^{99m}Tc-HMPAO leucocyte scintigraphy fails to detect Crohn's disease in the proximal gastrointestinal tract

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Abstract

Objective—To investigate the use of ^{99m}Tc-HMPAO (hexamethyl propylene amine oxime) leucocyte scintigraphy as a non-invasive screening test for inflammatory bowel disease.

Patients—10 children with suspected Crohn's disease, in whom routine investigation using barium contrast radiology, upper gastrointestinal endoscopy, colonoscopy, and mucosal biopsies had identified severe gastroduodenal and/or jejunal involvement.

Design—^{99m}Tc-HMPAO leucocyte scintigraphic studies performed in each of these cases were assessed by a radiologist who was blinded to the disease distribution.

Results—In nine cases there was no scintigraphic evidence of inflammation in the proximal gastrointestinal tract. The 10th child had both gastroduodenal and jejunal involvement, but scintigraphy only revealed faint jejunal positivity.

Conclusions—^{99m}Tc-HMPAO leucocyte scintigraphy should not be depended upon as a screening test for Crohn's disease. False negative results are likely in cases with Crohn's disease confined to the proximal gastrointestinal tract.

(Arch Dis Child 2001;85:43–46)

Keywords: inflammatory bowel disease; Crohn's disease; ^{99m}Tc-HMPAO; scintigraphy

^{99m}Tc-HMPAO (hexamethyl propylene amine oxime) leucocyte scintigraphy has been widely advocated as an investigative technique for patients with suspected inflammatory bowel disease.¹ It can reveal the presence and distribution of inflammation in the gastrointestinal tract, and it has been reported to compare well with conventional techniques such as barium contrast radiology and colonoscopy.^{1–19} Scintigraphy has several clear advantages: it is associated with much lower levels of radiation exposure than contrast radiology²⁰; unlike colonoscopy, it is non-invasive and so intravenous sedation and general anaesthesia are not required²¹; finally, it avoids the troublesome and unpleasant process of laxative bowel preparation necessary for colonoscopy. For these reasons, it has been proposed that ^{99m}Tc-HMPAO leucocyte scintigraphy could be used as a screening test for patients with suspected inflammatory bowel disease.¹

We were aware of individual patients with gastroduodenal Crohn's disease in whom the

proximal involvement had not been identified on ^{99m}Tc-HMPAO leucocyte scintigraphy. We therefore questioned its reliability as a screening test for patients with Crohn's disease confined to the proximal gastrointestinal tract. Our aim in this study was to determine whether ^{99m}Tc-HMPAO leucocyte scintigraphy reliably detected the presence of gastric, duodenal, or jejunal Crohn's disease.

Methods

Routine evaluation of all children presenting to our department with suspected Crohn's disease included barium contrast radiology with small bowel follow through, upper gastrointestinal endoscopy and colonoscopy with serial and targeted mucosal biopsies, and ^{99m}Tc-HMPAO leucocyte scintigraphy. Based on barium contrast radiology, endoscopy, and mucosal biopsies, 10 children with Crohn's disease were identified in whom there was severe gastric, duodenal, or jejunal involvement. In two of these the disease was confined to the proximal gastrointestinal tract, while in eight there was also distal ileal or colonic disease. In all 10 cases the disease was active at the time of investigation, and none of the children was receiving anti-inflammatory or immunosuppressive treatment.

Radiolabelled leucocyte scintigraphy was undertaken using conventional protocols. A 30 ml blood sample was labelled with ^{99m}Tc exametazime (d,l)-HMPAO (Ceretek, Nycomed Amersham, UK) according to the manufacturer's instructions. The maximum administered activity was 200 MBq, the dose being scaled in proportion to body weight in accordance with ARSAC guidelines.²² Five minute anterior and posterior images (approximately 200 000 counts) were acquired at 45 minutes and 3.5 hours following injection of the labelled blood sample, using a single headed gamma camera (Toshiba GCA901A/SA) with a high resolution collimator. Oblique or lateral images were obtained if necessary.

The scintigraphic images were reported by a radiologist (SC) who was unaware of the disease location as determined by the other investigative methods. Abdominal isotope uptake equal to or greater than that associated with the bone marrow was considered to indicate significant inflammation.² The gastrointestinal site of inflammation was determined both on the basis of abdominal location and from the configuration of the involved segment.

