

The Role of Scintigraphy in the Management of Inflammatory Bowel Disease

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From the Case Records of the Hospital of the University of Pennsylvania

J Nucl Med 1991; 32:856-859

CASE PRESENTATION

A 41-yr-old man with a 12-yr history of Crohn's disease was admitted for abdominal pain, nausea, diarrhea, fever, and abdominal distension. He was found to have a complete small bowel obstruction. Despite nasogastric suction and bowel rest, the patient did not improve, and therefore surgical intervention became necessary.

At laparotomy, the terminal ileum was noted to be thickened and edematous with prominence of mesenteric fat. The terminal ileum and the ascending colon were resected and an ileal-transverse colon anastomosis was performed. Macroscopically, the bowel wall of the lumen was significantly thickened with a markedly decreased lumen. The mucosa had a cobblestone appearance. Histologic examination of the terminal ileum revealed acute transmural inflammation with ulcerations and fissures. Discrete granulomas were seen. Both the macroscopic and microscopic findings were consistent with Crohn's disease. The patient did well postoperatively and was discharged in stable condition.

His past history revealed that four years prior to admission, he had crampy abdominal pain, loose stools, and fatigue. At that time, his stool was hemoccult-positive, he was anemic (hemoglobin of 11.0 g/dl normal range, 13.5-17.5 g/dl), and proctoscopy revealed noninflamed hemorrhoids and normal-appearing mucosa of the rectum and distal sigmoid. A barium enema demonstrated irregular ulcerations in the neoterminal ileum. Therapy with sulfasalazine was started, which resulted in improvement of his symptoms and disappearance of his anemia.

Three years prior to admission he developed vague upper abdominal pain, with hematemesis. He was brought to the emergency room where hypotension was treated with i.v. fluids. Emergency endoscopy revealed an actively

bleeding duodenal ulcer, which was thermally coagulated. The remainder of the examination did not reveal significant findings due to the presence of a large amount of blood in the lumen. The patient responded to histamine 2 antagonists and antacids.

One year prior to his present admission he again presented with gastrointestinal bleeding. Evaluation demonstrated an actively bleeding gastric ulcer with pyloric channel stenosis. The patient responded to histamine 2 antagonist therapy and was discharged.

Nine months before the present admission he was readmitted with abdominal pain, chills, fever up to 102°F, and diarrhea. The pain was crampy and was located in the right mid- and lower quadrant. Stool studies, blood cultures, and abdominal films were unremarkable. The patient was begun on sulfasalazine and prednisone and was discharged in improved condition.

The week before the present admission, the patient again developed the onset of abdominal pain in the right mid- and lower quadrant, fever, and diarrhea. The pain was occasionally crampy and was partially relieved by vomiting. On physical examination, there was abdominal distension, diminished bowel sounds, and moderate discomfort on palpation of the right lower abdomen. Rectal exam revealed fullness on the right side and hemoccult-negative stools. A stool specimen demonstrated fecal leukocytes. An upright abdominal film revealed a dilated loop of small intestine in the right mid-abdomen. Food and liquids were withheld, and the patient was started on broad-spectrum antibiotics. There was no growth of organisms by stool and blood cultures.

An upper gastrointestinal barium study with a small bowel follow-thru demonstrated evidence of one or more fistulae from the neoterminal ileum to the duodenum and probable recurrent Crohn's disease at the anastomosis between the ileum and the transverse colon (Fig. 1A-B). An abdominal CT scan demonstrated a single loop of thickened bowel in the right mid-abdomen. There was no evidence of any abnormal collections (Fig. 2). To further evaluate his continued fever and abdominal complaints, an ¹¹¹In-labeled white cell scan was obtained (Fig. 3). At 24 hr, there was an intense focal accumulation of the administered radiolabeled cells in the right upper quad-

Received Feb. 22, 1991; accepted Feb. 22, 1991.

