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CASE REPORT

In-vivo characterization of DALM in ulcerative colitis with high-resolution probe-based confocal laser endomicroscopy

Giovanni D De Palma, Stefania Staibano, Saverio Siciliano, Francesco Maione, Maria Siano, Dario Esposito, Giovanni Persico

Giovanni D De Palma, Saverio Siciliano, Francesco Maione, Dario Esposito, Giovanni Persico, Department of Surgery and Advanced Technologies, Center of Excellence for Technical Innovation in Surgery, Section of Diagnostic and Therapeutic Endoscopy, University of Naples Federico II, School of Medicine, 80131, Naples, Italy
Stefania Staibano, Maria Siano, Department of Biomorphological and Functional Sciences, Section of Pathology, University of Naples Federico II, School of Medicine, 80131, Naples, Italy
Author contributions: De Palma GD and Staibano S contributed to conception and design, analysis and interpretation of data, drafting the article, critical revision of the article, final approval of the article; Siciliano S, Siano M, Esposito D and Maione F contributed to data gathering, analysis and interpretation of the data, drafting the article, final approval of the article; Persico G contributed to critical revision of the article and final approval of the article.
Correspondence to: Giovanni D De Palma, Professor, Department of Surgery and Advanced Technologies, Center of Excellence for Technical Innovation in Surgery, Section of Diagnostic and Therapeutic Endoscopy, University of Naples Federico II, School of Medicine, Via Pansini, 5, 80131, Naples, Italy. giovanni.depalma@unina.it
Telephone: +39-81-7462773 Fax: +39-81-7462752
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Abstract

Recently, the use of confocal laser endomicroscopy (CLE) in the diagnosis of chronic ulcerative colitis (CUC) was reported. In this brief report we aimed to assess the application of probe-based CLE to characterize colonic mucosa and dysplasia in CUC. The study involved a patient presenting long-standing CUC. Confocal imaging of both the inflamed mucosa, a circumscribed lesion (dysplasia-associated lesional mass), and adjacent colonic mucosa are demonstrated and the correlation between the CLE and histological images. Inflamed mucosa and dysplasia showed specific alteration of crypt architecture, cellular infiltration, and vessel architecture with an excellent correlation between CLE and standard histological examination.

Key words: Colonoscopy; Confocal laser endomicroscopy; Chronic ulcerative colitis; Dysplasia-associated lesional mass; Histology

Peer reviewer: Dr. Sanchoy Sarkar, Department of Gastroenterology, Royal Liverpool University Hospital, Prescot Street, Liverpool, L78XP, United Kingdom

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INTRODUCTION

The term dysplasia-associated lesional mass (DALM) has been adopted to describe the group of endoscopically visible lesions, within the colitic colon (in the course of IBD), that refers to a heterogeneous population of lesions that demonstrate plaque-like, mass, stricture, sessile, or pedunculated morphology, that have an associated dysplasia in the surrounding mucosa[1-3].

With recent rapid advances in videoendoscopic instrument systems, improved endoscopic skills, and improved detection techniques such as pan-colonic dye spraying, the proportion of lesions that are discovered macroscopically is likely to increase[4].

Recently, the use of confocal laser endomicroscopy

(CLE) in the diagnosis of chronic ulcerative colitis (CUC) was reported[5,6].

This report describes the CLE findings in a case of DALM in CUC in correlation with histopathology diagnosis.

CASE REPORT

A 48-year-old woman with a 23 years history of left-sided ulcerative colitis underwent a surveillance colonoscopy.

A mild anemia (hemoglobin level, 110 g/L) with low serum iron levels (210 μg/L); normal value, 53-167 μg/L) and a high erythrocyte sedimentation rate (37 mm/L per hour; normal value, 1-10 mm/L per hour) were the only blood chemistry abnormalities identified.

Colonoscopy revealed a left-sided Mayo CU-1 CUC with a 2 cm plaque-like lesion at the sigmoid colon (Figure 1A and B). A morphological characterization of the lesion with CLE was undertaken.

