Tc-99m Diphosphonate and Sulfur Colloid Uptake by the Spleen in Sickle Disease: Interrelationship and Clinical Correlates: Concise Communication

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To determine the clinical significance of splenic uptake in bone scintigraphy and functional asplenia on the radionuclide liver-spleen image, bone and spleen scintigrams of 38 patients with sickle cell disease were reviewed. Eighteen underwent bone and liver-spleen studies, 15 had only bone images, and five had only liver-spleen studies. Sixteen of 33 who had bone scintigraphy showed splenic uptake, but the frequency of homozygous sickle cell (SS) disease was not greater than heterozygous sickle cell disease (S-hetero) in this group. SS patients with splenic uptake of Tc-99m diphosphonate had significantly fewer painful crises of the abdomen and extremities, and fewer inpatient and outpatient hospital visits than SS patients whose bone imaging did not visualize the spleen. Functional asplenia on liver-spleen images (16 cases) was seen only in SS disease. One SS patient, age 8, still had a spleen capable of phagocytizing colloid.

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Functional asplenia (Fig. 1), the inability of the anatomically present spleen to clear intravenously administered radiocolloid, has been described in homozygous sickle cell anemia (SS) (*1*,*2*), heterozygous sickle cell disease states—including S-C, S-E, and S-thalassemia, (S-hetero)—and a variety of other splenic disorders (*3*).

In contrast to this diminished uptake of radiocolloid, splenic accumulation of Tc-99m diphosphonates may occur in sickle cell disease (*2*,*4*,*5*) as well as in a variety of other disease states that involve the spleen (*3*) (Fig. 2).

This study was undertaken in a group of patients with sickle disease to determine the prevalence of these phenomena, their interrelationship, effect of patient age, and clinical significance.

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MATERIALS AND METHODS

We reviewed the charts of 38 patients, 26 with SS, 12 with S-hetero (nine with SC, three with S-thalassemia) who had had bone or spleen imaging, or both, within a 3-mo period. At the time of the imaging, the ages ranged from 5 to 56 yr, mean 22.9 ± 11.7 yr. Eighteen of the 38 had both bone and liver-spleen scintigraphy, 15 had bone images only, and another five had only liver-spleen scintigraphy. Thus 33 patients had images of the bones and 23 images of the liver and spleen (Table 1). These studies were generally ordered to detect infection or infarction. A detailed clinical profile for each patient was obtained from a retrospective chart review, including number of hospitalizations, frequency of infection, frequency and location of painful crises, percent hemoglobins S and F, age, and sex.

The liver-spleen scintigrams were performed with 3mCi Tc-99m sulfur colloid (Tc-SC) for adults and with appropriate weight-related reductions of activity for pediatric patients. Anterior, right and left lateral, and posterior views were obtained. If the spleen was not ini-

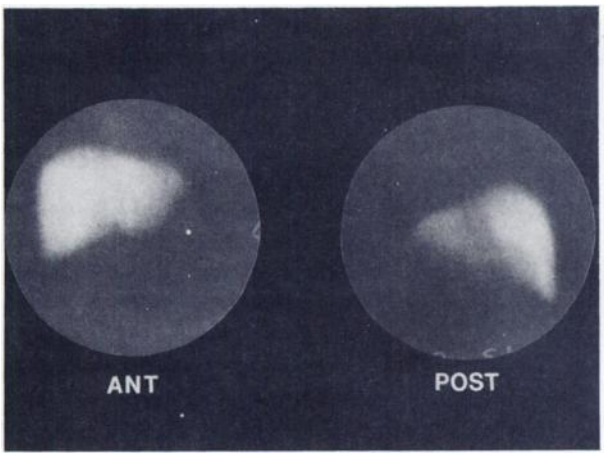

FIG. 1. Nonvisualization of spleen by Tc-99m sulfur colloid in sickle cell disease.

