General Surgery Grand Grounds

University of Colorado Health Sciences Center

Case Presentation

December 24, 2009

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- 27 YO female with chief complaint of abdominal pain.
- PMHx:
  - seizure disorder
  - colonic polyps (age 15)
  - Hemorrhoids
  - Constipation
  - Dyspepsia
  - hematemesis with EGD showing esophagitis, gastritis, duodenitis.

- G2P2
- PSurgHx: none
- Allergies: none
- Medications: none
- SHx: smokes ½-1ppd X 12 yrs. No EtOH. No illicits per px.
- ROS: mid-epigastric abd pain, diffuse and poorly defined

- Family Hx:
  - Father: colon cancer at age 7 (?)
  - Grandfather with colon cancer
  - No history of breast or ovarian cancer
  - No other significant malignancies
  - Family was told “polyposis coli”

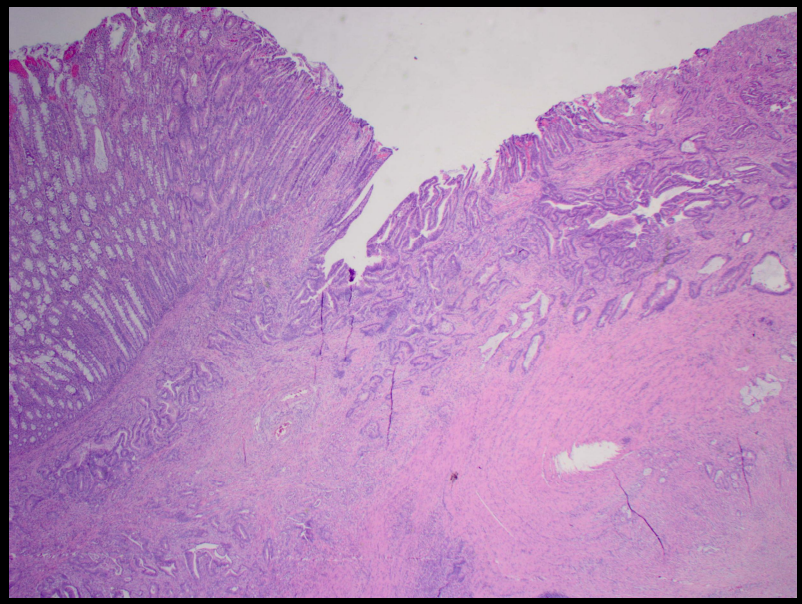
- Colonoscopy 8/09
  - Sessile polyp at rectosigmoid
  - Pedunculated polyps in descending and transverse
  - Multiple polyps in ascending colon
  - Cecal cancer
- CT scan
  - Mesenteric inflammation posterior to cecum, no metastatic disease

- O.R. 9/23/2009
  - Subtotal colectomy
  - Intraop sigmoidoscopy-ensure resection encompassed rectosigmoid polyp
  - Primary ileorectal anastamosis

- Pathology
  - Invasive mod-diff adenoCA, 5.5cm, T3/No in cecum, completely obstructing