Probe-based CLE procedure

The procedure was performed using the Cellvizio® Endomicroscopy System (Mauna Kea Technologies, Paris, France) by a Coloflex UHD-type probe (1 μm lateral resolution; 12 frames/s).

This system uses a 2.5-mm catheter probe (Coloflex UHD-type probe) that is inserted through the endoscope-working channel to obtain dynamic imaging of the mucosa. This probe has a field of view of 240 μm × 200 μm, with a lateral resolution of 1 μm. Probe-based CLE (pCLE) imaging data were collected at a scan rate of 12 frames/s with a scanning field of 30 000 pixels. Single video frames were reconstructed into 1 larger static image (4 mm × 2 mm) by a special computer software ("mosaicing" Mauna Kea Technologies).

Five mililiters of 10% sodium fluorescein were injected intravenously before CLE image acquisition as a contrast agent.

Confocal imaging of both the inflamed mucosa, the circumscribed lesion (DALM), and adjacent colorectal mucosa was performed by placing the tip of the probe in direct contact with the target tissue site.

Mucosal biopsy specimens were collected from the observation sites using biopsy forceps. Fixed samples were embedded in paraffin and sectioned transversely, and stained with hematoxylin-eosin to facilitate the comparison between confocal images and histology.

pCLE Images

pCLE imaging of inflamed mucosa showed dilation of crypt openings, more irregular arrangement of crypts, and enlarged spaces between crypt, crypt destruction, and/or crypt fusion and crypt abscess. Microvascular alterations with fluorescein leaks into the crypt lumen (therefore making the lumen brighter than the surrounding epithelium) were observed (Figure 2A and B).

DALM was characterized by "dark" cells, with mucin depletion and goblet cell/crypt density attenuation; the architectural pattern was irregular, as well as the epithelial thickness, with villiform structures and "dark" epithelial border. The blood vessels were dilatated and irregularly-branching, with poor orientation to adjunct tissue, and fluorescein extravasation (Figure 3A and B).

pCLE imaging of colorectal mucosa adjacent to lesion (1 to 2 cm around DALM) showed the switch from the inflamed mucosa, to the neoplastic mucosa as evidenced by DALM (Figure 4).

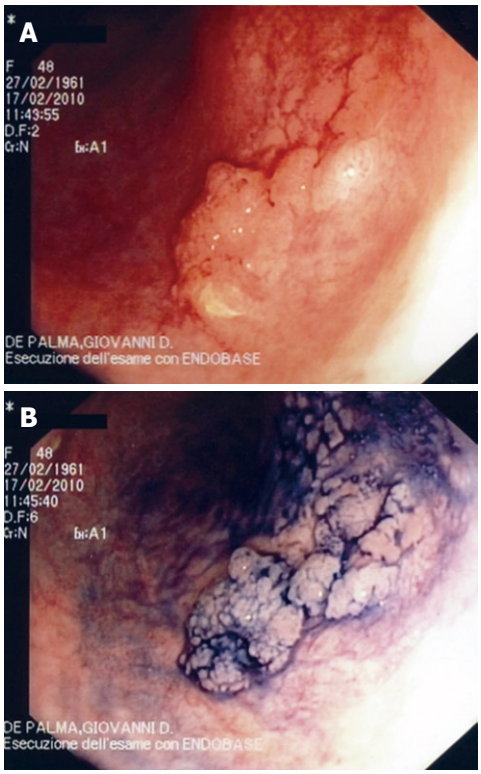

Figure 1 Conventional "white light" imaging of a plaque-like lesion of sigmoid colon in ulcerative colitis (A) and 0.5% indigo carmine chromoscopy of the lesion (B). The lesion is "unmasked" and clearly delineated.

