Case report

Familial adenomatous polyposis associated APC gene mutation - A case study

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Abstract
Familial adenomatous polyposis (FAP) is an autosomal dominant condition characterized by diffuse intestinal polyposis, specific gene mutation, and predisposition for developing colon cancer. Left untreated, patients with FAP will develop colorectal carcinoma during early adulthood. Hence, early detection and surgical intervention are of the utmost importance. Colectomy is required and may include an ileal pouch with ileo-anal anastomosis, which eliminates the colon and rectal disease while preserving fecal continence and avoidance of a permanent ileostomy. We report a case of colorectal cancer along with FAP showed features consistent with adenomatous polyposis coli and no evidence of malignancy was seen after the surgery.

Key words: APC gene, colorectal cancer, FAP

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Familial adenomatous polyposis (FAP) is most common, inherited as autosomal dominant disease with 80-100% penetrance and it was estimated the prevalence of 1 in 5000 to 7500¹. Despite attention to screening and surveillance ~25% of patient with FAP will have colon cancer at the time of colectomy². FAP disease goes in front just because of mutation in adenomatosis polyposis coli (APC) allele³. More unusual constitutional symptoms are an unexplained fever and one of several paraneoplastic syndromes. The most common paraneoplastic syndrome is thrombosis, usually deep vein thrombosis. A patient affected with colorectal cancer and FAP was studied and the case study presented here.

Case report

A 25 year old female patient had reported complaints of recurrent bleeding per rectum since 6 years. Stool mixed with blood and sometimes only fresh blood was passed. The stool frequency was once to thrice a day. The bleeding was accompanied with constipation and intermittent abdominal pain in lower abdomen prior to the passage of stools. Since 2 months bleeding episodes have been associated with the passage of mucus. The patient also suffered from general weakness and weight loss. She did not complain of anorexia, vomiting, and abdominal distension; or did not show any signs of jaundice or any lumps. There was no bleeding from skin, gums and any skin rashes or joint pains. She had no history of diabetes mellitus (DM), hypertension (HTN) and no other symptoms relating to cardiovascular disease (CVS), respiratory and central nervous system (CNS).

The patient was investigated and the test results showed hemoglobin (Hb)-7.4gm/dl, packed cell volume (PCV)-24%, prothrombin time (PT) / acti-
vated partial thromboplastin time (APTT)-normal and the rest of the complete blood picture (CBP), liver function test (LFT), renal function test (RFT) were normal. She underwent colonoscopy by which multiple sessile and pedunculated polyps were seen in the entire colon up to the cecum. Multiple biopsies were taken and report confirmed the diagnosis of adenomatous polyposis coli. Familial type was considered. The histopathology results showed colonic mucosa with intact surface epithelium, tubular glands of varying size with focal cystic dilatation and mucinous hypertrophy, juvenile polyposis coli. The ultrasound of abdomen and upper gastrointestinal endoscopy results were normal and hence no further treatment was given.

In February 2009, the patient’s father, aged 51 years, came and reported that he had a history of bleeding per rectum since 5 years. The symptoms were similar to his daughter; stools were mixed with blood and mucous. He suffered from weight loss, anorexia and increasing anemia since 3 months. He reported a history of hemorrhoidectomy in 1993 and was treated with homeopathy treatment for bleeding per rectum since 3 months. He had history of DM, HTN and coronary artery disease (CAD). Colonoscopy was performed and similar results were observed. In addition nodular, friable polypoidal growth was seen in the distal rectum close to the anal verge. His histopathology reports showed significant adenomatous polyps with severe dysplasia. Biopsy was done from the rectal growth showed moderately differentiated infiltrating adenocarcinoma rectum. The patient was referred for surgical treatment. The investigations done showed Hb-8.2gm/dl, LFT-was normal, carcinoembryonic antigen (CEA)-223ng/mL, computed tomography (CT) of the abdomen showed diffuse circumferential thickening of rectum with polypoidal soft tissue density mass lesion in the posterior wall of rectum measuring 3.5 x 3.6cm protruding into lumen (Fig 1). It also displayed multiple discrete soft tissue density lymph nodes in the pelvis along the iliac vessels, paraaortic and retroperitoneum (Fig 2).
Due to poor comorbid conditions, surgery was deferred and patient was advised to take chemotherapy. The patient received 3 cycles of chemotherapy (oxaplatinum, leurovirin, 5-FU). Subsequently developed neutropenia and condition deteriorated. The surgery was then performed including total proctocolectomy, J pouch, diversion ileostomy and ileoanal anastomosis (Fig 3). The histopathology results after the surgery showed features consistent with adenomatous polyposis coli and no evidence of malignancy was seen.

**Discussion**

Colonoscopy and biopsy needed to diagnose adenomatous changes and dysplasia and the presence of more than 100 polyps is confirming the diagnosis of Familial adenomatous polyposis (FAP). 10 years elapses between the appearance of polyps and development of cancer and is not advisable to delay surgery even in presymptomatic patients in individual who have not completed puberty. FAP gene is located in chromosome 5q21-q22. One mutated APC allele is inherited as germ line mutation from the affected parents and adenomas develop when the second allele (from the unaffected parents) become mutated or lost. In 1991 the APC gene was cloned and was reported to have ~2844 amino acid. Germ line mutations are found in patients with FAP Gardner’s syndrome creating a stop codon and truncated protein. Germ line mutations are dispersed throughout the 5’ half of the gene and somatic mutation of APC tend to accumulate in the mutation cluster region. Patient who inherits the APC mutation usually does not develop adenomas until 10-12 years of the age but rarely polyps appears in the 1st decade. Average age at onset of polyps was 25 yrs but symptoms did not appear until 33yrs of age. 90% of the FAP case have identified by 40yrs of age. Colorectal cancer is inheritable consequence in the natural history of FAP which used to appear ~10-15yrs after the onset of polyposis. Important components of the overall care of patient with FAP are to detect mutant gene carriers. Genetic testing is performed by extracting DNA from peripheral blood leucocytes and sequencing offers the best sensitivity for mutation of the APC but this method is highly expensive. In family with a known mutation, children who test positive can then undergo screening sigmoidoscopy to determine the disease status. COX-2 gene also plays the important role in the carcinogenesis by inhibiting the apoptosis, increase angiogenesis, modulation of inflammation, immunosuppression and conversion of precarcinogens which lead to the carcinogens. Sulindac (150mg BD) compared with placebo X for 9 months and there were reduction in mean number of polyps and polyp size. The Sulindac used for 3 month it was observe number & size of polyps were increased in patients with FAP and when (75 or 150mg BD) compared with placebo X for 48 month in patients with FAP (genotypically affected) there were no difference noted in mean number and size in both groups and didn’t prevent the developments of adenomas. 77 patients were treated with Celecoxib (100/400 mg BD) and placebo X for 6 month. After 6 month it was observed 28% reduction in mean number of polyps (p=0.003) and 30.7% reduction on polyps size (p=0.001) compared with 4.5% and 4.9% reduction in placebo.

**Conclusion**

In this case study, we report a patient and her father with colorectal cancer associated with FAP, showed features consistent with adenomatous polyposis coli and no evidence of malignancy was seen after the surgery.
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References