RETICULOENDOTHELIAL SCANS IN DISORDERS INVOLVING THE BONE MARROW

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Reticuloendothelial (RE) scans were performed on 58 patients with diseases affecting the bone marrow. All leukemic patients had decreased marrow activity and variable degrees of hepatosplenomegaly. The pattern of RE marrow activity in patients with lymphomas was variable but focal defects on marrow scan were usually associated with histologic evidence of lymphoma in the marrow. Decreased RE marrow activity occurred in multiple myeloma and two patients had focal defects on scan when skeletal x-rays were normal. Hemolytic or hemorrhagic anemias were associated with increased RE marrow activity but scans in aplastic anemia were normal. Myelophthisic anemia and myelofibrosis were associated with decreased central marrow activity and peripheral expansion of the marrow space. Fifty percent of patients with terminal renal disease had decreased RE marrow activity. Certain patterns of RE activity and distribution have been established for some disorders but these patterns may not always reflect the distribution or activity of hemopoietic tissue.

Until recently, bone marrow aspiration and biopsy were the only direct methods available for examination of the hematopoietic tissue. The value of these procedures is unquestioned in hematologic diagnosis but only a very small portion of the total blood-forming organ can be sampled. Furthermore, some diseases affect the bone marrow diffusely whereas other disorders produce localized abnormalities. Therefore it may be of importance to examine the entire marrow organ in some manner.

Technetium-99m-sulfur colloid has proved to be a satisfactory reticuloendothelial (RE) scanning agent because of its relatively low gamma energy, short half-life, and low radiation dose to the patient. It is quite commonly used for liver–spleen scanning and is readily available in most laboratories. In this report ^{99m}Tc-sulfur colloid has been used to evaluate the RE bone marrow as well as the liver and spleen in 58 patients with various diseases known to affect the bone marrow. The purpose of this study was to determine the patterns of RE scans in such diseases and to determine the diagnostic usefulness of RE scanning.

METHODS

Technetium-99m-sulfur colloid was prepared according to the instructions provided with a commercial kit (Tesuloid, E. R. Squibb & Sons, Inc.) and 171 μCi/kg body weight was given i.v. A flood source containing ^{57}Co was scanned prior to RE scanning in order to establish field uniformity. Approximately 5 min after injection of the isotope, scanning was started with a Pho/Gamma III scintillation camera using a low-energy, straight multihole collimator with appropriate window and intensity settings. Scans of the RE marrow included a lateral view of the skull, both shoulders, elbows, hips, knees, and anterior and posterior views of the pelvis and lumbosacral spine. Each of the multiple views of the bone marrow were taken with preset time exposures of 3 min. When peripheral expansion of the marrow space was noted, scans of the forearms, hands, legs, and feet were also performed. Because both the injected dose and marrow scanning time remained constant, it was possible to com-

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pare the intensity of marrow activity in different patients. For liver and spleen scans, total counts of 300,000 and 150,000, respectively, were accumulated. All scans were recorded on Polaroid positive prints or 35-mm Tri-X film or both.

The RE scans were interpreted in the following manner. The activity in the central or axial marrow was graded as slightly, moderately, or markedly increased (+, ++, +++) (Fig. 1) or decreased (−, −−, −−−) (Fig. 2). Normally, the axial marrow and the proximal one-third of the humeri and femora should show activity (Fig. 3). Activity present farther down into the femoral or humeral shafts, in the bones of the forearms, elbows, knees, lower legs, hands, or feet was considered to be peripheral expansion of the marrow space (Figs. 4 and 5). Peripheral expansion was graded as slight, moderate, or marked (+, ++, +++). The presence of focal defects in the marrow (Fig. 6), liver or spleen, and the size of the liver and spleen were also noted.

RESULTS

Patterns of reticuloendothelial activity are summarized in Table 1.

