Scintigraphic Findings in Gaucher's Disease

Ora Israel, Jacqueline Jerushalmi, and Dov Front

Department of Nuclear Medicine, Rambam Medical Center; and Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel

Gaucher's disease involves the liver, the spleen, and the bone. Liver-spleen and bone scintigraphy were used during an 8-yr period to evaluate changes caused by this disease. Patients were investigated with a liver-spleen scan for abdominal pain, mechanical discomfort, enlarged liver or spleen on physical examination, abdominal mass, abnormal liver function tests, and symptoms of hypersplenism. Fourteen liver-spleen scans were performed in nine patients. Liver scintigraphy showed various degrees of enlargement and inhomogenous uptake. In two patients focal defects were detected. In one, focal defects were due to liver involvement with Gaucher's disease, but in the other they were caused by metastatic pancreatic carcinoma. The study was also useful in detecting splenic infarction and in following enlargement of the spleen after partial splenectomy. The main indication for bone scintigraphy in six patients was bone pain. This was found to be caused by either aseptic necrosis of the head of the femur, bone infarction, pathological fractures, or osteomyelitis. Loosening after total hip replacement was ruled out in three patients and missed in one patient. Scintigraphy appears to be a simple, sensitive test for evaluation of the liver, spleen, and bony skeleton in patients with symptomatic Gaucher's disease.

J Nucl Med 27:1557–1563, 1986

Gaucher's disease is a hereditary lysosomal storage disease which involves the reticuloendothelial system (*1–3*). There is a paucity of publications (*4–8*) concerning scintigraphic findings in this disease which causes changes in the liver, spleen, and bone, and the role of scintigraphy is not well defined. Our experience with scintigraphy of patients suffering from Gaucher's disease, accumulated over a period of 8 years, is reported in the present communication.

PATIENTS AND METHODS

Fourteen patients with histologically proven Type I Gaucher's disease were evaluated in our department during the period from 1976–1984 for changes in the liver, spleen, and bone caused by the disease. All patients were Jews of Ashkenazi origin. Only one patient had both liver and bone evaluation. Scintigraphy was performed using a small field or digital large field-of-view camera* and scintigraphic findings were correlated with clinical, radiologic, and surgical results.

Liver-Spleen Evaluation

Nine patients underwent 14 liver-spleen scans after an i.v. injection of 3 mCi of technetium-99m (^{99m}Tc) phytate, or, in the case of two children, the administered dose was adjusted to weight. Patients were referred for evaluation of enlargement of liver and spleen, newly developed ascites, sudden onset of abdominal pain, evaluation of abdominal mass, and follow-up of spleen size after partial splenectomy.

Bone Evaluation

Six patients underwent 20 bone scans. They were performed after the i.v. injection of 20 mCi of [^{99m}Tc] methylene disphophonate (MDP). Patients had bone scintigraphy for repeated episodes of diffuse or localized bone or joint pain. In one patient a gallium scan was also performed due to suspicion of osteomyelitis in a region of closed fracture. This study was repeated 6 mo later. Four patients with total hip replacement were investigated for pain, possibly caused by loosening of the prosthesis.

RESULTS

The average age of patients with liver involvement was 31 yr (range 10–60 yr), and with bone involvement 37 yr (range 15–70 yr). Patients with liver and spleen involvement first presented with abdominal discomfort and patients with skeletal involvement first presented with bone pain.

The results of liver scintigraphy are summarized in Table 1. The liver was enlarged in eight patients (Table

Received May 2, 1985; revision accepted Mar. 31, 1986.

For reprints contact: Dov Front, MD, PhD, Dept. of Nuclear Medicine, Rambam Medical Center, Haifa 35254, Israel.