25LNs, no malignancy

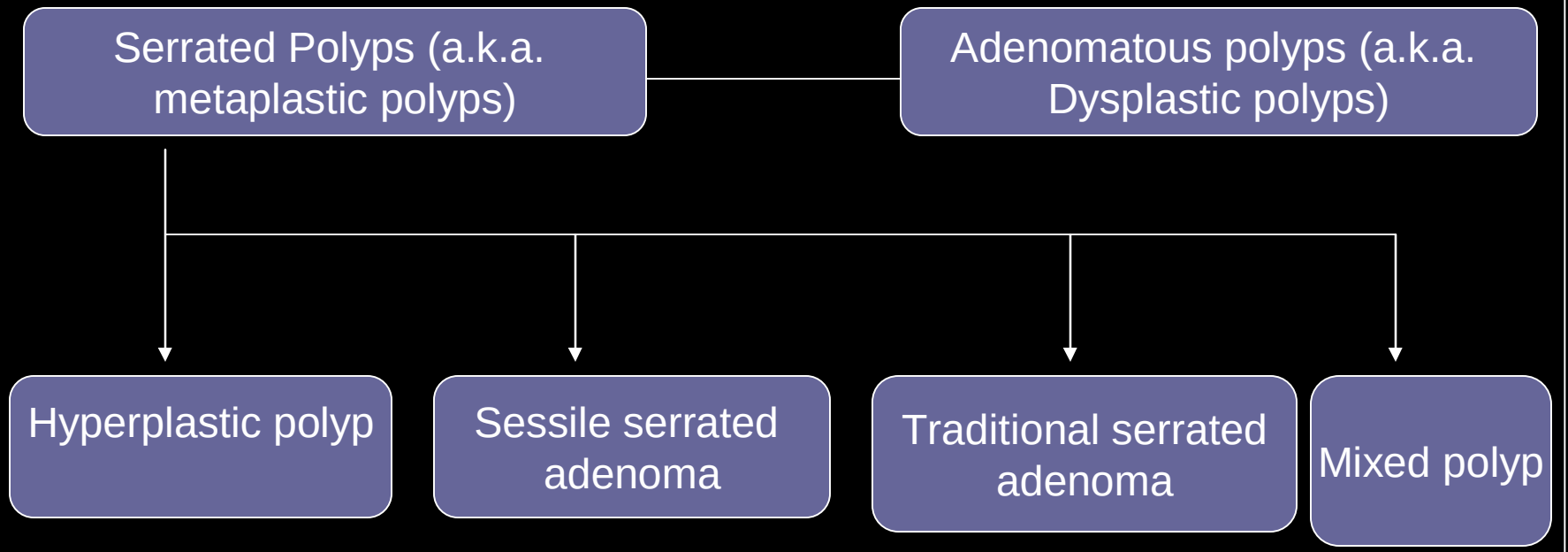
Nrml appendix



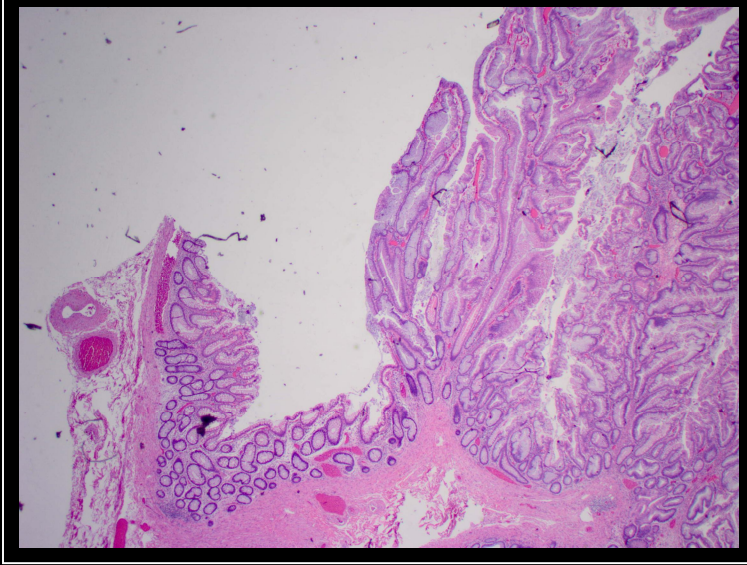
- Pathology (continued)
  - Multiple traditional serrated adenomas, 3.8cm max dimension, primarily right colon
  - (+) staining for MLH1, MSH2, MSH6 mismatch repair genes
  - No immunohistochemical evidence for microsatellite instability

