SCINTIGRAPHIC VISUALIZATION OF ABDOMINAL LYMPH NODES WITH ^{99m}Tc-PERTECHNETATE-LABELED SULFUR COLLOID

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Methods for determining whether para-aortic and pelvic lymph nodes are involved by lymphomas have been valuable in establishing the extent of disease and in planning treatment. These methods have included excretory urography, inferior vena cavagrams, and lymphangiography. This is a preliminary report of a new scintigraphic technique which seems to offer promise in the evaluation of such patients; it is relatively rapid, well-tolerated by patients, and appears to have no significant risk.

MATERIALS AND METHODS

Technetium-99m-pertechnetate was obtained by elution from a commercially available generator resin containing ^{99}Mo. Sulfur colloid was prepared from a commercially available kit (Tesuloid from Squibb) containing, in a sterile, nonpyrogenic solution, a mixture of sodium thiosulfate, gelatin, potassium phosphate, and hydrochloric acid. The ^{99m}Tc-pertechnetate was added to this solution, and the mixture was then heated at 100°C for 12 min. This resulted in the formation of a colloidal suspension with uniform particles about 0.3 micron in diam. The ^{99m}Tc-colloid so formed was drawn into two syringes in volumes sufficient to contain 500–1,000 μCi of ^{99m}Tc per syringe. Hyaluronidase, 75 mg in 0.5 ml of sterile water, and lidocaine, 0.5 ml of 2% solution, also were drawn into each syringe. The final volume in each syringe was 1.5–2 ml. The medial two interdigital webs of each foot were infiltrated with 0.25 ml of 2% lidocaine and then each of these four interdigital webs was injected with half the contents (0.7–1 ml) of a syringe containing the ^{99m}Tc-colloid-lidocaine-hyaluronidase mixture. The patient was instructed to walk about as much as possible for the next 1 hr and to return to the laboratory in 2 hr.

The scintigraphic image was made with a Nuclear-Chicago Pho/Gamma III scintillation camera with a multihole, 1.75-in.-thick, low-energy collimator (Model 821742). Occasionally, a pinhole collimator (Model 820728) was used in an attempt to resolve confluent masses. Pictures were taken over the lower abdomen and inguinal area with a 100-sec exposure and over the upper abdomen and epigastrium with 100-, 300-, or 500-sec exposures.

The patients studied constituted four distinct groups. In Group 1 were five patients in whom the presence of malignant lymphoma was suspected but who subsequently were found to have other disorders which were unlikely to affect abdominal lymph nodes. Two of these patients had nasopharyngeal lymphoepitheliomas, two had refractory anemia unassociated with malignancy, and one had a primary neurologic disorder. In Group 2 were 16 patients with proven malignant lymphoma in whom involvement of abdominal lymph nodes was regarded as improbable on the basis of findings at laparotomy or lymphangiography. In Group 3 were eight patients with malignant lymphoma with known involvement of abdominal lymph nodes on the basis of lymphangiographic studies. Group 4 consisted of two patients with known malignant lymphoma for whom interpretations of lymphangiograms were equivocal.

Scintigrams obtained from patients of Groups 1 and 2 were used to establish criteria for normality. Criteria for abnormality were based on a review of scintigrams obtained in Group 3. The reliability of these criteria was then tested by submission of the scintigrams to five observers who had not previously reviewed the scintigrams and who had no information as to the patient's clinical status or results of lymphangiography or other studies. These observers were briefly instructed in the techniques used and the criteria proposed and then were given the scintigrams to interpret.