TABLE 1
Liver Scan Findings in Gaucher's Disease

Patient no.	Age (yr), sex	Time after diagnosis of Gaucher's (yr)	Clinical findings	Scintigraphy	Diagnosis
1	35, F	22	Hepatomegaly and ascites; abnormal liver function	Hepatomegaly, inhomogeneous uptake of colloid	Liver involvement by Gaucher's disease
2	60, F	Diagnosed after liver scan	No known Gaucher's disease; clinical suspicion of hepatomegaly on routine checkup; normal LFT	Riedel's lobe; splenomegaly, shift to spleen	Gaucher's cells in liver
3	50, F	13	Anemia, leucopenia, thrombocytopenia, patient investigated for size of spleen	Normal spleen; enlarged liver	No hypersplenism; scan indicated normal size of spleen
4	47, M	10	Ascites; suspected enlargement of liver; abnormal liver function tests	Enlarged liver with focal defects	Adenocarcinoma of pancreas with liver metastases; focal defects here due to pancreas carcinoma and not liver involvement with Gaucher's disease
5	30, F	27	Mass in upper abdomen, abnormal liver function tests	Enlarged liver with focal defects	Gaucher's disease of liver caused focal defects
6	11, M	9	Partial splenectomy due to anemia and thrombocytopenia; hepatomegaly	5 mo postsurgery, size of spleen 11 cm; enlarged liver	State after splenectomy with slightly enlarged spleen
7	10, F	4	Enlarged spleen after partial splenectomy; enlarged liver	Enlarged spleen, shift; after surgery (span = 14 cm); enlarged liver	Recurrence of spleen enlargement after surgery
8	14, F	8	State after splenectomy for anemia, leucopenia, and thrombocytopenia	7 days postsurgery, span = 10 cm; enlarged liver with inhomogeneous uptake; 6 mo postsurgery, span = 12 cm; 1 yr postsurgery span = 13 cm	Follow-up showed mild enlargement of spleen
9	17, F	6	Abdominal pain; enlarged spleen and liver; anemia, leucopenia; abnormal liver function tests	Enlarged spleen with focal defects; enlarged liver with inhomogeneous uptake of colloid	Enlarged spleen with infarction; enlarged liver

1, Patients 1,3–9). The distribution pattern of the radiocolloid was inhomogeneous in four patients (Fig. 1). Two patients had focal defects on their scan (Patients 4 and 5). One patient was in a state of advanced stage of Gaucher's disease which was diagnosed 27 yr previously. In the other patient, adenocarcinoma of the pancreas was eventually diagnosed and the focal defects proved to be metastatic.

Enlargement of the spleen was present in four patients and it was associated with increased colloid uptake ("shift") in Patients 2 and 7. One patient (Patient 9) showed triangular focal defects in his spleen which on histology was found to be involved with Gaucher's disease and multiple infarctions. In three patients (Patients 6–8) after splenectomy, follow-up scintigraphy was of great value in detecting recurrence of splenic enlargement (Fig. 2).

The results of bone scintigraphy are summarized in

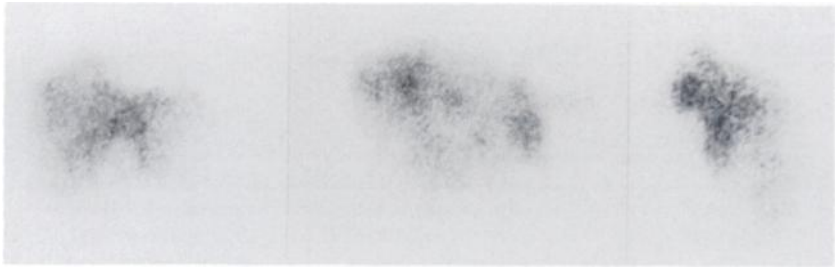

FIGURE 1
Inhomogenous uptake of colloid in large liver (Table 1, Patient 1)

