Corticosteroid treatment for asthma has been regarded as potentially dangerous because of the risk of side effects.⁷ Studies in children with acute asthma who had received an eight day course of methylprednisolone compared with a similar group of children who had received placebo showed that in both groups adrenal responsiveness was decreased seven days after the end of treatment; the decrease was no greater in the group given methylprednisolone than in the group given placebo.⁸ It is thus highly unlikely that a single three day course of corticosteroids would have any adverse effect. Provided that the day to day treatment of patients with asthma is properly supervised the need for repeated courses of corticosteroids for acute attacks should be minimal.

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Technetium-99m autologous phagocyte scanning: a new imaging technique for inflammatory bowel disease

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Abstract

A method to determine the extent of active inflammatory bowel disease using selective labelling of autologous neutrophils and monocytes by phagocytosis of a technetium-99m (^{99m}Tc) stannous oxide colloid is described. Unlike leucocyte scanning techniques using Indium-III (¹¹¹In), the ^{99m}Tc colloid scan uses a cheap, readily available isotope, which specifically labels phagocytes. Scan results in 20 patients with inflammatory bowel disease were compared with barium examinations and colonoscopic appearances. There was close agreement in 15 of 20 patients as to the extent of mucosal disease. In four cases the scan showed more extensive disease than was suggested by barium examination. The scan showed terminal ileal Crohn's disease in three patients in whom the barium studies of the ileum had been reported as normal. In four patients with inactive disease and normal barium examinations no activity was seen on the scans.

The ^{99m}Tc phagocyte scan is a sensitive, reliable means of determining the extent of active inflammatory bowel disease and can be used to quantify disease activity.

Introduction

Previous studies of patients with inflammatory bowel disease have established that scanning after intravenous injection of autologous leucocytes labelled with radionuclides determines the extent of

active disease and facilitates objective assessment of activity.¹⁻⁵ The technique is safe in the acutely ill patient⁶ and has proved beneficial in the study of the terminal ileum, for which conventional radiological and colonoscopic examinations are not always successful.

Most of the scanning techniques available use the radioisotope oxine labelled with indium-III (¹¹¹In), which is expensive and is produced by a cyclotron and hence has limited availability.¹⁻⁵ These factors mitigate against its widespread use in hospitals. Moreover, ¹¹¹In-oxine labels all the blood cell types,⁷ and purified populations of blood neutrophils must be prepared for optimal scanning.^{2,3,5}

We recently described a new scanning technique using stannous oxide colloid labelled with technetium-99m (^{99m}Tc) to label specifically autologous phagocytes in whole blood.⁸ We report the use of this readily available, inexpensive, and simple technique in scanning the intestine in patients with inflammatory bowel disease.

Patients

Twenty patients (nine men and 11 women, age range 16-70) suffering from inflammatory bowel disease (table) were studied after they had given informed consent to this study, which was approved by the Hospitals' Ethics Committee. Duration of disease ranged from two months to 15 years. Sixteen patients were diagnosed as having Crohn's disease and four as having ulcerative colitis using conventional clinical, radiological, colonoscopic, and histological criteria. Clinical disease activity was graded according to a modification of the criteria established by de Dombal as absent, mild, moderate, or severe.¹⁰ Fourteen of the 20 patients were receiving treatment with one or more of three agents: corticosteroid, sulphasalazine, and azathioprine (see table).

Methods

Autologous leucocytes (phagocytes) were selectively labelled in heparinised whole blood by phagocytosis of ^{99m}Tc coupled to a stannous colloid (<2 µm spheres) as described previously.^{8,9} Briefly, 20 ml of blood was taken and incubated for one hour with 400 MBq of ^{99m}Tc colloid and citrate buffer. After excess colloid had been removed by centrifugation the labelled blood was returned to the patients. Immediately before abdominal scanning, which was performed at three and six hours after injection using a modern, wide field gammacamera, patients were asked to empty their bladders.

