had proven metastatic neuroblastoma in his left tibia that was first detected 3 months after intensive chemotherapy and peripheral blood stem cell transplantation (PBSCT). ^{201}Tl scintigraphy was performed after 2 cycles of chemotherapy for recurrence.

^{201}Tl scintigraphy was performed after fasting for more

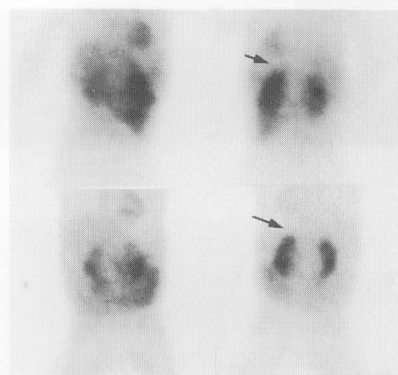


(a)MRI T1WI



(b)¹²³I-MIBG

(c)-1



(c)-2

Ant. Post.

Fig. 1 Patient 1 MRI T1WI (a) demonstrates a left suprarenal solid mass with 3 cm diameter. ¹²³I-MIBG (b) shows clear accumulation in the mass. But ²⁰¹Tl scintigrams ((c)-1: early image, (c)-2: delayed image) show no abnormal accumulation in the mass. Arrows show the tumor lesion.

than three hours to avoid intestinal accumulation. Ten minutes and 4 hours after intravenous administration of 1–2 mCi (37–74 MBq) ²⁰¹Tl, the whole body scans and SPECT of the abdomen or other required site were performed with a dual-head gamma camera (PRISM2000XP, Picker) with low-energy high-resolution parallel collimators. In case 7, no delayed whole body scan was obtained, but SPECT of the abdomen and head were performed instead. ¹²³I-MIBG images were obtained 30 hours after intravenous administration of 37–80 MBq, and the whole body scans and abdominal SPECT were performed with the same equipment as the ²⁰¹Tl studies. These two studies were performed with an interval of 3–8 days between the two studies in each case. For patients with abnormal accumulation in the skeletal lesions, additional bone scintigraphy was performed to differentiate bone metastases from bone marrow metastases. Bone scintigrams were obtained about 3 hours after intravenous injection of 185–555 MBq of ^{99m}Tc-HMDP. Images were visually estimated by two experienced nuclear physicians, who reached a consensus.

In all cases, the parents of patients, who well understood about the features of neuroblastoma, were informed that ²⁰¹Tl scintigraphy is thought to have high affinity for many kinds of tumors and that there is still the possibility of its usefulness for this disease. They consented to the study for the patients in addition to many other examinations.

