CASE REPORT

Feasibility of CEUS and strain elastography in one case of ileum Crohn stricture and literature review

Andrea Giannetti¹ · Marco Biscontri¹ · Marco Matergi¹ · Michela Stumpo² · Chiara Minacci²

Received: 26 February 2016 / Accepted: 12 May 2016 / Published online: 29 June 2016
© Società Italiana di Ultrasonologia in Medicina e Biologia (SIUMB) 2016

Abstract Contrast-enhanced ultrasonography (CEUS) and strain elastography (SE) are diagnostic imaging methods, which are still not routinely used in the clinical management of inflammatory bowel diseases. However, there are studies in the literature reporting on the use of both CEUS and SE in patients with bowel obstruction due to Crohn's disease, documenting the usefulness of these two methods in the differentiation between inflammation and fibrosis affecting the bowel wall. The aim of this case report is to evaluate the usefulness of CEUS and SE performed in a patient with Crohn's disease, who was admitted to hospital with bowel obstruction due to terminal ileal stricture and submitted to ileocecal resection. CEUS and SE identified and to some extent also characterized the inflammatory and fibrotic processes affecting the bowel wall. Macroscopic and microscopic examinations of the surgical specimen confirmed the presence of inflammatory phenomena (exudates, ulcers, and fistulas) and fibrosis as suggested by ultrasound (US) imaging methods.

Sommario L'ecografia con mezzo di contrasto (CEUS) e la elastografia strain (SE) sono metodiche recenti, ancora poco utilizzate nel management clinico delle malattie infiammatorie croniche intestinali. Riguardo alle stenosi intestinali nel morbo di Crohn, in Letteratura sono pubblicati studi sia con la CEUS che con la SE che hanno documentato l'utilità delle due metodiche nel differenziare

la natura flogistica o fibrotica del tratto patologico. Scopo di questo report è di valutare l'utilità delle due metodiche in un paziente affetto da morbo di Crohn, ricoverato per occlusione intestinale da stenosi dell'ultima ansa ileale ed operato di resezione dell'ileo terminale e del ceco. La CEUS e la Elastografia Strain hanno permesso la documentazione ed in un certo grado anche una misura dei processi flogistici e fibrotici a carico della parete intestinale affetta. L'esame macroscopico e microscopico del tratto resecato ha consentito di confermare la presenza dei fenomeni flogistici e fibrotici come ipotizzato con le due metodiche ecografiche.

Introduction

In patients with intestinal stricture due to Crohn's disease, characterization of the affected bowel wall is essential as medical therapy is indicated in the presence of mainly inflammatory phenomena, whereas surgical resection is required in the presence of mainly fibrotic phenomena.

Ultrasonography (US) is useful for diagnosis and staging of Crohn's disease affecting the terminal ileum, equivalent to CT enterography and MRI enterography according to the ECCO guidelines [1]. Changes in the terminal ileum wall are diagnosed using grayscale US, and lumen caliber can be assessed after administration of oral contrast agent.

Recently two US methods have been suggested for characterization of bowel obstruction, i.e. contrast enhanced US (CEUS) which permits correlation of the intensity of bowel wall enhancement with that of inflammatory activity in the examined portion [2] and strain elastography (SE) a method assessing the elasticity of the tissues.

✉ Andrea Giannetti
brgia@tin.it; andrea.giannetti@uslsudest.toscana.it

¹ Gastroenterology Unit, Misericordia Hospital, Via Senese 169, 58100 Grosseto, Italy

² Pathology Department, Misericordia Hospital, Via Senese 169, 58100 Grosseto, Italy

The basic physical principles and performance of CEUS and SE are described in other recent publications including the EFSUMB guidelines [3–5].

We describe a case of small-bowel subocclusive Crohn's disease due to terminal ileum stricture in which CEUS and SE were performed to characterize the affected bowel loop.

In this study, grayscale US, color Doppler US (CDUS), CEUS and SE were carried out on a high end US scanner (Mylab Twice, Esaote, Italy) equipped with appropriate convex and linear probes as well as contrast-specific and elastography software.