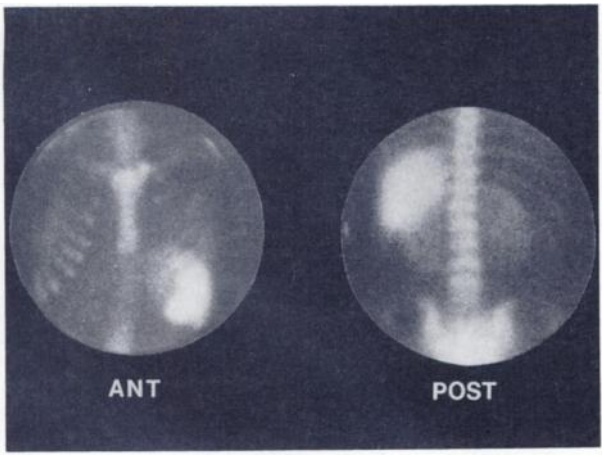

FIG. 2 Splenic uptake Tc-99m MDP in same patient.

tially visualized, left anterior and posterior oblique views were performed in all but one case. For bone scintigraphy, patients were hydrated with at least 250 ml of fluid in the 3 hr between injection and imaging; we used 20–25 mCi Tc-99m diphosphonate, again with dose reductions appropriate for size in children. We used standard nontomographic gamma cameras for both studies. Differences between two groups were analyzed by the unpaired Student's t-test, and between more than two groups by analysis of variance.

RESULTS

Sixteen (48%) of the 33 patients with SS (*13*) or S-hetero (*3*) who had a bone image had spleen visualization on this study, with Tc-99m diphosphonate uptake ranging from faint to strikingly increased (Table 1). All seven (100% with SS) with spleen visualization on the bone image and who also received Tc-SC had no sulfur colloid uptake by the spleen, whereas only six of 11 without Tc-99m diphosphonate splenic uptake and who had spleen scintigraphy had no splenic uptake with sulfur colloid ($p < 0.05$). On the other hand, if there was splenic function by liver-spleen image, this organ was never seen on the bone image (Table 1). Of four S-hetero patients who had bone scintigrams, none had splenic Tc-99m diphosphonate uptake. The mean age of the seven SS patients with functional asplenia and Tc-99m diphosphonate uptake was 23.1 ± 9.4 yr—not significantly different from the six SS functionally asplenic patients without the bone tracer concentration (28.5 ± 5.7 yr).

Seventeen patients of the 33 did not concentrate Tc-99m diphosphonate; ten of this group had SS disease while seven had S-hetero. The difference in the prevalence of SS between the groups whose spleens did or did not concentrate the bone imaging agent is not statistically significant ($p > 0.1$).

Thirteen of 23 patients with SS disease had visualization of the spleen with Tc-99m diphosphonate and three of ten cases with S-hetero demonstrated this phenomenon ($p > 0.1$). Thus SS homozygotes were no more likely to have spleen uptake on bone imaging than S-heterozygotes.

Out of 23 liver-spleen images, only seven (30%) showed splenic function (Table 1). Of these seven only one (age 8) had SS. The mean age of the 16 patients with functional asplenia, all with SS, was 23.3 ± 9.3 (range 5–39 yr).

TABLE 1. INTERRELATIONSHIP BETWEEN SICKLE CELL DISEASE, SPLEEN FUNCTION, AND SPLENIC CONCENTRATION OF Tc-99m DIPHOSPHONATE

Tc-99m sulfur colloid uptake	Tc-99m diphosphonate in spleen: Yes		No		Not done		Total
	SS*	S-het†	SS	S-het	SS	S-het	
Yes	0	0	1	4	0	2	7
No	7	0	6	0	3	0	16
Not done	6	3	3	3	0	0	15
Total	13	3	10	7	3	2	38

* Homozygous sickle cell disease.

† Heterozygous sickle cell disease (sickle-C, sickle-thalassemia).

TABLE 2. SPLEEN UPTAKE OF Tc-99m DIPHOSPHONATE

	Yes		No	
	SS	S-het	SS	S-het
Hematocrit	26.8 ± 5.0	32.1	26.6 ± 2.0	36.9 ± 4.2
Fetal hemoglobin	5.2 ± 3.9	—	9.0 ± 9.1	11.2 ± 10.9
No. painful crises in extremities	9.5 ± 8.0	—	29.9 ± 27.5	21.2 ± 18.4
No. painful crises in abdomen	5.6 ± 6.5	—	15.2 ± 9.9	7.8 ± 8.0
No. infections requiring hospitalization	3.7 ± 2.9	—	5.9 ± 3.5	4.2 ± 4.7
No. outpatient visits	7.0 ± 6.5	—	23.0 ± 25.7	16.2 ± 15.2
No. inpatient visits	11.2 ± 8.9		25.2 ± 15.7	10.2 ± 11.5

* $p < 0.001$.
† $p < 0.05$.
‡ $p < 0.02$.
(For all other comparisons $p > 0.1$).

