Endoscopic Ultrasound Miniprobe and Single Balloon Enteroscopy: A Diagnostic Tool for Investigating Small Bowel Lesions

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Research Article

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Abstract

Objectives: The set of balloon-assisted enteroscopy and endoscopic ultrasonography (EUS) together can further improve the diagnosis of small bowel submucosal lesions. We reported our experience on clinical utility of the EUS miniprobe UM-3Y in the investigation of lesions of small bowel during single balloon enteroscopy (SBE).

Methods: Between 2014 and 2017 we investigated 14 consecutive patients with symptoms, the suspect of small bowel tumor or inflammatory bowel disease. Almost all patients underwent video-capsule endoscopy before SBE.

Results: EUS permitted us to better characterize lesions detected with SBE procedure with no complications and it permitted to exclude the presence of lesions in some doubtful cases.

Conclusions: Our data demonstrated that EUS with miniprobe UM-3Y, associated with SBE, is an important diagnostic tool for investigating, with high accuracy, small bowel lesions. This can let to establish a better management of small bowel lesions.

Introduction

Small intestine is the longest part of digestive system and most of it is inaccessible by traditional endoscopic abilities. Recent advances in endoscopic equipment like the development of video capsule endoscopy (VCE) and balloon-assisted enteroscopy has permitted detailed observation of the entire small bowel [1–7]. The set of balloon-assisted enteroscopy and endoscopic ultrasonography (EUS) together can further improve the diagnosis of small bowel submucosal lesions, in spite of the difficulty to have a histological definition of them [8, 9].

The development of ultrasonographic miniprobes that can be passed through the working channel of standard endoscopes improve the usefulness and effectiveness of EUS [10, 11].

We reported our experience on clinical ability of the ultrasound miniprobe UM-3Y coupled with single balloon enteroscopy (SBE) to improve the diagnosis of small bowel lesions, especially that affecting submucosa.

Methods

Data from consecutive patients referred to the Oncological Gastroenterology Unit of Centro di Riferimento Oncologico Aviano, from October 2014 to January 2017, with diarrhea, anemia, submucosal neoformations or small bowel thickening, endoscopic video capsule image suggestive of Crohn's disease, abdominal pain and in follow up for non-hodgkin lymphoma were prospectively collected. Patients under 18 years, those with severe co-morbidity (American Society of Anesthesiologists’ [ASA] score of 4 or greater) and those unable or unwilling to give informed consent were exclude.

This observational prospective study was carried out in accordance with Declaration of Helsinki and has been approved by the Institutional Board of CRO-IRCCS, National Cancer Institute of Aviano (PN), Italy (CRO-2010-38 of 2 September 2010). Written informed consent to collect data anonymously was obtained from each patient on the day of the procedure. All patients underwent to SBE (EVIS EXERA II SIF-Q180, Olympus, Tokio, Japan) Fig. 1. Histological samples were collected performing standard small bowel biopsy in case of mucosal lesions while bite on bite biopsy in case of submucosal lesions. During SBE an ultrasound miniprobe “UM-3Y” (Olympus, Tokyo, Japan) (Fig. 2A-B) was used.
Results

14 patients (6 males and 8 females; mean age 57.2; range 34-80) with anemia (5/14), suspect of SBT (4/14), abdominal pain and diarrhea (3/14), follow-up for SBT and IBD (3/14) were investigated. 10 patients underwent to VCE which revealed 5/10 submucosal lesion, 2/10 mucosa involving neoplasia, a jejunum/ileum edema, a polypoid neoplasia and multiple ulcerations of jejunum and ileum.

SBE detected lesions in 10 patients: 3/10 submucosal mass, 3/10 neoplasia of which 2 ulcerated and 1 red volcano shaped, a jejunal or ileal edematous mucosa (2/10), a polypoid lesion and a substenosis (Table 1 and Fig. 3).
**Table 1**

Patients' clinical characteristics: Clinical Characteristic of patients according with clinical question, video-capsule endoscopy, single balloon enteroscopy, UM-3Y miniprobe analysis and histological result. NET Neuroendocrine Tumor; GIST Gastrointestinal Stromal Tumor; F-U follow up; NHL Non-Hodgkin Lymphoma; CT scan Computed Tomography scan.