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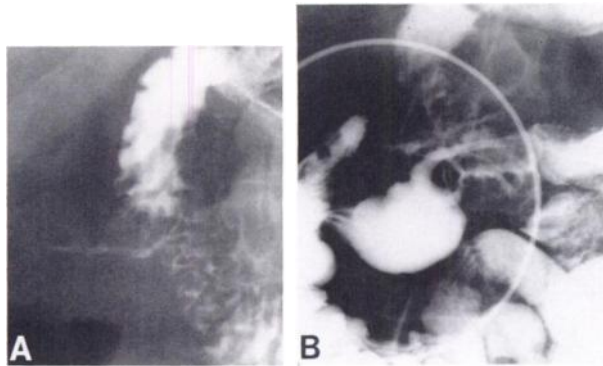


FIGURE 1. (A-B) A barium radiograph of the upper gastrointestinal tract with a small bowel follow-thru demonstrates one or more fistulae in the area of the neoterminal ileum to the duodenum. There is recurrent disease at the region of the anastomoses.

rant. Despite medical intervention, the patient continued to have diarrhea, pain, and fever and a laparotomy was performed.

At surgery, there was an extensive phlegmon at the site of the ileal-colonic anastomosis with a fistulae arising from the anastomoses to the duodenum. The phlegmon and fistulae were excised and a new ileal-transverse colon anastomosis was made. The patient tolerated the procedure well and had an uneventful postoperative course.

DISCUSSION

This case helps demonstrate the utility of scintigraphy in the management of patients with inflammatory bowel disease (IBD). Persistent symptomatology in this patient suggested ongoing inflammation or infection. However, both the barium study and the abdominal CT scan failed to define the abnormality. Indium-111-labeled white cell imaging was useful in identifying and localizing an inflammatory mass. Surgery was performed to excise the phlegmone and fistulae. Thus, white cell imaging altered the course of therapy in this patient.

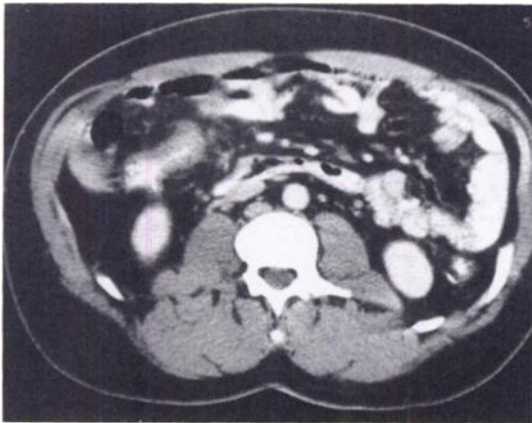


FIGURE 2. An abdominal CT scan demonstrates a single loop of thickened bowel in the right mid abdomen.



FIGURE 3. An intense focal accumulation in the right upper upper abdomen is noted on the 24-hr image using an ^{111}In -labeled white cell scan. This was interpreted to represent an inflammatory site in that location.

The diagnosis and management of patients with IBD can be challenging and fraught with difficulties. Therefore, the development of a simple, rapid, noninvasive, and safe modality for the evaluation of these patients is crucial. Barium radiography and endoscopic studies play an important role in the assessment of IBD patients, but these tools may be insufficient or potentially unsafe in some patients with IBD.

Gallium-67-citrate was one of the first radionuclides to be used in the evaluation of patients with IBD, but it has several limitations. It is excreted into the gastrointestinal tract, which may obscure areas of inflammation or falsely suggest regions of involvement. In addition, as imaging with gallium-citrate may require several days for completion, its utility for assessing the acutely ill patient is diminished.

Indium-111-labeled leukocytes have several advantages over other radiopharmaceutical preparations and modalities, including conventional and specialized radiographic techniques and endoscopy. It is rapid, since images can be obtained as early as 4–6 hr after injection. Indium-111-leukocyte scintigraphy can be performed safely in the critically ill patient, since bowel preparation and intubation are not needed. In addition, neither bound nor unbound ^{111}In appears in the gastrointestinal tract nor in the urinary system, so that regions of inflammation are not obscured.

Indium-111-labeled leukocyte scans are also helpful in the evaluation of complications of IBD, such as abscess formation. An abscess may be distinguished from inflammatory bowel disease, since labeled WBCs usually are more localized and this pattern is not in the distribution of the intestines. In a study by Goldman of 36 patients with IBD and suspected abscesses, 11 patients accurately were demonstrated to have focal abscesses. There were no false-positive nor negative results (1).

