$^{99m}$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. 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.

Scintigraphy has several clear advantages: it is associated with much lower levels of radiation exposure than contrast radiology; unlike colonoscopy, it is non-invasive and so intravenous sedation and general anaesthesia are not required; 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.

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 (Ceretec, 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. 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 was equal to or greater than that associated with the bone marrow was considered to indicate significant inflammation. The gastrointestinal site of inflammation was determined both on the basis of abdominal location and from the configuration of the involved segment.
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 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

| 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 | 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 | 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 | Stomach: marked antral nodularity | Gastric antrum: acute and chronic inflammation, ulceration, granulomas Duodenum: acute and chronic inflammation, crypt abscesses, villous atrophy, granulomas | Jejunum positive |

Jejunum: marked separation of loops
gastrointestinal endoscopy and mucosal biopsy in suspected Crohn's disease has revealed gastroduodenal inflammation in a high proportion of patients.1

Numerous studies, mostly based on adult patients, have examined the reliability of 99mTc-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.1,11–14 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%.14,16 Evidence regarding its reliability in detecting small bowel Crohn's disease is limited.1 There are few systematic studies on the use of 99mTc-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.11,17 When compared with histology, sensitivities of 90% and specificities of 75% to 90% have been reported for ileocolonic disease.10,11 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 99mTc-HMPAO leucocyte scan in a symptomatic patient virtually excludes inflammatory bowel disease.1 However, our study shows that false negative results do occur in children with active symptomatic Crohn's disease. 99mTc-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.

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 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

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 hunger cries. During his stay in hospital, the boy quickly put on weight with formula feed. 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.

ULRICH HEININGER
European editor

EUROPE CALLING
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Arch Dis Child 2001 85: 43-46
doi: 10.1136/adc.85.1.43

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