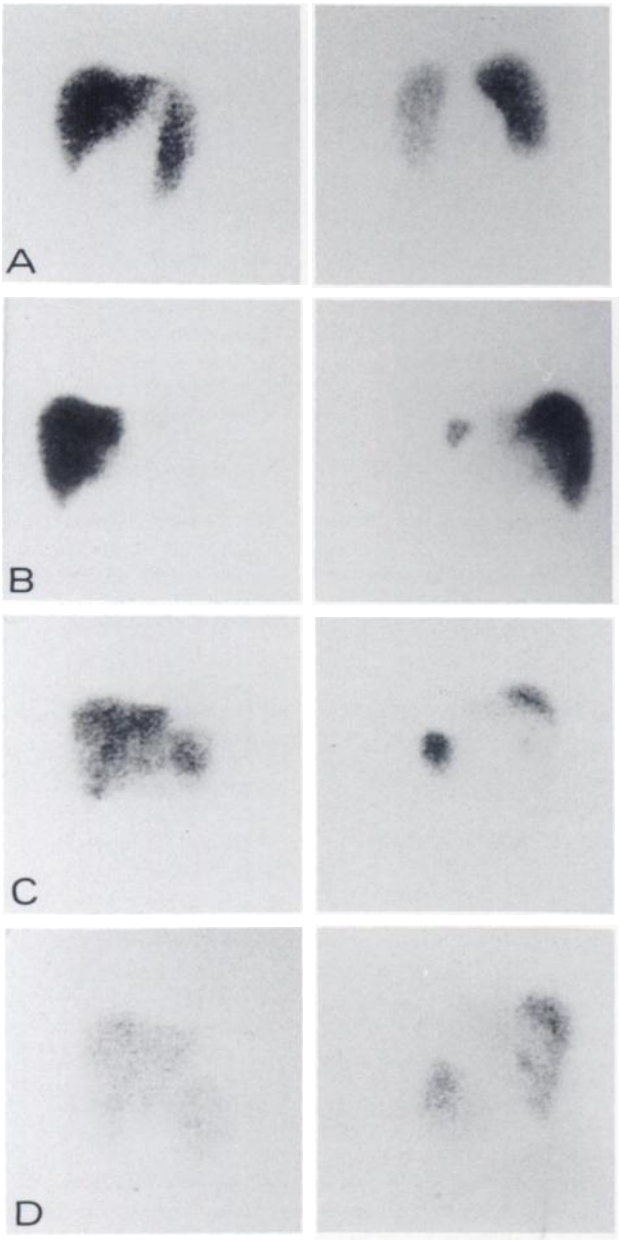

FIGURE 2
Followup of enlargement of spleen after partial splenectomy (Table 1, Patient 8). A: Preoperative scintigraphy showing enlargement of spleen. B: Scintigraphy after partial splenectomy. C and D: Enlargement of spleen on follow-up scintigraphy

Table 2. In four patients (Table 2, Patients 1,3–5) scintigraphy showed decreased uptake in the femoral head with increased uptake in repeat scans (Fig. 3). Aseptic necrosis and collapse of the femoral head were subsequently diagnosed by x-ray and confirmed by surgery.

Areas of increased uptake in the femoral shaft associated with sudden onset of pain were observed in two patients (Patients 4,5). In subsequent followup scintigraphy the findings disappeared and a photopenic area was observed in the shaft (Fig. 3). The clinical findings and followup radiological features confirmed the scintigraphic diagnosis of bone infarction.

In two patients (Patients 1,2) pathological features seen on x-ray appeared as persistent regions of increased uptake. In one of them (Patient 2) there were symptoms of infection. Gallium-67 (^{67}Ga) scintigraphy showed markedly increased accumulation of the radionuclide in the region. Osteomyelitis was confirmed by histology. The patient responded to treatment and the abnormal gallium uptake disappeared. Deformation of the distal epiphysis of the long bone in the lower limb—the "Erlenmeyer flask pattern"—was seen in four patients (Patients 1–3,5) (Fig. 3). Scintigraphy revealed scoliosis due to collapse of vertebral bodies in Patients 5 and 6.

Four patients (Patients 1–4) who were referred for bone pain after total hip replacement had negative findings for loosening of the prosthesis. In one patient (Patient 2) loosening of the acetabular component was found. In the other three, pain was due to causes other than loosening.

DISCUSSION

There are only a few reports on the scintigraphic findings in Gaucher's disease (*4–8*). Cheng et al. (*4*) described in detail the scintigraphic findings in three patients and in the other reports scintigraphy is only referred to in a general manner.

Our experience in 14 patients with involvement of the liver, the spleen, and the bone indicates that scintigraphy is useful in evaluating some of the clinical manifestations of Gaucher's disease. This disease is an inborn error of metabolism with autosomal recessive inheritance, due to a primary enzymatic deficiency in

TABLE 2
Bone Scan Findings in Gaucher's Disease

Patient no.	Age (yr), sex	Time after diagnosis of Gaucher's (yr)	Clinical findings	Scintigraphy	Diagnosis
1	70, F	Unrecorded (disease for many years)	Pain right hip	Abnormal uptake in head of right femur; "Erlenmeyer flask" sign	Avascular necrosis and collapse head right femur caused bone pain
			Pain left humerus	Increased uptake shaft of left humerus	Gaucher's changes in bone; fracture left humerus
			Total right hip replacement; pain right hip	No abnormal uptake in right hip to indicate loosening or infection	No abnormality left hip
2	28, F	21	Bilateral total hip replacement; pain right hip	No evidence for loosening; "Erlenmeyer flask" sign both femoral shafts	Loosening of acetabular component right prosthesis—false negative
			Recurrent pain 6 mo postsurgery for loosening right hip	No evidence for loosening	Radiological and clinical follow-up negative for loosening—true negative
			Trauma; closed fracture and signs of infection left femur; x-ray showed only a fracture	Uptake of both [^{99m}Tc] MDP and ^{67}Ga; negative ^{67}Ga after treatment	Fracture and infection left femur. True-positive, gallium scintigraphy. True-negative ^{67}Ga after treatment
3	34, F	26	Pain left hip	Increased uptake left femoral head	Avascular necrosis left femoral head diagnosed on operation for hip replacement
			Pain left knee; pain right hip	"Erlenmeyer flask" sign of left femur; increased uptake right femoral head	Avascular necrosis right femoral head
			Pain left hip, suspected loosening	No evidence for loosening	No evidence for loosening in 12-mo follow-up
4	18, F	Since childhood	Pain right hip	Decreased uptake right femoral head	Avascular necrosis of right femoral head
			Pain right hip, suspected loosening; pain left knee; pain left hip	No evidence for loosening; increased uptake distal left femur; increased uptake left femoral head	Follow-up—no loosening Avascular necrosis left femoral head