There are several indications for the use of a leukocyte scintigraphy scan in patients with IBD. First, it may be helpful in evaluating the patient with Crohn's disease who has had recent onset of symptoms and normal barium studies. Second, if disease of the terminal ileum is suspected and the area is not approachable by endoscopy,

scintigraphy may be extremely helpful for the detection of active inflammation. Third, the location, extent of disease activity, and severity may be assessed by a single image.

There have been several studies that reported the efficacy of ^{111}In -labeled leukocytes in the evaluation and management of patients with IBD. Stein et al. studied 10 patients with active ulcerative colitis and 5 with active Crohn's colitis and prospectively compared conventional radiography, endoscopy, and surgical findings with ^{111}In -white cell scintigraphy. There was excellent correlation in 11 patients, good correlation in 2 patients, and poor correlation in 3 for location of disease. The degree of inflammation by scintigraphy also correlated well with clinical assessment (2).

In 100 patients with suspected IBD, ^{111}In -granulocyte scintigraphy was compared to barium radiography and rectal histology. Thirty patients were found to have IBD by standard evaluation. Nuclear medicine scans were abnormal in 28 of the 30 patients. Both patients with normal scans were noted to have mild disease, normal radiologic studies, and mild symptoms. In the remaining 70 patients without IBD, 66 had normal scans and 4 were false-positive (3). In a study by Crama-Bohbouth, 39 patients with IBD were examined by indium-granulocyte scintigraphy and the studies were compared to clinical, radiologic, endoscopic, and/or histologic findings. Twenty-eight had positive scans, six had false-negative scans, five had true-negative results, and no patient had a false-positive scan. Thus, the scans proved to be both sensitive and specific for detecting inflammation (4).

The degree of inflammation can also be evaluated by examining fecal excretion of ^{111}In -granulocytes. Fifty-two patients with Crohn's disease or ulcerative colitis were studied in a prospective trial (5). In addition to an excellent correlation between endoscopy and histology for extent of disease, fecal excretion of ^{111}In -granulocytes was found to closely correlate with severity.

A troublesome problem in IBD is the assessment of strictures. Patients with Crohn's disease may develop strictures of the small intestine. It may be impossible to assess if the stricture is fibrotic or inflammatory by routine radiography. Indium-111-white cell scintigraphy may help differentiate inflammatory from fibrotic changes, since only the inflammatory stricture will demonstrate uptake of the radiolabeled white cells. In a study of 19 patients with IBD and strictures, ^{111}In -leukocyte scintigraphy accurately differentiated inflammatory and fibrotic strictures (6).

Another diagnostic dilemma is the patient who has undergone ileal resection and has recurrent diarrhea. It may be difficult to establish if the diarrhea is secondary to recurrent disease or bile salt loss. Patients with recurrent Crohn's disease will have uptake in the region of inflammation. Patients with choleretic diarrhea will not have a positive scan.

Indium-111-white cell scintigraphy may be used to

monitor and assess disease activity in response to medication (7). The medications used in IBD can be potentially toxic with numerous side effects. White cell scintigraphy can be used to serially monitor the patient's clinical course to help determine the medication dose. Alternatively, scintigraphy can be used to help evaluate complications that may arise. IBD patients may have concomitant irritable bowel syndrome (IBS), which may also cause gastrointestinal symptoms. Based on symptoms alone, it may be difficult to determine if patients have active inflammation or IBS. Nuclear scanning with ^{111}In -labeled leukocytes allows for objective evidence for inflammation.

There are disadvantages, however, with ^{111}In -white cell scintigraphy (8,9). Separation of leukocytes from other cells and plasma is a lengthy and labor-intensive process because multiple centrifugations and washings are required. Because white cells are then incubated with indium and resuspended in plasma, the entire process may take 2-4 hr and not all nuclear medicine departments have the capacity to perform this process. An additional problem is the high radiation exposure to lymphoid tissue, especially the spleen, which may be significant (10). This high dose of radiation to the spleen limits the usefulness of ^{111}In -leukocyte imaging in serially monitoring disease response to medication. In addition, since patients with IBD are often young, radiation exposure is more of a concern. However, this agent is currently approved for routine use by the Food and Drug Administration and is offered by many nuclear medicine laboratories on demand.

