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Visualization of the bone/bone marrow of lower extremities in Ga-67 whole-body images

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Patients whose Ga-67 whole-body images showed increased uptake by the bone/bone marrow of the lower extremities were selected and classified into three types according to the extent and the grade of the visualization. These types were then compared with their serum iron levels, iron-binding capacities, and the results of several other serum biochemical tests. Of 374 consecutive whole body 72-hr images reviewed, 59 (15.8%) showed increased uptake of the tracer by the bone/bone marrow of the lower extremities. The three classified types were as follows: type T—visualization of both tibiae and femurs; type S—strong visualization of the femurs; and type W—weak visualization of the femurs. The serum iron concentration was significantly high in type T and low in type S. In conclusion, the pattern of Ga-67 uptake by the bone/bone marrow of the lower extremities fairly closely reflects the status of iron metabolism.

Key words: Ga-67 scan, Serum iron, Serum UIBC, Bone/bone marrow visualization

INTRODUCTION

BIODISTRIBUTION of Ga-67 citrate is known to be affected by the serum iron concentration and iron binding capacity;[1–5] hyperferremia is reported to cause increased blood clearance and bone deposition of Ga-67.[6,7] Visualization of the bone/bone marrow in Ga-67 images is a normal finding,[8,9] while its visualization is quite prominent in some diseases and conditions.[10–12] Patients whose Ga-67 images showed increased uptake by the bone/bone marrow of the lower extremities were selected, classified, compared with the results of various serum biochemical tests, and analyzed with regard to the possible mechanisms.

MATERIALS AND METHODS

Consecutive Ga-67 whole-body images taken during a 9-month period at the University Hospital of Yamanashi Medical College were reviewed. Patients under 10 years old were excluded from this study because of physiologically strong uptake by the bone/bone marrow of children.[9] Ga-67 whole-body images were taken 72 hours after intravenous injection of 3 mCi (111 MBq) of Ga-67 citrate; a Toshiba GCA-405 gammacamera equipped with a medium energy collimator was used. Both anterior and posterior whole-body images were reviewed to judge whether the bone/bone marrow of the lower extremities were visualized. Serum iron, unsaturated iron-binding capacity (UIBC), ferritin, and immunoelectrophoretically measured transferrin were determined within two weeks before or after the imaging, and compared with the scan findings. The findings of bone marrow biopsy/aspiration from the iliac bone or the sternum and the effect of chemotherapy were also compared with the scan findings. Statistical analysis was done by Welch's t-test.

RESULTS

Of 374 consecutive images reviewed, 59 (15.8%) showed increased uptake of the tracer by the

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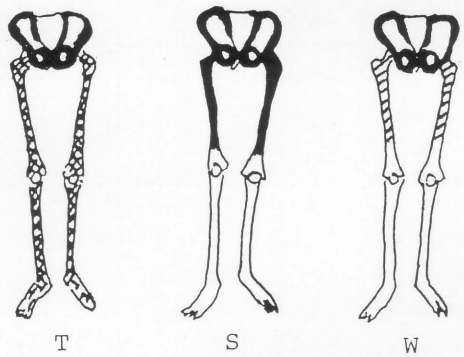

Fig. 1 Schematic illustration of types of visualization of lower extremities: type T—visualization of both tibiae and femurs; type S—strong visualization of the proximal or the whole femurs; and type W—weak visualization of the proximal or the whole femurs.

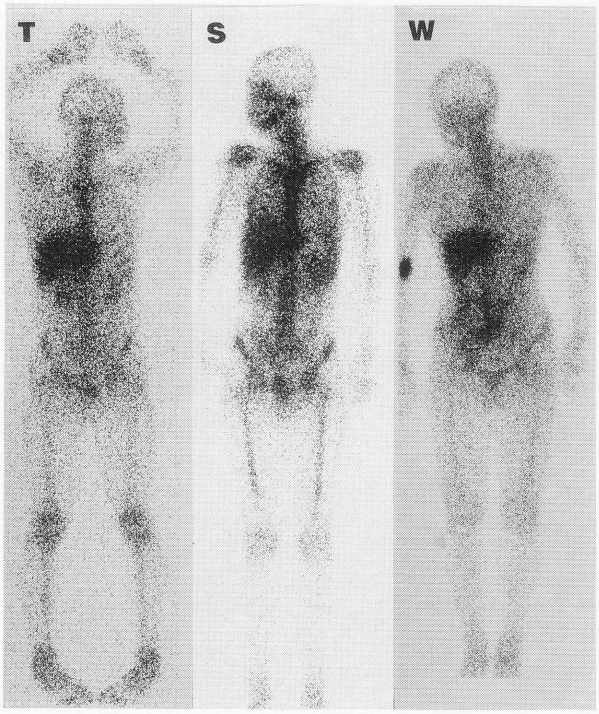

Fig. 2 Representative images of each type.