CEUS was performed using a second-generation contrast agent currently available in Europe (Sonovue, Bracco, Italy) administered as an intravenous bolus of 2.4 ml.

Fig. 1 **a** Contrast enhanced CT shows terminal ileum obstruction with wall thickening and bowel wall enhancement (arrow); the ileum is dilated (lumen caliber >2.5 cm). **b** Endoscopic image of the terminal ileum showing absence of mucosal lesions

The quantification of the enhancement after contrast administration was calculated using a dedicated software, Vuebox (Bracco SA, Switzerland) by manually drawing a region of interest (ROI) on the image depicting the affected bowel.

The software calculates the intensity/time curves (TICs) and related indices, i.e. the area under the curve (AUC), peak enhancement (PE), mean contrast transit time (MTT) and other parameters.

SE is a qualitative examination, and the elastic properties of the tissues are mapped in a color scale. Our scanner shows tissue elasticity values in 100 color shades ranging from blue indicating “maximum stiffness” to red indicating “maximum elasticity”. To obtain a better reproducibility and comparability, the outcome of SE can be classified using a colorimetric score already proposed in the literature [6]. Normal bowel wall thickness is <3 mm and the SE color map will be predominantly green.

US examinations were performed by a single operator (AG) with expertise in US imaging of the digestive tract including CEUS and SE.

Fig. 2 **a** Grayscale US shows the terminal ileum with thickened walls (>7 mm); bowel wall echo-stratification is partially lost. **b** CDUS of the same portion as **a** shows vascular signals within the bowel wall classified as Limberg 2–3

Fig. 3 CEUS of the terminal ileum, the portion proximal to the iliac artery. Grayscale US image on the left; CEUS image on the right. Enhancement of the bowel wall appears intense and slightly inhomogeneous

Case history

A 32-year-old patient with Crohn's disease affecting the terminal ileum (disease extension: about 20 cm). The patient had occasionally been administered medical therapy during the previous 3 years and was referred to our

department due to an episode of small-bowel obstruction confirmed by contrast enhanced CT carried out at admission (Fig. 1a).

Colonoscopy from the rectum to the cecum allowed exclusion of abnormalities affecting the colon and permitted visualization through the ileocecal valve of about 2 cm of the ileum which appeared normal (Fig. 1b). Medical therapy (corticosteroids and metronidazole) was administered and the episode resolved in a few days. Grayscale US confirmed the extension of the ileal disease, wall thickening up to 7 mm and loss of echost stratification of the bowel wall (Fig. 2a). CDUS showed vascular signals within the bowel wall which were assigned a Limberg score of 2 or 3 depending on the portion (Fig. 2b).

CEUS and SE were performed after resolution of bowel obstruction.

CEUS performed on two target segments of thickened bowel wall provided assessment of bowel wall enhancement classified as inhomogeneous, intense and prolonged (Fig. 3).

Quantitative parameters obtained with CEUS time/intensity curves of the thickened bowel wall suggested severe inflammation (Fig. 4: first target AUC 29 %, compared to the AUC of the time/intensity curve of the iliac artery as reference target).

Fig. 4 CEUS of the terminal ileum, the portion proximal to the iliac artery: **a** grayscale US image on the left, CEUS image on the right. The ROI (yellow) includes the bowel wall, the reference ROI (green) is on the iliac artery; **b** grayscale US image on the left; parametric map of the AUC values for wash in–wash out superimposed on CEUS image on the right; **c** enhancement with Sonovue linearized to arbitrary units together with the modeled time-intensity curve (yellow

curve is referred to ROI on the intestinal wall, the green curve is referred to the ROI on the iliac artery); **d** the table shows the absolute and relative values obtained from the analysis of time/intensity curves. AUC of TIC from the bowel wall is 29 % compared to the reference ROI on the iliac artery. These data suggest severe inflammation of the bowel wall

Fig. 5 **a** Elastography shows the terminal ileum wall (distal portion) in a mixed *color* pattern, mainly *blue*, *green* and *red* with preserved echo-stratification (*arrow*). This pattern indicates altered elasticity of the intestinal wall. **b** Elastography shows the terminal ileum wall, proximal to the portion shown in **a**, an inhomogeneous mixed color pattern, mainly *blue* and *green* with preserved echo-stratification. This pattern indicates reduced elasticity of the intestinal wall

SE provided further characterization of the bowel wall showing mildly abnormal elasticity of a short portion of the ileum close to the ileocecal valve and higher stiffness values in the portion of the ileum which was more distant from the ileocecal valve (Fig. 5a, b).

