
Indium-111-White Blood Cell Scintigraphy in Crohn's Patients with Fistulae and Sinus Tracts

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Method: Indium-111-white blood cell (^{111}In -WBC) images of 17 Crohn's patients with fistulae and sinus tracts were reviewed and correlated with radiographic results ($n = 16$ patients) and surgery ($n = 16$ patients), to characterize the scintigraphic appearance of fistulization and to determine the role of ^{111}In -WBC scintigraphy in this clinical setting. These were compared to 50 consecutive abnormal ^{111}In -WBC studies obtained in Crohn's patients with suspected active disease but no known fistulae or sinus tracts. **Results:** Scintigraphic findings which suggested the presence of fistulae were: (1) the presence of concomitant intestinal and extraintestinal lesions and (2) the absence of luminal activity on delayed images when early images detected bowel activity. The extraintestinal lesions were the drainage site of the fistula ($n = 7$) or an accompanying abscess ($n = 6$). Absence of luminal activity occurred in seven patients with fistulae and in two without fistulae; two patients had a proximal colostomy, two patients had bowel obstruction and five patients had fistulae to the skin ($n = 3$) or between the ileum and distal colon ($n = 2$). The distribution of active bowel disease as assessed scintigraphically was in complete agreement with surgery in 14 of 17 cases (82%) compared to 9 of 15 cases (60%) when correlating radiographic assessment with surgery. All surgically proven abscesses were detected on ^{111}In -WBC images. **Conclusion:** These results indicate that ^{111}In -WBC scintigraphy adds useful information to radiographic studies that is essential for appropriate management of Crohn's patients with fistulae and sinus tracts.

Key Words: intestines; disease fistula; radioactive radionuclide imaging; comparative studies; indium-111-leukocyte; Crohn's disease; gastrointestinal inflammation

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Crohn's disease is characterized by transmural inflammation which may lead to the formation of fistulae and sinus tracts in up to 40% of patients (1-4). Communications most commonly occur between loops of small bowel or the small bowel and large bowel but also between the bowel and the urinary bladder, the vagina, the skin, adja-

cent solid organs, muscles, the mesentery, pelvic bones and the spine (1,3-5). Patients with internal fistulae usually present with nonspecific symptoms of active bowel disease. Patients with fistulae to the genitourinary tract may complain of pneumaturia, fecaluria or fecal vaginal discharge (1,4,6).

Radiologic imaging modalities, particularly barium examinations are commonly obtained in Crohn's patients and may be the first to identify fistulization (4,7,8). Recent studies reported enhanced CT scans and MRI to be useful for the demonstration of fistulae and sinus tracts (9-11).

The role of ^{111}In -white blood cell (WBC) scintigraphy in the assessment of disease activity and disease extent in Crohn's patients has been cited in a large number of publications (12-15). Its role in Crohn's patients with fistulization has not been established. We reviewed ^{111}In -WBC images in 17 Crohn's patients with fistulae and sinus tracts, and correlated them with the radiographic and surgical results in order to characterize the scintigraphic appearance of fistulae and sinus tracts and to determine the role of ^{111}In -WBC scintigraphy in this clinical setting.

PATIENTS AND METHODS

Using the computerized hospital database, 53 Crohn's patients were identified as having been discharged with the diagnosis of fistulae or sinus tracts during the past 5 yr. Seventeen of these patients had an ^{111}In -WBC study while in the hospital. The indication for ^{111}In -WBC scintigraphy was to assess disease activity, disease extent and the presence of abscesses. Indium-111-WBC images were reviewed retrospectively. One patient had two episodes of fistulization and the studies obtained at the different times were reviewed separately for a total of 18 examinations.

Indium-111-WBC images were correlated with radiographic GI studies (upper and lower barium examinations and sinography) which were performed at the time of the fistulae ($n = 16$ patients) and with surgery ($n = 17$ operations in 16 patients). The diagnosis of fistulae and sinus tracts was confirmed at laparotomy except for one patient who was treated conservatively and in whom the diagnosis was made radiographically.