The extent of disease was determined within eight weeks of the scan by air contrast barium enema examination and, where appropriate, by small bowel

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series (nine patients). The patient in case 5 underwent only colonoscopy. Colonoscopic assessment was available for five patients. The extent of colitis or ileitis, or both, was assessed by a radiologist, who was unaware of the results of scanning. Disease was anatomically classified as occurring in one or more of five segments of the bowel: the terminal ileum or the ascending, transverse, descending, or rectosigmoid regions. Two nuclear medicine physicians, who were unaware of the diagnoses or the results of previous radiological or endoscopic assessment, independently assessed all scans.

FIG 1—Six hour ^{99m}Tc scan showing no bowel uptake in a patient with quiescent Crohn's disease and hepatomegaly.

Radionuclide activity was reported as present or absent in each of the five segments of the bowel surveyed.

Results

The table shows the patients' clinical details and extent of disease. All 16 patients with disease classed as clinically active showed evidence of disease on scanning. In four patients whose inflammatory bowel disease was clinically inactive no activity was seen on the scans (fig 1), and the barium examinations were reported as normal in each case. In 15 of 20 patients there was close agreement as to the segments of bowel affected. In the patient in case 14, whose symptoms were mild, active disease of the terminal ileum and colon was detected by scanning, and the same region showed mucosal disease when viewed at barium examination. In particular, active disease in the terminal ileum is clearly shown by scanning (fig 2). In four cases the scan showed more extensive disease or active disease in sites other than those suggested by barium studies (case 1). Crohn's disease of the terminal ileum was clearly shown by scanning in three patients in whom no mucosal abnormality was evident on barium examination (see table). In one patient (case 20) who was suffering from severe ulcerative colitis the appearances of the rectosigmoid region were normal at barium examination but the phagocyte scan showed active inflammation of the region, which was confirmed by histology (fig 3).

In two of the 20 patients studied the areas of disease appeared more extensive when viewed by barium examination (fig 4). Treatment with corticosteroids, azathioprine, or sulphasalazine did not affect the performance of the scan (see table).

Discussion

The ^{99m}Tc labelled autologous leucocyte scan accurately identifies actively inflamed intestine in patients with inflammatory bowel disease. This imaging method showed more extensive disease than barium examination in three of the 20 patients studied and was particularly valuable in identifying disease of the terminal ileum,

FIG 2—Three hour ^{99m}Tc phagocyte scan in a patient with Crohn's disease showing active inflammation in the terminal ileum and ascending colon in agreement with radiological appearances.

Clinical details of patients and extent of disease

Case No	Diagnosis	Disease activity	Activity on scanning	Sites of disease*		Treatment
				On radiology or colonoscopy	On scanning	
1	Crohn's disease	Moderate	Active	TC, DC, R	TI, R	Prednisone 25 mg
2	Ulcerative colitis	Moderate	Active	TC, DC, R (colonoscopy)	TC, DC, R	Prednisone 60 mg
3	Crohn's disease	Severe	Active	AC, TC, DC	TI, AC, TC, DC, R	—
4	Crohn's disease	Mild	Active	TI	TI	Prednisone 20 mg
5	Crohn's disease	Moderate	Active	DC, R (colonoscopy)	DC, R	—
6	Crohn's disease	Moderate	Active	AC, TC, DC, R	DC, R	Prednisone 10 mg, azathioprine 50 mg
7	Crohn's disease	Moderate	Active	AC	AC	Prednisone 20 mg
8	Ulcerative colitis	Mild	Active	R (colonoscopy)	R	Prednisone 50 mg
9	Crohn's disease	Mild	Active	TI, AC, TC, DC	TI, AC, TC, DC, R	—
10	Crohn's disease	Absent	Inactive	No disease (colonoscopy)	No uptake	Prednisone 5 mg
11	Crohn's disease	Moderate	Active	TI	TI	Prednisone 25 mg, azathioprine 100 mg
12	Crohn's disease	Mild	Active	TI, AC	TI, AC	—
13	Crohn's disease	Moderate	Active	DC, R	DC, R	Hydrocortisone 300 mg
14	Crohn's disease	Mild	Active	TI, AC	TI, AC	—
15	Crohn's disease	Mild	Active	TC, DC, R	TI, AC, TC, DC, R	Prednisone 50 mg, azathioprine 100 mg
16	Crohn's disease	Absent	Inactive	No disease	No uptake	Sulphasalazine
17	Crohn's disease	Absent	Inactive	No disease	No uptake	Sulphasalazine
18	Ulcerative colitis	Mild	Active	DC, R	DC, R	Prednisone 40 mg
19	Crohn's disease	Absent	Inactive	No disease	No uptake	—
20	Ulcerative Colitis	Severe	Active	AC, TC, DC, R (colonoscopy)	AC, TC, DC, R	Prednisone 60 mg