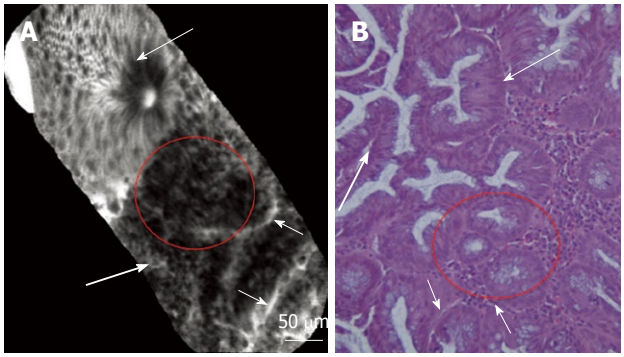

Figure 2 Confocal (A) and histological (B) images of colonic mucosa showing the switch from normal mucosa to inflamed mucosa. Normal crypt architecture is classically represented by ordered and regular crypt orifices covered by a homogeneous epithelial layer with visible "black-hole" goblet cells within the subcellular matrix (long thin arrows). Inflamed mucosa showing irregular arrangement of crypts, crypt fusion (red circles) and capillaries alterations (short arrows) and inflammatory cells (lymphocytes: long thick arrows). Magnification, × 200.

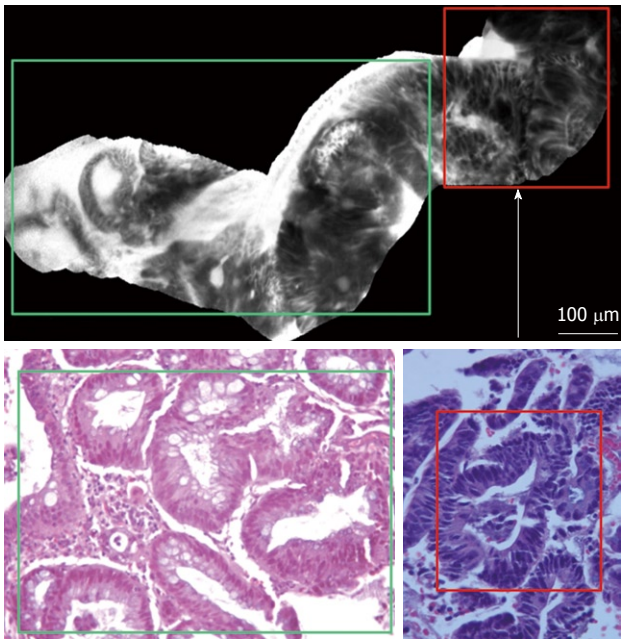

Figure 3 Confocal images of colonic mucosa evidencing the switch from the inflamed mucosa, to the neoplastic mucosa. Inflamed mucosa (green rectangle) is characterized by dilation of crypt openings, enlarged spaces between crypt, and microvascular alterations with fluorescein leaks into the crypt lumen (white arrow) therefore making the lumen brighter than the surrounding epithelium. Dysplastic mucosa (red rectangle) is characterized by "dark" cells, irregular architectural patterns with villiform structures and a "dark" epithelial border. Histology images show high-power hematoxylin and eosin stain of the tissue sampled, evidencing respectively inflamed area with features suggestive of chronic ulcerative colitis (green rectangle) and low grade dysplasia (red rectangle). Magnification, × 200.

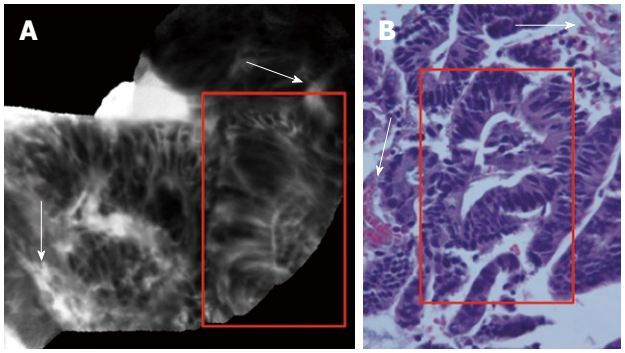

Figure 4 Confocal (A) and histological (B) images of dysplasia-associated lesional mass showing "dark" cells, with mucin depletion and goblet cell/crypt density attenuation; the architectural pattern is irregular, as well as the epithelial thickness, with villiform structures and "dark" epithelial border (red rectangles). There is gross distortion of the vascular architecture with tortuous and dilated vessels (white arrows). The hematoxylin and eosin stain histology shows a low grade dysplasia (red rectangle; hematoxylin and eosin staining; original magnification, × 200).