White cell scans may falsely overestimate the area of inflammation if there is migration of white cells within the bowel lumen. Early images may be better because there may be insufficient time for white cell migration to occur through an inflamed bowel wall. Late films should be obtained, however, if early images are negative. An additional method for reducing white cell migration in the bowel lumen is the use of intravenous glucagon, which reduces bowel motility.

False-positive ^{111}In -white cell scans occur in a myriad of settings, including hematomas, intramuscular injections, accessory spleens, swallowed or aspirated contaminated pulmonary or oral secretions, and gastrointestinal hemorrhage (11). Radioactive fecal material may collect in a colostomy or ileostomy if there is active inflammation. To the unsuspecting physician, this may be interpreted falsely as a positive scan. Simply repositioning the bag or emptying the contents would rectify the problem (12).

Indium-111-leukocyte scintigraphy is not always specific or diagnostic for IBD. This imaging technique is also useful in patients with other inflammatory or infectious processes, including pseudomembranous colitis, infectious or ischemic colitis, or diverticulitis (13).

Other agents have been used for nuclear imaging of IBD, including technetium-labeled preparations. Phagocytes labeled with $^{99\text{m}}\text{Tc}$ -colloid particles can be used. Technetium offers several advantages over indium, includ-

ing greater availability, lower cost, less irradiation to lymphoid organs, and greater ease of preparation, because technetium selectively labels neutrophils and monocytes.

Imaging with technetium-labeled phagocytes has been shown to be reliable and sensitive. In a report of 20 patients with IBD, there was a close correlation in 15 patients between scans, barium studies, and colonoscopy (14). In a follow-up study of 51 consecutive patients with IBD, quantification of counts over the area of interest and 24-hr fecal excretion rates correlated with the clinical disease activity index (15). Abscess location and identification can also be evaluated using ^{99m}Tc-labeled leukocytes (16).

Other new agents have also been used for scanning. Sucralfate is an aluminum salt used in the treatment of peptic ulcer disease. Thirty-three patients with Crohn's disease, 10 patients with ulcerative colitis, and 29 control patients were studied after oral administration of sucralfate labeled with ^{99m}Tc. Positive scans were obtained in 29 of 31 patients with active Crohn's disease and in all patients with ulcerative colitis. The sensitivity and specificity was 95% and 97%, respectively (17).

Technetium-99m-labeled hexamethylpropyleneamine-oxime (HMPAO) has been used for brain scanning with great success. This agent, which is rapidly incorporated into white cells, is ideal for imaging inflammation in IBD patients. In six patients with suspected or known IBD, ^{99m}Tc-HMPAO scans were taken. All six patients had positive scans, with five patients demonstrating positivity as early as 30 min after injection. Overall, it was felt that the quality of the images was superior to those obtained with indium (18). In 32 patients suspected of having IBD, all scans were positive for inflammation within the first hour. There were no false-positives. Later images at 24 hr were not helpful because there was bowel excretion of ^{99m}Tc-HMPAO. However, it was felt that the bowel excretion of this agent did not hinder the utility of the scan (19). Technetium-99m-HMPAO is not specific for IBD and has been used in patients with diverticulitis and intestinal infarction (20,21).

A potentially useful reagent for scanning is ¹¹¹In-labeled nonspecific immunoglobulin. It has been used in the evaluation of focal sites of inflammation in 128 patients (22). Sixty-two patients had possible abdominal or pelvic infections. Compared to surgical intervention or CT scanning, there were 21 true-positives, 30 true-negatives, 3 false-negatives, and 8 unusable scans. Thus, early results suggest that ¹¹¹In-labeled nonspecific immunoglobulin may be useful in the evaluation of abdominal infection. However,

it remains unclear if this imaging technique will be useful for the evaluation and management of patients with IBD.

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