After discharge, during gradual reduction in corticosteroid dosage, the patient had a second subocclusive episode and was submitted to surgical removal of the cecum along with the terminal ileum and the appendix.

The ileal wall was described by the pathologist as “stiff and thickened with irregular “cobblestone” appearance of the mucosa”. At low magnification, histological examination showed overall thickening of the ileal wall involving particularly the submucosa and associated with muscular hypertrophy (Fig. 6a).

High magnification showed areas of chronic productive follicular type inflammation with transmural extension into the tunica serosa (Fig. 6b), areas of acute exudative inflammation with mucosal and submucosal ulcers and fistulas (Fig. 6c), submucosal fibrosis with extension into the tunica muscularis (Fig. 6d) and muscular hypertrophy.

Discussion

Our 32-year-old patient had ileal stricture with wall thickening, partial loss of echo-stratification and vascular signals within the bowel wall (US and CEUS). These findings are commonly detected in patients with Crohn’s disease submitted to grayscale US in daily clinical practice.

CEUS performed on the target portion of the affected ileum suggested persistent severe inflammation of the bowel wall. After resection, histological examination of the surgical specimen confirmed “acute inflammation with exudates, necrosis, ulceration and fistula” (Fig. 6c).

SE performed on the terminal ileum wall showed altered elasticity (Figs. 5a, b, 7b) with a higher percentage of “blue” areas within the bowel wall (suggesting stiffness) in the portion which was more distant from the ileocecal valve compared to the portion next to the valve.

The outcome of SE was confirmed by macroscopic examination of the surgical specimen revealing a stiff, thickened bowel wall while microscopic analysis showed diffuse fibrosis of the bowel wall extending from the submucosa to the muscle tunic and muscular hypertrophy.

It should be pointed out that CEUS and SE provided evidence of severe inflammatory and fibrotic phenomena coexisting in the same portion of the ileal stricture (Fig. 7a, b). It is likely that not only fibrosis, but also exudation and interstitial edema may have contributed to the reduced elasticity of the bowel wall. In our patient, decision to perform surgery was influenced by the outcome of US including SE suggesting structural alteration of the ileal wall which is usually unresponsive to medical therapy.

There are still few data in the literature on CEUS and SE in bowel obstruction due to Crohn’s disease.

It has been assumed that CEUS would be useful in the study of bowel obstruction in patients with Crohn’s disease in the belief that strictures are caused mainly by inflammation or fibrosis, and that CEUS can evidence inflammation thanks to more intense enhancement of the affected bowel wall [7–10]. However, studies in the literature are not concordant. Schirin-Sokhan et al. found no correlation between the nature of the stricture and some of the quantitative indices of CEUS [7]. According to Quai et al., CEUS with elaboration of time/intensity curves and calculation of AUC permits adequate differentiation between

Fig. 6 **a** Hematoxylin–eosin stain, $\times 1$ magnification. Ileal wall thickening involving the submucosa (*arrowheads*) and tunica muscularis, associated with a fistula extending from the mucosa to the tunica muscularis (*arrow*). **b** Hematoxylin–eosin stain, $\times 10$ magnification. Inflammatory, mainly chronic, follicular infiltrate with extension into the tunica muscularis (*arrow*) and diffuse involvement of the tunica serosa (transmural extension of the inflammatory activity, *arrowheads*). **c** Hematoxylin–eosin stain, $\times 10$ magnification.