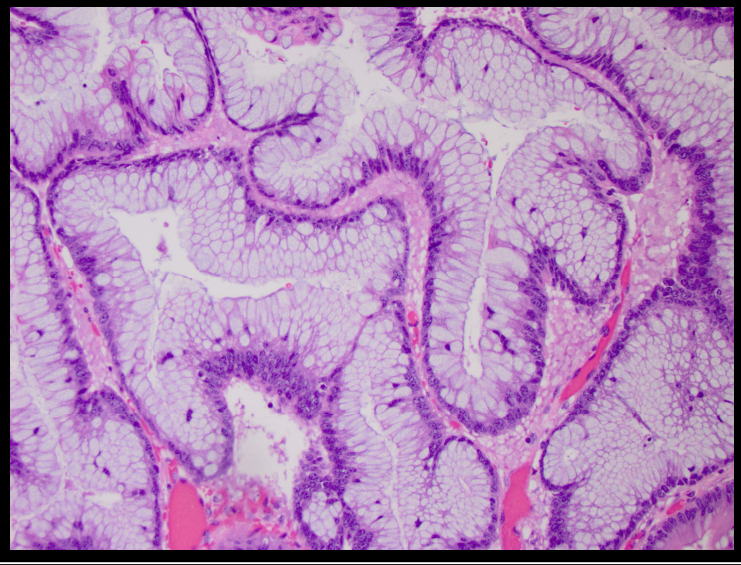
- Px did well postoperatively,
- D/c’d home POD 5
- Referred to heritable cancer clinic

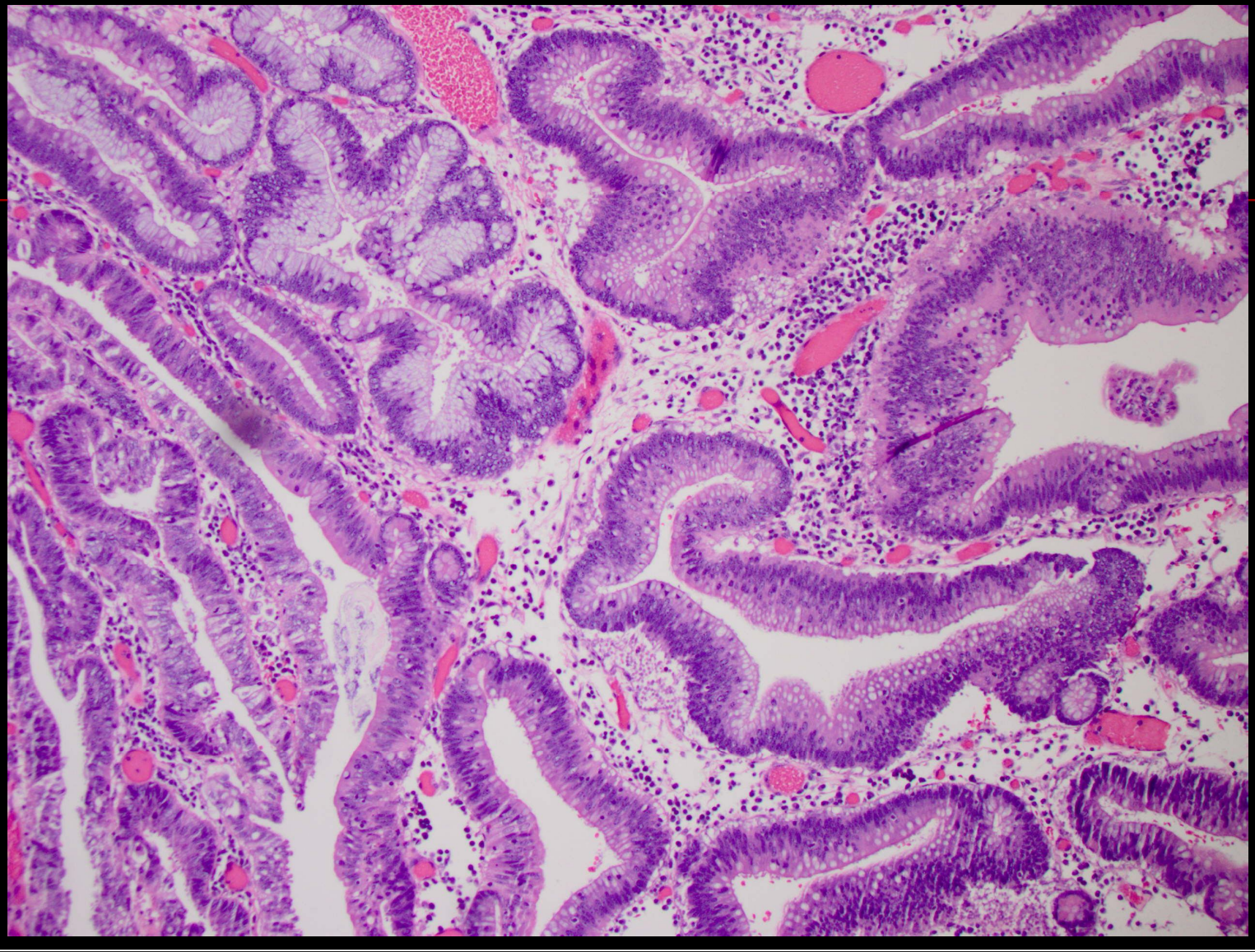
What is a traditional serrated adenoma?