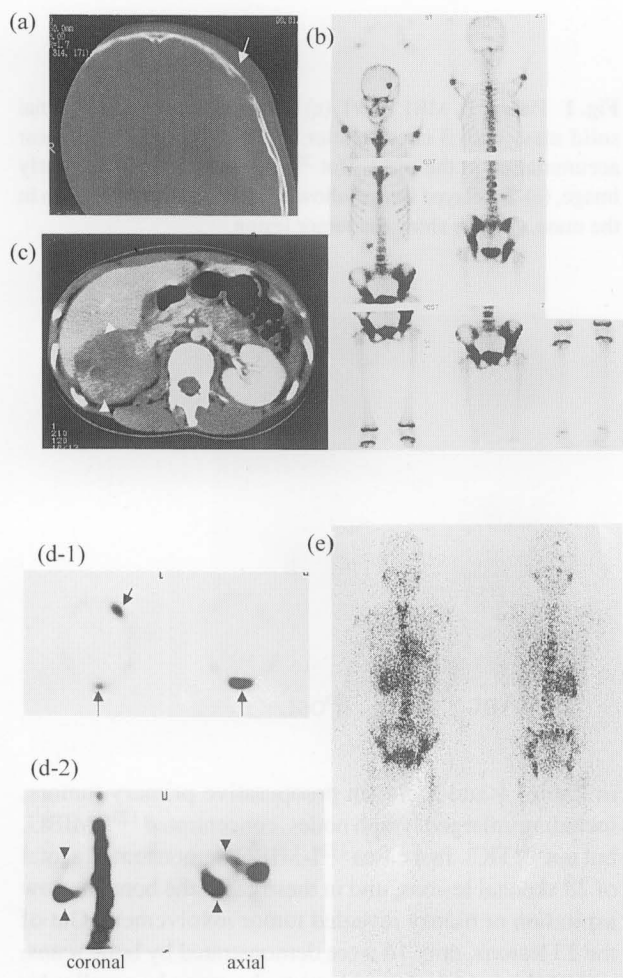
RESULTS

The overall patient characteristics and results are shown

in Tables 1 and 2. Seven preoperative primary tumors, including enlarged lymph nodes, concentrated ¹²³I-MIBG, but not ²⁰¹Tl. In 4 cases ¹²³I-MIBG demonstrated a total of 23 skeletal lesions, and in these cases the bone marrow aspiration or biopsy revealed tumor involvement. Out of the 23 lesions, only 14 were demonstrated by bone scans, and of these 14 lesions 11 were shown to be smaller by bone scan than by ¹²³I-MIBG. The lesions in which only ¹²³I-MIBG accumulated were interpreted as bone marrow metastases, and the lesions with both tracer accumulations were estimated as bone metastases. Of these 23 skeletal lesions, 21 were visualized on ²⁰¹Tl early images. Although the ²⁰¹Tl intensity was weaker than the intensity of ¹²³I-MIBG accumulation, ²⁰¹Tl distribution resembled the ¹²³I-MIBG accumulation (not like the accumulation in bone scintigrams), but they were not seen on the delayed images.

Patient 8 had a biopsy which confirmed recurrent neuroblastoma at the diaphysis of the left tibia. The abnormal ¹²³I-MIBG accumulations in the lesion, which were observed on admission, were no longer seen in the second study performed after 2 cycles of chemotherapy, but ²⁰¹Tl accumulated in the lesion despite the absence of MIBG uptake, but it was not retained on the delayed image.

After the ²⁰¹Tl studies, patients 1, 2 and 3 underwent resection of the tumor and no additional chemotherapy. Patients 4 and 5 underwent chemotherapy at first, and then a second look operation, and chemotherapy after tumor resection again. Chemotherapy is now being repeated for patients 6 and 7. For patient 8, who had already undergone the chemotherapy, second look operation, and re-chemo-



therapy with PBSCT, another chemotherapy regimen, was performed.

Patients 1, 2, 3 and 4 remain well without any evidence of disease for 5, 3, 0.5 and 3 years without therapy. Patients 5, 6 and 7 had very refractory diseases; patient 5 died after 1.5-years of hospitalization, and patients 6 and 7 are still undergoing intensive chemotherapy. Patient 8 has been free from disease for 4 months since the second PBSCT.

Case Reports

Patient 1

A 2-year-old boy was admitted to the hospital for further examination of increased urinary catecholamine metabolites discovered in a mass-screening examination at 18 months. He was asymptomatic, but abdominal ultrasonography and MRI demonstrated a left suprarenal abnormal mass. I-123-MIBG accumulated in the tumor, but ^{201}Tl scintigraphy showed no abnormal accumulation (Fig. 1). Preoperative biopsy of the tumor confirmed the diagnosis of neuroblastoma, rosette-fibrillary type.

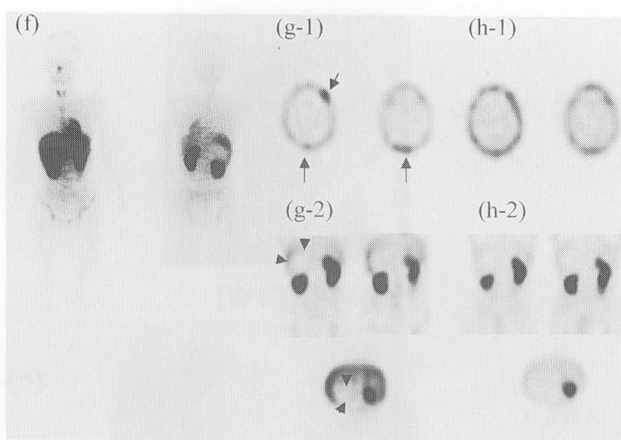


Fig. 2 Patient 7 CT scans (a) of the skull shows an osteolytic lesion with unclear border in the frontal bone (arrow). Bone scintigrams (b) show abnormal accumulations in the left frontal bone, some spines (Th2, L1), right 6th rib, left sacro-iliac joint, upper part of left acetabulum, and right ischium to acetabulum. Abdominal contrast CT scans (c) show a large right suprarenal mass with a necrotic center (arrow heads). ^{123}I -MIBG SPECT images (d-1: head, d-2: abdomen) show abnormal uptake by the tumors (arrows: skull mass, arrow heads: abdominal mass), and the whole body scans (e) demonstrate diffuse accumulation of the bone marrow (vertebrae, ribs, pelvic bones, proximal long bones of the extremities, and the proximal ends of the distal long bones) as well as the known lesions. ^{201}Tl early scans (f) demonstrate diffuse bone marrow accumulations like as ^{123}I -MIBG scans. ^{201}Tl early SPECT (g-1: head, g-2: abdomen) also demonstrate diffuse bone marrow accumulation as well as the skull (left frontal lesion) hot spots (arrows), but show the cold area at the abdominal tumor (arrow heads), while delayed images (h-1: head, h-2: abdomen) could not detect these accumulations.

