Is scintigraphic double-track appearance a sign of severe acute episodes of ulcerative colitis?

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SUMMARY

Aim — In comparison to endoscopy, clinical and biological criteria are less predictive of severity in attacks of ulcerative colitis (UC). Our aim was to assess the value of the double-track scintigraphic appearance in the assessment of the severity of acute UC by comparing it to endoscopic criteria.

Patients and methods — We reviewed medical records of 52 patients hospitalized for an acute attack of UC, who had undergone within 48 hours of presentation both a technetium 99m hexamethyl propylene amine oxime (99mTc-HMPAO) granulocyte scintigraphy and endoscopic examination (colonoscopy: n=20; rectosigmoidoscopy: n=32).

Results — Taking into account the colonic segments examined together with both methods in the same patient or results obtained with colonoscopies, there was an excellent agreement between the double-track scintigraphic appearance and endoscopic criteria of severity.

Conclusion — In patients with previously diagnosed UC, 99mTc-HMPAO granulocyte scintigraphy when available may replace endoscopic examination to assess the severity of attacks.

The full text of this article is available in English, free of charge, on the web on: www.2med.com/gcb.
Patients and methods

Patients

Medical files of 52 patients (27 women, 25 men, mean age 36 years, age range: 17-83 years) hospitalized between 1994 and 2000 for an acute episode of ulcerative colitis (UC) were reviewed retrospectively. Diagnosis of UC had been established on the basis of typical clinical presentation, disease course and endoscopic and histological findings [16]. These patients had had UC for a mean 6 years (range: 2-12 years) with an average of four acute flare-ups (range: 2-7). On admission, 45 patients were taking medications: oral steroids (n = 20, dose = 0.5 to 1 mg/kg/d prednisone equivalent), local steroids (n = 7), aminosalicylates (oral and/or local, n = 14), azathioprine (n = 4). Seven patients had no ongoing treatment. Mean time between onset of the attack and admission was 44 days (range: 3-72) and 14 patients (27%) were referred from another hospital.

All patients underwent technetium 99m granulocyte scintigraphy and endoscopy within a 48 hour period. The order of the explorations was not programmed nor randomized and depended solely on availability. Granulocyte scintigraphy was performed before the endoscopic exploration in 20 of the 52 patients.

Methods

Scintigraphic scans were obtained after labeling polymorphonuclear neutrophils in accordance with the technique described by Peters et al. [17] and modified by addition of a separation step to isolate mononuclear cells in order to obtain specific granulocyte labeling [18, 19]. Briefly, a 45 mL blood sample, drawn with anticoagulant, was allowed to settle for 30-90 minutes at 37 °C followed by density gradient flotation using 2 centrifugations to isolate polymorphonuclear neutrophils which were then labeled with 20 mCi technetium 99m hexamethyl propylene amine oxime (99mTc-HMPAO, Ceretec Amersham, UK). Labeling yield was 40-80% and cell viability was greater than 98%, in line with data in the literature [20].

After reinfusion as rapidly as possible of isolated and labeled granulocytes, the patient underwent an anterior-view dynamic scintigraphy lasting 20 minutes, performed with a high-resolution low-energy parallel collimator equipped with a broad field gamma camera centered on the thorax and the abdomen. This dynamic scan was used to check the integrity of the granulocytes in vivo as it is known that polymorphonuclear cells which have been activated or injured in vitro during the separation or labeling steps exhibit persistent intense pulmonary activity associated with high liver uptake due to the destruction of damaged cells. Rapid pulmonary clearance associated with low liver uptake demonstrates proper cell preparation. This step is no longer necessary after achieving sufficient skill with the cell labeling process.

The scintigraphic exploration consisted of anterior and posterior acquisition of planar scans centered on the abdomen 1 and 2 hours after infusion of the labeled cells [21]. Acquisition time was 10 minutes. A tomographic scan was useful in certain cases to better identify inflammatory foci (overlap of gut and bone uptake) or obtain a specific view: rectal foci, oblique or lateral scans to follow the bowel loops. The double-track appearance was generally visible on the anterior views but three-quarter oblique views were sometimes necessary for proper identification.

All scintigrams were interpreted by the same operator blinded to endoscopic findings. All scintigrams were reviewed by a second investigator for the purpose of this study. The colon was divided into 5 segments: rectum, sigmoid, descending, transverse and ascending colon. Lesions visualized on the scintigrams were considered to be severe if a double-track aspect was identified in one or several segments. Intensity of uptake was expressed in comparison with bone marrow uptake, 0 = absence of uptake, 1 = uptake less intense than bone marrow uptake, 2 = uptake equivalent to bone marrow uptake, 3 = uptake more intense than bone marrow uptake. Maximal uptake and the most significantly involved colonic segment were noted.

