



CLINICAL RESEARCH

Abdominal computed tomography in refractory coeliac disease and enteropathy associated T-cell lymphoma

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Abstract

AIM: To evaluate computed tomography (CT) findings, useful to suggest the presence of refractory coeliac disease (RCD) and enteropathy associated T cell lymphoma (EATL).

METHODS: Coeliac disease (CD) patients were divided into two groups. Group I: uncomplicated CD ($n = 14$) and RCD type I ($n = 10$). Group II: RCD type II ($n = 15$) and EATL ($n = 7$).

RESULTS: Both groups showed classic signs of CD on CT. Intussusception was seen in 1 patient in group I vs 5 in group II ($P = 0.06$). Lymphadenopathy was seen in 5 patients in group II vs no patients in group I ($P = 0.01$). Increased number of small mesenteric vessels was noted in 20 patients in group I vs 11 in group II ($P = 0.02$). Eleven patients (50%) in group II had a splenic volume $< 122 \text{ cm}^3$ vs 4 in group I (14%), 10 patients in group I had a splenic volume $> 196 \text{ cm}^3$ (66.7%) vs 5 in group II (33.3%) $P = 0.028$.

CONCLUSION: CT scan is a useful tool in discriminating between CD and (Pre) EATL. RCD II and EATL showed more bowel wall thickening, lymphadenopathy and intussusception, less increase in number of small mesenteric vessels and a smaller splenic volume compared with CD and RCD I.

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Key words: Coeliac disease; Refractory coeliac disease; Enteropathy associated T-cell lymphoma; Computed tomography; Bowel wall thickening; Lymphadenopathy; Intussusception; Splenic volume

INTRODUCTION

Coeliac disease (CD) is one of the most common immunologically mediated gastrointestinal diseases. The prevalence varies between approximately 1:100 and 1:300 worldwide. Refractory coeliac disease (RCD) is considered when patients show persistent or relapsing symptoms and villous atrophy despite adherence to a gluten-free diet (GFD), especially those over the age of 50 years^[1]. Two forms of RCD can be discriminated. RCD I which is defined as RCD with normal intra-epithelial T lymphocytes (IEL's) in intestinal biopsies and RCD II defined as RCD with aberrant IEL's^[2,3]. In RCD enteropathy associated T-cell Lymphoma (EATL) can evolve with a 20 time higher relative risk compared to the general population^[4-6]. Therefore it is necessary to be able to discriminate uncomplicated CD from its malignant complications.

Computed tomography (CT) is one of the first radiological examinations performed for different indications in patients with CD, especially those with RCD to exclude malignancy. A variety of findings like jejunoileal fold pattern reversal^[7], small bowel intussusception^[8] and (benign) mesenteric lymphadenopathy^[9] have been recognized on CT images in patients with CD. However, no discriminating or specific CT signs have been recognized and described regarding RCD II or EATL. Therefore, we evaluated both the spectrum of abdominal CT findings, useful for suggesting CD and those findings which might be useful to suggest the presence of EATL in adult coeliac patients.

MATERIALS AND METHODS

Patients

Between January 2003 and January 2005 a total of 46 patients (18 M, 28 F; mean age 58 years, range 18-88 years) with proven CD according to UEGW criteria (2001), were enrolled. All patients were previously diagnosed as having CD, RCD I, RCD II or EATL by clinical evaluation,

serology and intestinal biopsy^[10]. Patients were divided into two groups: Group I consisted of 24 patients with uncomplicated CD ($n = 14$) and RCD type I ($n = 10$), group II consisted of 22 patients with RCD type II ($n = 15$) and EATL ($n = 7$). Informed consent was obtained from all the patients who participated in this study. All procedures followed in this study were in accordance with the standards of the institutional ethical committee.

Computed tomography.

The indications for CT scan were assessment of unexplained recurrent abdominal complaints and/or suspicion of EATL. After overnight fasting, examinations were performed either on a 4-detector (Somatom 'Volume Zoom', Siemens, Erlangen, Germany) or on a 64-detector ('Sensation 64', Siemens, Erlangen, Germany) CT scanner, using either a 2.5 mm or a 0.6 mm collimation, reconstructed in 5 mm contiguous axial slices. Forty-three out of 46 patients received an orally administered diluted solution of barium sulphate suspension (46 mg/g, 49 mg/mL, 900 mL E-Z-CAT, E-Z-EM Canada Inc, Montreal Canada) divided into two doses (450 mL), the night before and the morning of the investigation. Forty-five minutes prior to imaging, patients received an extra 300-500 mL oral contrast. Because of severe abdominal symptoms or refusal of contrast, 3 patients did not receive oral contrast. Intravenous non-ionic contrast [Ultravist, Iopromide (300 mL/L), Schering, Berlin, Germany] was administered in 42 patients (2 patients refused intravenous contrast and 2 patients supposed to be allergic to contrast) at an injection rate of 3 mL/s (maximum total amount of 100 mL, depending on body weight) with CT acquisition after 70 s.