Fifty consecutive abnormal ^{111}In -WBC studies obtained in Crohn's patients with suspected active bowel disease but no known fistulization were reviewed for purposes of comparison. These patients had neither clinical manifestation of an external fistula nor radiographic evidence of fistulization. Since these patients were not operated on, the presence of asymptomatic fistulae

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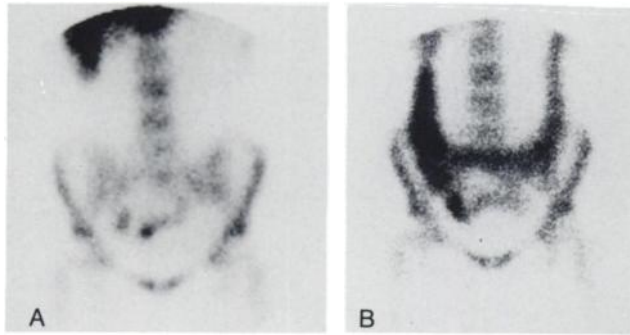


FIGURE 1. Active Crohn's disease. (A) Early image. (B) Delayed image. Early abnormal activity at the distal small bowel and delayed luminal activity throughout the colon.

cannot be excluded. However, even if present, these fistulae were not associated with morbidity requiring surgery.

Clinical Data on Crohn's Patients with Fistulae and Sinus Tracts

There were 12 women and 5 men with an average age of 38.9 yr (range 20–64) and an average duration of Crohn's disease of 10.4 yr (2–23). Six patients had previous abdominal surgery; four had bowel resection and reanastomosis; one had resection of bowel and colostomy and one had a recent cholecystectomy. Ten patients presented with symptoms of active bowel disease, including abdominal pain, diarrhea and vomiting but the presence of fistula was not suspected clinically. The three patients with enterovesical fistulae and the two patients with rectovaginal fistulae presented with fecaluria and vaginal fecal discharge, respectively. Four patients with fistulae between the bowel and the skin presented with a subcutaneous abscess which was drained prior to imaging in three patients.

Scintigraphic Technique

Mixed leukocytes were labeled with ^{111}In -WBC using the technique described by Datz and Taylor (16). Planar images of the abdomen and pelvis were obtained 2–4 hr postinjection of approximately 500 μCi of ^{111}In -WBC (early images) and 18–26 hr postinjection (delayed images) using a medium energy collimator and 20% energy window settings over the 173 keV and 247 keV photopeaks of ^{111}In . SPECT studies were not routinely performed but were occasionally added for better localization of lesions detected on planar images. A 360° rotation was performed in 64 projections, 30 sec each. The data were reconstructed in two slice thicknesses using Hanning prefiltering (cutoff 0.6) and backprojection with a ramp filter.

Scintigraphic and Radiographic Interpretation

Indium-111-WBC images from both groups of Crohn's patients with and without fistulae were reviewed independently by three nuclear medicine physicians blinded to the radiographic and surgical results. The scintigraphic findings were recorded on forms which included the following data: the presence of intestinal or extraintestinal lesions, the change in activity between early and delayed images, the presence of intraluminal activity distal to the intestinal abnormality on delayed images and whether SPECT, when available, added data to the planar images. An intestinal lesion was recognized on early images by the distribution of activity in the anatomic location of the small or large bowel and the presence of luminal activity distal to it on delayed images (17).

Barium examinations and sinography were available for corre-

lation in 16 patients with fistulae and sinus tracts. They were interpreted retrospectively by a radiologist experienced in GI radiology who was blinded to the scintigraphic and surgical results. The interpretation included data on the presence of fistulization and the distribution of bowel disease.