bone/bone marrow of the lower extremities. These findings were classified into 3 types (Fig. 1): type T —visualization of both tibiae and femurs; type S—strong visualization of the proximal or the whole femurs; and type W—weak visualization of the proximal or the whole femurs. Typical images are shown in Figure 2. The numbers of cases showing these types were 6, 16 and 37, respectively, for types T, S and W.

Figure 3 shows the serum iron concentration in patients of each type. The mean value in type T patients, 160 ± 71, is significantly higher ($p<0.001$) than that in the control patients, 58 ± 34, which was calculated for 50 patients without visualization of the bone/bone marrow of the lower extremities. The mean value in type S patients, 18 ± 7.3, is also significantly lower ($p<0.001$) than that in the control patients.

Type T and S cases are summarized in Table 1. Four of 6 type T patients had malignant lymphoma although type T does not seem to be specific for this disease. Several non-malignant diseases are included in both T and S types; that is, there seems to be no correlation between the kind of disease and the type of visualization. The serum ferritin concentration also showed no correlation with these types. UIBC was not measured for any of the type T, but it showed rather high values in type S patients. Serum transferrin in two type T patients was markedly decreased.

Thirteen patients underwent bone marrow biopsy/aspiration. The results are shown in Table 2. There seems to be no correlation between the bone marrow findings and the type of visualization.

To evaluate the chemotherapeutic effect on the visualization of bone/bone marrow, the chemotherapeutic history was checked for each patient. The results are shown in Table 3. Half of the patients showing type T had recently received chemotherapy; however, both treated and untreated patients showed all types of visualization.

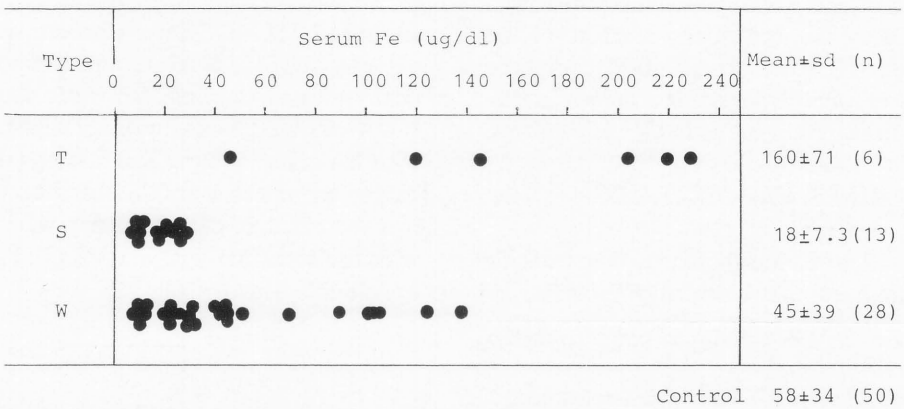

Fig. 3 Serum iron concentration measured in each type. Mean value for type T is significantly higher than that for control, and mean value for type S is significantly lower.

Table 1 Summary of cases showing types T and S

Type	Diagnosis	Age	Sex	Fe	Ferritin	UIBC	Trfr*
T	Malignant lymphoma	46	F	220	—**	—	↓↓
	Malignant lymphoma	29	M	229	234	—	—
	Malignant lymphoma	17	M	46	—	—	—
	Brain lymphoma	18	M	120	—	—	—
	Uterine cancer	69	F	204	555	—	—
	RA & acute renal failure	19	F	145	324	—	↓↓
S	Gastric cancer	55	M	26	—	200	—
	Gastric cancer	72	M	10	—	—	—
	Gastric cancer	62	M	—	—	—	—
	Metastatic skin tumor	41	F	—	—	—	—
	Breast cancer	72	F	7	10	—	—
	Oral cancer	73	F	29	—	—	—
	Lung cancer	54	M	25	1,240	—	—
	Uterine cancer	57	F	12	—	—	—
	Ovarian & uterine cancer	47	F	19	133	—	—
	Malignant lymphoma	50	F	10	—	—	—
	(Malignant lymphoma	50	F	25	—	—	—)***
	Polycythemia vera	63	F	20	18	282	→
	AML	33	M	—	—	—	—
	SLE	49	F	17	73	264	—
	Perirenal abscess	71	F	20	—	—	—
	FUO	38	F	10	55	178	↓