CT parameters

The following CT findings were evaluated: (1) abnormalities of intestinal fold pattern, (2) bowel dilatation, (3) air excess, (4) fluid excess, (5) bowel wall thickening, (6) intestinal intussusception, (7) ascites, (8) lymphadenopathy, (9) increased number of lymph nodes, (10) mesenteric vascular changes, and (11) splenic size. All CT scans were analyzed by two dedicated radiologists in consensus (MM and JHvW).

Definition of CT parameters

Abnormalities of the intestinal fold pattern were defined quantitatively as a decreased number of jejunal folds and/or an increased number ('jejunization') of ileal folds, measured as the mean number of folds per 2.5 cm in three segments at different locations^[7]. Less than 4 jejunal folds per 2.5 cm were considered to be decreased and more than 4 ileal folds per 2.5 cm were considered to be increased^[7]. The presence of an equal number of intestinal folds in ileum and jejunum (ileum/jejunum fold ratio ≥ 1) was defined as 'jejunoileal fold pattern reversal' (JFPR)^[11-13]. In cases of doubt, abdominal loops in the left upper quadrant were considered to be jejunal and loops in the right lower quadrant were considered to be ileal. Intestinal loops were considered dilated if more than three segments measured equal or more than 3 cm in diameter on transverse images^[14].

Fluid excess and air excess were scored directly in

patients with dilated intestinal loops on a Likert scale (none/mild/moderate/severe). Fluid excess was indirectly assessed by dilution of oral contrast (flocculation). Air excess was scored as present in case more than 3 segments were dilated with air.

The bowel wall was considered thickened when it measured more than 3 mm in the transverse plane of a fully distended loop^[15]. Intussusception was denoted as a target mass or as a more complex layered mass within the bowel lumen^[16].

Lymph node enlargement was considered present if nodes measured greater than 1 cm in diameter in their shortest axis. The number of lymph nodes within the mesentery were scored on a Likert scale (none/mild/moderate/severe). Cavitation of nodes was present by showing a low-density center within the lymph node.

Ascites was evaluated by visual inspection. Increase in splanchnic circulation was scored as the transverse diameter 2-3 cm caudal of the origin of the superior mesenteric artery. Also an increase of number of small vessels within the mesentery was noted on a Likert scale (none/mild/moderate/severe).

Splenic volume was calculated by the following formula; $(30 + 0.58 \times (\text{length} \times \text{width} \times \text{height}))$. The longest axis in the transversal plane is considered as length, the perpendicular distance is considered the width and the longest cranio-caudal distance is considered as the height of the spleen^[17].

Statistical analysis

Student's paired *t*-test, Mann-Whitney, or Fisher's exact test were used for data analysis when indicated. *P* values of less than 0.05 were considered to be statistically significant. All statistical analysis was performed using the Statistical Software Package version 11.0 (SPSS Inc., Chicago, Illinois, USA).

RESULTS

Fold pattern and small bowel dilatation

Because of lack of intraluminal contrast or lack of distension of the small bowel loops, jejunal fold pattern could only be analyzed in 26 patients whereas ileal fold pattern could be assessed in 29 patients. Ten out of 26 (38%) patients showed a decreased number of jejunal folds, 16 (62%) showed an increased number of folds. Ileal folds were found increased in 5 out of 29 (17%) patients and decreased in 24 (83%) patients. No significant difference was found in JFPR between who both groups. Small bowel dilatation ranged from 30-35 mm and was found in 11/46 patients in total ($P = \text{NS}$). All CT findings are summarized in Table 1.

Fluid and air excess

Excess of air was not visible in 24/46 patients, mild in 13 patients, moderate in 7 patients and severe in 2 patients in total. Fluid excess and flocculation were scored as none in 20 (43%) patients, mild in 8 (17%) patients, moderate in 12 (26%) patients and severe in 6 (13%) patients. All findings were equally distributed between the groups.

