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Comparison of Scintigraphy with Indium-111 Leukocyte Scan and Ultrasonography in Assessment of X-Ray-Demonstrated Lesions of Crohn's Disease

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The aim of this study was to compare the results obtained with an indium-111 scan with those obtained with less expensive and harmless ultrasonography to evaluate the location and inflammatory activity of Crohn's disease. Thirty-one patients previously studied with x-ray underwent abdominal ^{111}In scans and ultrasonography (US). Sensitivity and specificity of US in detecting lesions seen with ^{111}In scan were 77% and 92.8%, respectively. Sensitivity and specificity of ^{111}In scan in detecting x-ray-defined lesions were 69.2% and 92.7%; the figures for US were 73% and 93.3%, respectively. Considering the evaluation of disease activity, ultrasonographic bowel wall thickness was significantly related to scintigraphic intensity of emission ($r = 0.75$ $P < 0.01$). Our experience suggests that US provided information about the location and inflammatory activity of lesions similar to that obtained from ^{111}In scan.

KEY WORDS: abdominal ultrasonography; 111-indium scan; Crohn's disease.

New diagnostic tools have recently been proposed for the assessment of Crohn's disease (CD). Autologous indium-111-labeled leukocyte scans have gained increasing popularity in defining disease extent (1) and have been proposed as a "gold standard" in assessing disease activity (2). Disadvantages of this technique include the radiation exposure and the time required.

Abdominal ultrasonography (US) has also been proposed for the diagnosis (3, 4) and evaluation of CD activity (5). It is less expensive and avoids radiation exposure. The relationships between ^{111}-In scan and US findings have recently been studied (6) in terms of disease extent. The current study is the second (6) to compare the results of these two methods for localization and activity of CD.

MATERIALS AND METHODS

Thirty-one patients with a well-established diagnosis of CD were studied. Twelve patients had been operated on

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for CD (3 ± 1 years before the study). For each patient a thorough clinical evaluation was obtained and reported as the Crohn's disease activity index (CDAI) (7). Fourteen patients were in clinical remission (CDAI < 150), 17 had clinically active disease, and 12 were on steroid treatment. Laboratory investigations, including erythrocyte sedimentation rate (ESR; normal <15 mm first hour), C reactive protein (CRP; normal <0.8 mg/dl), α_1-glycoprotein (normal <140 mg/dl), were used to monitor the laboratory activity of the disease.

Autologous ^{111}In-labeled leukocyte scan was carried out according to the labeling method described elsewhere (8), allowing a 95% prevalence of granulocytes in the infused leukocytes. The examination was performed by an experienced nuclear physician (C.C.) informed as to diagnosis and any previous surgical resections carried out in the patient being examined. Using anterior and posterior scans at the 4th hour, the location of the lesion(s) was registered for each patient. The activity of each lesion detected with the ^{111}In scan was expressed by emission intensity obtained by dividing the emission unit area of the lesion by the emission unit area of the iliac crest, used as the reference standard. Overall emission intensity in patients with multiple lesions was obtained by calculating the mean of the emission intensity of the single lesions, weighted against their extent (measured by number of pixels contained in the inflamed area, which is proportional to lesion extension).

Within three days of the ^{111}In scan, each patient also underwent abdominal US, performed by an experienced physician (V.A.) unaware of the previous scan findings and informed as to diagnosis and any surgical resections previously performed. Longitudinal, transverse, and oblique plane US scans on the right and left abdomen were obtained for each patient, with a 5-MHz linear transducer probe (Siemens SL2). Bowel wall thickness, measured in millimeters, was considered abnormal when >4 mm (9, 10) and the maximum measurement obtained in each section of the bowel was used as the US marker of activity. For patients with more than one lesion, the highest bowel wall thickness value was used.

The US physician and the nuclear physician divided the abdomen into areas, and the lesions seen by ^{111}In scan or US were ascribed to a certain section of the bowel (jejunum; ileum; ascending, transverse, descending, and sigmoid colon; and rectum) in accordance with information about the anatomical features.

For each patient, a complete radiological study of the gastrointestinal tract (small and large bowel double-contrast studies), made within the three months preceding the study, was available for comparison with the ^{111}In scan and US findings. For each section of the bowel, the sensitivity and specificity of US in detecting lesions seen with ^{111}In scans were calculated. We considered lesions seen both by US and ^{111}In scan as true positive (TP), lesions detected only by US as false positive (FP), and lesions seen by ^{111}In scan and not by US as false negative (FN). The true negatives were calculated for each intestinal section according to the following formula: 31 (total number of patients) − (FP + TP + FN).

To evaluate overall sensitivity and specificity, we added up the TP, FP, TN and VN of each intestinal section. The sensitivity and specificity of US and ^{111}In scan in detecting x-ray-demonstrated lesions was also evaluated using the same criteria described above.