The endoscopic exploration consisted of a total colonoscopy in 20 patients performed under general anesthesia and a rectosigmoidoscopy in 32 patients. The endoscopic explorations were performed by senior operators. The colon was prepared with 3-4L polyethylene glycol for total colonoscopy and two Normacol® enemas for rectosigmoidoscopy.

Assessment of the severity of UC was based on the criteria described by Carbanniel et al. [5]. UC was considered severe when at least one of the following criteria was present: deep ulcers extending over at least 10% of the colonic surface examined, detached mucosa on the borders of the ulcers, well-like ulcerations, extensive abrasion of the mucosa.

Results

Scintigraphic findings

The double-track appearance was observed in 23 patients. The two observers (a clinician and a nuclear medicine physician) were in full agreement for presence or absence of a double-track. Typical images are presented in figure 1 (isotopic aspect of colitis without double-track appearance) and figure 2 (isotopic aspect of colitis with double-track appearance).

Among the 23 patients with a double-track scintigram, uptake intensity was scored 3 in 14 (61%) and 2 in 9 (39%), but never 1. The double-track aspect was not observed for 29 patients whose uptake intensity scores were 3 (n = 10, 34%), 2 (n = 13, 45%) and 1 (n = 6, 21%). When present, the double-track appearance involved one colonic segment in most of the patients,
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Comparison between endoscopic and scintigraphic criteria of severity defined on the presence or absence of a double-track

We first compared the two sets of diagnostic criteria in patients for whom given colonic segments could be compared. Since rectosigmoidoscopy had been performed in most patients, we assumed that the proximal portion of the colon was free of severe lesions if the lesions observed in the distal colon were not severe at endoscopy. The results of this first analysis are presented in table I. Among the 52 patients, we had discordant results in 4. This could be explained by the absence of signs of severity in three patients who had undergone rectosigmoidoscopy alone and who exhibited a double-track aspect involving the descending or transverse colon. The results were truly discordant in only one patient whose rectosigmoidoscopy had been performed to the hepatic flexure without evidence of severe lesions (shallow ulcers without mucosal detachment; histology: moderately active subacute rectosigmoiditis) but whose scintigram displayed a double-track sigmoid colon. This patient had clinical and biological signs of severe disease (6 bloody stools/day, serum hemoglobin 8.9 g/dL, erythrocyte sedimentation rate above 55 the first hour, serum albumin 28 g/L) and 223 transmural inflammation (figures 2 and 3). If the attack is severe, ulcers penetrate deeper, detaching the submucosa; labeled polymorphonuclear cells are dispersed into all the layers of the colonic wall producing a thickened appearance resulting from the submucosal detachment [22-25]. The wider aspect of the colonic wall gives a double-track image and signals transmural inflammation (figures 2 and 3). This deeper extension is a common finding in active Crohn’s disease, but in UC represents a sign of severity.

The precision of endoscopic assessment of the severity of colonic lesions has been demonstrated in comparison with anatomic data obtained after surgery for severe UC [5]. The good agreement between the endoscopic evaluation of severity and the presence of a double-track on the scintigram was first suggested by the team at the Cochin hospital in Paris who reported several observations [15, 19, 26]. The purpose of our work was thus to ascertain the significance of the double-track scintigraphic aspect in patients with known UC experiencing an acute attack using endoscopic findings for comparison.

Discussion

Labeled polymorphonuclear cells are distributed in the normal depth of the mucosa and submucosa during mild flare-ups of ulcerated colitis [22-25], explaining the homogeneous image observed on scintiscan (figures 1 and 3). If the attack is severe, ulcers penetrate deeper, detaching the submucosa; labeled polymorphonuclear cells are dispersed into all the layers of the colonic wall producing a thickened appearance resulting from the submucosal detachment [22-25]. The wider aspect of the colonic wall gives a double-track image and signals transmural inflammation (figures 2 and 3). This deeper extension is a common finding in active Crohn’s disease, but in UC represents a sign of severity.

There are several limitations to our study. Firstly, the retrospective nature of the data prevented use of clinical course under treatment as an evaluation criterion for severity of the attack.

Table I – Scintigraphic double-track and endoscopic signs of severity (colonoscopies and recto-sigmoidoscopies) in 52 patients with an acute attack of ulcerative colitis.

<table>
<thead>
<tr>
<th>Double-track sign</th>
<th>present</th>
<th>absent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endoscopic signs of severity</td>
<td>19</td>
<td>0</td>
</tr>
<tr>
<td>No endoscopic signs of severity</td>
<td>4</td>
<td>29</td>
</tr>
</tbody>
</table>

Table II – Scintigraphic double-track and colonoscopic signs of severity in 20 patients with an acute attack of ulcerative colitis.

<table>
<thead>
<tr>
<th>Double-track sign</th>
<th>present</th>
<th>absent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endoscopic signs of severity</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>No endoscopic signs of severity</td>
<td>0</td>
<td>11</td>
</tr>
</tbody>
</table>

Table III – Scintigraphic double-track and colonoscopic signs of severity in 20 patients with an acute attack of ulcerative colitis.

