A Plethora of Colon Polyps

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Background

• Clinical history:
  – 45 year old female with complaint of blood in stool
  – Underwent colonoscopy
    • Five 3-9 mm polyps throughout colon and internal hemorrhoids
  – Polyps completely removed and sent for pathology
4 mm cecal polyp
3 mm ascending colon polyp
6 mm hepatic flexure polyp
8 mm sessile trans colon polyp
9 mm descending colon polyp
Just a bunch of polyps?

- Lymphoid aggregate
- Tubular adenoma
- Ganglioneuroma
- Intramucosal lipoma
- Inflammatory (juvenile) type polyp
Ganglioneuroma

• Sporadic
• FAP
• Multiple endocrine neoplasia, type IIB
• Neurofibromatosis 1
• Cowden syndrome (CS)
Inflammatory (juvenile) polyp

- Sporadic (especially in children)
- Chronic injury response
  - IBD, ischemia, or chronic infections
- Juvenile polyposis
- Cowden syndrome
PTEN Hamartoma Tumor Syndrome
**PTEN Hamartoma Tumor Syndrome (PHTS)**

- Unifies heterogeneous germline *PTEN* disorders
- Cowden syndrome (CS), Bannayan-Riley-Ruvalcaba syndrome (BRRS), Proteus syndrome
- Multiple hamartomas and distinctive phenotypes
- *PTEN* (10q22-23) tumor suppressor gene
  - Mutated in 80% CS, 60% BRRS
- 20-30% familial, 70-80% de novo (autosomal dominant, penetrance ~80%)
CS

- CS is the only PHTS disorder associated with a documented predisposition to malignancies
  - Other PHTS with PTEN mutations assumed to have Cowden-associated cancer risks
- Incidence of 1 in 200,000
  - Likely underestimated
- Extra-intestinal findings predominate, 30-80% have intestinal polyps
CS Cancer Risk

- CS clinical criteria + PTEN mut
- Est cumulative lifetime cancer risks:
  - 85% breast
  - 35% thyroid
  - 28% endometrial
  - 9% colorectal
  - 34% renal cell
  - 6% melanoma

PHTS/CS Clinical Dx Criteria (NCCN)

• Major criteria: Breast, Endometrial, Thyroid follicular cancer
  – Gastrointestinal hamartomas (≥3)
    • Ganglioneuromas, others but not HP’s
  – Macrocephaly (≥97 percentile)
  – Macular pigmentation penis
  – Adult Lhermitte-Duclos disease (LDD)
  – Multiple mucocutaneous lesions
    • Trichilemmomas, acral keratoses, mucocutaneous neuromas, oral papillomas

PHTS/CS Clinical Dx Criteria (NCCN)

- **Minor criteria**
  - Autism spectrum disorder
  - Colon cancer
  - Esophageal glycogenic acanthosis ($\geq 3$)
  - Lipomas ($\geq 3$)
  - Mental retardation (ie, IQ $\leq 75$)
  - Renal cell carcinoma
  - Testicular lipomatosis
  - Thyroid adenoma, multinodular goiter
  - Vascular anomalies (multiple intracranial developmental venous anomalies)

Working diagnosis of PHTS/CS

EITHER/OR:

1. Three or more major criteria, must include macrocephaly, Lhermitte-Duclos disease, or GI hamartomas

2. Two major and three minor criteria
PHTS/CS: Frequent GI findings

- Esophagus
  - Glycogen acanthosis 40-60%
- Stomach
  - Fundic gland polyps, Inflammatory (juvenile) type polyps
- Colon and small bowel
  - Inflammatory (juvenile) type polyps
  - Ganglioneuromas
  - Lymphoid polyps
  - Intramucosal lipomas
  - Adenomas
Glycogen acanthosis

Endoscopic image from www.gastrointestinalatlas.com
CS: intestinal findings

• GI polyps at U of U reviewed in CS patients
  – 12/19 had *PTEN* mutations
  – Inflammatory (juvenile) polyps most common (95%)
  – Expansive lymphoid follicles (63%)
  – Ganglioneuromas (53%)
  – Mucosal lipomas (26%)

• Two or more hamartomatous polyp types/pt: highly prevalent in Cowden syndrome
PHTS/CS Management

Women
- Breast exam q 6-12 mon, starting 25yo or 5-10 years before earliest breast ca in family
- Annual mammogram and breast MRI screening starting 30-35yo
- Consider annual endometrial bxs and/or US starting 30-35yo
- Discuss risk reduction mastectomy, hysterectomy

Men and Women
- Annual PE starting 18yo
- Annual thyroid US starting 18yo
- Colonoscopy, starting 35yo, then q5 yr or more
- Consider renal US starting 40yo, they q1-2 yr
When to raise suspicion for PHTS in your pathology report?

• Multiple gastrointestinal hamartomas
  – Combinations of inflammatory (juvenile) polyps, ganglioneuromas, mucosal lipomas distributed throughout the GI tract

• Diffuse esophageal glycogenic acanthosis
Glycogenic acanthosis in esophagus
Thanks for your attention!