RESULTS

The most common scintigraphic findings in Crohn's patients with suspected active disease but no known fistulae (the comparison group) were early intestinal lesions which were less intense on delayed images and the presence of luminal activity distal to these sites on delayed images (Fig. 1). Of 69 intestinal lesions identified in this group of patients, only 9 showed an increase in activity with time. Seven of these lesions were the most distal abnormal segments in multisegmental disease. Intraluminal labeled white blood cells from the more proximal sites of disease most likely contributed to the increase in activity in these distal segments. Distal intraluminal activity was present on delayed images in 48 patients and absent in 2 patients; a patient with a proximal colostomy and a patient with small bowel obstruction. Extraintestinal abnormality was detected in one patient at the site of a recent surgical incision.

Two scintigraphic findings found in Crohn's patients with fistulae and sinus tracts but not in Crohn's patients with no known fistulization were: the presence of concomitant intestinal and extraintestinal lesions and the absence of distal luminal activity in patients without colostomy or bowel obstruction to account for this lack of activity. Table 1 summarizes the scintigraphic results in Crohn's patients with fistulae and sinus tracts.

The extraintestinal lesions detected on ^{111}In -WBC images were the drainage site of the fistula ($n = 7$) or accompanying deep abscesses ($n = 6$). In the three patients with enterovesicle fistulae, activity was detected in the bladder (Fig. 2). The activity disappeared postvoid in one patient and was detected for the first time on delayed images in another patient, suggesting that extravasated luminal labeled white blood cells rather than inflammation in the bladder wall was the cause for the bladder activity. In one of two patients with rectovaginal fistula, ^{111}In -WBC images detected abnormal activity in the perineum. In the other patient, ^{111}In -WBC images detected a persistent site of activity in the pelvis, found on laparotomy to be a perirectal abscess, but did not detect perineal activity. In the four cases of enterocutaneous fistulae, skin activity showed an increase from early to delayed images in the presence of a subcutaneous abscess ($n = 1$) and a decrease when a drain had been inserted prior to imaging ($n = 3$).

Distal luminal activity was absent on delayed images in seven patients, although the early images detected sites of active bowel disease; one patient had a colostomy, one patient had bowel obstruction, three patients had fistulae to the skin and two patients had fistulae between the proximal bowel and distal colon (Fig. 2). These conditions may explain the lack of distal luminal activity.

The extent of active bowel disease as determined scin-

TABLE 1
The Scintigraphic Findings in Crohn's Patients with Fistulae and Sinus Tracts

Patient no.	Abnormal uptake on early images	Change in intensity on delayed images [†]	Presence of distal luminal activity on delayed images	Additional information on SPECT	Final diagnosis
1	I: IC RS EI:	↓ → n—bladder	Present	Confirming the EI activity to be in the urinary bladder	Ileovesicle fistula
2	I: IC RS EI: low pelvis	↓ ↑ ↑	Present	Localizing the pelvic lesion to the urinary bladder	Ileovesicle fistula
3	I: IC EI: low pelvis	↓ ↑ (disappeared postvoid)	Present	Localizing the pelvic lesion to the urinary bladder	Ileovesicle fistula
4	I: IC, RC, TC, LC, RS (segmental) EI: perineum	↓ ↓ 0	Present (faint)	ND	Rectovaginal fistula
5	I: IC RS EI/I: upper pelvis	↓ ↑ ↑ ↑	Present	Localizing the pelvic lesion posteriorly	Rectovaginal fistula, perirectal abscess
6	I: IC EI: right pelvis left pelvis	↓ ↓ ↑	Absent	Localizing the pelvic right lesion to the skin and the left lesion to the iliac crest	Enterocutaneous fistula on the right, left psoas abscess
7	I: IC	0	Absent	ND	Enterocutaneous fistula
8	I: proximal to colostomy EI: adjacent to colostomy opening	↓ ↑ ↑	Absent	ND	Enterocutaneous fistula
9	I: EI: left upper abdomen	↑ ↑	Present*	ND	Sinus tract from transverse colon, mesenteric abscess
10	I: IC EI/I: right mid abdomen	→ ↑	Present	ND	Fistulae between loops of small bowel, mesenteric abscess
11 [†]	I: IC RS I: SB EI: right pelvis	↓ ↓ → ↑	Absent Absent	ND Uptake in right pelvis extending anteriorly to the skin and posteriorly to the iliac crest. Connection to SB?	Ileosigmoid fistulae Enterocutaneous fistula, sinus to right iliac crest
12	I: IC RS EI/I: upper abdomen	→ ↑ ↑	Absent	ND	Ileosigmoid fistulae, bile leak, intraabdominal abscess
13	I: IC	↓	Present	ND	Ileosigmoid fistula (small)
14	I: IC	↓	Present	ND	Ileosigmoid fistulae (small)
15	I: IC	→	Present	ND	Ileocecal to proximal small bowel fistula
16	I: IC, RC, RS	↓	Present	ND	Ileosigmoid fistulae
17	I: IC, RC, TC (prox.) EI/I: above the hepatic flexure (duodenum?)	↓ 0	Absent	ND	Duodenocolic fistula, colonocolic fistula, bowel obstruction