Patient 7

An 11-year-old girl was admitted with a head mass and a continued low-grade fever lasting over 2 weeks. She had been treated first with antibiotics, because osteomyelitis had been suspected, but her symptoms did not changed. CT images of the skull showed focal osteolytic change with mild periosteal reaction in the left frontal bone. On her bone scintigrams, many abnormal accumulations were seen in her vertebrae, ribs, and pelvic bones as well as in the left frontal bone. Physical examination revealed a large abdominal mass, and abdominal CT showed a large tumor occupying the right retroperitoneal suprarenal space. Since urinary vanillylmandelic acid (VMA) and homovanillic acid (HVA) levels were very high, neuroblastoma was suspected. An ^{123}I -MIBG scintigram showed an abnormal hot spot in the head, and ring-like uptake by the abdominal tumor, and diffuse accumulation was seen in bone marrow or the bone of vertebrae, and proximal extremities, which meant that she had progressed neuroblastoma with metastases in diffuse bone marrow and several cortical bones. There was an especially intense hot spot on the parietal bone, which corresponded to the

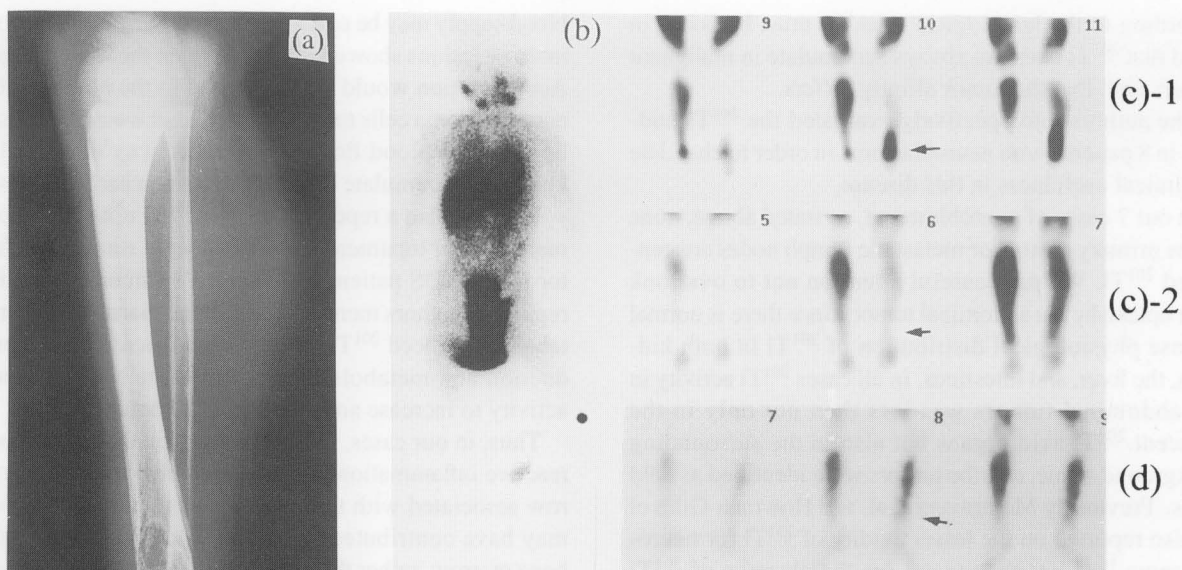


Fig. 3 Patient 8 An X-ray radiograph (a) of the left lower leg shows the osteolytic lesion with periosteal reaction at the distal metaphysis of the tibia. ^{123}I -MIBG (b) accumulates in the same lesion. ^{201}Tl SPECT performed after the chemotherapy shows marked uptake on the early image ((c)-1), but it is washed out on the delayed image ((c)-2). And the accumulation of ^{123}I -MIBG is disappeared at the second study (d). Arrows show the tibia lesion.

initially noticed lesion. The early ^{201}Tl scintigram showed no abnormal accumulation by the abdominal tumors, but diffuse bone marrow uptake was seen as in the MIBG scintigram. As to the skull lesion, a hot spot in the diffuse accumulation pattern was seen on the ^{201}Tl early images as in the ^{123}I -MIBG images. Although a delayed whole body scan could not be obtained, the alternatively obtained delayed SPECT images of the head and the abdomen demonstrated no abnormal accumulation (Fig. 2).