| ID | Age | Sex | Clinical question | Video-capsule endoscopy | Single Balloon Enteroscopy | UM-3Y miniprobe | Histology |
|----|-----|-----|-------------------|-------------------------|---------------------------|-----------------|-----------|
| 1  | 80  | F   | Jejunal submucosal neoformation | Jejunal submucosal neoformation | Jejunal submucosal mass | Submucosal hypoechoic nodule of 1cm | NET       |
| 2  | 55  | F   | Anemia            | Proximal jejunal ulcerated neoformation | Proximal jejunal ulcerated neoformation | Non-homogeneous hypoechoic neoformation of 1.6cm of the 3th and 4th layer | GIST CD117/cKit+ |
| 3  | 34  | M   | HIV+              | Jejunal red volcano-shaped neoformations | Jejunal red volcano-shaped neoformations with fibrin and hemosiderin | Mucosal and submucosal non-homogeneous hypoechoic neoformation | Sarcoma Kaposi |
| 4  | 57  | M   | Jejunal loops thickening | Not performed (previous intestinal resection) | Edematous jejunal mucosa | Mucosal and submucosal hypoechoic thickening (NHL?) | NHL       |
| 5  | 64  | M   | Diarrhea          | Distal jejunum and ileal edema | Ileal mucosa and proximal jejunum slightly edematous | No alterations of ileum and proximal jejunum | Eosinophilic ileitis |
| 6  | 46  | F   | Anemia            | Polypoid neoformation of distal jejunum | Polypoid neoformation of 4cm with ulcer | Mucosal and submucosal anechoic areas | Hamartomatous polyp |
| 7  | 51  | F   | Crohn's disease   | Proximal jejunum submucosal formation | Proximal jejunum submucosal formation | Submucosal capsulated anechoic formation (simple cyst) | No histology |
| 8  | 71  | F   | Anemia            | Jejunal and ileal multiple lacerations | Proximal jejunum ulcerated neoformation | Non-homogeneous hypoechoic neoformation of all the layers | Low differentiated adenocarcinoma |
| ID | Age | Sex | Clinical question | Video-capsule endoscopy | Single Balloon Enteroscopy | UM-3Y miniprobe | Histology |
|----|-----|-----|-------------------|-------------------------|---------------------------|-----------------|-----------|
| 9  | 61  | M   | Anemia            | Proximal jejunum submucosal neoformation | Submucosal neoformation?  | Normal aspect   | Negative  |
| 10 | 45  | F   | Anemia            | Ileum submucosal neoformation | Normal aspect             | Normal aspect   | Negative  |
| 11 | 67  | F   | Chronic diarrhea  | Not evaluable            | Normal aspect             | Normal aspect   | Negative  |
| 12 | 51  | F   | CT scan for retroperitoneal sarcoma - Jejunal infiltration? | Not performed | Substenosis and lumen dilation | Normal aspect   | Negative  |
| 13 | 67  | M   | F-U NHL           | Not performed            | No alterations of the terminal ileum | Normal aspect   | Negative  |
| 14 | 34  | M   | Abdominal pain    | Proximal jejunum submucosal neoformation | Normal aspect             | Jejunal wall regularly stratificated | Negative  |

In all cases we were able to insert EUS miniprobe “UM-3Y” through the enteroscope channel and finally obtain a high-resolution image that let to differentiate all layers of the wall. 1 of the 3 submucosal masses was described by EUS as hypoechoic submucosal area, 1 as anechoic formation (capsulated) and in the last no alterations were found. Final histological diagnosis of the hypoechoic submucosal area was neuroendocrine tumors while no alterations were found in the other cases. Neofomations were all described by EUS as non-homogeneous hypoechoic neoformation. Lesions were histologically classified as a gastrointestinal stromal tumor, an adenocarcinoma and a Kaposi’s sarcoma. One of the 2 cases of edematous mucosa was described as a hypoechoic thickening of mucosa and submucosa and histological diagnosis reveal a Non-Hodgkin Lymphoma. In the other case no lesions were found. Polypoid lesion was described as anechoic areas of mucosa and submucosa and histologically as an hamartomatous polyp.

Results of SBE versus miniprobe analysis and definitive diagnosis are collected in Table 1.

Surgery was performed in patients with adenocarcinoma and submucosal lesions and post operative histology confirmed biopsy data and ultrasound miniprobe conclusion.

All patient that underwent surgery were clinically followed and no relapses were found. Patients with inflammatory bowel disease were treated with biological therapy and followed according to IBD guidelines.

Discussion
EUS and balloon-assisted enteroscopy were previously tested only in a few studies and all with a double balloon enteroscopy (DBE) [3, 8, 9]. Fukumoto et al. compared abdominal ultrasonography (US) with EUS image quality during DBE, for various type of small bowel diseases. In this study EUS images provided more detail than US images and may contribute to accurate diagnosis of small bowel lesion. During the study, however, they found some technical issues. Images obtained at a distance from the miniature probe showed poor quality and they found difficulty in controlling EUS probe when bends occur in the small bowel [3].