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Accepted 20 February 2001

Table 1 Gastroduodenal and jejunal Crohn's disease: comparison of findings on barium contrast radiology, endoscopy, mucosal histology, and ^{99m}Tc -HMPAO scintigraphy

Case No	Barium contrast radiology	Endoscopy	Gastric and duodenal histology	Scintigraphy
1	Jejunum: distorted thickened folds	Normal	Gastric antrum: acute and chronic inflammation, glandular destruction Duodenum: acute and chronic inflammation, villous atrophy	Negative
2	Normal	Normal	Gastric antrum: acute focal inflammation, glandular involvement Duodenum: acute and chronic inflammation	Negative
3	Normal	Duodenum: red thickened folds, extensive ulceration	Gastric antrum: acute and chronic inflammation, granulomas Duodenum: acute and chronic inflammation	Negative
4	Duodenum: distorted folds Jejunum: distorted folds	Normal	Gastric antrum: acute and chronic inflammation Duodenum: acute and chronic inflammation, villous atrophy	Negative
5	Duodenum: distorted thickened folds	Stomach: red, swollen rugae	Gastric antrum: acute & chronic inflammation	Negative
6	Duodenum: distorted folds Jejunum: distorted folds	Duodenum; red, thickened folds, multiple aphthous ulcers	Duodenum: acute and chronic inflammation, villous atrophy	Negative
7	Jejunum: distorted folds, separation of loops	Stomach: marked antral nodularity	Duodenum: acute and chronic inflammation, villous atrophy	Negative
8	Jejunum: distorted folds	Normal	Duodenum: acute and chronic inflammation	Negative
9	Normal	Stomach: antral nodularity and superficial ulcers Duodenum: superficial ulcers	Gastric antrum: acute and chronic inflammation Duodenum: acute and chronic inflammation, marked cryptitis, villus atrophy	Negative
10	Stomach: swollen rugae Duodenum: featureless, loss of folds Jejunum: marked separation of loops	Stomach: marked antral nodularity Duodenum: pale, featureless, narrow, non-distensible	Gastric antrum: acute and chronic inflammation, ulceration, granulomas Duodenum: acute and chronic inflammation, crypt abscesses, villous atrophy, granulomas	Jejunum positive

Results

The results are shown in table 1.

Upper gastrointestinal barium contrast radiology with small bowel follow through showed unequivocal signs of proximal gastrointestinal disease in seven of the 10 children. Abnormal features observed included swollen gastric rugae, thickened and distorted intestinal mucosal folds, loss of folds, and abnormal separation of bowel loops because of bowel wall thickening. There were radiological abnormalities in the stomach in one case, in the duodenum in four, and in the jejunum in five.

Upper gastrointestinal endoscopy revealed unequivocal signs of disease in the stomach or duodenum in six of the 10 cases. Gastric abnormalities included mucosal redness, swollen rugae, nodularity, and ulceration and were present in four cases. Duodenal abnormalities included mucosal pallor or redness, loss of mucosal folds, thickened folds, and ulceration and were also present in four cases.

Obvious histological abnormalities were found in the gastric or duodenal biopsies in all 10 children. Gastric abnormalities included moderate to severe mixed acute and chronic inflammation in seven, neutrophil infiltration of glandular epithelium and glandular destruction in two, ulceration in one, and granulomas in two. Duodenal abnormalities included moderate to severe mixed acute and chronic

inflammation in nine, moderate to severe villous atrophy in six, cryptitis in one, crypt abscess formation in one, and granulomas in one.

Overall, unequivocal radiological or endoscopic signs of gastroduodenal or jejunal disease were present in nine cases. In one child (case 2), although contrast radiology and upper gastrointestinal endoscopy were normal, the mucosal biopsies revealed active inflammation with glandular destruction in the gastric antrum, and inflammation with severe patchy villous atrophy in the duodenum.

In nine of these 10 cases, ^{99m}Tc -HMPAO leucocyte scintigraphy totally failed to reveal the presence of inflammation in the stomach, duodenum, or jejunum. In one child (case 10) with barium contrast, endoscopic, and histological evidence of gastroduodenal involvement and barium contrast evidence of jejunal involvement, only the jejunum was positive on scintigraphy. In the eight patients who also had distal ileal or colonic disease, scintigraphy was successful in demonstrating the inflammation in those areas.

Discussion

Because ^{99m}Tc -HMPAO leucocyte scintigraphy is non-invasive and is associated with minimal radiation it appears ideally suited to paediatric investigation. However, the 10 cases described

here show that it cannot be relied upon completely as a screening test for Crohn's disease. In each of these patients there was unequivocal evidence of active disease in the proximal gastrointestinal tract. The abnormalities were neither subtle nor trivial. In nine cases macroscopic disease was evident on barium contrast radiology or upper gastrointestinal endoscopy, and all had unequivocal histological evidence of gastroduodenal inflammation. Despite this, scintigraphy failed to reveal the presence of inflammation in the proximal gastrointestinal tract in nine. In one child with both gastroduodenal and jejunal disease only the jejunum was positive, and in that case the scintigraphic abnormality was faint.

The radiologist reporting the scintigraphic images in this study was blinded to the results of the other investigations and did not know the disease distribution. The presence of distal ileal or colonic disease in eight of the 10 children provided an important positive control. The distal disease in those cases was evident on the scintigraphic images, and so the absence of proximal scintigraphic positivity was not because of a general technical failure.

In the two cases with Crohn's disease confined to the proximal gastrointestinal tract scintigraphy completely failed to reveal the presence of gut inflammation, and had it been used as a screening test it would have been misleading. The eight with distal disease would also have had a false negative result if the inflammation had been confined to the proximal gut. ^{99m}Tc-HMPAO leucocyte scintigraphy appears to lack sensitivity in patients with gastroduodenal or jejunal Crohn's disease compared with conventional radiology, endoscopy, and mucosal biopsy.