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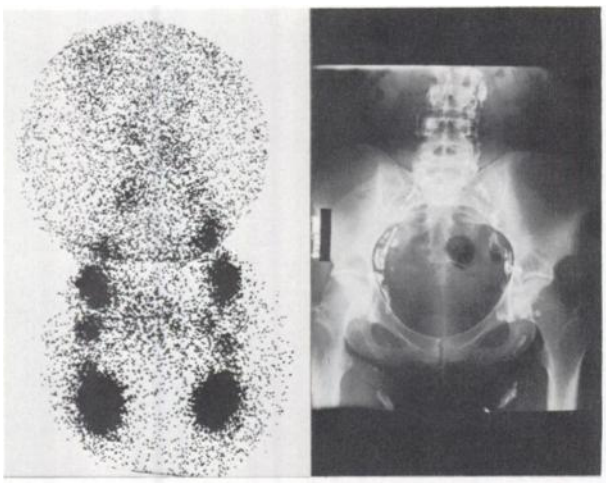

FIG. 1. Left: normal lymph node scintigram with visualization of nodes to level of second lumbar vertebra. There is equal activity on both sides. Activity diminishes progressively cephalad. Exposure was 500 sec for upper part and 145 sec for lower. Patient was 27-year-old woman with clinical Stage 1 nodular sclerosing Hodgkin's disease involving mediastinum. All observers interpreted this as normal scintigram. Right: lymphangiogram of same patient. Upper para-aortic nodes appear equivocally involved. Laparotomy disclosed slight lymph node hyperplasia in this area, which was found histologically to be inflammatory in nature.

RESULTS

Normal scintigram. In the control subjects (Groups 1 and 2), the inguinal nodes invariably produced the dominant images (Fig. 1). These nodes usually were round and contained equal radioactivity. However, in several of the control patients the nodes were oval or irregular in shape. The prominence of the inguinal nodes may be due in part to the fact that they are the first to trap the labeled colloid (popliteal nodes were never visualized) and in part to their superficial location (absorption, by overlying tissue, of radiation emanating from these nodes would be less than for deeper nodes). The diameter or intensity of the flare in the inguinal area bore no apparent relationship to size of the nodes. Even nodes which were not palpable produced an image approximately 3 cm in diam. Above the inguinal area, the lymph node images usually became progressively less intense. By laying the lymphangiogram over the scintigram, the extent of visualization of lymph nodes was readily ascertained. Although in some instances there was visualization of nodes as high as the L-2 or L-3 vertebral level, more commonly the nodes above the external iliac group showed very faint uptake of ^{99m}Tc-colloid. This was particularly true with an exposure time of 100 sec. Therefore, as a routine, exposures at 500 sec also were obtained over the upper abdominal area. Scintigrams obtained later than 2 hr after injection did not provide better lymph node images than those at 2 hr. Furthermore, if exposures were made more than 3 hr after injection, there was uptake of ^{99m}Tc-colloid by epithelial surfaces of the bowel and bladder.

Abnormal scintigram. In patients with involvement of retroperitoneal lymph nodes, the pattern was different from that in the control group. Contrary to

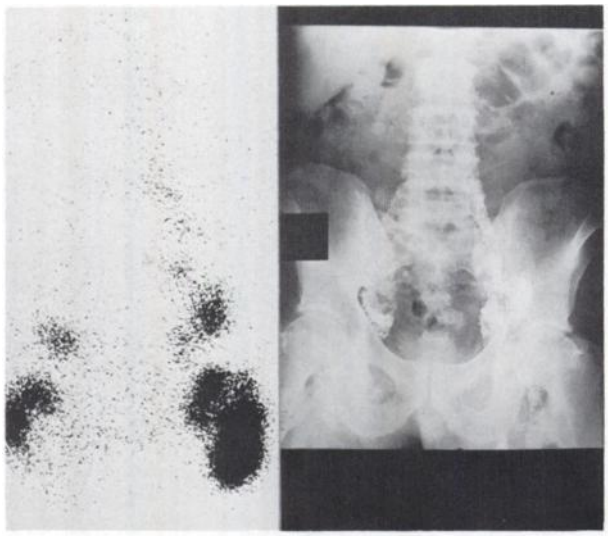

FIG. 2. Left: abnormal scintigram from 49-year-old man with Hodgkin's disease. Biopsy of enlarged left inguinal node had been interpreted as showing benign inflammation. Scintigram disclosed marked enhancement in activity in left inguinal area compared with right and substantially less activity on right as high as para-aortic area. Exposure was 500 sec for upper part and 135 sec for lower. Right: lymphangiogram of same patient shows such extensive bilateral involvement of inguinal, iliac, and lower para-aortic nodes that lymphatic obstruction is present with medium still in lymphatic vessels on this delayed film. Nodes are enlarged with radiolucent filling defects because of disease.

