Familial Adenomatous Polyposis: A Review of Treatment and Associated Syndromes

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Abstract:

Familial adenomatous polyposis is (FAP) is a rare and largely inherited cancer predisposition syndrome[5]. FAP occurs in around 1 in 10,000 people[1]. With this condition, individuals will develop numerous, precancerous adenomatous polyps throughout their colon and rectum[1]. The polyps start to develop in the teen years to early 20's (mean age of 16), and by 35 years old, 95% of patients will have polyps[5]. With age these polyps will increase in number and in size, and eventually one of these polyps will become cancerous. In fact, colon cancer is inevitable without colectomy, and adenocarcinoma develops at a mean age of 39 in untreated patients[2].

This is a genetically inherited, autosomal dominant condition involving APC gene mutation (5q21)[5]. The term "familial" points out that this is a largely inherited syndrome, but up to 30% of FAP patients have no family history of the disease and the APC mutation is produced at conception[2]. The APC gene is normally involved in the apoptosis of colonic epithelial cells[4]. The APC gene is a negative regulator of beta-catenin[4]. When APC is mutated, beta-catenin is no longer downregulated and can function to stimulate cell growth[4]. Thus, the APC gene is categorized as a tumor suppressor gene, and mutations can lead to the development of various cancers[1,4]. Germline APC mutations can serve as diagnostic, though classic FAP is classically diagnosed clinically when a colonoscopy finds more than 100 polyps on exam[1]. However, other diagnostic criteria exist such as the finding of any colorectal adenomas in a patient under 30 years old who has a family history of FAP[3].

This poster will review the case of patient TM, and discuss gross specimen handling as well as provide an overview of the disease, it's associated syndromes, and management.

Patient Background:

- 16-year-old, Caucasian male
- Family history of FAP (Mother and maternal Grandmother)
- Patient genetic testing
  - Identified pathologic mutation in the APC gene (5q21)
- Colonoscopy reveals innumerable polyps
  - Biopsy results: adenomatous polyps
- Treatment
  - Total proctocolectomy

Rationale and Hypothesis:

A total proctocolectomy was determined necessary, and this is a standard operation for FAP patients. An ileal pouch-anal anastomosis was created as well as a diverting loop ileostomy. In a separate surgery, the ileostomy will be closed to restore function for the patient. As stated above, this seemingly drastic measure is quite necessary in order to prevent colon cancer[2]. Patient's with classic FAP will have the mutated APC gene present in every cell[2]. If left untreated, the number and size of the adenomatous polyps will increase, and colon cancer is inevitable[1].

Cancer in adenomas correlates well with size. Cancer is extremely rare in adenomas less than 1cm in diameter, and nearly 40 % of adenomas greater than 4cm will have cancerous foci[5]. In addition to the standard total colectomy sections obtained for microscopic evaluation (proximal and distal margins, appendix, IC valve), the Pathologists' Assistant must pay very close attention to this specimen, ensuring that all polyps greater than 1 cm in size are entirely submitted. It is in these polyps that cancer is most likely to be identified and upwards of 25% of patients will be diagnosed with adenocarcinoma at the time of presentation[4].

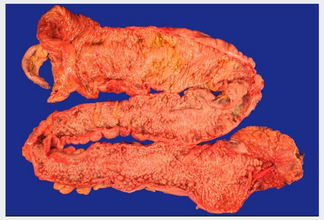
Conclusion:

FAP is a largely inherited, autosomal dominant cancer predisposition syndrome involving APC gene mutation[5]. This mutation can lead to various additional intestinal and extraintestinal manifestations and cancers[1]. Patients with FAP will develop hundreds to thousands of adenomatous polyps beginning in the early teen years[2]. These polyps cannot be individually removed, and therefore the entire colon and often the rectum must be removed[2]. Without treatment, all FAP patients will develop colon cancer, usually by age 40[2].

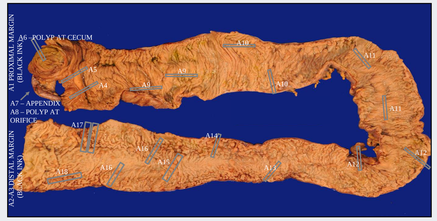
Following surgery, most patients can eat normal diets, and lead normal lives[2]. Increased surveillance will be required for these patients; regular endoscopy every 3 years (or more frequently if abnormal polyps are detected), and sigmoidoscopy every 1-4 years if all rectal tissue was removed[2].