DISCUSSION

CLE is a new technology that has enabled endoscopists to collect real-time *in vivo* histological images or "virtual biopsies" of the gastrointestinal mucosa during endoscopy.

CLE can be performed currently with 2 devices: one integrated into an endoscope (Pentax, Japan, herein termed eCLE) and one as a stand-alone probe (herein termed pCLE) capable of passage through the accessory channel of most endoscopes (Cellvizio, Mauna Kea Technologies, Paris, France)[7-9]. There are no data, at present, comparing pCLE with eCLE to demonstrate the superiority of any one system. pCLE has several advantages and disadvantages compared with eCLE. Advantages include the greater versatility of pCLE probes, which can be used in conjunction with virtually any endoscope (high-resolution endoscopes, NBI, cholangioscope, *etc.*), ad hoc usage (such as when a lesion is detected with a normal endoscope) and acquisition at video frame rate of 12 frames/s. allowing *in vivo* imaging of capillary flow. Disadvantages include a slightly lower resolution (approximately 1 μm compared with 0.7 μm for eCLE) and smaller field of view (240-600 μm).

Recently, the use of eCLE in the diagnosis of CUC was reported. Watanabe *et al*[5] and Li *et al*[6] reported on real-time inflammation activity assessment by CLE. The inflammation activity assessment includes crypt architecture, cellular infiltration, and vessel architecture. These studies evidenced that images taken with the CLE provided information that was equivalent to conventional histology, differentiating between active and non-active CUC patients during ongoing endoscopy.

Hurlstone *et al*[10] assessed the clinical applicability and predictive power of the CLE for the *in vivo* differentiation of ALM and DALM in CUC. The study evidenced that ALM and DALM can be differentiated with a high overall accuracy, enabling the safe selection of patients suitable for endoluminal resection *vs* immediate referral for surgery.

To the best of our knowledge, this is the first report that addressed the application of pCLE for the *in vivo* characterization of colonic mucosa and DALM in a patient with CUC during ongoing videocolonoscopy.

Our study showed that the pCLE system permits high-quality cellular, subsurface vascular and stromal imaging *in vivo*, with an excellent correlation between CLE and standard histopathologic examination for both inflammation and dysplasia in ulcerative colitis.

Post-acquisition specifically-developed software ("mosaicing", Mauna Kea Technologies) was used to reconstitute the dynamic high-resolution pictures into a larger static image. By the use of mosaicing, the image area could be increased 2- to 4-fold, and image definition could be further enhanced to allow finer detail visualization. As a result of the large static image comprising of many single pictures of a video sequence, evaluation of the examination is easier and more efficient. Thereby, these features lead to an excellent correlation between CLE and standard histopathologic examination (Figures 1-4).

The main aspect of inflamed mucosa consisted of dilation of crypt openings, enlarged spaces between crypt, and microvascular alterations with fluorescein leaks into the crypt lumen (therefore making the lumen brighter than the surrounding epithelium); DALM showed typical neoplastic features of Mainz CLE criteria for prediction of intraepithelial neoplasia[11] (Figure 4).

In conclusion, this is the first study to address the novel applicability of pCLE for the *in vivo* characterization of mucosal inflammation and dysplasia in CUC. With appropriate training and careful patient selection, CLE imaging may become a suitable imaging modality in patients with CUC. The ability to target biopsies to areas suggestive of dysplasia *in vivo* allows rapid, highly accurate diagnosis "on table", reducing inappropriate, non-significant histopathology.

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