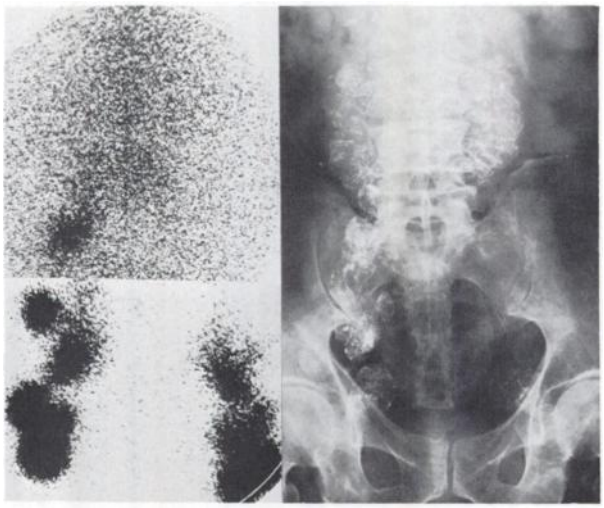

FIG. 3. Left: abnormal scintigram from 68-year-old man with chronic lymphocytic leukemia. Inguinal and external iliac nodes show markedly enhanced activity and appear to be nearly confluent. There appears to be broad, marked, filling defect in iliolumbar area on left. Broad, diffuse zone of increased activity is seen in left para-aortic area. Exposure was 300 sec for upper part and 100 sec for lower. Right: lymphangiogram of same patient shows massive involvement of right iliac and para-aortic nodes bilaterally, with nodes grossly enlarged and filled with radiolucent defects. These findings are consistent with involvement by leukemia. Left iliac nodes are not as well seen as on scintigram.

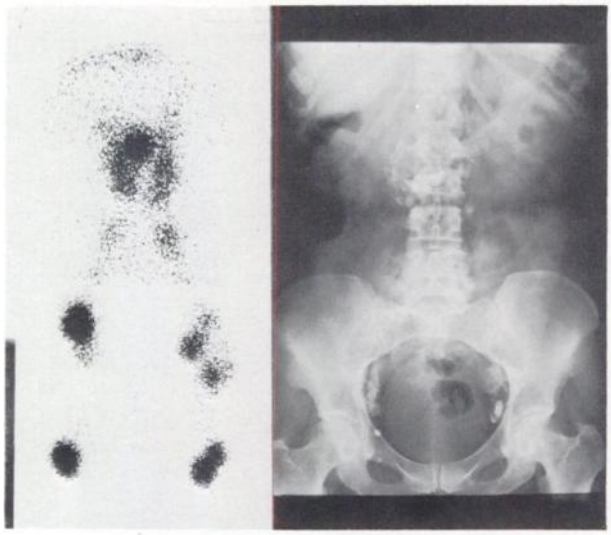

FIG. 4. Left: abnormal scintigram showing cluster of left external iliac nodes and apparently confluent mass at level of L-2 and L-3 vertebrae, which exhibited unusually high activity. Exposure was 328 sec for upper part and 89 sec for lower. Patient was 58-year-old woman with mixed cellularity Hodgkin's disease, clinical Stage IIB. Right: lymphangiogram of same patient, showing enlarged iliac and upper para-aortic lymph nodes, especially on right, containing radiolucent defects consistent with extensive involvement by Hodgkin's disease.

our expectation, lymphomatous involvement of nodes often resulted in marked enhancement of uptake of ^{99m}Tc-colloid. Confluent masses and asymmetrically prominent nodes also were seen in these patients (Fig. 2). Occasionally, apparently confluent, rope-like masses were seen extending cephalad from the inguinal area.

