Familial Adenomatous Polyposis (FAP)

Background

1. Definition: Autosomal dominant disease caused by a mutation in the adenomatous polyposis coli gene resulting in early development of hundreds to thousands of colorectal adenomas. Confers a 100% risk of developing colorectal cancer[1]
2. General Information
   - Gardner's syndrome: familial adenomatous polyposis variant associated with extraintestinal manifestations (desmoid tumors, epidermoid cysts, lipomas, osteomas, supernumerary teeth, gastric polyps, and juvenile nasopharyngeal angiofibromas).[2]
   - Turcot's syndrome: rare variant of familial adenomatous polyposis associated with brain tumors.
   - Attenuated familial adenomatous polyposis: familial adenomatous polyposis variant with less than 100 colorectal adenomas, greater right sided colonic involvement, fewer extracolonic manifestations, and a delayed onset of colorectal cancer.[2]

Pathophysiology

1. Pathology of Disease[3]
   - Caused by mutation in adenomatous polyposis coli gene located on chromosome 5q21-q22
   - More than 800 mutations have been described
   - Various expressions of the disease and extraintestinal manifestations
   - One-third of patients have no family history and may represent a new germline adenomatous polyposis coli mutation or mutY homolog gene mutation causing autosomal recessive mutY homolog associated adenomatous polyposis.
2. Incidence, Prevalence[4]
   - Incidence: 1 in 6,850 to 1 in 18,000
   - Prevalence: 1 in 21,505 to 1 in 30,000
3. Risk Factors
   - Family history of FAP
   - Affects both genders equally
   - FAP seen in second and third decades of life (mean age 16)
4. Morbidity / Mortality
   - 100% develop colon cancer if colectomy not performed
   - At risk for several extracolonic malignancies[5]
     - Duodenal ampullary carcinoma
     - Follicular or papillary thyroid cancer
     - Childhood hepatoblastoma

- Gastric carcinoma
- CNS tumors (mostly medulloblastomas)

Diagnostics

1. History[1]
    - Asymptomatic if detected early
    - Increasing bowel movements
    - Looser stools
    - Mucous discharge
    - Rectal bleeding
    - Abdominal or back pain
    - Family history of colon cancer
2. Physical Examination
    - Normal if detected early
    - Congenital hypertrophy of the retinal pigment epithelium (brown to black round lesions on the retina)
    - Nasopharyngeal angiofibromas
    - Supernumerary teeth
    - Thyroid mass
    - Abdomen mass
    - Epidermoid cysts
    - Lipomas
3. Diagnostic Testing
    - Diagnosis is based upon the presence of 100 or more colorectal adenomas on colonoscopy.
    - Consider familial adenomatous polyposis gene testing for the following indications: Patient with 100 or more colorectal adenomas (affected with adenomatous polyposis coli); first degree relatives of familial adenomatous polyposis patients; Patient with 20 or more cumulative colorectal adenomas (suspected attenuated familial adenomatous polyposis); First degree relatives of patients with attenuated familial adenomatous polyposis.[6]

Differential Diagnosis

1. Key Differential Diagnoses (Genetic syndromes with increased colorectal cancer risk)[7]
    - Hereditary nonpolyposis colorectal cancer (aka Lynch syndrome)
    - Familial juvenile polyposis
    - Peutz-Jeghers syndrome
    - MutY homolog associated adenomatous polyposis
2. Extensive Differential Diagnoses (Genetic syndromes with gastrointestinal polyposis)[7]
    - Cowden disease

- Intestinal ganglioneuromatosis
- Ruvalcaba-Myhre-Smith syndrome
- Devon family syndrome
- Cronkhite-Canada syndrome

Therapeutics

1. Prophylactic colectomy when polyposis is at a premalignant stage.
2. Consider sulindac, tamoxifen, chemotherapy, or radiotherapy for progressive intra-abdominal and abdominal wall desmoids.[1]

Follow-Up

1. Return to office: For annual thyroid exam and evaluation for extraintestinal manifestations
2. Refer to specialist: Gastroenterology referral for endoscopic evaluation[1]
   - Symptomatic patients of any age
   - Upper endoscopy for screening and surveillance
   - Annual flexible sigmoidoscopy beginning at age 10-12 for confirmed or suspected familial adenomatous polyposis
   - Repeat colonoscopy every 6-12 months after subtotal colectomy to evaluate for colon cancer or remnant polyps[9]

Prognosis

1. Colorectal cancer develops in 100% of patients: mean age of 39 years in familial adenomatous polyposis; mean age of 54 years in attenuated familial adenomatous polyposis.[1]
2. Risk of small bowel obstruction (7%), desmoids tumors (13%), small bowel adenocarcinomas (3%), and pouch or ileal adenomas (35-47%) after colectomy.[10]

Prevention

1. Hereditary disorder, no known prevention
2. NSAIDs may be considered after colectomy and as an adjunct to endoscopy to reduce rectal polyp burden.[1]

Patient Education

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2. http://www.cancer.net/patient/Cancer+Types/Familial+Adenomatous+Polyposis

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