Original article

Is ^{99m}Tc-LeucoScan scintigraphy useful in the assessment of location in Crohn's disease?

A.N. Kapsoritakis[1], S.I. Koukouraki[2], I.E. Koutroubakis[3], F. Dimoulios[3], A. Delidaki[2], S. Potamianos[1], N. Karkavitsas[2], E.A. Kouroumalis[3]

SUMMARY

Background/Aims: Scintigraphy with ^{99m}Technetium HMPAO labelled white blood cells (^{99m}Tc HMPAO-WBC) is routinely used for the assessment of inflammatory bowel disease (IBD). The main disadvantages of this diagnostic test are the time consuming in vitro cell labelling and the handling of blood itself. To overcome these problems, new, equally effective agents are under development. To assess the value of a new, easily prepared agent, the ^{99m}Tc-Leucoscan, in IBD, we performed a pilot scintigraphic study in patients with active Crohn's disease (CD). In the event of negative results, it was envisaged, that another agent ^{99m}Tc (V) dimercaptosuccinic acid (DMSA) would be tested.

Patients - Method: We performed ^{99m}Tc-Leucoscan scintigraphy in 7 patients with clinically active CD and in 3 of them an additional scintigraphy with 99mTc (V) DMSA. Two of the 7 patients were males and 5 females; aged 26-70 years (mean age 42 years). Two of them had extra-intestinal manifestations with joint involvement.

Results: In one of these patients ^{99m}Tc-Leucoscan scintigraphy was considered as indeterminate because of relatively increased uptake in the bowel and in the other 6 it was false negative. In the 2 patients with joint involvement ^{99m}Tc-Leucoscan images did show increased uptake in the involved bone areas. Three of all patients subsequently underwent ^{99m}Tc (V) DMSA scintigraphy and all 3 were considered true positive.

Conclusion: Our study concludes that ^{99m}Tc-Leucoscan scintigraphy has no place in the assessment of gastrointestinal inflammation in CD. ^{99m}Tc (V) DMSA could be suggested as a reliable tracer that could substitute for ^{99m}Tc-HMPAO WBC scintigraphy in IBD patients.

Key Words: Crohn's disease, ^{99m}Tc-Leucoscan, ^{99m} Tc (V) DMSA, Scintigraphy, Intestinal inflammation.

[1]Department of Internal Medicine, Gastroenterology Unit, University Hospital of Thessaly, Departments of [2]Nuclear Medicine and [3]Gastroenterology, University Hospital of Crete, Greece

Author for correspondence:

Andreas N. Kapsoritakis MD, Lecturer of Gastroenterology, Iroon Politechniou 144, 41223 Larissa, Greece, Tel: (+2410) 682435, Fax: (+2410) 237117, e-mail: kapsoritakis@her.forthnet.gr

INTRODUCTION

Crohn's disease (CD) is an inflammatory bowel disease in which the inflammation may be present throughout the gastrointestinal tract and in addition extra-intestinal manifestations may be observed. Mucosal infiltration with leukocytes is a characteristic histological feature in CD, particularly during periods when the disease is active. For the assessment of the location of disease throughout the gastrointestinal tract, at least one radiological and two different endoscopic techniques are necessary.

Scintigraphy, is a non-invasive technique that makes possible the visualization of active CD in the entire bowel. Several scintigraphic techniques have been used for the assessment of location of intestinal inflammation in CD. The most widely used, for a number of years, has been scintigraphy with techetium-99m hexamethyl-propylamine-oxime labeled white blood cells (^{99m}Tc HMPAO-WBC), because of its high sensitivity and specificity.[1-4] The main disadvantages of this diagnostic procedure are; the interaction with patient's blood and the time-consuming in vitro cell labelling, that takes about 2 hours. In order

to overcome these problems, new radiopharmaceutical agents are under evaluation.

^{99m}Tc-Leucoscan (a Fab' fragment of monoclonal antibody) is a relatively new agent that has registered for the detection of infections in soft tissue and bone[5]. The preparation of ^{99m}Tc-Leucoscan takes about 5 min for in vitro labelling and does not require direct interaction with patient's blood. Because of these properties it was thought to be an ideal candidate for our study.

^{99m}Tc (V) dimercaptosuccinic acid (DMSA) scintigraphy is effective in the detection of bone and joint infections[6], and as has been recently suggested a useful diagnostic test for the localization of intestinal inflammation.[7] It is inexpensive and has the advantages of simple preparation, like Leucoscan.

To assess the value of a new, easily prepared agent, we performed a pilot scintigraphic study with ^{99m}Tc-Leucoscan in patients with active CD. In the event of negative results it was envisaged, that another radiopharmaceutical agent ^{99m}Tc (V) DMSA could be tested.

MATERIALS AND METHODS

Patients: We performed ^{99m}Tc-Leucoscan scintigraphy on 7 patients with active CD. All patients had a definitive diagnosis of active CD confirmed by radiological, endoscopic and histological studies. All patients had active disease, with a Crohn's disease activity index (CDAI)[8] >150. Patients with previous bowel surgery were excluded. Two of the 7 patients were males and 5 females (pregnancy was excluded); aged 26 to 70 years (mean age 42 years). The mean CDAI score was 247 (range 160-391). Two of the patients were newly diagnosed and two had extra-intestinal manifestations with joint involvement.