Table 1 CT findings: comparison between subgroups in coeliac disease. All signs are described by number of patients affected and mentioned otherwise in case of deviation

CT findings	CD and RCD I	RCD II and EATL	Total
Number of patients	24	22	46
Gender (F/M)	18/ 6	10/12	28/18
Mean age (yr)	56	61	58
Jejunal/ileal fold ratio (No of folds/2.5 cm)	4.5/3.0	3.7/2.9	4.1/3.0
JFPR	3	6	9
Bowel dilatation	5	6	11
Air excess	14	8	22
Fluid excess	12	14	26
Increased wall thickness	10	14	24
Intussusception	1	5	6
Ascites	0	1	1
Lymphadenopathy	0	5	5
Increased No of lymph nodes	16	12	28
Lymph node cavitation	0	1	1
Increased splanchnic circulation	20	11	31

CT: Computed tomography; CD: Coeliac disease; RCD: Refractory coeliac disease; EATL: Enteropathy associated T-cell lymphoma; JFPR: Jejunoileal fold pattern reversal.

Wall thickness and intussusception

Increased wall thickness ranged from 4 to 11 mm in group I (mean 7.7 mm, median 7 mm) and from 5 to 15 mm (mean: 9.6 mm, median 10 mm) in group II. Nine patients in group II showed a thickness of more than one cm versus only 4 in group I ($P = \text{NS}$). Intussusception was observed in only 1 patient in group I, compared to 5 patients in group II ($P = 0.06$). Only one patient (RCD II, 67 years old male) showed a small amount of intra-abdominal fluid in the rectovesical pouch.

Lymph nodes

Enlarged lymph nodes were only found in 5 patients in group II ($P = 0.013$). Both groups showed an increase in non-enlarged lymph nodes ($P = 0.295$). Only one lymph node showed cavitation (59 year old male with RCD II).

Vascular findings

An increase in the number of small mesenteric vessels was observed in 20/24 (83%) patients in group I *vs* 11/22 (50%) patients in group II ($P = 0.02$). The diameter of the superior mesenteric artery was measured in a total of 23 patients and this varied from 4-7 mm.

Splenic volume

Splenic volume of all patients ranged from 37-321 cm³ (mean 162 cm³) in normal distribution. No significant differences were found between mean volumes in both groups I and II (178 cm³ *vs* 144 cm³). However, after allocating the patients into 3 arbitrary groups according to the splenic volume, as shown in Table 2, the RCD II and EATL group showed significant more patients with a smaller spleen than RCD I and uncomplicated CD ($P = 0.028$).

DISCUSSION

In patients clinically suspected of having CD, biopsies

Table 2 Splenic volume: comparison between subgroups in coeliac disease *n* (%)

Splenic volume	CD and RCD I	RCD II and EATL	Total patients
Group A: 37-122 cm ³	4 (27)	11 (73)	15
Group B: 124-196 cm ³	10 (63)	6 (38)	16
Group C: 196-321 cm ³	10 (67)	5 (33)	15
Mean volume (cm ³)	178	144	162

CD: Coeliac disease; RCD: Refractory coeliac disease; EATL: Enteropathy associated T-cell lymphoma.

are mandatory to confirm or exclude the diagnosis^[18]. In uncomplicated cases, radiological examination is not required. However, in clinical practice pre-malignant and malignant complications of CD have to be excluded in patients who have persistent complaints despite strict adherence to a GFD. Furthermore CT, performed in patients presenting with atypical abdominal symptoms, can suggest a diagnosis of CD^[13]. The most striking features found in CD are jejunoileal fold pattern reversal, small bowel intussusception, and benign mesenteric lymphadenopathy^[7-9,12,13]. However, to our knowledge, no discriminating findings between CD/RCD I and (Pre) EATL have been described using CT.

Regarding jejunal and ileal fold abnormalities; especially jejunoileal fold pattern reversal and total loss of jejunal folds may be considered specific findings in CD^[7,12,13]. In our study, only in 52% (24 out of 46 patients) both jejunal and ileal folds could be assessed because of lack of contrast or lack in distention of small intestinal loops, probably due to suboptimal bowel preparation because of progressive abdominal complaints. In only 9 out of 24 (38%) patients a jejunoileal fold pattern reversal was observed. This is a low percentage compared to that reported by Tomei *et al*^[7], however we included a high percentage of patients with RCD I, RCD II and EATL. Furthermore, both increased ileal folds, decreased jejunal folds, and jejunoileal fold pattern reversal were equally distributed between the subgroups, which demonstrates that the number of folds is not a good discriminator between both groups.

Transient intussusception of the small bowel was present in 5 patients in group II compared to one patient in group I ($P = 0.06$). The majority of patients showed an increase in the number of nodes (< 1 cm), which was not significantly unequally distributed between both groups CD. However, mesenteric lymphadenopathy (short axis > 1 cm) was only found in the (Pre) EATL group, whereas cavitation, which is considered to be a rare complication associated with a poor outcome^[22-24], was found in one patient with RCD II (Figure 1). In this patient additional examinations, including 18F-FDG-PET scan and laparoscopic mesenteric lymph nodes resection, did not show any evidence of EATL.