Bone marrow aspiration from the iliac crest and open biopsy of the abdominal tumor confirmed the diagnosis of neuroblastoma, rosette-fibrillary type.

Patient 8

A 5-year-old boy who had undergone resection of abdominal neuroblastoma and 3 months previously achieved complete remission after intensive chemotherapy and peripheral blood stem cell transplantation (PBSCT), was readmitted for left leg pain. An X-ray radiograph showed an osteolytic lesion with obvious cortical disruption and periosteal reaction in the distal metaphysis of the left tibia. ^{123}I -MIBG accumulated at the same site, and the biopsy confirmed the diagnosis of the metastatic neuroblastoma. ^{201}Tl scintigraphy was performed after 2 cycles of chemotherapy, and demonstrated abnormal uptake in the lesion on the early image and reduced activity that was indistinguishable from the background on the delayed image. The second MIBG scintigraphy, performed one week after the ^{201}Tl scintigraphy, demonstrated no abnormal distribu-

tion, even though there had been no treatment between the two studies (Fig. 3). Although periosteal reaction continued on the X-ray radiographs, no tumor cell was detected by bone marrow aspiration.

DISCUSSION

^{201}Tl was first used for myocardial perfusion imaging in the early 1970s.^{13,14} It behaves like potassium, and it is thought to be transported through a similar Na-K ATPase pump, Ca ion channel, and co-transport system, instead of potassium ion.^{7,14} It now has another significant role as a positive indicator for tumors in various organs. The exact mechanism of ^{201}Tl uptake by tumors is not completely known, but the activity of ^{201}Tl uptake is thought to be influenced by many factors: i) blood flow to the tumor and the nature of the tumor vessels, ii) tumor cell viability, iii) cell membrane permeability, iv) tumor cellularity, v) proliferation potential, and vi) some tumor types.⁷

A number of clinical investigations have shown that the accumulation in potentially malignant lesions persists longer than in benign lesions,^{7-9,15} and because of this feature ^{201}Tl scintigraphy is now being used to differentiate between benign and malignant lesions, but it is not always entirely reliable, and some exceptions have been reported. The above rule does not apply to certain types of soft tissue tumors, and Tonami et al. reported that in cases of lung cancers the degree of ^{201}Tl accumulation to the malignant lesion and the clearance from lesions vary

according to the histological type.⁹ It must be borne in mind that ^{201}Tl does not always accumulate in malignant tumors and, that the tumor affinity differs.

The authors retrospectively evaluated the ^{201}Tl findings in 8 patients with neuroblastoma in order to elucidate its clinical usefulness in this disease.

In our 7 cases of neuroblastoma, as stated above, none of the primary tumors or metastatic lymph nodes concentrated ^{201}Tl . We paid careful attention not to overlook faint uptake by the abdominal tumor, since there is normal intense physiological distribution of ^{201}Tl in both kidneys, the liver, and intestines. In all cases ^{201}Tl activity in the abdominal tumors was less than not only in the adjacent ^{201}Tl avid organs but also in the surrounding background tissue, and the tumors were identified as cold areas. Previously Montravers et al. and Howman-Giles et al. also reported on the lesser avidity of ^{201}Tl for neuroblastoma,^{16,17} but the reason for the absence of ^{201}Tl accumulation has not yet been clarified. Some features of neuroblastomas, perhaps ion-transport systems, tumor cell-membrane permeability, tumor cellularity, viability, or some other factors, would interfere with the mechanism of ^{201}Tl accumulation. Our results for primary lesions are in accordance with previously published reports, and it seems that the lack of ^{201}Tl uptake would be one of the characteristics of neuroblastoma, irrespective of the degree of malignant behavior of the individual tumor. These results made us less enthusiastic about examining more patients.

On the other hand, interestingly, the ^{201}Tl scintigraphy findings in the bone marrow and cortical bone lesions differed from those in the intra-abdominal tumors. Skeletal metastatic lesions were visualized on the early ^{201}Tl scans, and the accumulation showed fast washout.

