Scintigraphy with ^{99m}Tc(V)-DMSA in monitoring patients with inflammatory bowel disease

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Abstract

The clinical significance of pentavalent technetium-99m dimercaptosuccinic acid (^{99m}Tc(V)-DMSA) scintigraphy in diagnosing inflammatory bowel disease (IBD) has not yet been fully elucidated. *The aim* of this prospective paper was to study the above. *This study included* 54 patients, 22 females and 32 males (mean age: 36.68±11.49; range: 18-63 years) with IBD who came to our clinics for follow-up and were examined clinically by colonoscopy and ^{99m}Tc(V)-DMSA scintigraphy. *On the follow-up studies*, five patients (9.25%) relapsed, and 49 (90.74%) remained at a steady condition. There was a good correlation between the scintigraphic results and the clinical and colonoscopy data of the patients (P<0.05). *In conclusion*, our results indicated that ^{99m}Tc(V)DMSA scintigraphy can be complementary to colonoscopy for the diagnostic evaluation of IBD.

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Introduction

Inflammatory bowel disease (IBD) includes two chronic idiopathic diseases, Crohn's disease (CD) and ulcerative colitis (UC). There has been an increase in the incidence of IBD in recent years, mostly because of changes in lifestyle and eating habits [1, 2]. Optimal management of IBD requires appropriate localization, determination of the severity and therapeutic management [3]. The extent of the inflammatory process can be investigated by colonoscopy with multiple biopsies is the gold standard for the investigation of the large intestine and the terminal ileum; however, colonoscopy in cases of abnormal shape of the bowel (octoid, zig-zag dolichocolon) is not always applicable, as usually in cases of progressed IBD [4].

Several studies demonstrated the reliability of various scintigraphic imaging procedures for the assessment of disease activity in IBD [5-11], while radiolabeled leukocytes are still widely used due to their high sensitivity and specificity [12, 13]. However, high cost, time-consuming labeling procedures and radiation dosimetry may limit the application of some of the scintigraphic techniques [14, 15]. Pentavalent technetium-99m-dimercaptosuccinic acid (^{99m}Tc(V)-DMSA) has been successfully used for the scintigraphic diagnosis of inflammatory processes such as osteomyelitis, psoas major abscess, and bone and joint infections [16-18]. Although this procedure offers high patient acceptability, low cost, easy preparation, and good image quality, there are rather few papers on the efficacy of ^{99m}Tc(V)-DMSA scintigraphy in IBD [19-21]. The aim of this prospective study was to investigate the clinical significance of ^{99m}Tc(V)-DMSA scintigraphy in the diagnosis of disease activity in patients with IBD.

Subjects and methods

Participants and study design

This study was conducted on 54 patients with IBD 52 patients with UC and 2 patients with CD, 22 females and 32 males (mean age: 36.68±11.49; range: 18–63 years). The duration of disease was 6.06±3.19 years and patients referred for follow-up examinations. Patients were recruited from a university hospital in Gorgan, Golestan Province, Iran, between May 2011 and December 2012. The diagnosis was supported by history, laboratory tests, colonoscopy, histology, and radiology. The patients underwent dynamic and static planar ^{99m}Tc(V)-DMSA scintigraphy. Exacerbation was defined as recent worsening of the symptoms, with a CD activity index greater than 150 in CD cases [17] or a simple clinical colitis activity index greater than 3 in UC cases [18]. Standard labora-

tory parameters included: red and white blood cell counts, hemoglobin, hematocrit, platelets count, erythrocyte sedimentation rate, and C-reactive protein. Furthermore, colonoscopy and biopsy were performed in all patients.

This study complies with the Declaration of Helsinki and was approved by the institutional ethics committee of Golestan University of Medical Science; all patients gave their informed written consent.

Imaging protocols

The patients received 370MBq of ^{99m}Tc(V)-DMSA by intravenous injection. A commercial (V)-DMSA kit (AEOI, Tehran, Iran) was applied and the labeling and quality control procedures were carried out according to the manufacturer's instructions.

Scans were performed initially at the first minute, for 30min, in dynamic mode. Then, anterior planar projections of the abdomen and pelvis were acquired at 60, 120, and 180min after the radiotracer injection, each for a duration of 10min. The images were obtained on a large field of view by a double head gamma camera (PRISM Picker 1000XP, GE, USA) with a 15% energy window centered on 140keV and a low energy, all-purpose collimator.