Imaging technique: In all cases the scintigraphy was performed within a week after colonoscopy. Twenty mCi (740MBq) of ^{99m}Tc- Leucoscan were intravenously injected in all patients included in our study. Three of these patients subsequently underwent scintigraphy with 20 mCi (740 MBq) of ^{99m}Tc (V) DMSA. The minimum interval between these two radioisotopic studies was 2 days.

A γ camera GE Millennium (Millwakee, USA) equipped with a low energy general purpose collimator (LEGP) was used. Planar views of the abdomen were obtained 1 hour after intravenous injection of ^{99m}Tc Leucoscan and 3 hours after the ^{99m}Tc (V) DMSA injection, with the patient in supine and upright position. Before imaging, patients were requested to void their bladders to avoid false results.

All scintigrams were visually evaluated by two nuclear medicine physicians without knowledge of diagnosis and endoscopic data. The bowel was divided into 5 segments: small bowel, ascending colon, transverse colon, descending colon and rectosigmoid. Scintigraphic images were considered as true positive when an increased uptake was observed in the bowel. A false negative study was considered when there was no uptake of the tracer in the bowel, although the other diagnostic procedures were positive for inflammation. The scintigraphic results were compared with the endoscopic, radiological and clinical data of the patients.

RESULTS

^{99m}Tc Leucoscan and ^{99m}Tc (V) DMSA scintigraphies were well tolerated by all patients and no complications were observed. In one out of 7 cases, ^{99m}Tc-Leucoscan scintigraphy was considered as indeterminate because of a relatively increased uptake in a single bowel segment, although the patient was known to have diffuse inflammation. In the other 6 patients ^{99m}Tc-Leucoscan revealed no increased uptake in the bowel at all and was considered as false negative. In the two patients with joint involvement ^{99m}Tc-Leucoscan images showed increased uptake in the involved bone areas. In all patients, a normal distribution was seen with physiological uptake in bone marrow, liver, spleen and kidneys. Owing to these disappointing (false negative) results the study with ^{99m}Tc-Leucoscan was stopped.

Three of these false negative cases underwent ^{99m}Tc (V) DMSA scintigraphy. All of them were evaluated as definitely positive because of an increased uptake in all bowel segments with active disease (true positive).

DISCUSSION

Endoscopy and radiology are the cornerstones in the assessment of Crohn's disease, especially for establishing the diagnosis in the initial work-up, for diagnosing strictures and fistulae, and detecting malignant degeneration. These methods, however, are invasive, require bowel preparation and may not be suitable for all situations. Scintigraphy may have an important role in the follow-up of CD patients, especially in cases of suspected recurrence and in monitoring therapy.[1,2,4,9] A precondition for the success of bowel scintigraphic imaging is the presence of active disease.[1]

Noninvasive scintigraphy with labelled leukocytes has been demonstrated as a reliable technique for the assessment of location in CD patients, and has been shown to correlate well with Endoscopy.[10] Because of its easy preparation, rapid binding of the antibody on granulocytes and the use of ^{99m}Tc as radionuclide, Leucoscan was thought to be an ideal replacement for the ^{99m}Tc HMPAO-WBC labelling procedure, but this could not be confirmed in our study. The failure of Leucoscan to detect gastrointestinal inflammation in our study, as well as in another study by Stokkel *et al*.,[11] allows us to conclude that ^{99m}Tc-Leucoscan cannot replace ^{99m}Tc HMPAO-WBC in IBD investigation. These negative findings were probably due to a difference in the mechanism of uptake of Leucoscan compared to ^{99m}Tc HMPAO-WBC.[11] The evaluation of joint involvement with Leucoscan in patients with CD, restricts its usefulness only to this purpose. However, in a small number of pediatric patients with IBD, SPECT imaging with 99m-Tc antigranulocyte monoclonal antibody detected the presence of inflammation in the majority of patients.[12]

The failure of Leucoscan to detect the inflammatory foci in CD patients in this study stands in contrast to the true positive images obtained using ^{99m}Tc (V) DMSA. Despite the small number of patients presented herein, the continuation of the study has shown that ^{99m}Tc (V) DMSA scintigraphy provides a non-invasive, practical, safe and accurate assessment of IBD location[13]. ^{99m}Tc (V) DMSA could be suggested as a reliable tracer to substitute for ^{99m}Tc HMPAO-WBC scintigraphy in IBD patients.

In summary, the failure of ^{99m}Tc-Leucoscan to detect gastrointestinal inflammation allows us to conclude that it cannot replace ^{99m}Tc HMPAO-WBCs in IBD investigation. The visualisation of joint involvement by Leucoscan, suggests that it may be of use for this purpose only. On the other hand, despite the small number of cases in the present study, ^{99m}Tc (V) DMSA could be suggested as a reliable tracer that could substitute for ^{99m}Tc HMPAO-WBC scintigraphy in IBD patients.

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