Normally there is no significant physiological accumulation of ^{201}Tl by bone or bone marrow¹³ except for uptake in the normal growth plates of the long bones in children. Clear accumulation in the vertebrae and the diaphyses of long bones indicates a pathological condition.

There have been reports of ^{201}Tl accumulation in the bone marrow in relation to tumor cell infiltration in myeloma¹⁸ and Hodgkin's lymphoma.¹⁹ As a tumor-seeking agent, ^{201}Tl is a useful tool for evaluating patients with malignancy, and it detects the affected bone marrow, but it is difficult to understand why ^{201}Tl accumulates only in bone marrow and bone metastatic lesions and not in abdominal neuroblastomas. Metastatic tumor cells may have almost the same characteristics as the primary and lymph node lesions in terms of cell membrane permeability or ion transport systems, cellularity and tumor viability. If there is any difference between the features of intra-abdominal lesions and skeletal lesions, it would be the vascularity and capillary formation in the tumor. A solid mass is usually fed by one or more vessels, whereas in the bone marrow the tumor cells are disseminated and are surrounded by an abundant blood supply. This form of

blood supply may be one of the reasons why only the bone marrow lesions showed ^{201}Tl uptake on the early images. Accumulation would not be related to the ability of the neuroblastoma cells to pick up ^{201}Tl , but would be caused by regional blood flow, in the same way that ^{201}Tl is known to accumulate in inflammation on early images.²⁰

There is also a report on diffuse ^{201}Tl uptake by bone marrow after treatment with granulocyte stimulating factor in an AIDS patient with Kaposi's sarcoma.²¹ In that report the authors mentioned that bone marrow hypermetabolism induced ^{201}Tl accumulation. Increased cell production and metabolism may cause the Na-K ATPase activity to increase and result in ^{201}Tl uptake.

Thus, in our cases, the form of regional blood supply, reactive inflammation or hyperfunction of the bone marrow associated with the presence of the metastatic foci may have contributed to the ^{201}Tl accumulation in the bone marrow, rather than the characteristics of the tumors themselves. As to the cortical involvement, the periosteal reaction may contribute to the ^{201}Tl uptake. There is no conclusive proof of these hypotheses, but the fact that the bone marrow uptake did not persist confirms that the uptake mechanism is independent of the malignant behavior of the tumor. In case 8, after the resolution of MIBG accumulation, inflammation of the bone and persisting periosteal reaction may have led to the ^{201}Tl accumulation.

It is noteworthy that ^{201}Tl accumulation by the skeleton does not always mean tumor cell infiltration. Lebtahi et al. reported that on MRI studies abnormal bone marrow signals often persist after chemotherapy for neuroblastoma, despite complete normalization of the MIBG scan, and that an abnormal MRI signal does not necessarily indicate the presence of disease.²² It may also be true that early ^{201}Tl early accumulation in the bone marrow or bone does not necessarily indicate the presence of a viable tumor, and this might be observed in other tumors besides neuroblastoma. In cases of suspected malignant tumor, the mechanism of early ^{201}Tl uptake by skeletal lesions would include the tumor characteristics and other factors. But when uptake does not persist on the delayed image, it may indicate that the early uptake reflects hypervascularity, inflammation, hypermetabolism of the bone marrow, or periosteal reactions. Careful attention must be paid to the interpretation of skeletal ^{201}Tl distribution.

Many more cases need to be examined to describe the reliable features of ^{201}Tl scintigraphy in neuroblastoma. The experience described here suggests that ^{201}Tl scintigraphy is not very useful in the diagnosis or follow-up of neuroblastoma, but it shows one interesting possible mechanism of ^{201}Tl accumulation in bone marrow and bone. The uptake by affected bone marrow or bone might be independent of the tumor characteristics, so we must take care in the interpretation of skeletal ^{201}Tl accumulation.