The Mann-Whitney rank sum test was used to test differences between unpaired observations. Differences in bowel wall thickness and overall emission intensity in patients with active and inactive CD were calculated considering the greatest value of bowel wall thickness and the mean emission intensity of lesions for each patient. In lesions seen both by US and ^{111}In scan, a variable regression analysis was applied in order to study relationships between bowel wall thickness and emission intensity. R coefficients were then calculated, the significance being evaluated by Student's t statistic with $n - 2$ degrees of freedom.

All numerical values are expressed as means ± SD unless otherwise stated. P values less than 0.05 were considered significant.

RESULTS

Location of Lesions. Of the 31 patients, disease was confined to the ileum in 17, to the colon in five, and to both the ileum and colon in six. A total of 52 intestinal lesions were detected by x-ray examination. In three patients, who had recently been operated on, there was no radiological sign of disease recurrence. US was positive in these three patients, ^{111}In scan was positive in two of these three.

The ^{111}In scan was negative in three cases and US in one case. In the other patients, 48 sites of activity were detected by ^{111}In scan (21 ileal and 27 colonic lesions), and 49 were identified by US (21 ileal and 28 colonic lesions).

Sensitivity and specificity of US in detecting lesions that were positive with ^{111}In scan were 77% and 92.8%, respectively (Table 1).

Sensitivity and specificity of ^{111}In scan in detecting x-ray-detectable lesions were 69.2 and 92.7%; the figures for US were 73% and 93.3%, respectively (Tables 2 and 3).

Disease Activity. For abdominal lesions detected both by US and ^{111}In scan, bowel wall thickening was significantly related to the corresponding emission intensity (Figure 1). There was no statistical difference between emission intensity of lesions also detected by US and those which were not (EI 1.74 ± 1.0 vs 1.23 ± 0.47 P = NS). Differences in bowel wall thickness and overall emission intensity between different classes of patients, divided according to CDAI and to laboratory tests studied, are shown in Table 4.

TABLE 1. SENSITIVITY AND SPECIFICITY OF US IN DETECTING ^{111}IN SCAN LESIONS

Site of lesions	In-111 lesions (N)	Ultrasound lesions (N)			Sensitivity (%)	Specificity (%)
		True positives	False positives	False negatives		
Jejunum*	4	4				
T. ileum	17	14	3	3	82.3	78.5
Ascending colon	5	3	2	2	60	92.3
Transverse colon*	3	2	2	1		
Descending colon	8	7	3	1	87.5	86.9
Sigmoid	10	7	1	3	70	95.2
Rectum*	1		1	1		
Total lesions	48	37	12	11	77	92.8

*Sensitivity and specificity were not calculated due to the small number of lesions detected.

DISCUSSION

There is growing evidence that scanning after reinjection of ^{111}In-labeled autologous leukocytes is useful in the evaluation of CD patients (1, 2). This is particularly true for patients unsuited to more invasive methods, such as double-contrast radiology or endoscopy, due to very active disease; when there is suspicion of an intraabdominal abscess; or when one must differentiate between symptoms due to active disease (warm lesions) and those explained by the presence of fibrotic strictures (cold lesions) (11). This method has also proved useful in evaluating the inflammatory activity of the disease, whether by the percentage of fecal excretion of injected leukocytes (12) or by the numerical scoring systems using the uptake rate of the lesions on the screen (13). However, radiation exposure and the time taken up by leukocyte isolation and labeling procedures make this method poorly suited to routine follow-up of CD patients. The utility of US has not been extensively evaluated in CD. Some US patterns (thickening of the bowel wall with target sign, stiffening and matting of the loops, mesenteric enlargement) have been repeatedly described in CD (3, 5), although they cannot be considered specific. Bowel wall thickening seems to be the most typical and constant finding (5), and it can be easily measured. In this study, 77% of inflamed sites of the bowel seen as warm lesions on ^{111}In scan appear as thickened bowel loops with US. There is only one report in the literature on this aspect (6), in which percentages regarding ulcerative colitis and CD are given together. The results are similar to ours. Some discrepancies between the two techniques could be due to the attribution of detected lesions to a different section of the intestine. Sensitivity of US in identifying lesions detected with ^{111}In scan was lower in the ascending and sigmoid colon and rectum, if compared to ileum and descending colon. In order to explain some US false positive lesions, we could suggest that some fibrotic strictures, which were undetected by ^{111}In scan because they were cold lesions, are identified as thickened loops by US. A comparison between US or ^{111}In scan and standard radiology revealed that both techniques seem to miss roughly 25–30% of lesions documented by radiology. We could not identify specific subsets of patients more liable to produce negative scans or negative US when positive with radiology. It is possible that discrepancies between ^{111}In scan

TABLE 2. ABILITY OF US AND ^{111}IN SCAN IN DETECTING LESIONS SEEN BY X-RAY

Site of lesions	X-ray lesions (N)	Indium scan lesions (N)			Ultrasound lesions		
		True positives	False positives	False negatives	True positives	False positives	False negatives
Jejunum	5	3	1	2	3	1	2
T. ileum	20	14	3	6	14	3	6
Ascending colon	3	2	3	1	2	3	1
Transverse colon	5	3		2	4		1
Descending colon	9	7	1	2	8	2	1
Sigmoid	9	7	3	2	7	1	2
Rectum	1		1	1		1	1
Total lesions	52	36	12	16	38	11	14