(continued)

TABLE 2—*continued*

Patient no.	Age (yr), sex	Time after diagnosis of Gaucher's (yr)	Clinical findings	Scintigraphy	Diagnosis
5	15, F	9	Pain right hip	Decreased uptake right femoral head; "Erlenmeyer flask" left femur	Avascular necrosis right femoral head
			Pain left hip and right femoral shaft	Uptake right femoral head; decreased uptake left femoral head; increased uptake surrounding a photopenic area in right femoral shaft; scoliosis	Aseptic necrosis left femoral head; bone infarction right femoral shaft; scoliosis
6	58, F	8	Back pain	Collapsed vertebraes and scoliosis	Scoliosis

glucocerebrosidase. This causes defective degradation of glucocerebrosides and their storage in large reticuloendothelial (Gaucher) cells. These cells massively infiltrate the liver, spleen, bone marrow, and other organs containing reticuloendothelial system.

Three variants have been described with different pathological and clinical features correlating with various levels of residual tissue glucocerebrosides in the body (*2,3*). Type II and III, acute and subacute neuropathic forms (known also as infantile and juvenile types), involve the central nervous system of newborns and young children. They have a rapidly progressive course resulting in death in a number of years (*3*). Type I, chronic, nonneuropathic, or "adult" Gaucher's disease, affects children or adults and has a slowly progressive course and a wide variety of clinical features.

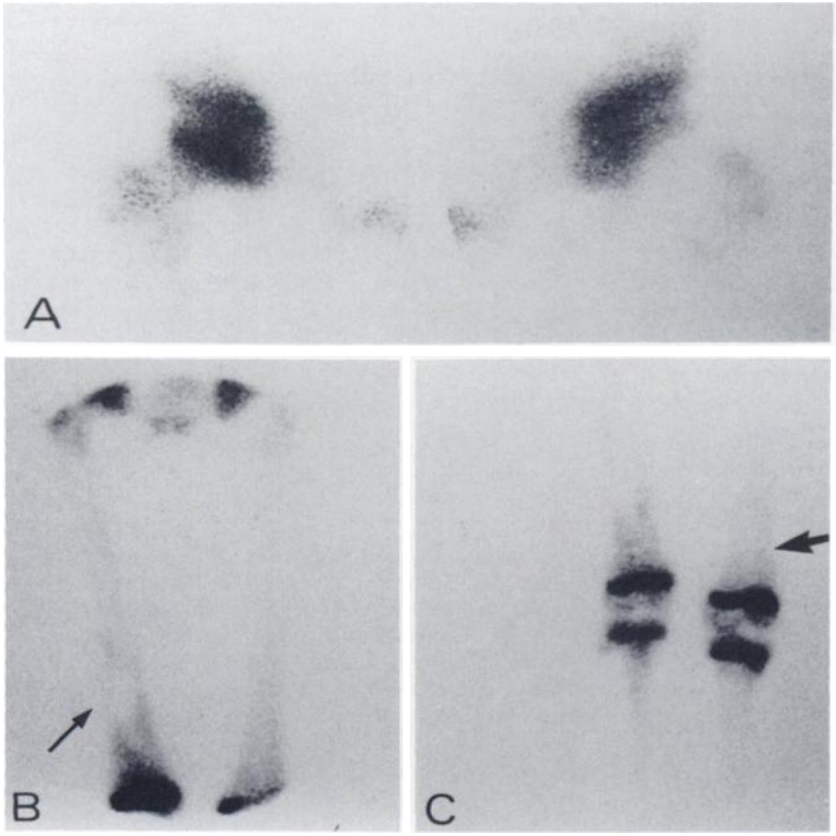

FIGURE 3
Avascular necrosis of head of both femurs. Bone infarction, left femoral shaft (Table 2, Patient 5). A: Bone scintigraphy of pelvis showing increased uptake in head of right femur and decreased uptake in head of left femur. B: Scintigraphy of femurs showing increased uptake in distal part of right femur and photon deficient area (arrow). C: "Erlenmeyer flask" pattern, left pattern, left distal femur (wide arrow)

Patients with juvenile and adult type Gaucher's disease may be observed within members of the same family. The disease is ~30 times more frequent in Ashkenazi Jews with an incidence of 1:2,500 (*9*). All our 14 patients belonged to this ethnic group.

