

DYSPLASIA IN ULCERATIVE COLITIS

Introduction

- One of the most complex and frightening aspects of the diagnosis of IBD is risk of malignancy
- Colorectal cancer (CRC) develop from precursor lesions; window of opportunity for early detection and cure
- Understanding dysplasia is crucial to proper management of CRC
- Sporadic CRC—dysplastic precursor is adenomatous polyp managed endoscopically
- IBD
 - dysplasia polypoid or flat, localized, diffuse, or multifocal
 - marks entire colon as being at heightened risk
- Cancer surveillance more challenging in IBD than general population

Risk of colorectal cancer

- *Pancolitis*: incidence of colorectal cancer 2% at 10 yrs; 8% at 20 years; 18% at 30 years of disease
- *Left-sided disease*: No risk with proctitis or proctosigmoiditis; left sided colitis risk between 1 - 5% at 20 years

Factors influencing development of cancer

- Duration and extent of disease: Rarely seen with disease duration less than 8 years: no surveillance until > 8years of disease in pancolitis; 12 years of left-sided disease
- Strictures in UC and Crohn's
- Disease severity
- Age of onset
- PSC: Uncertainty as to whether there is increased risk and whether these patients need to have surveillance started earlier
- Family History CR Cancer: question whether patients should get more intensive, earlier onset surveillance

Colonoscopic surveillance

- Damaged colonic mucosa → low grade dysplasia → high grade dysplasia → cancer
- Detect patients with dysplasia before development of cancer or detect cancer in earlier stages
- Limited data and considerable uncertainty as to the course of development of low-grade dysplasia, the inevitability of progression to high grade dysplasia and cancer, and efficacy of surveillance

Dysplasia

- Macroscopically: heterogeneous; elevated (endoscopically visible) or flat (microscopically detectable)
- Microscopically replacement of native epithelium by unequivocally neoplastic but noninvasive epithelium
- Interobserver variation in determining presence

- IBD Dysplasia Morphology Study Group classification of dysplasia: questionable reproducibility
- Dysplasia should be distinguished from reactive inflammation
- Other concerns: sensitivity or sampling error

Colonoscopic surveillance studies

- No randomized trials (unlikely)
- Most surveillance studies from institutions following subjects > 8 years with disease beyond splenic flexure; q3 year interval
- Favorable non-randomized data

Technical aspects of colonoscopic surveillance

- Generally q1-2 years starting at 7-8 years of disease unless suspicious lesions require closer f/u
- Surveillance biopsies sample fraction of mucosa at risk
- Algorithm is 4 quadrant biopsies every 10 cm starting at cecum to descending colon; sampling every 5 cm beginning in sigmoid; average 44 biopsies
- new advances: laser-induced fluorescence spectroscopy

Management of patients with dysplasia

- Dysplasia associated lesion or mass (regardless of whether high grade or low grade) has 40% risk of associated malignancy
- High grade dysplasia in flat mucosa has risk of malignancy 42-67%
- DALM or high grade dysplasia → colectomy

Controversial low-grade dysplasia

- Advising colectomy in setting of low grade dysplasia is reasonable and the current recommendation of the American College of Gastroenterology
- Patients with low grade dysplasia may already have CR cancer
 - Bernstein et al Lancet 1994 with 42% (10/24) patients with HGD and 16% (3/19) patients with LGD with CRC in colectomy
 - Ullman et al Gastro 2003 27% (3/11) with colectomy 6 months after diagnosis of flat LGD with cancer or HGD
- If no colectomy, rate of progression?
 - 33-54% progression of LGD to cancer in five years
 - Some authors with substantially lower rates 0-10% five year progression
- Some physicians say colectomy only if LGD is repeatedly confirmed on repeat colonoscopy or in more than one specimen (multifocal)
 - risky because negative exam doesn't afford reassurance
 - most patients will eventually be found to have LGD or worse on subsequent colonoscopies
 - rate of progression of multifocal and unifocal LGD to cancer is same
- Weight of evidence points in direction of colectomy for LGD

Adenoma in setting of UC

- Adenoma by definition dysplastic
- May be a subtype of DALM not associated with high predictability for CR cancer
- Distinction between sporadic adenoma and DALM important
 - lesion outside extent of chronic UC distribution, then sporadic adenoma likely and colectomy not advised
 - adenoma that is endoscopically and histologically compatible with sporadic adenoma lies within distribution of chronic UC and is completely removed, multiple biopsies of flat surrounding mucosa
 - if negative, surveillance with repeat biopsies every 3-4 months for one year, then yearly thereafter
 - colectomy for patient with dysplasia in flat mucosa or patients with polypoid dysplasia not resected endoscopically

Ileal pouch anastomosis and risk of cancer

- with stapled technique, anal transition zone consisting of residual colonic epithelium
- very small risk of cancer unless patients had dysplasia or CR cancer in original specimen
- no formal recommendations — some clinicians survey Transition Zone q 2-3 years
 - low grade dysplasia followed closely with repeat multiple biopsies
 - persistent dysplastic mucosa or high grade dysplasia—mucosectomy or laser ablation
 - ? need for anal mucosectomy in subgroup with dysplasia or CR cancer in original specimen

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