TABLE 3. SENSITIVITY AND SPECIFICITY OF ^{111}IN SCAN AND US IN DETECTING LESIONS SEEN BY X-RAY

Site of lesions	Indium scan		Ultrasonography	
	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
Jejunum	60	96.1	60	96.1
T. ileum	70	72.7	70	72.7
Ascending colon*				
Transverse colon	60	100	80	100
Descending colon	77.7	95.4	88.8	90.9
Sigmoid	77.7	86.3	77.7	95.4
Rectum*				
Total lesions	69.2	92.7	73	93.3

*Sensitivity and specificity were not calculated due to the small number of lesions detected.

TABLE 4. DIFFERENCES IN BOWEL WALL THICKNESS (BWT) AND OVERALL EMISSION INTENSITY (OEI) BETWEEN PATIENTS WITH ACTIVE AND INACTIVE DISEASE

Test	Patients (N)	BWT	OEI
CDAI			
<150	14	5.3 ± 2.2	1.26 ± 0.75
>150	17	5.8 ± 2.2	1.49 ± 1.22
ESR			
<20	13	5.2 ± 2.2	0.96 ± 0.77
>20	18	6.5 ± 2.2*	1.70 ± 1.11*
α_1-glycoprotein			
<140	14	5.2 ± 2.4	0.98 ± 0.74
>140	17	5.9 ± 2.1	1.73 ± 1.14*
CRP			
<0.8	12	4.5 ± 1.9	0.94 ± 0.75
>0.8	19	6.3 ± 2.2*	1.6 ± 1.1*

*$P < 0.05$.

or US and x-ray are related to the mean three-month interval between the studies. However, similar results have been reported by other studies where the time interval was shorter (11).

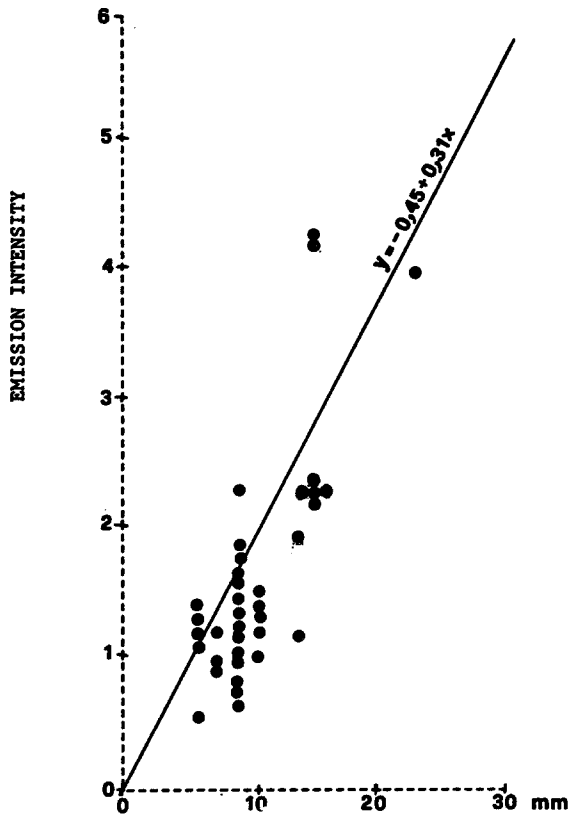

Fig 1. The relationship between emission intensity of the lesions seen with indium scan and the bowel wall thickening seen with ultrasound ($r = 75$; $P < 0.01$).

With regard to evaluation of activity, in our study bowel wall thickness was significantly higher in patients with increased ESR and CRP, but patients with clinically active CD did not have thicker bowel walls than patients in clinical remission. Also in other studies (4, 14) no clear relationships have been established between bowel wall thickening and disease activity, although bowel wall thickening seems to decrease after successful steroid treatment of disease recurrence (5). This study confirmed the result that uptake rates of detected lesions (overall emission intensity) are higher in patients with increased ESR, α_1-acid glycoprotein, and CRP but not with high CDAI values. A correlation between ^{111}In scan and CDAI or laboratory parameters was found in some studies (9, 15), but not in others (16). In our experience, bowel wall thickness measured by US for lesions also identified by ^{111}In scan was significantly related to emission intensity, suggesting that measurement of inflammatory activity with these two methods gives comparable results.

In conclusion, in this study abdominal US has provided information about the location of CD lesions similar to that obtained with autologous ^{111}In leukocyte scan (sensitivity 77%) and for these lesions, it also gave comparable information about CD activity. Abdominal US is preferable to ^{111}In scan in most circumstances for detection and evaluation of x-ray-demonstrable lesions of the intestine.

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