Extensive acute inflammation with exudates, mucosal ulceration and fistula extending to the submucosa (*arrow*). The inflammatory infiltrate is in the acute phase, with neutrophil granulocytes and occasional eosinophils associated with necrotic and fibrinoid material from the ulcer base. **d** Hematoxylin–eosin, $\times 10$ magnification. High magnification showing the thickened submucosal layer with deposits of collagen fibers and hyalinosis (*arrows*)

inflammatory and fibrotic strictures. The authors also provide cutoff values for an accurate diagnosis [8]. In their study, Nylund et al. confirmed that fibrotic strictures present reduced blood volume and blood flow [9]. Ripollés et al. examined 28 patients with Crohn's disease affecting the bowels subsequently submitted to surgery. They found correlation between several US parameters: vascular color signal intensity (CDUS), enhancement percentage (CEUS), signs of transmural pathologic changes (grayscale US) and the degree of bowel wall inflammation revealed by histological examination [10].

Baumgart et al. performed SE in 10 patients with Crohn's disease who subsequently underwent surgical resection, and they found that SE can differentiate fibrosis from normal bowel wall. Increased bowel wall stiffness evidenced at SE correlated with the outcome of histological examination of the surgical specimens showing

hypertrophy of the tunica muscularis and presence of collagen fibers within the bowel wall [11].

Fraquelli et al. examined 23 patients with Crohn's disease who subsequently underwent surgical resection and compared with 20 patients who were not indicated for surgical treatment. They confirmed the usefulness of SE in detecting fibrosis within the bowel wall. Particularly the calculation of "strain ratio" (between the affected bowel wall and the adjacent mesentery) was more accurate than the "visual score" in differentiating between severe fibrosis, moderate fibrosis and inflammation affecting the bowel wall [12].

Coexistence of fibrosis and inflammation in intestinal strictures caused by Crohn's disease has recently been found by other Authors in studies comparing the outcome of MRI enterography with that of histological examination [13, 14]. In these studies inflammatory and fibrotic

Fig. 7 **a** CEUS of the terminal ileum, proximal to the portion shown in Fig. 3. Grayscale US image (left), CEUS image (right); intense, homogeneous enhancement of the bowel wall (arrow). **b** Elastography shows the wall of the terminal ileum, the same portion as the one shown in **a**, proximal to the portion shown in Fig. 5b. The bowel wall appears mainly blue (indicating stiffness, arrow)

processes do not exclude each other, as they are proportional to one another in most intestinal strictures submitted to histological examination after resection. Contrast enhanced MRI enterography has a late interstitial phase which is useful for detecting moderate or severe fibrosis of the bowel wall [14].

Contrast enhanced MRI enterography is in clinical practice considered the gold standard for the diagnosis and monitoring of small-bowel Crohn's disease due to the high diagnostic accuracy [15, 16]. However, according to the recent review of Bettenworth et al., also CEUS and SE seem to be promising, and a combination of these two methods could improve stricture characterization in Crohn's disease [16]. Further targeted studies are required to confirm this hypothesis.

In conclusion, the purpose of this report is to document the usefulness of combined CEUS and SE in the characterization of one case of intestinal stricture due to Crohn's disease. In this patient CEUS and SE added diagnostic information to the outcome of grayscale US and these findings were subsequently confirmed at histological examination.

Compliance with ethical standards

Conflict of interest Authors have no conflict of interest to declare related to this study.

Informed consent All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki declaration of 1975, as revised in 2000. The patient provided written informed consent to enrolment in the study and to the publication of information that could potentially lead to his identification.

Human and animal studies The study described in this article does not involve the use of animal subjects.