In some instances, there was a marked decrease in activity in an area of extensive lymphomatous infiltration. In two cases there was a diffuse pattern of activity over a large area, which corresponded to a large mass on the lymphangiogram. Thus three scintigraphic patterns were seen to be characteristic of lymphomatous disease of the retroperitoneal lymph nodes:

1. Marked difference in activity between the two sides as a result of either enhanced or diminished uptake of ^{99m}Tc-colloid (Figs. 2 and 3).
2. Prominent, broad pattern of increased activity in para-aortic area (Figs. 2 and 4).
3. Linear confluence of nodes, resembling a rope, without clear demarcation as distinct nodes or cluster of nodes (Figs. 5 and 6).

Certain apparently confluent node masses could be resolved by use of the pinhole collimator (Fig. 7). Because of the apparent magnification of nodes as a consequence of radiation scatter, we have not based criteria on size of lymph nodes.

Evaluation by independent observers. The correlation between radiologists' interpretations of lymphangiograms and interpretations of corresponding scintigrams is given in Table 1.

DISCUSSION

Lymphangiography of abdominal lymph nodes has aided in the evaluation of para-aortic and retroperitoneal nodes which cannot be evaluated by palpation or by other roentgenographic methods (*1–4*). For example, it has been shown (*2*) that, of patients thought to have Stage I disease above the diaphragm on the basis of physical examination, 35% have lymphangiographically demonstrable involvement of subdiaphragmatic para-aortic nodes and therefore have Stage III. On the other hand, lymphangiography has its limitations (Table 2). Although the complications listed as "adverse effects" of lymphangiography may be very serious (*5–7*), they are infrequent except in patients with chronic pulmonary disease.

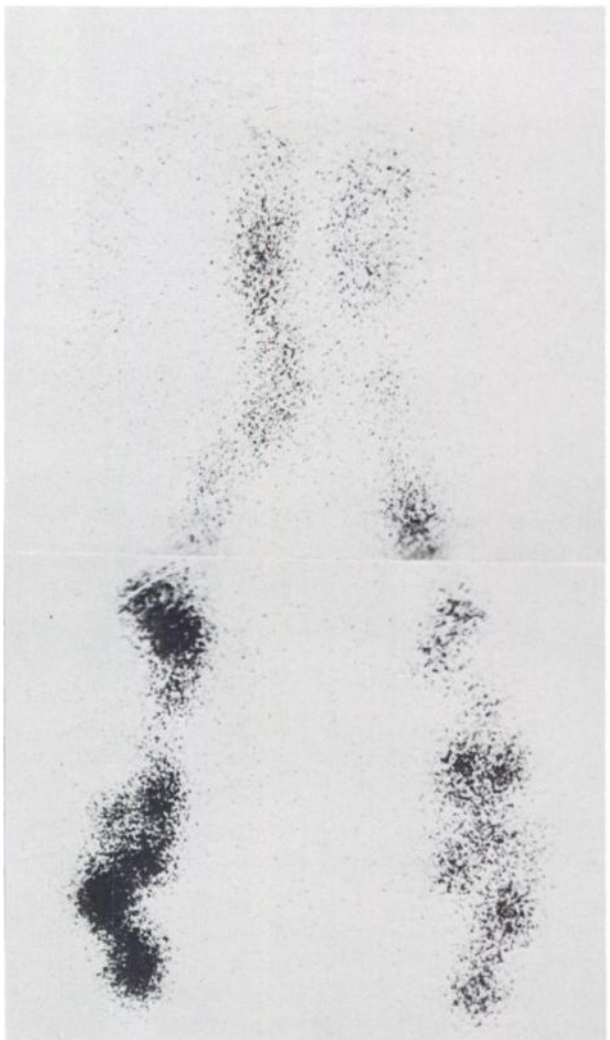

FIG. 5. Abnormal scintigram from 69-year-old man with Hodgkin's disease, clinical Stage IIA. Lymph nodes show increased activity in confluent pattern extending from inguinal to para-aortic areas. Although pattern is similar on each side, uptake is relatively greater on right. Exposure was 500 sec for upper part and 300 sec for lower. Extensive involvement of these nodes was confirmed by findings at laparotomy.