*No abnormal intestinal site was identified on early images but delayed images detected intraluminal activity.

[†]This patient had two episodes of fistulization.

I = intestinal; EL = extraintestinal; EI/I = cannot be distinguished; SB = small bowel proximal to the terminal ileum; IC = terminal ileum and ileocecal area; RC = right colon; TC = transverse colon; LC = left colon; RS = rectosigmoid; ↑ = increased; ↓ = decreased; → = no change; 0 = disappeared; n = new lesion; ND = not done.

tigraphically was in complete agreement with surgery in 14 of 17 patients (82%). In one patient with a large ileosigmoid fistula, early images detected an abnormality in the sigmoid that appeared normal on surgery (Fig. 3). It may be that by

4 hr, the time of imaging, luminal white blood cells originating in the diseased ileum migrated to the sigmoid through the fistula, thus giving the false impression of disease in the sigmoid. In another patient, active disease in the

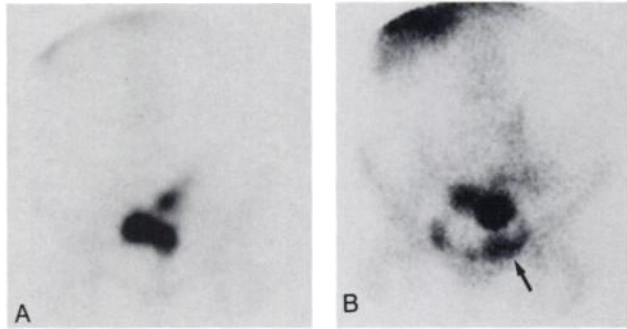


FIGURE 2. Enterovesicle fistula. (A) Early image. (B) Delayed image. Concomitant with the bowel abnormality, delayed images detect activity at the site of urinary bladder (arrow).

proximal small bowel was not noted scintigraphically and in a third patient a diseased segment of bowel was obscured by activity in an accompanying abscess.

The extent of disease as determined radiographically was in complete agreement with surgical results in 9 of 15 cases (60%). In four cases, radiographic abnormality was identified in segments that were not actively inflamed. In two patients, barium examinations underestimated the full extent of disease.

SPECT images, which were available for six patients, were helpful in differentiating intestinal from extraintestinal distribution and more accurately localizing the site of activity (Figs. 4 and 5).

In four patients with internal fistulae, the scintigraphic appearance was identical to that of Crohn's patients with active disease but no known fistulization, in that early intestinal lesions and distal luminal activity were detected on the delayed images.