Figure 1. Anterior ^{99m}Tc(V)-DMSA dynamic scintigram in a 39 years old male with active ulcerative colitis showed uptake in the transverse and hepatic flexture colon, congruent with the colonoscopy findings.

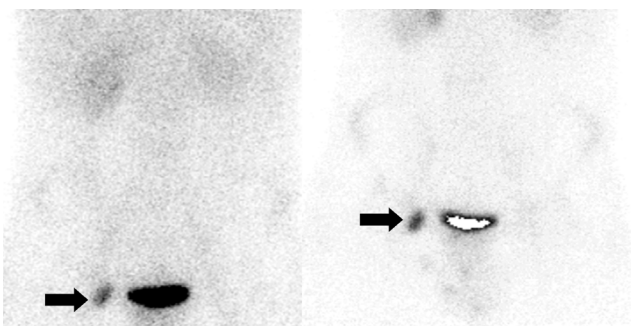

Figure 2. Anterior ^{99m}Tc(V)-DMSA scintigram in a 21 years old male patient with active Crohn's disease showed an intense activity adjacent to the bladder on the right side (terminal ileum), congruent with the colonoscopy findings.

Table 1. *The clinical efficacy of ^{99m}Tc(V)-DMSA scan for the diagnosis of active inflammatory bowel disease*

Statistical parameters	Number
True positive	5
False »	0
True negative	95
False »	0

PPV, NPV, sensitivity, specificity and accuracy were all 100%

Image interpretation

Scintigraphic data were interpreted by two nuclear medicine specialists unaware of the clinical or laboratory findings and differences of judgment were solved by consensus. The bowel was divided into the following five segments: small intestine, ascending, transverse and descending colon, and rectosigmoid. A discrete focus of increased ^{99m}Tc(V)-DMSA activity on the scintigraphy in the abdomen and pelvis was considered positive for disease activity.

Statistical analysis

The data were represented as mean±SD. The scintigraphic results of ^{99m}Tc(V)-DMSA imaging were compared with clinical data, laboratory data, and/or colonoscopy and histology findings. Patients with active disease and radiotracer activity on the scans were defined as true positive (TP), while those with active disease and negative tracer activity were considered false negative (FN). Patients with inactive disease without abnormal radiotracer activity were defined as true negative (TN), whereas those with inactive disease and radiotracer activity were considered false positive (FP). Sensitivity, specificity, negative and positive predictive values, and also accuracy were determined for each scan.

A chi-squared test was used to compare the statistical parameters of this technique. A value of $P<0.05$ was considered significant.

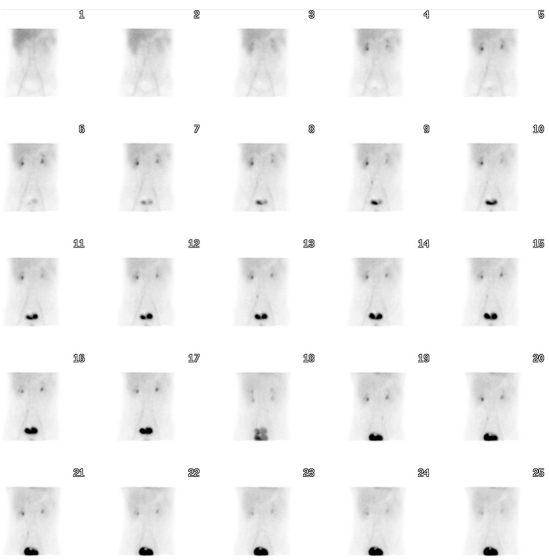

Figure 3. Anterior ^{99m}Tc(V)-DMSA scintigram in a 36 years old male patient with inactive ulcerative colitis showed no abnormal activity in the abdomen and pelvis.

Statistical analysis was performed using an IBM computer and PASW software, version 18.0 (SPSS, Inc., Chicago, IL).

Results

On our follow-up studies, relapse of the disease was confirmed in 5/54 (9.25%) of the patients and no change in the disease status with no tracer uptake was observed in the remaining 49/54 (90.74%) patients. Examples are shown in Figures 1-3.