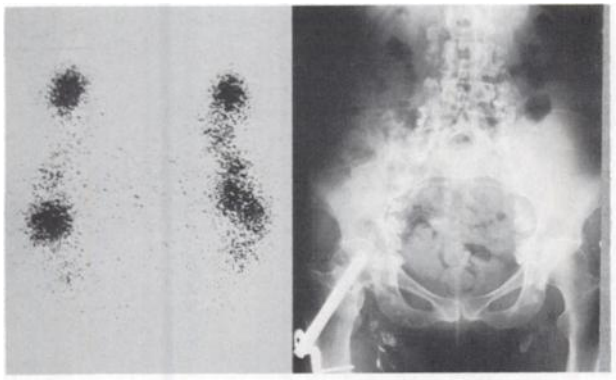

FIG. 6. Left: Abnormal scintigram from 69-year-old man with lymphosarcoma. Rope-like appearance of right inguinal to external iliac nodes was regarded as indicative of lymphoma. No nodes were visualized above external iliac level. Only scintigram obtained over lower abdomen is shown; exposure was 100 sec. Right: lymphangiogram of same patient, showing extensive filling of iliac and para-aortic lymph nodes up to L-2 level with all nodes enlarged and with filling defects due to extensive involvement by Hodgkin's disease. Para-aortic node involvement is striking on lymphangiogram but was not visualized on scintigram.

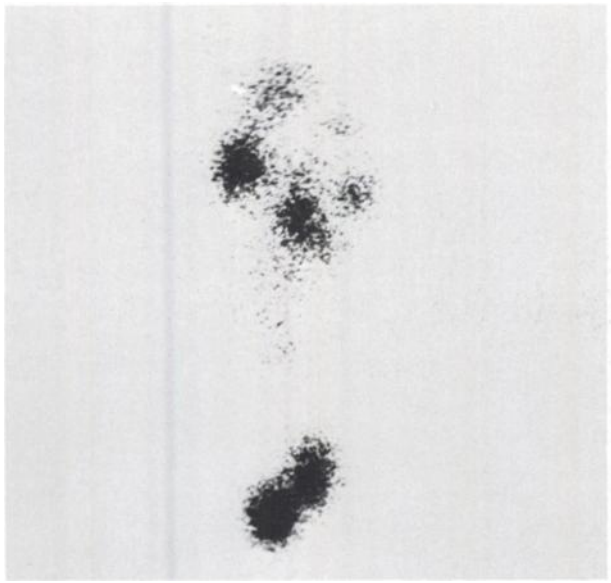

FIG. 7. Same case as Fig. 4, showing effect of pinhole collimator in resolving apparent left external iliac mass into several discrete nodes.

The advantages which lymph node scintigraphy might offer are (A) it appears to be entirely innocuous, (B) it requires little time on the part of personnel and physician and only a brief commitment of physical facilities, and (C) the study may be completed in a few hours, during most of which the patient need not be under supervision.

Reports on the use of colloidal ^{198}Au in the scintigraphic study of cervical and abdominal lymph nodes (*8–13*) indicated favorable results. Breit and coworkers (*13*) reported their experience with lymph node scintigraphy using ^{198}Au in more than 800 patients, including 337 with carcinoma of uterus, ovary, or testis, and 168 with malignant lymphoma. Using criteria similar to those reported here, they compared concomitant lymphangiography and scintigraphy of retroperitoneal nodes in 193 patients (111 with lymphoma). Results with the two methods agreed in 167 (86.5%). Hauser and coworkers (*14*) have reported preliminary studies of the use of ^{99m}Tc-colloid for lymph node scintigraphy in experimental animals and in a few patients with lymphoma. No comparison was made with other techniques.