Sixteen patients had 17 operations for fistulae and sinus tracts. One patient was treated with antibiotics, corticosteroids and TPN. Eighteen bowel segments were found on laparotomy to be inflamed and the origin of fistulae and sinus tracts. Fistulae and sinus tracts included ileosigmoid fistulae (n = 5), fistulization between loops of small bowel (n = 1), ileocecal (n = 1), enterovesicle (n = 3), enterocutaneous (n = 4) and enterovaginal fistulae (n = 2), a sinus tract to the mesentery (n = 1) and a sinus tract to the iliac bone (n = 1). The fistulized segments showed evidence of active inflammation on surgery and were abnormal on ¹¹¹In-WBC images except in one patient

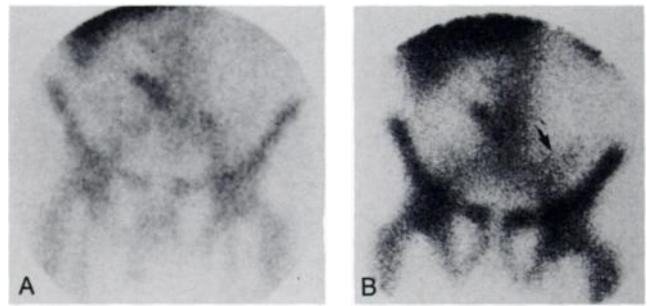


FIGURE 3. Ileosigmoid fistula. (A) Early image. (B) Delayed image. Although early images detect a proximal intestinal lesion, there is no luminal activity distal to it (note the activity in the sigmoid, arrow).

where the bowel disease was obscured by activity in an adjacent abscess.

Barium examinations and sinography obtained in 15 patients prior to surgery identified fistulization in 12 patients. In seven patients, the tract itself was delineated. In two patients with enterovesicle fistulae, barium examinations showed extravasation of barium to the pelvis but failed to delineate the urinary bladder. They did not identify the presence of a small ileosigmoid fistula, fistulization between loops of small bowel and a sinus tract to the mesentery.

Accompanying deep abscesses were found on laparotomy in six patients. All were identified on ¹¹¹In-WBC images as persistent foci of activity (Fig. 6).

Patients with bowel disease localized to the site of the fistula had resection of the fistulized bowel segment, closure of the tract and primary reanastomosis (n = 5). Patients with an accompanying abscess had fecal diversion, resection of bowel when the disease was limited to the site of the fistula and the abscess was drained (n = 6). The patients with enterovesicle fistula had resection of the fistulized bowel segment but the bladder was treated conservatively. One patient with rectovaginal fistula had a defunctioning ileostomy due to the presence of active bowel disease in the terminal ileum and entire colon. The repair of the fistula was postponed to a later date (Fig. 7). One patient with extensive disease and multiple fistulae had proctocolectomy and a permanent ileostomy and one patient who had previous colostomy had resection of the fistulized segment and a new colostomy was created.

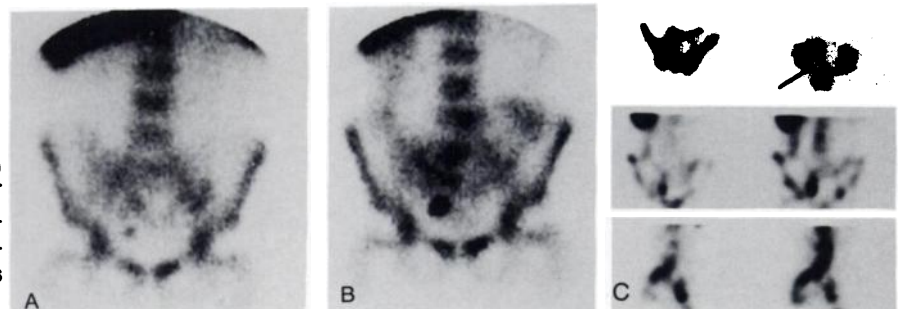


FIGURE 4. Enterovesicle fistula. (A) Early image. (B) Delayed image. (C) SPECT images. Planar images detected a pelvic lesion. SPECT images localized it to the bladder. Connection with the diseased bowel is suggested (arrows).