In visual analysis of the scintigraphic images of the 5 patients in relapse, uptake was observed in the transverse, the descending, the rectosigmoid colon, the terminal ileum and finally, the hepatic flexure and transverse colon. There was a good correlation between the scintigraphic results and the clinical data of the patients (Table 1, P value <0.05). The ^{99m}Tc(V)-DMSA scintigraphy was in all cases accurate in the diagnosis of disease activity (Table 1).

Colonoscopy with biopsy was carried out on all 5 patients with active disease which correlated completely with the scintigraphic findings.

Discussion

Diagnosis and follow-up of patients with IBD is mainly based on endoscopy and histology [5, 22]. Radiological methods such as computed tomography (CT), magnetic resonance imaging (MRI), and ultrasound are also being used as secondary to endoscopy [2, 23, 24]. However, patient compliance with these methods is poor, due to the necessity for adequate bowel preparation and the increased risk of complications, especially in the acute phase of bowel inflammation [2, 25, 26].

Several nuclear medicine studies have also been applied, like radiolabeled autologous leukocytes, human polyclonal immunoglobulins, antigranulocyte monoclonal antibodies, monoclonal antibodies against activated endothelial adhesion molecules, and fluorine-18-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET) scans [5-8, 27, 28]. Although radiolabeled leukocytes are still widely used because of their high sensitivity and specificity [12, 13, 28], high cost, labor-intensive in vitro labeling procedures, radiation microdosimetry, and the handling of blood are main drawbacks of this procedure [14, 15].

Pentavalent ^{99m}Tc-DMSA is a tumor-seeking agent that has also been used successfully for the diagnosis of other diseases [29-31] and of inflammatory processes [16, 18]. The mechanism of ^{99m}Tc(V)- DMSA activity in inflammatory processes remains uncertain, although its radiotracer infiltration into the interstitial space due to increased capillary permeability has been suggested as the main mechanism of DMSA uptake into the inflammatory lesions [17, 20].

To our knowledge, this is the fourth clinical study to assess ^{99m}Tc(V)-DMSA scintigraphy for the detection, localization, and assessment of disease activity in patients with IBD [19-21]. In 2001, Lee et al. (2001) in 62 patients [21] showed a sensitivity, specificity and accuracy of more than 94%. In 2003, Koutroubakis et al. (2003) studied patients at early IBD stage at exacerbation and at remission and reported diagnostic sensitivity, specificity, negative and positive predictive value for active disease between 85%-92% [19]. In the third paper, Stathaki et al. (2008) [20] reported agreement between endoscopy and scintigraphy of 91.9% and 84.4% for ^{99m}Tc labelled WBC and ^{99m}Tc(V)-DMSA, respectively. False negative results for ^{99m}Tc(V)-DMSA scintigraphy were found in two patients and were associated with a mild degree of inflammation [20]. Although ^{99m}Tc(V)-DMSA scintigraphy seems to provide a useful tool for the assessment of disease activity in IBD patients, it may not replace ^{99m}Tc- HMPAO WBC in patients with ischemic colitis [32, 33].

In the three above-mentioned studies, there were a few FN results for ^{99m}Tc(V)-DMSA scintigraphy, which were associated with mild degrees of inflammation in IBD and might explain small differences in accuracy between ours and the three previous studies.

According to our results, ^{99m}Tc(V)-DMSA scintigraphy has excellent diagnostic sensitivity and specificity. Moreover, ^{99m}Tc (V)-DMSA has many advantages compared with other radiopharmaceuticals, such as low cost, availability, good physical characteristics (good counting statistics in imaging), no need for blood manipulation, and an easy preparation procedure. The cost of (V)-DMSA scintigraphy is approximately one half of the cost of WBC scintigraphy and also less than the cost of colonoscopy in our country.

The favorable results of the three previous studies, in combination with the advantages of the method, could establish this technique as an ideal alternative scintigraphic method. This study may recommend to the clinicians that the ^{99m}Tc(V)-DMSA scintigraphy can be included in the work up of patients with IBD.

We have studied a relatively small sample size of our patients and excluded other types of colitis. We did not perform semi-quantitative analysis and colonoscopy. The other limitation of the study is that disease activity was determined based on composite indices of disease activity and we did not do colonoscopy in all patients.

In conclusion, our results indicate that ^{99m}Tc(V)-DMSA scintigraphy can provide reliable and reproducible information to the clinicians (accuracy 100%) and we suggest when possible, to be included in the diagnostic algorithm of patients with IBD.

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The authors declare that they have no conflicts of interest.

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