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.

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RÉSUMÉ

Le double contour scintigraphique est-il un marqueur de gravité des poussées de rectocolite hémorragique ?

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Objectif — Les critères endoscopiques de sévérité ont une meilleure sensibilité que les critères clinico-biologiques dans l’appréciation de la gravité des poussées de rectocolite hémorragique (RCH). Notre but était de préciser la valeur d’un double contour scintigraphique dans l’appréciation de la gravité par comparaison aux données endoscopiques.

Malades et méthodes — Nous avons revu les dossiers de 52 malades hospitalisés pour une poussée aiguë de RCH et ayant eu dans un intervalle de temps ne dépassant pas 48 heures une scintigraphie aux polynucléaires marqués au Technetium 99 m hexaméthyl propylène amine oxime (Tc 99°-HMPAO) et un examen endoscopique (coloscopie totale : n = 20 ; recto-sigmoidoscopie : n = 32).

Résultats — En ne tenant compte que des segments coliques explorés conjointement par les 2 techniques chez le même malade ou des résultats obtenus en coloscopie totale, il existait une très bonne concordance entre l’existence d’un double contour scintigraphique et la présence de critères endoscopiques de gravité.

Conclusion — Chez un malade ayant une RCH connue, la réalisation d’une scintigraphie aux polynucléaires marqués au Tc 99°-HMPAO dans les centres disposant de cet examen peut se substituer à l’endoscopie pour juger de la gravité de la poussée.

The severity of acute episodes of ulcerative colitis (UC) can be assessed on the basis of clinical and biological criteria proposed by Truelove and Witts in 1955 [1] then modified in 1986 [2]. These criteria were defined before the widespread use of corticosteroids and as such lack sensitivity for assessing the severity of UC attacks, particularly in patients referred after institution of treatment [3-5].

Certain teams employ colonoscopic criteria for assessing patients with acute exacerbations which appears to be superior to severity assessment on clinical criteria [4, 5]. Colonoscopy offers a direct assessment of the severity and extent of the rectocolonic lesions and also a way of selecting patients with a high risk of complications. Carbonnel et al. [5] found that 43 of their 46 patients with active UC and severe lesions at endoscopy underwent surgery because of the lack of satisfactory response to corticotherapy or onset of complications. Pathological examination of the surgical specimen confirmed the presence of ulcers reaching the muscularis propria. Only two-thirds of these same patients also had clinical and biological signs of severe disease. The drawback with colonoscopy is its invasive nature, the risk of complications, and the need for anesthesia, which for certain authors would limit its use in patients with clinically severe disease [6-9].

Scintigraphy with labeled granulocytes is a non-invasive method allowing an objective exploration of the inflammatory colon. It can be performed without preparation or anesthesia and exposes the patient to minimal radiation [10-14]. Based on observations in a small cohort of patients, Guimbaud et al. [15] proposed in 1998 that a double-track appearance of the colon is an expression of transmural inflammation and can be considered to be a sign of severe active UC. In the present retrospective analysis, we wanted to ascertain the value of this scintigraphic double-track appearance for evaluating the severity of acute attacks of UC in comparison with endoscopic findings.
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 fractionation using 2 centrifugations to isolate polymorphonuclear neutrophils which were then labeled with 20 mCi technetium 99m hexamethyl propylene amine oxime (Tc-99m-HMPAO, Cerevac, 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 faci, 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 the literature [20] and to patient Identity. 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 when a double-track aspect was identified in one or several segments. Intensity of uptake was expressed in comparison with bone marrow uptake in the following manner: 1 = 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 3-4 L polyethylene glycol for total colonoscopy and two Normacol® enemas for rectosigmoidoscopy.

Assessment of the severity of UC was based on the criteria described by Carbanné 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.

Fig. 1 – Grade 3 scintigraphic uptake from rectum to hepatic flexure without double-track appearance. Fixation scintigraphique de grade 3 du rectum jusqu’à l’angle colique droit sans aspect de double contour.

Fig. 2 – Grade 3 scintigraphic uptake from rectum to left part of transverse colon with double-track appearance from proximal sigmoid to left part of transverse colon. Fixation scintigraphique de grade 3 du rectum jusqu’à la partie gauche du côlon transverse avec double contour s’étendant de la partie haute du sigmoïde jusqu’à la partie gauche du côlon transverse.
Présence ou absence d’un double contour colique en scintigraphie et résultats endoscopiques (colonoscopies et recto-sigmoidoscopies) chez 52 malades en poussée de rectocolite hémorragique.

<table>
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<tr>
<th>Double-track sign</th>
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<th>absent</th>
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<tbody>
<tr>
<td>Endoscopic signs of severity</td>
<td>19</td>
<td>0</td>
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<tr>
<td>No endoscopic signs of severity</td>
<td>4</td>
<td>29</td>
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more rarely 2 or 3 segments which were adjacent or not (13, 7 and 3 patients, respectively). The segments involved were, in decreasing order : sigmoid colon (n = 14), descending colon (n = 9), transverse colon (n = 9), ascending colon (n = 3), rectum (n = 3).

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 histological 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 improved rapidly with intravenous corticosteroids.

When colonic segments could be compared, the agreement between the endoscopic and scintigraphic evaluation of extension was excellent. In 85% of cases, at least one of the double-track images was located at the same site as the endoscopic lesions considered to be the most severe. We also conducted a second analysis retaining the 20 patients who underwent total colonoscopy (table II). For these 20 patients, the agreement between endoscopic assessment of severity and the presence or absence of a double-track appearance on the scintigram was excellent. Six of the 9 patients with a double-track appearance and endoscopic signs of severity had maximal uptake scored at 3 ; this level was also noted in 4 of the 11 patients without a double-track scintigram or endoscopic signs of severity.

Colectomized patients

Seven patients who failed to improve after 5 to 10 days of intravenous corticosteroids (n = 3) or cyclosporin (n = 4) underwent emergency colectomy. These 7 patients all had endoscopic signs of severity and a double-track scintigram. The extent of the double-track image was not greater in colectomized patients than in non-colectomized patients. Pathology examination of the surgical specimens confirmed the presence of deep ulcers reaching the muscularis propria and located at the same site as the double-track image and the severe lesions identified endoscopically.

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]. This 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.

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.

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.

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

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


