[\textsuperscript{67}Ga]Citrate Scintiscanning in Active Inflammatory Bowel Disease

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Twenty-five hospitalized patients were studied prospectively with [\textsuperscript{67}Ga]citrate (GA) abdominal scintillation scanning in an attempt to define its role in the evaluation of patients with active inflammatory bowel disease (IBD). There were nine patients with ulcerative colitis (UC), seven with Crohn’s disease (CD), and nine controls. In four patients, two with UC and two with CD, a tissue/plasma radioactivity ratio was obtained and compared to normals. All the UC patients had positive GA scans and only one of seven of the CD patients had a positive scan. There were no false positive scans. Scans performed after a 3- or 5-day delay were more accurate than 6-hr scans alone. Well-delineated colonic radioactivity 6 hr after injection which persists for 3 to 5 days indicates the presence of UC in patients with IBD, while a negative scan is more consistent with active CD. Colonic uptake at 6 hr which clears by 48 or 72 hr is not indicative of UC. This procedure aided in following the course of UC, delineating the extent of disease, and in differentiating active CD from an intraabdominal abscess. Tissues from UC patients had increased tissue/plasma radioactivity ratios while tissues from CD patients had normal or decreased ratios which were consistent with the imaging data.

The use of [\textsuperscript{67}Ga]citrate (GA) scanning to visualize tumors was initially reported by Edwards and Hayes in 1969 (1). Since then other workers have confirmed the tumor-seeking properties of GA and clarified its role in the evaluation of a number of neoplasms (2–5). Experience has demonstrated that GA concentrates in many nonneoplastic tissues (6, 7). Of particular interest is the observation that GA localizes in inflammatory tissues, which is especially significant for detection of infectious processes and abscesses (8–12).

A characteristic feature of acute inflammatory bowel disease (IBD) is the extensive infiltration of the intestinal wall by inflammatory cells. Experimental studies using autoradiography have shown the association of GA with lysosome or lysosome-like granules in the walls of abscesses and in other focal sites of inflammation (13, 14). A recent study reported diffuse radioactivity within the entire colon in a patient with pseudomembranous colitis (15). Kaplan et al (16) observed intense visualization of the colon 6 hr after an injection of GA in a patient with ulcerative colitis. Several studies directed primarily to the localization of GA in septic processes have suggested possible localization in patients with IBD, but necessary clinical information and documentation has not been available (10–12).

This prospective study was aimed at defining the role of GA scanning in hospitalized patients with active IBD.

MATERIALS AND METHODS

Sixteen consecutive hospitalized patients with IBD seen by the Gastroenterology Division were studied. In-
formed consent was obtained according to the Human Research Protocol of the University of Miami. Nine patients had UC, and seven had CD (three with regional ileitis, two with ileocolitis, and two with colitis without ileal involvement).

Seven commonly used clinical parameters were evaluated: temperature (oral temperature >100°C during first hospital day), pulse rate (>90/min), hematocrit (<30% of normal), white blood cell count (>10,000 mm³), erythrocyte sedimentation rate (>30 mm/hr), serum albumin (<3.0 g/100 ml), and the number of stools per day (>5 per day). Each patient had at least three abnormal parameters for entry in the study. Patients with three abnormal parameters were considered moderately ill and patients with four or more abnormal parameters were considered severely ill. Antibiotic and/or corticosteroid therapy was underway in all cases at the time of scanning. Nine patients without known IBD were used as controls. The GA scans in this group were ordered by their attending physicians for reasons unrelated to suspected IBD, and all were for detection of neoplastic disease or intraabdominal abscess.

**Scanning Technique.** The patients were injected intravenously with 6 mCi [153Ga]citrate (New England Nuclear, North Billerica, Massachusetts). Scanning was performed using a multiplane tomographic whole-body scanner (Pho-Con, Searle Radiographics) and a large field gamma-scintillation camera (LFOV, Searle Radiographics) with medium-energy parallel hole (MEP) collimators. Tomographic studies were done on the tomo 2 setting using a 65- x 65-cm format and speed at 250 cm/min. The 184 and 289 keV photopeaks were included using a dual analyzer. Anterior and posterior abdominal and pelvic views were obtained when the scintillation camera was used. The triple analyzer in the camera was set for 93, 184, and 289 keV photopeaks using 30%, 20%, and 20% windows, respectively. All displays for both instruments were on SO-179 transparency film (Eastman Kodak Co.) exposed in Micro-Dot imager (Searle Radiographics) using 11 x 14 size for Pho-Con studies and 8 x 10 size for camera studies.

To determine the optimal time for imaging GA in the bowel, images were obtained at 6 hr, 24–48 hr, 72 hr, and 5 days. Two patients had scans repeated at a later date because of a change in their clinical course. Since approximately 10–15% of an intravenous dose of GA is excreted via the intestine (17), laxatives and cleansing enemas were administered to control patients, but not to the IBD patients since most had diarrhea as a manifestation of their disease.

The scans of all 25 patients were coded and read by three observers, experienced at reading GA studies in a variety of disease states, using the same film and imaging instruments. These observers had no prior knowledge of the patient’s clinical diagnosis or of any prior reading. A study was considered positive if large-bowel topography was well defined and intensely labeled regardless of the time of scan after GA injection. If the bowel topography became less well defined or the labeling less intense during the 5 days of scanning, the study was considered negative. Recognition of more specific bowel luminal labeling versus bowel wall labeling can be difficult or impossible unless the findings correlated with the degree of bowel cleansing or diarrhea in each patient. Some experience is required to avoid overinterpretation since background variations, other labeled structures and other disease entities must be recognized by the observer.

**Tissue Sampling.** Four patients with IBD, two with UC, and two with CD had plasma samples and biopsy specimens of actively diseased tissue obtained simultaneously 4–6 days after initial GA injection. These were washed, weighed, and then counted in a gamma well counter for 4 min, with subtraction of a wash water blank as a background indicator. The tissues were rectal mucosa in two patients with UC, one patient with CD with active inflammation of the rectum, and ileal mucosa obtained as a surgical specimen from one patient with regional ileitis. A tissue/plasma ratio (cts/g vs cts/ml) was computed and compared with the data of Nelson et al (18), who investigated the localization of GA in the normal colon and suggested that the normal colon-plasma ratio is approximately 6.7:1.

**RESULTS**

The clinical data of the IBD patients are summarized in Table 1.

**Ulcerative Colitis.** All nine of the patients with UC had positive delayed (72-hr and 5-day) scans. Figure 1 shows a typical positive scan. Seven of the nine patients were judged severely ill by our criteria and two moderately ill. The two moderately ill patients had negative 6-hr studies which became positive at 28 and 48 hr, respectively, but the tissue to background activity was more pronounced with delayed scans.

One patient had an initial positive scan at all intervals when she was severely ill while scans performed two weeks later were negative when her clinical and laboratory picture was much improved following intensive medical therapy. One patient with left-sided colitis alone as judged by colonoscopy exhibited only descending and sigmoid colonic radioactivity on GA scan. One patient was thought to have clinical findings of isolated proctosigmoiditis on initial evaluation. However, the scans showed diffusely increased uptake over the entire colon; subsequent barium contrast x-rays demonstrated universal colitis.

**Crohn’s Disease.** Six of the seven patients with active CD had negative scans. One (patient 14) had a positive scan at all intervals. This patient had had a previous ileoproctostomy. She presented with fever, and a hypomotile dilated small bowel was demonstrated on her barium contrast x-ray studies. On her previous admission antibiotic alone were used, and she improved rapidly. During the last admission...