Replacement of Kupfer cells produce hepatomegaly and can lead in advanced, long-standing cases, to hepatic failure. James et al. (*5*), although not describing their scintigraphic findings in detail, found a uniform pattern of hepatomegaly and inhomogenous uptake of colloid. Cheng et al. (*4*) found in three patients various degrees of liver involvement on scintigraphy. The findings in the nine patients in our series showed a whole spectrum of changes in the liver. Findings varied from slight enlargement and inhomogeneity to markedly enlarged liver with frank focal defect and this could be correlated to the severity or course time of disease (Table 1). Focal defects due to liver involvement with Gaucher's disease should not be confused with metastatic disease as shown in Patient 4 (Table 1) who had both Gaucher's disease and metastatic pancreatic carcinoma.

Involvement of splenic tissue produces enlargement and symptoms of hypersplenism and in cases of massive splenomegaly, mechanical pressure and infarctions. Splenic enlargement is common and tends to recur after partial splenectomy. This is used as a compromise technique to resolve the hematologic and mechanical complications due to splenomegaly and hypersplenism, and to preserve the immunological properties of the spleen (*6*). Scintigraphy enables initial assessment and postoperative follow-up. Recurrences are common and splenic size should be assessed when symptoms of hypersplenism reappear (Patient 8, Table 1, Fig. 2). Left upper quadrant pain may be caused by splenic infarction as shown in Patient 9 (Table 1). Splenic uptake may be increased compared to the liver and is related to the degree of tissue replacement by Gaucher's cells in the liver.

Replacement of bone marrow with Gaucher cells may partly explain the hematologic features of the disease. Infiltration of the marrow can result in bone destruction and fracture. Increased intramedullary pressure interferes with the blood supply to the bone resulting in infarction and aseptic necrosis (*3*). These pathologic conditions can all cause bone pain which is a common symptom in Gaucher's patients (*10,11*). Scintigraphy is a sensitive method for early diagnosis of bone involvement by Gaucher's disease. Dynamic changes in bone structure due to avascular necrosis, infarction, or bone marrow expansion (Erlenmeyer flask) can be seen on scintigraphy (*12*). Diagnosis of osteomyelitis may be especially difficult due to the great variety of bone abnormalities. A case has been reported in which scanning with [^{99m}Tc]MDP followed by ^{67}Ga excluded the diagnosis of osteomyelitis (*8*). In Patient 2, Table 2, ^{67}Ga scintigraphy enabled us to establish the diagnosis of osteomyelitis and to monitor the response to treatment.

Due to compromise of blood supply to the head of the femur, aseptic necrosis may occur and is treated by total hip replacement. Since bone pain is common in Gaucher's disease it is not possible to determine clinically whether after surgery it is caused by loosening or due to symptoms of the primary disease. In a study of the orthopedic complications in Gaucher's disease, Goldblatt et al. (*10*) found good results of hip replacement. Other authors report less encouraging results (*11*).

In the cases presented here loosening was excluded in four devices in three patients, while in one patient loosening of the acetabular component was missed on scintigraphy. Four devices were well tolerated and pain was not due to any orthopedic complications in these cases.

In Matoth's series (*1*) describing Gaucher's disease in Israel, 15 out of 34 patients had involvement of liver, spleen, and bone. Liver and bone involvement are not considered different manifestations of the disease; however, in our patient population, only one patient was investigated for involvement of both liver, spleen, and bone.

In conclusion, our experience in 14 patients shows that Gaucher's disease often involves the liver, spleen, and skeleton and that a variety of changes in these organs can be detected by scintigraphy.

FOOTNOTE

*Elscint Dymax and Apex 415, Haifa, Israel.

ACKNOWLEDGMENTS

The authors thank Gerald M. Kolodny of the Division of Nuclear Medicine, Beth Israel Hospital, Boston, for his review of the manuscript, and to Phyllis Hiller and Ruth Rose for their secretarial assistance.

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