* Transferrin, ** Unknown or not done *** Different study in the same patient

Table 2 Results of bone marrow biopsy/aspiration in each type

Type	Bone marrow biopsy/aspiration			Not done or Unknown
	Tumor invasion	Hyper-plastic	Hypo-plastic	
T	2	1	1	2
S	0	2	2	12
W	2	2	1	32

Table 3 Chemotherapeutic history in each type

Type	Chemotherapy was done		Untreated	Unknown
	within 2 weeks	more than 2 weeks before		
T	3	0	3	0
S	2	1	8	5
W	4	5	24	4

DISCUSSION

Ga-67 citrate injected intravenously is known to be distributed to the bone and bone marrow.[8] From the scintigrams, however, it is rather difficult to discriminate between visualization of bone and that of bone marrow. We directed our attention to the lower extremities in order to discriminate between these two. Visualization of the femurs (types S and W) might be due to uptake by the bone marrow rather than the bone. On the other hand visualization of the tibiae (type T) is speculated to be due to uptake by the bone unless it is proven that there is tibial expansion of the bone marrow or tibial marrow invasion of malignant cells which have an affinity for Ga-67. To clarify this, bone marrow biopsy from the tibiae might be necessary. However, bone marrow biopsy/aspiration from the iliac bone or the sternum in type T cases did not always suggest hyperplastic bone marrow. Also, diffuse homogeneous invasion of the Ga-67-avid malignant cells to the tibial bone marrow might be improbable. Therefore, we think that type T reflects increased uptake of Ga-67 by the bone rather than the bone marrow. Ga-67 is known to have been investigated as a bone scanning agent,[13]: and it acucumulates well in bone tissues or bone lesions.[14,15]

In several biochemical tests, the serum iron concentration correlated well with the type of visualization of the lower extremities. That is, type T patients apparently showed increased serum iron concentration, while type S patients showed a decreased serum iron concentration. On the other hand, type W patients did not show any particular tendency with regard to the serum iron concentration. Unfortunately, only few patients had their UIBC or serum transferrin concentration measured in our study. Therefore, no conclusion can be drawn, but some type T patients showed a decreased serum transferrin concentration and some type S patients showed

rather increased UIBC. These findings coincide quite well with the results of Scheffel et al[3] and Higashi et al.[16] Only one type T patient showed a normal serum iron concentration. His UIBC or serum transferrin concentration might be low, although neither was measured. The reason why increased serum iron causes increased uptake of Ga-67 by the bone is only speculative. However, it has been shown that when the protein-binding of Ga-67 is blocked by stable gallium, the bone uptake of Ga-67 increases.[6,13,17] In patients with increased serum iron, the protein-binding of Ga-67 is easily blocked by the iron. Thus the rapid clearance of Ga-67 from tissues other than bone might occur and the bone might be visualized clearly. Among the bone of lower extremities, tibiae are especially easily visualized in the anterior view because of lack of overlapping soft tissues.

Why was the serum iron concentration in type T patients high? First, chemotherapy is a possibility. Chilton et al[5] showed higher levels of serum iron after methotrexate treatment of animals, resulting in altered Ga-67 tissue distribution. Second, radiation is another possibility. Bradley et al[1] showed increased concentration of serum iron after whole-body irradiation of animals, resulting in increased urinary excretion of Ga-67. Third, blood transfusion is known to increase the serum iron concentration. In our type T cases, except the patient with RA, their hyperferremia can be explained by at least one of these factors. Though some types S and W patients received these therapies, their serum iron concentration did not become high for some reason.

In conclusion, visualization of the tibiae in Ga-67 whole-body images, which we classified as type T, is based on the uptake of the tracer by the bone rather than the bone marrow, and is due to increased serum iron and/or probably decreased serum UIBC. On the other hand, visualization of femurs only, especially in cases with strong uptake such as type S, is based on uptake by the bone marrow rather than the bone, and is due to decreased serum iron and/or probably increased UIBC.

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