Journal of Crohn's and Colitis (2013) 7, 968–973

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Natural history of low grade dysplasia in patients with primary sclerosing cholangitis and ulcerative colitis☆,☆☆

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Received 25 October 2012; received in revised form 24 January 2013; accepted 2 February 2013

KEYWORDS
Flat dysplasia;
Low grade dysplasia;
Ulcerative colitis;
Primary sclerosing cholangitis

Abstract

Background and Aim: Patients with ulcerative colitis (UC) and primary sclerosing cholangitis (PSC) are at increased risk of colon cancer. The aim of this study was to determine the natural history of LGD and its progression to high grade dysplasia (HGD)/colorectal cancer (CRC) in PSC–UC patients.
Methods: Ten PSC–UC patients with LGD who underwent surveillance colonoscopy from 1996 to 2011 were evaluated. Raised dysplasia was defined as a discrete raised lesion located in an area involved by either quiescent or active colitis that was endoscopically resected, while flat dysplasia was defined as the absence of documentation of a raised lesion.
Results: Of the 10 patients with LGD, 3 (30%) progressed to raised HGD over a mean follow-up of 13±11 months. Three of 10 patients had initial raised LGD while 7 had flat LGD. The location of HGD was in the proximal colon in all 3 patients. However all 3 patients who progressed to HGD had initial dysplasia located in the distal colon and had flat morphology. The incidence rate for detection of HGD/CRC was 9.4 cases per 100 person years at risk. Patients with LGD with flat morphology had an incidence rate of 17.8 cases per 100 person years at risk. HGD occurred more frequently within the first year of initial detection of LGD (23.5 per 100 patient years of follow-up).

Abbreviations: ACG, American College of Gastroenterology; 5-ASA, 5-aminosalicylic acid; CD, Crohn's disease; DALM, dysplasia associated lesion or mass; IBD, inflammatory bowel disease; IC, indeterminate colitis; HGD, high grade dysplasia; LGD, low grade dysplasia; PSC, primary sclerosing cholangitis; UC, ulcerative colitis.

☆ Grant support: The study is supported by a research grant from the Inflammatory Bowel Disease Working Group and American College of Gastroenterology Grant (both to U.N.).

☆☆ Specific author contributions:Study concept, paper preparation and revisions — Preethi GK Venkatesh.Data monitoring and paper preparation — Norma G Gutierrez and Ramprasad Jegadeesan.Study concept, paper revisions and critical review — M Sanaka and U Navaneethan.

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http://dx.doi.org/10.1016/j.crohns.2013.02.002

Conclusions: One-third of patients with LGD progressed to HGD/CRC in PSC–UC. Most patients progress within the first year of diagnosis of LGD supporting early colectomy in PSC–UC patients with LGD.

1. Introduction

Ulcerative colitis (UC) patients with concomitant primary sclerosing cholangitis (PSC) are at increased risk for developing colorectal cancer (CRC).[1–4] The 10-year and 20-year risks of developing colorectal neoplasia have been reported as 14% and 31% respectively in PSC–UC patients in contrast to 4.4% and 8.6% in UC alone.[3,5] Colonoscopy with biopsy needs to be performed at the time of diagnosis in patients with PSC-inflammatory bowel disease (IBD) with yearly surveillance thereafter.[6] Surveillance to detect early dysplasia to prevent colon cancer in IBD patients is recommended.[7–10] Dysplasia in UC patients can be classified as low grade dysplasia (LGD) or high grade dysplasia (HGD).[11]

For patients with HGD, colectomy is recommended because of increased risk of detecting synchronous adenocarcinoma.[12] Also the risk of progression to cancer over time is significantly elevated to 35%.[12] However the risk of progression of LGD is very variable. In particular, there is no consensus whether monitoring with endoscopic surveillance or surgery after a diagnosis of LGD is recommended in patients with PSC. In another study from our institution, we found a low rate of progression of LGD to HGD or cancer in UC patients without PSC on a surveillance program.[13] Patients with distal flat LGD were at highest risk of progression.[13] However the literature in PSC–UC patients is very limited with variable risks of progression and studies have clumped both PSC and non-PSC patients together.[14–16]

The primary aim of this study was to determine the natural history of LGD and study the progression to HGD/CRC in PSC–UC patients. The secondary aims were to evaluate when these were detected in patients with LGD undergoing follow-up surveillance colonoscopy and/or colectomy.

2. Patients and methods

2.1. Patients

The Cleveland Clinic electronic medical record database was queried for patients with UC and concomitant PSC who underwent two or more surveillance colonoscopies and diagnosed with low grade dysplasia (LGD) from January 1996 to December 2011. Demographic, clinical, and procedural data and adverse events were collected. The study was approved by the Cleveland Clinic Institutional Review Board.

2.2. Inclusion and exclusion criteria

The major inclusion criterion was presence of LGD on surveillance colonoscopy. Patients with Crohn's disease (CD) and indeterminate colitis (IC) were excluded. Patients who had insufficient follow-up after the diagnosis of LGD or underwent immediate colectomy within 1 month were excluded. Patients with lesions classified as indefinite for dysplasia and as non-dysplastic lesions were also excluded. It is a routine recommendation that patients with LGD in the setting of PSC–UC undergo colectomy in our institution. Patients who had lesions or mass which were not endoscopically removable went directly to colectomy and did not undergo follow-up surveillance at our institution were excluded. However, patients who were not willing for colectomy in the setting of flat LGD or raised LGD which was endoscopically removed get follow-up surveillance colonoscopy in our institution.

2.3. Demographic and clinical variables

PSC was diagnosed based on the finding of intra- and/or extra-hepatic bile duct abnormalities such as beading, duct ectasia, and structuring of the intra- or extrahepatic bile ducts based on the review of endoscopic retrograde cholangiopancreatography and/or magnetic resonance cholangiopancreatography.[17] Patient and disease characteristics including age, gender, age at PSC and UC diagnosis, and duration of UC were evaluated. Information on smoking history, and family history of IBD or colon cancer in first degree relatives was also obtained. Information regarding the type of UC treatment used (steroids, azathioprine, biologics) was also obtained, with patients having to use this medication continuously for atleast for 6 months for this to qualify as medication use.

All histopathology slides, including biopsies from colonoscopies performed elsewhere, were examined by atleast two experienced gastrointestinal pathologists at our institution in order to confirm the diagnosis of dysplasia. Proximal location of dysplasia was defined as dysplasia location anywhere proximal to the splenic flexure, while distal dysplasia was defined as dysplasia location distal to the splenic flexure. Flat dysplasia was defined as the absence of documentation of a raised mass, lesion, or polyp in endoscopy or pathology reports. Raised dysplasia was defined as a discrete raised lesion located in an area involved by either quiescent or active colitis that was endoscopically resected with biopsy confirmation of dysplasia. Raised lesions at endoscopy that were felt to be irregular or unamenable to excision and hence more suggestive of mass or plaque-like lesion i.e. DALM were excluded as these patients automatically underwent colectomy.[18] Thus, only raised lesions that could be endoscopically removed completely and without any evidence of surrounding flat dysplasia were included. Surveillance for dysplasia in our institution involves 4 quadrant biopsies every 10 cm of the colon as recommended by the American College of Gastroenterology (ACG).[19] A complete colonoscopy was done in all cases, without finding dysplasia in the proximal colon in