References

1. Panes J, Bouhnik Y, Reinisch W, Stoker J, Taylor SA et al (2013) Imaging techniques for assessment of inflammatory bowel disease: joint ECCO and ESGAR evidence-based consensus guidelines. *J Crohns Colitis* 7(7):556–585
2. Romanini L, Passamonti M, Lanzarotto F, Villanacci V, Grazioli L et al (2014) Quantitative analysis of contrast-enhanced ultrasonography of the bowel wall can predict disease activity in inflammatory bowel disease. *Eur J Radiol* 83(8):1317–1323
3. Piscaglia F, Nolsøe C, Dietrich CF, Cosgrove DO, Gilja OH et al (2011) The EFSUMB guidelines and recommendations on the clinical practice of contrast enhanced ultrasound (CEUS): update 2011 on non-hepatic applications. *Ultraschall Med* 33(1):33–59
4. Bamber J, Cosgrove D, Dietrich CF, Fromageau J, Bojunga J et al (2013) EFSUMB guidelines and recommendations on the clinical use of ultrasound elastography. Part 1: basic principles and technology. *Ultraschall Med* 34(2):169–184
5. Cosgrove D, Piscaglia F, Bamber J, Bojunga J, Correias JM et al (2013) EFSUMB guidelines and recommendations on the clinical use of ultrasound elastography. Part 2: clinical applications. *Ultraschall Med* 34(3):238–253
6. Fufezan O, Asavaoie C, Tamas A, Farcau D, Serban D (2015) Bowel elastography a pilot study for developing an elastography scoring system to evaluate disease activity in pediatric Crohn's disease. *Med Ultrason* 17(4):422–430
7. Schirin-Sokhan R, Winograd R, Tischendorf S, Wasmuth HE, Streetz K et al (2011) Assessment of Inflammatory and fibrotic stenoses in patients with Crohn's disease using contrast-enhanced ultrasound and computerized algorithm: a pilot study. *Digestion* 83:263–268
8. Quaia E, De Paoli L, Stocca T, Cabibbo B, Casagrande F, Cova MA (2012) The value of small bowel wall contrast enhancement after sulfur hexafluoride-filled microbubble injection to differentiate inflammatory from fibrotic strictures in patients with Crohn's disease. *Ultrasound Med Biol* 38(8):1324–1332
9. Nylund K, Jirik R, Mezl M, Hausken T, Pfeiffer F et al (2013) Quantitative contrast-enhanced ultrasound comparison between

- inflammatory and fibrotic lesions in patients with Crohn's disease. *Ultrasound Med Biol* 39(7):1197–1206
10. Ripollés T, Rausell N, Paredes JM, Grau E, Martínez MJ, Vizuite J (2013) Effectiveness of contrast-enhanced ultrasound for characterisation of intestinal inflammation in Crohn's disease: a comparison with surgical histopathology analysis. *J Crohn's Colitis* 7:120–128
 11. Baumgart DC, Müller HP, Grittner U, Metzke D, Fischer A et al (2015) US-based real-time elastography for the detection of fibrotic gut tissue in patients with stricturing Crohn disease. *Radiology* 275(3):889–899
 12. Fraquelli M, Branchi F, Cribiù FM, Orlando S, Casazza G et al (2015) The role of ultrasound elasticity imaging in predicting ileal fibrosis in Crohn's disease patients. *Inflamm Bowel Dis* 21:2605–2612
 13. Barkmeier DT, Dillman JR, Al Hawary M, Heider A, Davenport MS et al (2015) MR enterography—histology comparison in resected pediatric small bowel Crohn disease strictures: can imaging predict fibrosis? *Pediatr Radiol*. doi:[10.1007/s00247-015-3506-6](https://doi.org/10.1007/s00247-015-3506-6)
 14. Rimola J, Planell N, Rodríguez S, Delgado S, Ordas I et al (2015) Characterization of inflammation and fibrosis in Crohn's disease lesions by magnetic resonance imaging. *Am J Gastroenterol* 110:432–440
 15. Dambha F, Tanner J, Carroll N (2014) Diagnostic imaging in Crohn's disease: what is the new gold standard? *Best Pract Res Clin Gastroenterol* 28:421–436
 16. Bettenworth D, Nowacki TM, Cordes F, Buerke B, Lenze F (2016) Assessment of stricturing Crohn's disease: current clinical practice and future avenues. *World J Gastroenterol* 22(3):1008–1016