Regarding non-specific signs, bowel dilatation and excess of fluid (with flocculation of contrast) and air^[13,19], bowel dilatation and increased splanchnic circulation, as measured using the diameter of the superior mesenteric artery 2-3 cm distal to its origo, we found no significant differences between the two subgroups. However mesenteric vascularity, as measured using a semi-quantative scale,



Figure 1 Coronal reconstruction in a patient with RCD type II showing cavitation of lymph nodes and smaller non cavitated lymph nodes in combination with infiltrated mesenteric fat (arrows).



Figure 2 Axial CT image of a patient with RCD type I demonstrates (A) multiple small lymph nodes (arrowheads) and (B) thickening of the ileal wall (arrows) and infiltration of the mesenteric fat (*).



Figure 3 Axial CT image (A) demonstrates EATL (arrow) and prestenotic dilatation of jejunal loops. The coronal reformation (B) demonstrates dilated jejunum with infiltrated mesenteric fat (*) and multiple enlarged lymph nodes (arrowheads).

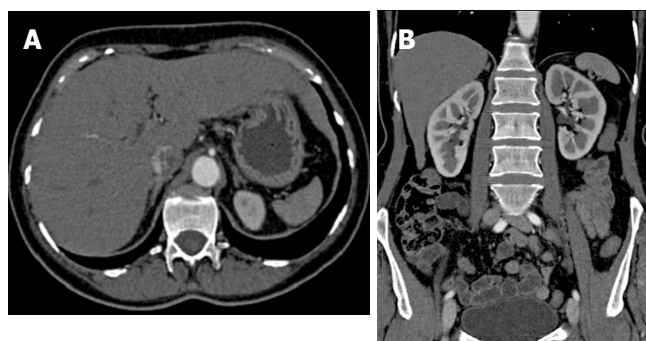


Figure 5 Hyposplenism in a patient with RCD type I demonstrated on axial image (A) and coronal (B) reconstruction.

was significantly increased in group I. We hypothesize that this increase of small vessels and small lymph nodes in group I may be due to the acute inflammatory process in this group (Figure 2). Also no significant difference in number of patients with increased wall thickness was found. However more patients in group II showed a wall thickness of more than 1 cm ($P = \text{NS}$, Figures 1, 3 and 4).

Splenic atrophy occurs frequently in patients with CD and is related to the severity of the disease and degree of dietary control and shows a significant correlation with an impaired function with the incidence rising with increasing age of starting treatment^[26]. Although no correlation was observed in literature between splenic size and the

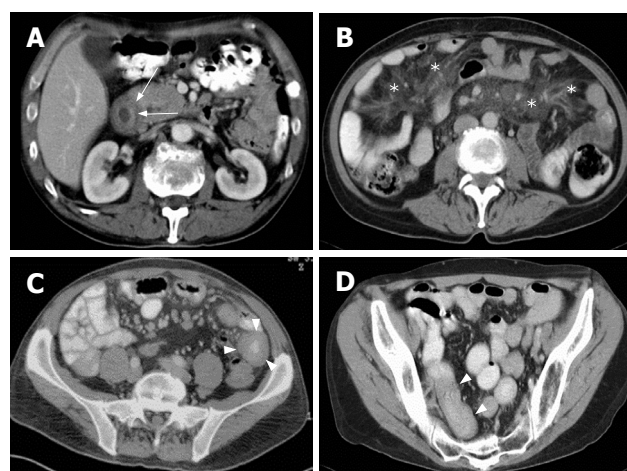


Figure 4 Axial CT images demonstrating locations of EATL. A: Duodenal localization of lymphoma (arrow); B: Mesenteric localization showing "misty mesenterium" (*) and multiple lymph nodes; C: Jejunal localization of lymphoma (arrowhead) and multiple lymph nodes; D: Ileal localization (arrowhead).

duration of the GFD as well as the percentage of splenic size recovery after gluten withdrawal, hyposplenism in adult CD was improved by a GFD^[27]. Furthermore regarding group II, hyposplenism was not related to the development of malignant disease in small samples^[28]. In this study however, significantly more patients in the RCD II /EATL group showed a smaller splenic size (Figures 4 and 5).

In conclusion, both groups showed classic signs of CD on CT. Though small groups were analysed, group II showed more bowel wall thickening, lymphadenopathy, intussusception and more hyposplenism and less increase in splanchnic circulation than group I. Therefore, we conclude that bowel wall thickening, lymphadenopathy, intussusception and hyposplenism should raise suspicion for RCD II and the development of EATL.

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