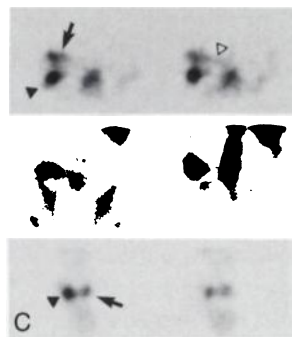
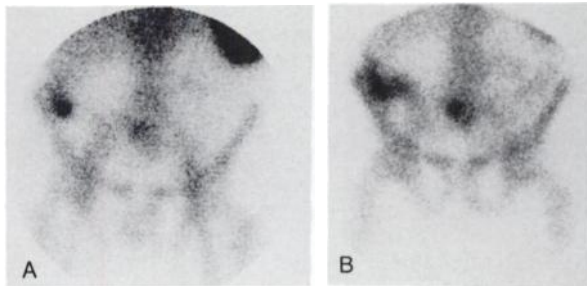


FIGURE 5. Sinus tract from small bowel to skin and to the iliac bone. (A) Early image. (B) Delayed image. (C) SPECT images. SPECT images show the lesion on the right to extend anteriorly to the skin (arrow) and posteriorly to the iliac bone (arrowhead). Connection with the diseased small bowel is suggested (empty arrow).

DISCUSSION

Fistulae and sinus tracts may cause significant morbidity and discomfort and often are associated with phlegmon and abscess formation. Longstanding tracts harbor the risk of malignant transformation (4,7).

Conservative treatment achieves healing of fistulae and sinus tracts only rarely. The standard treatment is surgery. The major factors in selecting the surgical procedure and the time of surgery are the location of the fistula, the distribution of active disease in other bowel segments and the presence of accompanying abscesses. Single stage surgical approach which includes resection of the fistulized bowel segment, local repair of the tract and primary reanastomosis is reserved for cases where the active bowel disease is limited to the site of the fistula. If the bowel disease is multisegmental, this approach is discouraged as it has a high incidence of failure. Bowel disease should be treated initially with aggressive medical therapy or by planning a multistaged surgical approach. In this approach, the initial surgery is aimed at fecal diversion. Repair of the tract and reanastomosis are performed at a later stage, once the extensive bowel disease is in remission. The site of fecal diversion is determined by the distribution of disease in the GI tract. Accompanying deep abscesses require surgical drainage and fecal diversion. In cases of enterovesicle fistula, the fistulized bowel segment is resected and the bladder is treated conservatively if its wall is not inflamed (1,2,4,6,18,19).

Gastrointestinal radiologic investigation with barium examinations and sinography identified the majority of fistu-

lae and sinus tracts in our patients. Indium-111-WBC images suggested the presence of fistula by detecting activity at the drainage site in seven patients with enterovesicle, enterovaginal and enterocutaneous fistulae. The delayed appearance of the bladder activity in one patient and the postvoid change in another suggest luminal white blood cells rather than inflammation of the bladder wall to be the cause for the scintigraphic abnormality.

Radiographic investigation of the upper and lower GI tracts is commonly used to determine the distribution of Crohn's disease. However, in patients with recurrent disease the distinction between active disease and chronic changes from previous episodes is often difficult. The distribution of active disease as assessed radiographically was in complete agreement with the surgical results in only 60% of cases, and 27% of cases showed disease in bowel segments that were not actively inflamed. Indium-111-WBC images have the advantage of being negative in fibrosis and scarring and positive in active inflammation (15,20). The distribution of active disease on scintigraphy was in complete agreement with surgery in 82% of the cases. Fistulization signals active bowel disease. In other series, as in our patients, fistulae and sinus tracts originated in actively inflamed bowel segments (1,19). These segments were identified on nuclide images as being actively inflamed except in one patient where the segment was obscured by activity in an adjacent abscess.

