Familial Adenomatous Polyposis

Familial adenomatous polyposis (FAP) is a disease that is inherited in an autosomal dominant manner and results from a mutation in chromosome 5. The mutation is in the adenomatous polyposis coli, or APC tumor suppressor gene. This causes an overexpression of beta-catenin which leads to unregulated cellular proliferation. The two-hit hypothesis is implicated in the pathophysiology of this disease. Clinical findings include a change in bowel habits and several colonic polyps. Diagnostic workup and screening are performed as a colonoscopy and/or upper endoscopy while management is prophylactic surgery to remove the colon. If not treated, FAP will progress to colorectal carcinoma.

PLAY PICMONIC

Pathophysiology

Autosomal Dominant

Dominoes

This disease is inherited in an autosomal dominant fashion. This means that, on average, 50% of the children of an affected parent will have the disease.

Mutation in Chromosome 5

Five-hand Mutant

The mutation in familial adenomatous polyposis occurs on the long arm of chromosome 5 at band 22, or 5q22.

APC Gene Mutation

Apple-PC

The adenomatous polyposis coli (APC) gene is a tumor suppressor gene located on the long arm of chromosome 5. This gene is mutated in familial adenomatous polyposis.

Overexpression of Beta-catenin

Up-arrow Beta-fish with Katana

The APC protein works by ubiquitinating and degrading beta-catenin, which is an oncoprotein in the Wnt signaling pathway. When APC is mutated, beta-catenin accumulates, causing unregulated cellular proliferation that leads to polyp formation.

Two-Hit Hypothesis

Poster of a Hippo-scientist wearing a Two-tutu and a Mutated-DNA being Hit.

The two-hit hypothesis suggests that a second genetic alteration occurs following the primary mutation that results in deletion of the other allele and further supports the development of unrestricted growth leading to a variety of cancers. The two-hit hypothesis is implicated in FAP.

Clinical Findings

Change in Bowel Habits

Delta Bowel-bowl

Patients are often asymptomatic. However, when symptoms arise, they may include abdominal pain and changes in bowel habits e.g. frequency, consistency, or even hematochezia.

Colonic Polyps

Polyp-guy holding Colon

FAP is characterized by the presence of profuse colonic carpeting from adenomas. Several hundreds of these polyps are common. This leads to the gastrointestinal features of the disease.

Screening

Colonoscopy

Colon-scope

Flexible proctosigmoidoscopy is performed annually as a screening measure to look for polyps in the rectum since FAP always includes rectal involvement. Screening begins at age 10 and then involves upper endoscopy at age 25 to screen for gastric and duodenal malignancy.

Management

Prophylactic Surgery

Toy-surgeon throwing Purple-axes

The treatment for FAP is removal of the colon and rectum to prevent progression to colorectal cancer. An anastomosis between the ileum of the small intestine and the external anus is performed to allow for defecation without an ileostomy. Patients may also opt for medical therapy with celecoxib or a particular NSAID (sulindac), but colectomy is preferred.

Considerations

Progresses to Colorectal Carcinoma

Colon-hat-wearing Car-gnome

100% of patients with FAP will go on to develop colorectal carcinoma (CRC). This often occurs by age 40. Therefore, these patients often receive a prophylactic colectomy.