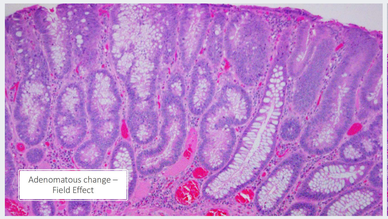
Findings:

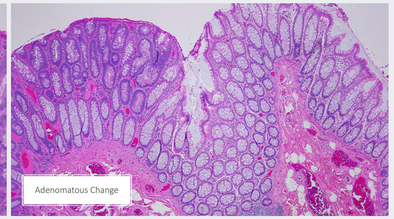
Opened colon, fresh

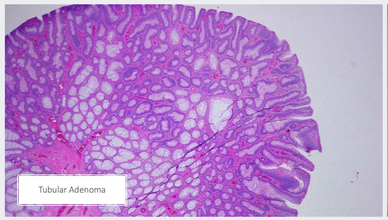


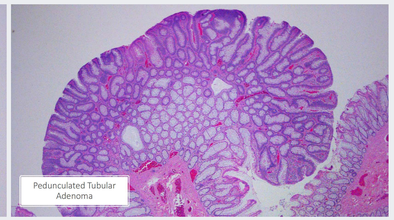
Fixed specimen, section map











Gross Description:

75 cm length proctocolectomy specimen with an average diameter of 4cm. There is an attached 1.5cm length portion of terminal ileum, and 7.6 x 0.8 cm grossly unremarkable appendix. The red-tan serosa is smooth and glistening, as is the moderate amount of soft, lobulated pericolonic adipose tissue. The ileocecal adipose tissue demonstrates prominent vasculature and several potential lymph nodes up to 0.8cm in greatest dimension. The mesorectal envelope is grossly complete.
The specimen is opened revealing coarsely granular, tan ileal mucosa with the usual folds. The mucosa of the ileocecal valve appears granular and focally heaped up (Cassettes A4-A5). The colonic mucosa demonstrates diffuse, innumerable sessile and pedunculated pale-red polyps that range from 0.1 cm up to 0.8 x 0.6 x 0.5 cm (Cassette A17), that are more prominent in the distal 20 cm. The mucosal surface of the cecum demonstrates sparse sessile polyps (greater than 5), the largest of which measures 0.4 x 0.3 x 0.2 cm (Cassette A6). Additionally, 0.2 cm polyp is noted at the appendiceal orifice (Cassette A8). The uninvolved colon mucosa is tan and has normal folds. The pliable wall has a uniform thickness of 0.2 cm.

Microscopic description:

- Total proctocolectomy showing multiple tubular adenomas with multifocal mucosal epithelial adenomatous change.
- No evidence of high-grade dysplasia.
- Lymph nodes, ileocecal region, without significant pathology.
- Appendix showing patchy intramural neutrophils and rare crypt abscess without additional significant mucosal or mural inflammation.
- Attached terminal ileum without significant pathology.
- Distal colonic resection margin (en face section) shows focal mucosal adenomatous change.

Variants and Post Surgery Management:

Familial Adenomatous Polyposis (FAP)

- ***VARIANTS***
  - ***Gardner Syndrome***
    - Somatic and germline mutations – inactivation of both alleles involved
    - FAP associated with development of epidermoid cysts, fibromas (mostly intra-abdominal), desmoid tumors, and osteomas
      - Variable penetrance – one or more of these manifestations may be present
  - ***Turcot Syndrome***
    - Variant of FAP or HNPCC (Lynch Syndrome)
    - Adenomatous polyps with increased risk of colorectal cancer
    - Increased risk of brain tumors
      - Glioblastomas associated with Lynch Syndrome
      - Medulloblastomas associated with FAP

Extracolonic Manifestations

- Congenital hypertrophy of the retinal pigment epithelium (CHRPE)
  - An early manifestation in up to 90%
- Polyps in gastric fundus and duodenum
- Desmoid tumors (aggressive fibromatosis)
- Hepatoblastoma (1-2%, usually under age 5)
- Papillary thyroid cancer (<2%)
- Pancreatic carcinoma (<1%)
- Benign dermatofibromas, lipomas, and bone lesions (osteomas, exostosis, cortical thickening of long bones, dental cysts)

MANAGEMENT

- ***Endoscopy and sigmoidoscopy post colectomy***
  - Regular intervals
    - Every 6-12 months if some rectal tissue remains
    - Every 1-4 years if all rectal tissue removed
- ***Yearly ultrasound of thyroid gland in late teens***
- ***Regular CT or MRI if personal or family history of desmoid tumors***

References:

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