Intra-abdominal abscesses may occur in 12%–28% of Crohn's patients during the course of the disease (2,4). Fistulization and previous laparotomy are the most com-

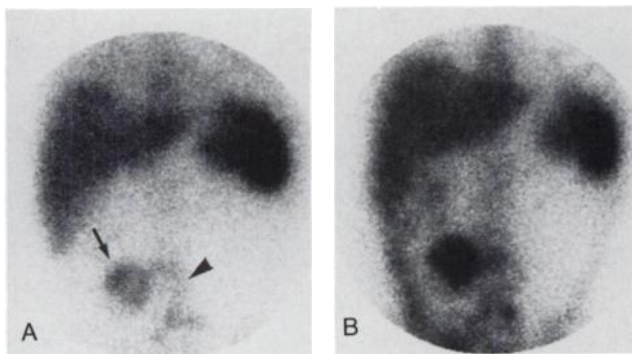


FIGURE 6. An accompanying abscess. (A) Early image. (B) Delayed image. A persistent focus of activity is detected (arrow) concomitant with intestinal disease (arrowhead).

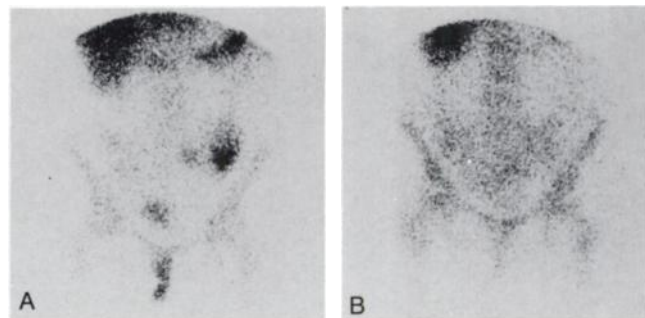


FIGURE 7. Rectovaginal fistula and extensive active bowel disease. (A) Early image. (B) Delayed image. In addition to abnormal perineal activity, there is evidence of multisegmental active disease. The patient had a functioning ileostomy with later repair of the fistula.

mon underlying conditions associated with abscess formation. An abscess can be the result of fistulized inflammatory loops of bowel which form an inflammatory mass with impaired blood supply. Sinus tracts, unlike fistula, do not connect the bowel with a free epithelium-lined surface but rather with muscles, bones, mesenteric fat or solid organs, provide a site for stagnation of fecal content and abscess formation. Ultrasound and CT scan are the radiologic techniques of choice for detection of abscesses and in selected cases guide percutaneous drainage of the abscess (5). Indium-111-WBC studies accurately determined the presence of abscesses and identified all surgically proven abscesses in our patients (21-23).

Indium-111-WBC scintigraphy was used to assess disease activity in Crohn's patients. Since patients may have fistulae and sinus tracts not uncommonly present with non-specific symptoms of reactivation of bowel disease, the possibility of fistulization should be considered. Fistulae and sinus tracts may present scintigraphically as activity at the recipient site of the fistula in addition to intestinal lesions which indicate the presence of active bowel disease. The detection of active bowel disease and abscess concomitantly should also raise the possibility of fistulization. Fistulae may be used by luminal white blood cells as a route for migration other than through the colon and therefore should be suspected when delayed images fail to detect luminal activity distal to the intestinal lesions. A proximal colostomy and bowel extractions were causes other than fistulization accounting for lack of luminal activity in our patients. Diarrhea was suggested to be the cause for absent luminal activity in a patient with active Crohn's colitis (24). However, it was not found to cause absent luminal activity in our patients with or without fistulae, including those patients with severe diarrhea.

In conclusion, in patients with Crohn's disease who are clinically or radiographically suspected of having fistulae or sinus tracts, ¹¹¹In-WBC scintigraphy may add information which is essential for appropriate clinical management and therefore should be included in their preoperative investigation.

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