Anemia. Patients with aplastic anemia had normal RE scans. Patients with marrows capable of responding to hemorrhage, hemolysis, or nutritional deficiency had increased RE marrow activity on scan. Patients with infiltrative diseases of the marrow, i.e., tumor cells or myelofibrosis, had decreased central marrow activity, peripheral expansion of the marrow space, and hepatosplenomegaly. Focal defects on scan were found in two of the four patients with myelophthisic anemia but not in the two patients with myelofibrosis.

FIG. 1. Increased central marrow activity (hemipelvis and upper femur).

FIG. 2. Decreased central marrow activity (hemipelvis and upper femur).

FIG. 3. Normal central marrow activity (hemipelvis and upper femur).

Polycythemia. Three patients with polycythemia vera had splenomegaly. Two patients treated by phlebotomy had increased central marrow activity and peripheral expansion of the marrow space. One patient treated successfully with ^{32}P had a normal marrow scan. One patient with polycythemia secondary to hypoxic lung disease had a normal marrow scan and no splenomegaly.

Leukemia. All eight patients with acute or chronic leukemia had a moderate to marked decrease in central RE marrow activity and three had peripheral expansion of the marrow space. All patients except one were anemic and all had hepatosplenomegaly by scan. The most marked splenomegaly occurred in the chronic leukemias. Focal defects were not observed.

Multiple myeloma. All six patients with multiple myeloma and radiologic evidence of bone involvement had diffusely decreased central marrow activity on scan. Another patient with localized myeloma had increased central RE marrow activity and eryth-

FIG. 4. Peripheral expansion of marrow (knee).

roid hyperplasia on marrow aspiration due to GI bleeding. In two patients with normal skeletal x-ray films, focal defects were found on marrow scan. Anemia was present in all but one patient and hepatosplenomegaly was slight or absent.

Lymphomas. Patients with lymphomas had variable patterns of RE marrow activity, and no correlation with hematocrit, organomegaly, or pretreatment with cytotoxic drugs or irradiation could be made. Peripheral expansion of the marrow space occurred in 12 of the 17 patients. Five of six patients with focal defects on RE marrow scan had histologic proof of lymphoma in the marrow. Hepatosplenomegaly by scan was found in all patients with Hodgkin's disease or lymphosarcoma. In contrast, organomegaly was mild or absent in reticulum cell sarcoma. Focal defects were found in the spleen in two patients with lymphosarcoma and one with Hodgkin's disease; defects on the liver scan were present in one patient with Hodgkin's disease.

Uremia. Eleven of 12 uremic patients had abnormal RE marrow scans. Six patients had decreased central marrow activity and all six had BUNs greater than 70 mg%. Of the remaining six patients, three had a BUN less than 70 mg% and three were greater than 70 mg%, but all had normal or increased RE marrow activity. Slight enlargement of the liver or spleen was found by scanning in 11 of the 12 patients. All but one of the patients were anemic and were in a program of intermittent hemodialysis. The degree of anemia could not be correlated with the RE marrow scan.

DISCUSSION

Anger produced the first RE marrow scan in a rabbit using colloidal ^{198}Au in 1953 (*1*). Since that time various techniques have been proposed for scanning the bone marrow. In 1958 Engstedt and coworkers, also using colloidal ^{198}Au, described the normal pattern of distribution of RE marrow activity as well as the patterns seen in polycythemia vera, myelofibrosis, chronic hemolytic anemia, and metastatic cancer (*2,3*). They also found that the RE activity on scans corresponded to areas of active hematopoiesis as demonstrated by bone marrow biopsies from various parts of the body.

With ^{52}Fe and ^{99m}Tc-sulfur colloid, Van Dyke and coworkers obtained both RE and erythropoietic scans in the same patient and found similar patterns of distribution of the two scanning agents in most patients (*4*). However, some patients have had RE and erythropoietic scans that did not correspond to

FIG. 5. Peripheral expansion of marrow (elbow).