REFERENCES

1. D'Angio GJ, Evans AE, Koop CE. Special pattern of widespread neuroblastoma with a favorable prognosis. *Lancet* 1971; 1: 1046–1049.
2. Jaffe N. Neuroblastoma: Review of the literature and an examination of factors contributing to its enigmatic character. *Cancer Treatment Rev* 1976; 3: 61–82.
3. Evans AE, D'Angio GJ, Randolph J. A proposed staging for children with neuroblastoma. *Cancer* 1971; 27: 374–378.
4. Shulkin BL, Shapiro B. Current concepts on the diagnostic use of MIBG in children. *J Nucl Med* 1998; 39: 679–688.
5. Okuyama C, Ushijima Y, Sugihara H, Okitsu S, Maeda T. ¹²³I-metaiodobenzylguanidine (MIBG) scintigraphy for the staging of neuroblastoma. *KAKU IGAKU (Jpn J Nucl Med)* 1998; 35: 835–842.
6. Maurea S, Lastoria S, Caracò C, Indolfi P, Casale F, Tullio MT, et al. Iodine-131-MIBG imaging to monitor chemotherapy response in advanced neuroblastoma: comparison with laboratory analysis. *J Nucl Med* 1994; 35: 1429–1435.
7. Tonami N. Diagnosis of Tumor with Thallium-201. *KAKU IGAKU (Jpn J Nucl Med)* 1994; 30: 449–455.
8. Ochi H, Sawa H, Fukuda T, Inoue Y, Nakajima H, Masuda Y, et al. Thallium-201 chloride thyroid scintigraphy to evaluate benign and/or malignant nodules. *Cancer* 1982; 50: 236–240.
9. Tonami N, Shuke N, Yokoyama K, Seki H, Takayama T, Kinuya S, et al. Thallium-201 single photon emission computed tomography in the evaluation of suspected lung cancer. *J Nucl Med* 1989; 30: 997–1004.
10. Sumiya H, Taki J, Tsuchiya H, Nonomura A, Miyauchi T, Tonami N. Midcourse thallium-201 scintigraphy to predict tumor response in bone and soft-tissue tumors. *J Nucl Med* 1998; 39: 1600–1604.
11. Lee VW, Sax EJ, McAneny DB, Pollack S, Blanchard RA, Beazley RM, et al. A complementary role for thallium-201 scintigraphy with mammography in the diagnosis of breast cancer. *J Nucl Med* 1993; 34: 2095–2100.
12. Oriuchi N, Tamura M, Shibasaki T, Ohye C, Watanabe N, Tateno M, et al. Clinical Evaluation of Thallium-201 SPECT in Supratentorial Gliomas: Relationship to Histologic Grade, Prognosis and Proliferative Activities. *J Nucl Med* 1993; 34: 2085–2089.
13. Atkins HL, Budinger TF, Lebowitz E, Ansari AN, Greene MW, Fairchild RG, et al. Thallium-201 for Medical Use. Part 3: Human Distribution and Physical Imaging Properties. *J Nucl Med* 1977; 18: 133–140.
14. Kawana M, Krizek H, Porter T. Use of ¹⁹⁹Tl as a Potassium Analog in Scanning. *J Nucl Med* 1970; 11: 333–336.
15. Jinnouchi S, Hoshi H, Ohnishi T, Futami S, Nagamachi S, Watanabe K, et al. Thallium-201 SPECT for Predicting Histological Types of Meningioma. *J Nucl Med* 1993; 34: 2091–2094.
16. Montravers F, Coutiris G, Sarda L, et al. Utility of thallium-201 and iodine-123 metaiodobenzylguanidine in the scintigraphic detection of neuroendocrine neoplasia. *Eur J Nucl Med* 1993; 20: 1070–1077.
17. Howman-Giles R, Uren RF, Shaw PJ. Thallium-201 Scintigraphy in Pediatric Soft-Tissue Tumors. *J Nucl Med* 1995; 36: 1372–1376.
18. Sayman HB, Sonmezoglu K, Altioek E, Devranoglu G, Ferhanoglu B. Unexpected Bone Marrow Uptake of Thallium-201 in nonsecretory Myeloma. *J Nucl Med* 1995; 36: 250–251.
19. Linde R, Basso L. Hodgkin's Disease with Hypercalcemia Detected Thallium-201 Scintigraphy. *J Nucl Med* 1987; 28: 112–115.
20. Tonami N, Matsuda H, Ooba H, Yokoyama K, Hisada K, Ikeda K, et al. Thallium-201 Accumulation in Cerebral Candidiasis. Unexpected Finding on SPECT. *Clin Nucl Med* 1990; 16: 397–400.
21. Abdel-Dayem HM, Sanchez J, Al-Mohannadi S, Kempf J. Diffuse Thallium-201-Chloride Uptake in Hypermetabolic Bone Marrow Following Treatment with Granulocyte Stimulating Factor. *J Nucl Med* 1992; 33: 2014–2016.
22. Lebtahi N, Gudinchet F, Nenadov-Beck M, Beck D, Delaloye BA. Evaluating Bone Marrow Metastasis of Neuroblastoma with Iodine-123-MIBG Scintigraphy and MRI. *J Nucl Med* 1997; 38: 1389–1392.