Subsequently, Wada et al. in 2014 [9] noticed that EUS during DBE enhances the endoscopists’ ability to establish a more qualitative diagnosis and select an appropriate therapeutic strategy [9]. They evidenced that this method can assess specific information about depth grading lesions and a correct evaluation of the structure of severe strictures prior to endoscopic balloon dilatation providing a more qualitative and powerful diagnostic value of the lesion [9]. In the same way, Murino et al. in 2016 [8] proved the efficacy of EUS during DBE on the investigation of submucosal lesions detected on their patient. They confirmed that the combination of EUS and enteroscopy can be the key for a correct and appropriate investigation and a subsequent management of SBT, especially for those which affect the submucosa [8]. At the best of our knowledge, our is the first study on ultrasound miniprobe and SBE. As Manno et al. demonstrate [2] SBE is a helpful and safe procedure with a diagnostic and therapeutic clinical impact and low complication rate [2].

The miniprobe UM-3Y is longer (2700 mm) respect that used by Fukumoto and Murino et al. with a diameter of 2,5 mm, smaller than that of Murino et al. and it incorporates a radial scanning system with a frequency of 20MHZ, higher respect probes used by Fukumoto et al., connected to an endoscopic ultrasonic observation unit (EU-M30; Olympus, Tokyo, Japan).

In all cases EUS images give a more detailed description of the lesion respect the results obtained with SBE and, mostly, it permitted to exclude the presence of lesions in some doubtful cases.

We noticed that the miniprobe can be useful as an added value for giving us a better characterization and evaluation if we detected a submucosal lesion on CT scan or to follow some patient treated for tumors and to exclude lesions detected on VCE or on radiology techniques. For these reasons, we suggest a major employment of this device that can be helpful for the endoscopists to have a clearer and immediately available diagnosis during enteroscopy especially if they detect suspects submucosal lesions. Despite the difficulty to obtain tissue from submucosal lesion during EUS-SBE, EUS can provides some information about the wall stratification that can help the endoscopist to exclude other lesions and can improve the differential diagnosis directly in the endoscopic room. EUS during SBE is feasible, safe, and rapidly available and can represent one of the must-have endoscopists’ device.

**Conclusion**

In conclusion, in our experience, endoscopic ultrasound with miniprobe UM-3Y during SBE is an important diagnostic tool for investigating with high accuracy small bowel lesions.

**Abbreviations**

DBE Double Balloon Enteroscopy
EUS  Endoscopic Ultrasonography
IBD  Inflammatory Bowel Disease
SBE  Single Balloon Enteroscopy
SBT  Small Bowel Tumor
US  Ultrasonography
VCE  Video Capsule Endoscopy

Declarations

Ethics approval and consent to participate: Ithas been approved by the Institutional Board of CRO-IRCCS, National Cancer Institute of Aviano (PN), Italy, number: CRO-2010-38 of 2 September 2010. Written informed consent to collect data anonymously was obtained from each patient on the day of the procedure.

Consent for publication Written informed consent was obtained from each patient on the day of the procedure.

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare no conflict of interest.

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Author’s contribution:

Renato Cannizzaro, Prof: conceived, designed and supervised the study; identified and recruited patients, wrote the manuscript and critically reviewed the manuscript. He approved the final draft submitted.

Raffaella Magris, PhD: analyzed data, wrote and reviewed the manuscript. She approved the final draft submitted.

Stefania Maiero, MD: identified and recruited patients. She approved the final draft submitted.

Luca Navarra, Dr: reviewed the manuscript. He approved the final draft submitted.

Mara Fomasarig, MD: identified and recruited patients and critically reviewed the manuscript. She approved the final draft submitted.

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**Figures**
Figure 1

EVIS EXERA II SIF-Q180 (Olympus, Tokyo Japan), with permission of Olympus
Figure 2

A-B The prototype longer ultrasound miniprobe UM-3Y (Olympus, Tokyo, Japan), with permission of Olympus.
Endoscopic images of small bowel lesions detected with endoscopic ultrasound and their specific endoscopic ultrasonography images. A. Endoscopic image of proximal jejunum ulcerated neoformation. B. 1.6 cm diameter non-homogeneous hypoechoic neoformation with irregular borders at the 3rd and 4th layers. C. Endoscopic image of ileal mucosa and proximal jejunum slightly edematous D. No alterations of ileum and proximal jejunum E. Endoscopic image of jejunal submucosal neoformation. F. 1 cm diameter submucosal hypoechoic nodule. G. Endoscopic image of a proximal jejunum submucosal neoformation. H. Anechoic capsulated submucosal formation (simple cyst). I. Endoscopic image of jejunal loop thickening. J. Mucosal and submucosal hypoechoic thickening K. Endoscopic image of red-volcano shaped neoformations. L. Non-homogeneous hypoechoic neoformations.