- Traditional serrated adenoma
  - Underlying architecture of hyperplastic polyps
  - Dysplastic features of an adenoma







- Hereditary Colon Cancer Overview
  - Estimated 5-15% of colon cancers
  - Linked to specific, heritable gene mutation
  - 2 most common are Lynch syndrome and F.A.P
  - Both of these progress through adenoma-carcinoma pathway
  - Together, these two syndromes encompass only 2-5% of all colorectal cancers

Familial Adenomatous Polyposis

- 1:30,000 prevalence
- Mutation of APC gene (Ch. 5)
- 100s-1000s polyps
- Average age of cancer is 39
- 90% have duodenal polyps, gastric polyps common
- Autosomal Dominant, 25% spontaneous mutations
- Adenoma-carcinoma pathway
- Rx: total abdominal colectomy and proctectomy

Lynch Syndrome

- A.K.A. Hereditary Non-polyposis Colorectal Cancer
- 5% of all CRC diagnoses
- Mismatch repair gene defect
- Microsatellite instability
- Proximal colon predominately affected
- Average age of cancer 45
- Adenoma-carcinoma pathway
- Rx is total abdominal colectomy, proctectomy

- Adenoma-carcinoma pathway
  - Progression of adenoma to dysplasia to adenocarinoma
  - Adenomas >10mm, estimated 1%/yr progression to carcinoma
  - 3% of all adenomas estimated to progress to cancer

Hawkins, N et al. "The Serrated Neoplasia Pathway." Pathology, 34:6 548-555

- Other pathways exist:

- Hyperplastic polyposis
  - Large serrated polyps throughout colon
  - Average 40-100 polyps, mixed subtypes
  - Initially thought to have no increased malignant potential
  - Longitudinal studies have now shown up to 50% present with eventual adenocarcinoma

What about the traditional serrated adenoma?

- Adenoma cytology but hyperplastic (serrated) architecture
- Thought to have similar malignant potential to adenomas
- May be faster growing due to the methylation pathway defects

- Does this patient have a hereditary syndrome that proceeds through a non-adenoma-carcinoma pathway?

- 2006 case report and review in Cancer: Epidemiology, Biomarkers, and Prevention
  - 11 families with primarily serrated polyps and colon CA
  - Appears to be AD, variably penetrant
  - High preponderance of BRAF mutation
  - Variable MSI
  - Majority of cancers occurred in the proximal colon and in females

- Young J and Jass J. "The Case for a Genetic Predisposition to Serrated Neoplasia in the Colorectum: Hypothsis and Review of the Literature." Cancer Epi Biomarkers Prev. 2006; 15(10). Oct 2006

- BRAF proto-oncogene implicated
  - Hypermethylation
- Occurrence of cancer linked with smoking
  - ? Weakly penetrant gene defect associated with environmental factors

- Take home points:
  - Serrated / hyperplastic polyps harbor malignant potential
  - Familial inheritance of serrated neoplastic pathways exist and should be considered
  - Serrated pathways are frequently proximal colon, may allow for rectal-sparing operations
  - Screening is paramount