Our limited experience with colloidal ^{198}Au, coupled with review of the experiences of others, has led us to believe that use of either radiocolloid for lymph node scintigraphy gives equivalent results in young patients. Czempiel (*15*) pointed out that colloidal ^{198}Au scintigrams are poor in older persons and in those unable to walk. However, we have not found old age or paraplegia to influence results with the ^{99m}Tc scintigram (provided even passive movements of the feet can be accomplished). These facts and the enormous advantage of ^{99m}Tc-colloid in terms of radiation safety* led us to abandon the use of colloidal ^{198}Au early in the course of the present study.

As can be seen from Table 1, there was, overall, 66% agreement between interpretations of scintigrams and lymphangiograms. These results are less impressive than those of Breit and coworkers (*13*). These differences should be placed in proper perspective. First, the scintigraphic technique is a com-

* A conventional 100-μCi dose of ^{198}Au gives a radiation dose at the site of injection of at least 100 rads [Breit et al (*13*) estimated the local tissue radiation dose from 200 μCi of ^{198}Au as being 1,000 rads] compared with a radiation dose of a fraction of a rad for a 1,000-μCi dose of ^{99m}Tc.

TABLE 1. RESULTS OF INDEPENDENT REVIEWS OF SCINTIGRAMS BY FIVE OBSERVERS

	No. of cases	No. of scintigrams reported as			% of concordant interpretations
		Normal	Abnormal	Equivocal	
Group 2: lymphangiograms reported as normal	16	59	17	4	74
Group 3: lymphangiograms reported as showing lymphomatous involvement of abdominal nodes	8	12	23	5	58
Group 4: lymphangiograms reported as equivocal	4	6	4	10	—

TABLE 2. COMPARISON OF SCINTIGRAM AND LYMPHANGIOGRAM

Aspect	Scintigram	Lymphangiogram
Resolution	Fair	Excellent
Time required (approx.)	Technician, 30 min; physician, 5 min	Nurse, 90 min; physician, 20 min; technician, 10 min
Possible adverse effects	None known	Cellulitis; fever; myalgia; pulmonary embolism; cerebrovascular accident; iodide sensitivity reaction; death rarely
Contraindications	Comatose or uncooperative patient	Iodide sensitivity; pulmonary disease

pletely new development. It is likely that further refinements in techniques, changes in size or character of colloid, and possibly the development of instruments which permit greater resolution will enhance its diagnostic accuracy. Second, in this study there was a bias toward inclusion of patients with minimal disease. Only a few patients with known Stage III disease were included. Most of the patients studied were believed on clinical grounds to have Stage I or Stage II disease, and in most this clinical impression was confirmed. It is in the evaluation of such cases that any technique is likely to be severely tested. The results reported by Breit and coworkers (*13*) appear to have been obtained in a series of patients with more advanced disease than those we have studied (89% of their patients with lymphoma had positive lymphangiograms, compared with 35% in the present study). Third, although we have evaluated the scintigraphic results in terms of the lymphangiographic findings, it has become quite clear that this approach has pitfalls. Only in the past few years has correlation been sought between the results of lymphangiography and findings at laparotomy in patients with lymphomas. These studies have shown a substantial inaccuracy in the results of lymphangiography (*16–18*). For this reason, future evaluations of scintigraphic methods must be based on comparison with findings at laparotomy.

SUMMARY

Scintigraphic study of abdominal lymph nodes may be performed using ^{99m}Tc-labeled sulfur colloid in a technique which appears to be without significant risk, is associated with little patient discomfort, and requires only a small expenditure of time by the patient and the laboratory personnel. A review of preliminary results indicates that the scintigraphic method may be useful for the identification of patients with lymphomatous involvement of retroperitoneal lymph nodes. Good visualization of nodes above the external iliac level is often not achieved whether the nodes are normal or involved with lymphoma. The method does not provide the fine morphologic details obtained in lymphangiographic studies. Both methods appear to have substantial errors of both false-positive and false-negative types. The scintigraphic technique at present appears to have some value in the study of patients with lymphoma or other malignancies involving retroperitoneal lymph nodes.

ACKNOWLEDGMENT

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