Diagnosing Dysplasia in IBD: A Brief Review
3rd Emirates Surgical Pathology Conference
15 December 2017
Dubai, UAE

Martine McManus, MD, FCAP
Pathology & Laboratory Medicine Institute
Cleveland Clinic Abu Dhabi
Outline

- Outline the risk of colorectal neoplasia in Inflammatory Bowel Disease (IBD)
- Review why dysplasia in IBD is difficult to diagnose
- Discuss and illustrate the classification/grading of dysplasia in IBD
Dysplasia-Carcinoma Sequence

Sporadic

Normal → Adenoma → Cancer

Colitis

Colitis → Dysplasia → Cancer
Sporadic colon cancer

Normal mucosa → Early adenoma → Intermediate adenoma → Late adenoma → Carcinoma

- Loss of APC function
- Aneuploidy, sialyl-Tn antigen expression, CpG island methylation, miRNA dysregulation
- Microsatellite instability, KRAS mutations, COX-2 activity
- DCC and DPC4 mutations
- SRC mutations
- P53 mutations

Colitis-associated colon cancer

Normal mucosa → Indefinite dysplasia → Low-grade dysplasia → High-grade dysplasia → Carcinoma

- PS3 mutations
- P53 LOH
- Aneuploidy, sialyl-Tn antigen expression, COX-2 activity, CpG island methylation, microsatellite instability, miRNA dysregulation
- DCC mutations
- SRC mutations
- KRAS mutations
- Loss of APC function

IBD-associated Colorectal Cancer: Risk

- 1%, 2% and 5% after 10, 20 and >20 years of disease duration.
IBD-associated Colorectal Cancer: Clinical Features

- 0.8% of all colorectal cancer cases
- Males > females
- Age < 65 years old
- Proximal colon
- Concomitant PSC
IBD-associated Colorectal Cancer: Prognosis

- Associated with worse mortality
- UC-associated CRC not associated with increased mortality relative to CD-associated CRC
Dyplasia in IBD is difficult to detect on endoscopy
Endoscopy: Dysplastic Lesions in IBD
Dyplasia is challenging to classify on histology (even when 2 GI Pathologists review the slides)
Dysplasia in IBD

NEG
Negative for Dysplasia

IND
Indefinite for Dysplasia

LGD
Low-grade Dysplasia

HGD
High-grade Dysplasia
Negative for Dysplasia

- “Normal colonic mucosa” - proximal to involved UC; skip area in CD
- “Inactive colitis” - treated (healed) quiescent colitis
- “Active colitis” - ongoing (untreated or refractory disease)
IBD Colitis: Histologic Features

- Surface epithelial degeneration
- Full thickness lymphoplasmacytosis
- Increased lamina propria eosinophils
- Crypt architectural distortion, or drop out
- Metaplasia – Paneth cell, pyloric gland
- Neutrophilic and/or eosinophilic cryptitis
- Neutrophilic and/or eosinophilic crypt abscesses
IBD Colitis: Reparative/Regenerative Changes

- **Hypermucinous architecture (Mucinous dysplasia)**
- **Serrated architecture (Serrated dysplasia)**
- **Crypt architectural disarray**
- **Nuclei: vesicular, minimal nuclear pleomorphism, regular nuclear contour**
- **Lacks epithelial atypia and complex architecture**
Indefinite for Dysplasia: When should you use this?

- Cannot classify as equivocally positive or negative for dysplasia
- The nuclear changes look dysplastic but there is inflammation involving the same epithelium
- Unusual growth pattern (villiform, serrated)
- Nuclear atypia disproportionate to the amount of inflammation
- Caution: This has the worst inter-observer agreement
Positive for Dysplasia

- Low-grade
- High-grade
Low-grade Dysplasia
Sporadic Adenoma vs Colitis-associated Dysplasia

Endoscopically Visible Polyp

Modified from Odze RD et al. Surgical Pathology of the GI Tract, 3rd ed, 2015
Sporadic Adenoma vs Colitis-associated Dysplasia

Endoscopically Visible Polyp

- Inside IBD
- Outside IBD

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Endoscopically Visible Polyp

Inside IBD

Outside IBD

Sporadic Adenoma

Polypectomy and regular surveillance

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Sporadic Adenoma vs Colitis-associated Dysplasia

Endoscopically Visible Polyp

Inside IBD
- + flat dysplasia
  - Colectomy
- - flat dysplasia
  - Polypectomy and increased surveillance

Outside IBD
- Sporadic Adenoma
  - Polypectomy and regular surveillance

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Endoscopically Visible Polyp

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Biopsy the Polyp

Modified from Odze RD et al. Surgical Pathology of the GI Tract, 3rd ed, 2015
Low-Grade Dysplasia
Sporadic Adenoma versus Colitis-associated Neoplasia?

- Report should contain 3 pieces of information:
  1. Grade the dysplasia in the polyp
  2. State whether the mucosa surrounding the polyp shows colitis
  3. State whether the mucosa surrounding the polyp shows dysplasia
- Pathologist should provide clinicopathologic correlation
Positive for Dysplasia: High-grade Dysplasia

- *High-grade*: best inter-observer agreement; nuclear pleomorphism and architectural complexity
Don’t rely on Immunohistochemistry!

✓ p53 overexpression
✓ Ki-67 proliferation
Invasive Adenocarcinoma

- Gross features may be subtle or even absent
- Multiple synchronous/metachronous lesions
- Unique grossing protocol for IBD colectomies
IBD Resections: Grossing Protocol

Grossing Note:
- 2 sections/cassette from each segment of colon
- Focus on areas identified endoscopically
- Sample strictures, plaques,
Low-grade Tubuloglandular Adenocarcinoma

Diagnosing Dysplasia in IBD

- Synthesize and interpret all information present: correlate with clinical and endoscopic context
- Consider the background disease when evaluating epithelium
- Maintain a high threshold for dysplasia, always show it to a second Pathologist
- Be careful with reparative/regenerative changes
- Partner with your Gastroenterologist: communicate and explain your findings