Correlations between hematologic and clinical measurements and spleen visualization on bone and liver-spleen imaging appear in Tables 2 and 3, respectively. As expected, the patients with S-hetero had significantly higher hematocrits than those with SS. There was no difference in hemoglobin F content between the two groups.

SS patients with spleen uptake of Tc-99m diphosphonate had fewer painful crises in both the abdomen ($p < 0.02$) and extremities ($p < 0.05$) than those without spleen visualization. This was also reflected in the fewer outpatient and inpatient visits required by the group with spleens seen on bone scintigrams. There was no difference in any of these clinical events between SS patients whose spleen did not visualize and S-heterozygotes. None of these groups differed in the prevalence of infection.

The clinical comparison between patients with spleens that concentrated Tc-SC normally and those that did not was essentially a comparison of S-heterozygotes and SS patients, respectively, since only one SS patient (age 8) still had a functioning spleen. There was no significant difference between these groups in any of the measurements except hematocrit (Table 3), although there was a trend toward fewer crises and hospital visits in the S-heterozygotes, as expected.

DISCUSSION

The data in Table 1 suggest that a relationship exists between loss of a spleen's phagocytosis of Tc-SC and its uptake of Tc-99m diphosphonate. No patient with sulfur colloid uptake (functioning spleen) had a spleen that concentrated the bone-imaging agent. All seven patients

TABLE 3. Tc-99m COLLOID SPLEEN IMAGING

	Spleen functioning		Functional asplenia	
	SS	S-het	SS	S-het
Hematocrit	27.8†	34.8 ± 3.0	26.4 ± 3.5	—
Fetal hemoglobin	25.8	6.4 ± 6.5	5.9 ± 6.1	—
No. of painful crises in extremities	47	25.4 ± 15.8	12.5 ± 7.8	—
No. of painful crises in abdomen	16	5.2 ± 6.6	11.7 ± 13.6	—
No. infections requiring hospitalization	12	4.2 ± 4.7	4.8 ± 3.4	—
No. outpatient visits	17	19.4 ± 13.5	10.3 ± 9.1	—
No. inpatient visits	45	13.0 ± 8.9	10.0 ± 7.7	—

* $p < 0.05$.
† All data in this column are from one patient, age 8.

with Tc-99m diphosphonate uptake had functional asplenia and SS. In 11 patients with no Tc-99m diphosphonate seen in the spleen and who also had a liver-spleen study, the spleen functioned in five, four of whom were S-heterozygotes; the fifth was only 8 yr old. S-heterozygotes generally have fewer episodes of splenic infarction than SS-homozygotes.

The most reasonable hypothesis to explain this is, of course, progressive splenic infarction, which causes functional, and eventually anatomic, asplenia. With infarction there is a focal deposition of calcium salts and iron, both of which have been shown to lead to Tc-99m diphosphonate localization (*6*,*7*). The presence of a residual vascular supply is obviously necessary as well. Perhaps certain sickle disease patients have special characteristics of their disease permitting some preservation of the blood supply; alternatively we may merely be seeing a continuum of diminishing splenic blood flow in a selected population of sickle patients.

We could not find differences between the groups with or without Tc-99m diphosphonate splenic uptake in age or percent erythrocyte hemoglobin F. (A high hemoglobin F may reduce the clinical severity of sickle disease.)

The significantly reduced number of painful crises in the abdomen ($p < 0.02$) and extremities ($p < 0.05$) in the SS patients with Tc-99m diphosphonate uptake was surprising. This group of patients, with their spleens visualized by bone scan, must have been able to maintain more splenic blood flow after infarction than those without a visible spleen, since some blood flow to the organ is required to deposit the Tc-99m diphosphonate. Perhaps these SS patients were also better able to perfuse the tissues and organs at risk for infarction, thus decreasing the number of painful crises. Further research into the rheology of sickled blood is required to determine precisely what reduces the number of painful crises in the group of SS patients we have identified by their ability to reperfuse an infarcted spleen.

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