FIG. 6. Focal defect in sacroiliac area (arrows).

each other. This discrepancy has been seen in diseases that affect the hemopoietic or erythropoietic marrow but spare the stroma and reticulum, e.g., aplastic anemia and pure red-cell aplasia.

More recently, RE scanning has been used to detect abnormalities in the bone marrow in Paget's disease (*5*) and to detect marrow infarcts in sickle cell anemia (*6,7*). Iron-52 has been used to show expansion of the erythropoietic marrow in five patients with megaloblastic anemia and extramedullary hematopoiesis in the spleen in one patient (*8*). Subramanian, et al have proposed the use of ^{99m}Tc-stannous phytate for RE scanning (*9*), and ^{111}In has been used as a substitute for ^{52}Fe in scanning the erythropoietic marrow (*10–12*).

In the present study, patients with erythroid hyperplasia (hemolytic or hemorrhagic anemias, polycythemia) had increased and expanded RE marrow activity. In comparison, patients with replacement of marrow with neoplastic cells (leukemia, carcinoma, myelofibrosis) or functional impairment of the marrow (uremia) had decreased RE marrow activity.

The RE scan pattern has been considered to represent the anatomic distribution of reticuloenthelial tissue, if not the hematopoietic tissue. Replacement of marrow tissue by tumor cells, leukemia, or myelofibrosis results in the expected decrease in RE activity on scans. However, decreased RE activity on scanning caused by a functional impairment of RE tissue has not been documented previously. The patients with severe uremia reported herein may well be the first example of decreased RE activity with normal marrow distribution. The pattern of RE activity in patients with uremia may have no relevance to the anatomic distribution of RE tissue in this disease. The presence of uremia should therefore be taken into consideration in the interpretation of any RE scan.

RE marrow scans were not of value in staging lymphomas unless focal defects were found. The fact that the phagocytic function of the RE system is increased in patients with Hodgkin's disease (*13*) may account for the increased central marrow activity in four of the seven patients in this series, and for the peripheral expansion in six of the seven.

Focal defects on RE marrow scans were found in patients with myelophthisic anemia, lymphoma, and localized myeloma. Patients with localized myeloma and focal defects on marrow scans had normal skeletal x-rays. This suggests that the RE marrow scan may be a more sensitive test than the skeletal x-ray. Focal defects in the liver or spleen were found in some patients with lymphoma.

Radiation or chemotherapy may have caused a decrease in RE marrow activity in some patients with lymphomas or multiple myeloma (*14*). However, this problem did not exist with the patients with leukemia or with other disorders because treatment with irradiation or cytotoxic drugs did not occur prior to RE scanning. Furthermore, in the patients with lymphomas, no correlation could be made between the use of chemotherapy and the RE scan pattern.

TABLE 1. PATTERNS OF RETICULOENDOTHELIAL ACTIVITY

Clinical examples†	Central marrow	Peripheral expansion	Hepatosplenomegaly
Healthy subject Aplastic anemia (2)	Normal	Absent	Absent
Hemorrhagic anemia (1) Sickle cell anemia (1)* Resolving megaloblastic anemia (1)	Increased	Present	Absent
Polycythemia vera (2)	Increased	Present	++
Acute leukemia (5)	Decreased	Absent	+
Chronic leukemia (3) Myelofibrosis (2) Myelophthisic anemia (4)*	Decreased	Present	++
Multiple myeloma (6)* Uremia (BUN > 70 mg%) (6)	Decreased	Absent	±
Hodgkin's disease (7)*	Variable	±	++
Lymphosarcoma (6)*	Variable	±	++
Reticulum cell sarcoma (4)*	Variable	±	±

* Focal defects on marrow scan may be present.
† Numbers in parentheses indicate number of patients studied.

Table 1 represents an attempt to identify patterns of RE activity in various disorders. It is recognized that there is overlap and individual variation in each class of disease. However, it appears useful to identify certain patterns that are most characteristic of each disease. It is hoped that this classification will be expanded when more disorders involving the marrow, directly or indirectly, have been studied.

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