*TI=Transverse ileum. AC=Ascending colon. TC=Transverse colon. DC=Descending colon. R=Rectosigmoid.

FIG 3—Three hour ^{99m}Tc phagocyte scan compared with barium enema examination performed four days later in a patient with ulcerative colitis. The scan shows pancolitis, but sparing of the rectosigmoid region is suggested by the barium study. Evidence of active mucosal inflammation of the rectosigmoid region was confirmed by histology.

which is inaccessible to colonoscopy and often poorly visualised by barium examination. The ^{99m}Tc phagocyte scan, like colonoscopy, detects active inflammation—a distinction not made by barium examination, in which the mucosal abnormalities outlined may represent fibrosis or other changes due to previous disease that is no longer active.

Several scanning techniques have been developed to exploit the advantages of radionuclide scans in identifying active inflammatory bowel disease. Gallium-67 scans require 24 to 48 hours before images can be interpreted reliably, and false positive results arise because of normal bowel excretion. Subsequently, ^{111}In -oxine leucocyte scanning has been shown to provide earlier images, to distinguish inflamed bowel from abscess more readily, and to allow faecal excretion of labelled cells to be measured for assessment of disease activity.⁵ Recently, a new test entailing oral administration

of sucralfate to detect mucosal inflammation has been reported.¹¹ This method, however, is unsuitable for use in the acutely ill patient and cannot readily be used to assess disease activity objectively. Moreover, the test depends on bowel transit of isotope and is therefore probably of limited value when there is partial bowel obstruction or greatly increased motility.

^{99m}Tc phagocyte scanning shares several important advantages with ^{111}In -oxine over conventional methods of assessment. Scanning entails minimal preparation and discomfort for patients and can be used in the acutely ill patient. Furthermore, disease activity can be assessed objectively. Preliminary studies in our patients indicate that inflammatory activity can be measured objectively from both temporal uptake of radioactivity with regional analysis¹² and faecal excretion of isotope (preliminary observations).

The ^{99m}Tc phagocyte scan reported here has several important

FIG 4—Six hour ^{99m}Tc phagocyte scan in a patient with longstanding Crohn's disease compared with barium enema examination. Extensive mucosal abnormalities apparently affecting the entire colon are seen in the barium study, but the scan suggests that active inflammation is confined to the descending colon and rectosigmoid regions.

advantages over ^{111}In -oxine scans. Firstly, ^{99m}Tc is readily available in hospitals and is fairly inexpensive, whereas ^{111}In requires a cyclotron for its generation and is very expensive, and thus its practical use is limited. Secondly, the ^{99m}Tc tin colloid labelling technique selectively labels neutrophils and monocytes in whole blood. This is a simple method that obviates the preparation of purified neutrophil populations required for optimal ^{111}In scans due to the propensity for ^{111}In to label all the blood cell types.⁶ Thirdly, the shorter half life of ^{99m}Tc (six hours) means that there is less irradiation of organs than with ^{111}In (half life 67.5 hours).

The ^{99m}Tc phagocyte scan offers a cheap, safe, sensitive, and reliable means of identifying active inflammatory bowel disease. The isotope is readily available in hospitals that perform radionuclide scans, and preparation of the radiopharmaceutical requires minimal technician time.

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