There are several possible explanations for this failure. First, the gastric region is sometimes partly obscured by the normal concentration of isotope in the liver and spleen. In the patients described here, however, gastric involvement was accompanied by duodenal disease. Second, the abnormalities seen with contrast radiology or at endoscopy might not necessarily be associated with acute inflammation, and if so ^{99m}Tc-HMPAO leucocyte scintigraphy might be negative.⁴ In the patients described here, however, the disease was clinically active and the mucosal biopsies revealed the presence of acute inflammation. Perhaps the most likely explanation is that the total mass of acute inflammatory cells infiltrating the gut wall tends to be smaller in gastroduodenal and jejunal Crohn's disease than in ileocolonic disease.

Involvement of the proximal gastrointestinal tract is not uncommon in Crohn's disease. Severe gastroduodenal disease is reported in about 5% of patients.^{23 24} Proximal Crohn's disease may occur more often in children. Halligan *et al* examined the small bowel disease distribution on barium follow through studies in 114 adults and 67 children with Crohn's disease.²⁵ Duodenal or jejunal disease was present in 15% of adults and 30% of children. The disease was confined to the stomach and proximal small intestine in 9% of the children. In recent years, the routine use of upper

gastrointestinal endoscopy and mucosal biopsy in suspected Crohn's disease has revealed gastroduodenal inflammation in a high proportion of patients.²⁶

Numerous studies, mostly based on adult patients, have examined the reliability of ^{99m}Tc-HMPAO leucocyte scintigraphy in the investigation of patients with inflammatory bowel disease.¹ When used in order to detect colonic inflammation, sensitivities of 65% to 100% and specificities of 50% to 100% have been reported.^{1 13 14} When used to assess the extent and distribution of disease, the reported concordance with conventional contrast radiology and endoscopy has ranged from 60% to 100%.^{2 4-6} Evidence regarding its reliability in detecting small bowel Crohn's disease is limited.³ There are few systematic studies on the use of ^{99m}Tc-HMPAO leucocyte scintigraphy in children with suspected inflammatory bowel disease. Overall, diagnostic sensitivities of 84% to 93% and specificities of 81% to 88% have been reported.^{11 12} When compared with histology, sensitivities of 90% and specificities of 75% to 90% have been reported for ileocolonic disease.^{9 16-18} The numbers of subjects included in most adult and paediatric studies have been small, and it should be appreciated that the unstated confidence intervals for reported sensitivities and specificities are therefore wide.

CONCLUSIONS

It has been stated that a negative ^{99m}Tc-HMPAO leucocyte scan in a symptomatic patient virtually excludes inflammatory bowel disease.¹ However, our study shows that that false negative results do occur in children with active symptomatic Crohn's disease. ^{99m}Tc-HMPAO leucocyte scintigraphy may have a role in the detection and assessment of gastrointestinal inflammation, but it should not be considered a completely reliable screening test. When Crohn's disease is suspected, barium contrast radiology and endoscopy remain the essential investigative techniques.

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EUROPE CALLING

World wide wasting?

Whether we like it or not, the world wide web has entered our professional and private lives. Electronic access to literature search tools such as MEDLINE, online availability of journals (like this one), sending and receiving documents, booking trains or flights—to mention just a few examples—have made our lives so much easier. However, there is another side of the coin. More and more parents confront us with information obtained from obscure sites on the internet, where potentially harmful recommendations are published without professional review. Already, case reports have been published of parents who have refused to immunise their child after websites have suggested that it was safer not to do so. You will not be surprised to hear that intemperate use of computers and the internet is now under discussion as a psychiatric disorder. Whether internet addiction really is an illness by itself or is symptomatic of other primary disorders remains to be seen.

Paediatricians and other providers of medical care for children should be prepared to deal with the “internet-(ed)ucated” parent today, and even more tomorrow. We may encounter new forms of child neglect, as the following case illustrates. A 6 month old infant was recently sent to our hospital for a diagnostic check up because of failure to

thrive. He was the first child of a young, well educated couple. The mother had been on maternity leave since delivery, the child's father was fully employed. The family had internet access at home. Although the child was healthy and had developed normally during the first 3 months of life, weight gain was insufficient thereafter. A careful history by the admitting house officer revealed that the infant had been breast fed for 3 months, but his mother then became increasingly impatient with the child, mainly because caring for him took away the time which she used to spend surfing the internet. She didn't react to her son's natural demands and ignored his hungry cries. During his stay in hospital, the boy quickly put on weight with formula and no other plausible cause for his malnutrition was found. Psychiatric help was offered to the mother which she accepted. Currently, a household helper has been engaged and the boy is making encouraging developmental progress.

Obviously, one more entity needs to be added to the already long list of possible causes for failure to thrive: parental Morbus Internet! Sad but true.

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