Fig. 3 – Schematic scintigraphic aspects: a) non severe attack of UC with mucosal and submucosal distribution of labeled granulocytes and homogeneous uptake; b) severe attack of UC with transmural distribution of labeled granulocytes through a thickened colonic wall and double-track appearance.

Représentation schématique des aspects scintigraphiques : a) pous-

sée non grave de rectocolite hémorragique avec distribution muqueuse et sous-muqueuse des polynucléaires marqués responsa-

ble d’une fixation homogène ; b) poussee de rectocolite hémorragi-

que grave avec distribution transmurale des polynucléaires marqués

dans la paroi colique responsable d’un aspect en double contour.
indications for treatment and the type of treatment administered not being predetermined. Secondly, a total colonoscopy was not available for most of the patients. This fact, which results from the difficulty encountered in obtaining a total colonoscopic exploration in this setting, prevented us from comparing clinical and biological severity criteria with endoscopic criteria (generally reported only for the distal colon). The lack of systematic colonoscopy data led us to compare endoscopic and scintigraphic criteria solely for colonic segments which had been explored by both techniques (table I). We found an apparent disagreement for 4 patients. For 3 patients, the scintigraphic double-track image was observed higher in the colon, beyond the segments explored endoscopically. For most patients, there was an excellent agreement between the scintigram (presence or absence of a double-track) and the endoscopy evaluation of severity. The results were confirmed for the 19 patients who exhibited both severe lesions at endoscopy and a double-track at scintigraphy. Results were more difficult to interpret in 29 patients who did not have endoscopic signs of severity in the explored segments. Eighteen of these patients had undergone rectosigmoidoscopy with an assumption that the more proximal portion of the colon would have a presentation similar to the explored segments, i.e. no signs of severity. This assumption appears to be acceptable for the following reasons: a) endoscopic signs of severity in patients with acute attacks of UC are generally observed in the distal colon [5], as was the case in our study; b) there was a perfect agreement between endoscopic and scintigraphic results observed in the subgroup of patients undergoing total colonoscopy (20 patients, table II); c) the site of the double-track sign was almost always the same as that of the most severe lesions observed endoscopically. Finally, most of the scintigraphic and endoscopic explorations were not performed on the same day. It would be reasonable to assume that treatment-induced changes during the 24-48 hours between the explorations would not modify severity significantly. We did not test the possibility that endoscopy performed before scintigraphy might modify the scintiscans, but the good agreement between the scintigraphic and endoscopic results despite the random order of the two explorations is probably an argument against any effect.

The main objective of this study was to ascertain the value of the double-track appearance as a marker of the severity of UC attacks in comparison with endoscopic findings. If the hypothesis of the analysis to colonic segments explored by both explorations is licit, our results demonstrated that the sensitivity of the scintigraphic double-track aspect is comparable with endoscopic criteria in acute attacks of UC. We observed discordance in only one patient who had a double-track aspect situated in the sigmoid colon without signs of severity identified at rectosigmoidoscopy. This patient had clinical and biological signs of severity but progressed favorably with treatment.

Tc 99m-HMPAO labeled granulocyte scintigraphy has demonstrated that tracer uptake, which corresponds to polymorphonuclear migration to the colon, is correlated with bioclinical and endoscopic criteria of disease severity [13, 21, 27-30]. While statistically significant on the population level, this correlation is not sufficient on the individual level: many patients exhibiting maximal uptake do not have clinically or endoscopically severe disease [21, 27-30]. In our study, 6 of the 9 patients with a double-track aspect and signs of severe disease at colonoscopy presented an uptake scored at 3, the same score as in 4 of the 11 patients without a double-track aspect or endoscopic signs of severity.

In their study, Carbonnel et al. [5] found that 43 of the 46 patients with endoscopic signs of severity underwent emergency surgery after failing to respond to corticosteroids or more exceptionally after developing a complication. Guimbaud et al. [15] had only 9 patients with endoscopic signs of severity and a double-track aspect at scintigraphy; 7 of these 9 patients required emergency colectomy due to the lack of improvement with corticosteroids; pathology confirmed the presence of ulcers penetrating the musculosa. Their 24 patients with no scintigraphic evidence of a double-track did not require surgery. In our series, only 7 of the 19 patients with a double-track appearance (and endoscopic signs of severity) required colectomy; the 12 others improved with medication. This lower rate of colectomy compared with the two earlier studies is related to frequent use of cyclosporin in our patients in the event of non-response to intravenous steroids.

In conclusion, when available, Tc 99m-HMPAO scintigraphy of the colon can be a useful alternative to colonoscopy to assess the severity of an attack in patients with recognized ulcerative colitis. Future prospective studies should be conducted to determine the prognostic value of the double-track appearance and its usefulness in predicting response to treatment.

REFERENCES


