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Confocal Endomicroscopic Evaluation of Colorectal Squamous Metaplasia and Dysplasia in Ulcerative Colitis

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Case Report

A 52 year old woman with 20 years of ulcerative colitis (UC) underwent surveillance colonoscopy. She had received prednisone and then started infliximab four months prior to colonoscopy, for diarrhea and rectal bleeding, which resolved, but arthralgias and paresthesias led to infliximab discontinuation after the third induction dose. At the time of colonoscopy, she was asymptomatic on mesalamine monotherapy.

Colonoscopy revealed only left-sided colitis and pseudopolyps abutting the anal verge. Random biopsies revealed moderate active colitis consistent with UC in the distal 40 cm of the colon. Rectal biopsies 10 cm from the anus incidentally also contained areas of squamous epithelium with at least intermediate grade squamous intraepithelial neoplasia. Biopsies of the distal rectum revealed inflammatory pseudopolyps, as well as squamous epithelium with high-grade squamous intraepithelial neoplasia.

The patient was brought back for sigmoidoscopy. White-light evaluation revealed only subtle changes at 10 cm from the anal verge (figure 1A), but narrow-band imaging (NBI) revealed two distinct fields of mucosa lining the rectum (figure 1B). Magnification endoscopy revealed a clear line demarcating two fields (figure 2A). Probe-based confocal laser endomicroscopy (pCLE) revealed the mucosa on the left of figure 2A to be squamous epithelium (figure 2B), confirmed by histology (figure 2C). Further examination of this mucosa with pCLE revealed foci suspicious for dysplasia (figure 2D) due to the irregular cellular architecture, lack of uniformity in cell size and increased density of cell nuclei

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leading to a dark appearance on pCLE imaging. The presence of squamous dysplasia was confirmed histologically with targeted biopsies (figure 2E). Curiously, the areas with the greatest mucosal irregularity by gross inspection did not contain dysplasia. Dysplasia extended all the way to the anal verge; therefore, the patient underwent total proctocolectomy and with an end-ileostomy. Her resected specimen confirmed squamous metaplasia in the rectum, with high-grade intraepithelial neoplasia but no evidence of invasion or involvement of resection margins.

Discussion

Isolated cases of squamous metaplasia and carcinoma of the colorectum have been described in longstanding UC¹⁻⁵. Such metaplasia and dysplasia may be a result of chronic mucosal inflammation, as in Barrett's esophagus. However, HPV is present in colonic squamous carcinoma⁴ and has a role in the pathogenesis of cervical cancer. Thus, the mucosal immunosuppression associated with UC or its treatment may permit HPV to promote cellular transformation in colonized individuals. Although our patient's HPV status was unknown, she had been exposed to recurrent courses of steroids over her lifetime. She had also been exposed to anti-TNF therapy, although the short interval between treatment and documented dysplasia makes it difficult to speculate that infliximab was a contributing factor.

Colonic squamous metaplasia in the absence of carcinoma is extremely rare, with only 10 cases evident in the English literature since 1950^{1-3, 5-11}. Some of these cases developed carcinoma or dysplasia^{1, 2, 6, 8}, indicating that squamous metaplasia of the colon is a precursor to carcinoma. The rarity of premalignant cases of colonic squamous metaplasia in the literature may reflect how difficult it is to identify pre-neoplastic metaplasia during conventional endoscopy.

NBI endoscopy facilitated our gross identification of metaplastic epithelium, as has been described previously³. We additionally used magnification endoscopy to reveal an abnormal vascular and pit pattern in this epithelium, and then used pCLE to confirm the diagnosis of squamous metaplasia in real-time. The greatest benefit of using pCLE was to identify areas that were highly suspicious for dysplasia within the metaplastic field to then perform targeted biopsies. Thus the use of NBI for characterization and pCLE for diagnosis may be an effective way to improve early detection of focal squamous metaplasia and dysplasia in longstanding UC.

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Reference List

1. Adamsen S, Ostberg G, Norrby C. Squamous-cell metaplasia with severe dysplasia of the colonic mucosa in ulcerative colitis. Report of a case. *Dis Colon Rectum*. 1988; 31(7):558–562. [PubMed: 3391065]

2. Cheng H, Sitrin MD, Satchidanand SK, Novak JM. Colonic squamous cell carcinoma in ulcerative colitis: Report of a case and review of the literature. *Can J Gastroenterol*. 2007; 21(1):47–50. [PubMed: 17225882]
3. Fu K, Tsujinaka Y, Hamahata Y, Matsuo K, Tsutsumi O. Squamous metaplasia of the rectum associated with ulcerative colitis diagnosed using narrow-band imaging. *Endoscopy*. 2008; 40(Suppl 2):E45–E46. [PubMed: 18300203]
4. Kong CS, Welton ML, Longacre TA. Role of human papillomavirus in squamous cell metaplasia-dysplasia-carcinoma of the rectum. *Am J Surg Pathol*. 2007; 31(6):919–925. [PubMed: 17527081]
5. Maruoka T, Hasegawa K, Nagasako K. Squamous cell metaplasia without dysplasia of the colonic mucosa in ulcerative colitis. *Gastrointest Endosc*. 1990; 36(1):65–66. [PubMed: 2311886]
6. Cabrera A, Pickren JW. Squamous metaplasia and squamous-cell carcinoma of the rectosigmoid. *Dis Colon Rectum*. 1967; 10(4):288–297. [PubMed: 6037409]
7. Langner C, Wenzl HH, Bodo K, Petritsch W. Squamous metaplasia of the colon in Crohn's disease. *Histopathology*. 2007; 51(4):556–557. [PubMed: 17880537]
8. Woods WG. Squamous cell carcinoma of the rectum arising in an area of squamous metaplasia. *Eur J Surg Oncol*. 1987; 13(5):455–458. [PubMed: 3666162]
9. Nishi T, Weinstein WM, Makuuchi H. Squamous cell metaplasia in the rectum: a case report and review of the medical literature. *Tokai J Exp Clin Med*. 2004; 29(4):163–166. [PubMed: 15717487]
10. Chen FC, Fink RL, Machet D. Squamous metaplasia of the rectum: a surgical curiosity. *Eur J Surg*. 1996; 162(2):155–156. [PubMed: 8639732]
11. Polivy C, Rosenthal II. Squamous metaplasia and papillomatosis of rectum. *Arch Surg*. 1964; 89:1077–1082. [PubMed: 14208455]

Figure 1.

White-light versus narrow-band imaging (NBI) of colonic squamous metaplasia: A proximal rectal field of squamous metaplasia in the upper left quadrant of images is only subtly evident by conventional white-light endoscopy (A) but stands out as a pale field with speckled vascular markings on NBI (B).

Figure 2.

Magnification and confocal endoscopic imaging of colonic squamous metaplasia and dysplasia: **A**, Magnification endoscopic image of proximal rectal mucosa, obtained with a friction-fit cap on the endoscope, reveals metaplastic squamous epithelium to the upper left and columnar epithelium to the lower right of the image, demarcated by an abrupt border. The confocal probe can be seen in contact with the mucosa to the upper left of the image. **B**, Confocal image of metaplastic but non-dysplastic squamous rectal epithelium, containing an intrapapillary capillary loop (in white), corresponding to one of the small red spots seen by magnification endoscopy in **A**. **C**, Conventional histology of non-dysplastic rectal squamous metaplasia with a capillary loop, as in **B**. **D**, Confocal images of squamous dysplasia in the rectum, containing disorganized vasculature and cells, with crowded, dense nuclei. **E**, Conventional histology of rectal squamous dysplasia, as in **D**.