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Dr. Anita Sajjanar
Associate Professor,
Department of Pathology,
Datta Meghe Medical College,
Shalinitai Meghe Hospital and
Research Center, Nagpur,
Maharashtra, India

Dr. Jushmita Pathak
Senior Resident, Department
of Pathology, D Y Patil
Medical College, Kolhapur,
Maharashtra, India

Corresponding Author:
Dr. Anita Sajjanar
Associate Professor,
Department of Pathology,
Datta Meghe Medical College,
Shalinitai Meghe Hospital and
Research Center, Nagpur,
Maharashtra, India

Adenocarcinoma of the sigmoid colon in familial adenomatous polyposis syndrome: A case report

Dr. Anita Sajjanar and Dr. Jushmita Pathak

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Abstract

Familial adenomatous polyposis (FAP) is an autosomal dominant inherited syndrome characterized by the development of numerous adenomatous polyps in the colon and rectum. A germline mutation in the APC gene (adenomatous polyposis coli) present on chromosome 5q21 is the molecular level defect causing this syndrome.

In this case series report, we report two cases of FAP from a single family of 10 members which included parents, four female siblings, and four male siblings. Apart from index cases, the rest of the family members detected to have polyps on colonoscopic evaluation. Literature review, data regarding timely surgery, surveillance, and chemoprevention are discussed.

The FAP phenotype determines the type of treatment. In severe polyposis, proctocolectomy with ileoanal anastomosis is the optimal method for minimizing cancer development risk. Genetic counselling should guide genetic testing and considerations of colectomy. This case report advocates complete rectal removal, especially in cases of poor patient compliance.

Keywords: familial adenomatous polyposis syndrome, adenocarcinoma, sigmoid colon

Introduction

Familial Adenomatous Polyposis (FAP) is characterized by the development of numerous polyps (typically more than 100) in the colon's epithelium. Extra colonic manifestations of the disease are also common, and 58-90% of FAP patients develop polyps in the stomach and duodenum. The disease is most commonly inherited as an autosomal dominant trait caused by a germline mutation of a tumor suppressor gene called the adenomatous polyposis coli gene in chromosome 5q21. Spontaneous mutation is a phenomenon occurring naturally and not as a result of mutagens. Spontaneous mutations arise from a variety of sources, including errors in DNA replication, spontaneous lesions, and transposable genetic elements [7].

It has a reported incidence of 1 in 5000 to 1 in 17000 live birth annually [1]. If left untreated, the predisposition of malignant transformation is significant and typically occurs in the third to fifth decade of life with 100% disease penetrance by 40 years of age.

A variant of FAP called attenuated APC (AAPC) is associated with a variable number of adenomas; usually, 20 –100, a tendency toward right-sided colonic adenomas, an age onset of colorectal cancer that is approximately ten years later than for FAP, and mutations near the 5-prime or 3-prime end of the APC gene [8-12]. Although sigmoidoscopy is adequate screening for most FAP, a colonoscopy should be used in those with AAPC, beginning in the late teens or early second decade of life, depending on the age of polyp expression in the family.

The most common symptoms manifest in the advanced stage of FAP and include rectal bleeding, anaemia, abdominal pain, tenesmus, and diarrhoea. In the majority of FAP patients, a genetic disorder resulting from a germline mutation in the adenomatous polyposis gene (APC gene) is responsible for the syndrome [3].

Other common clinical features in patients with FAP include multiple gastric fundic gland polyps, duodenal, periampullary or ampullar adenomas, while extraintestinal features are desmoid tumors, congenital hypertrophy of the retinal pigment epithelium, epidermoid cysts, osteomas, and thyroid cancer [2].

Case reports

Here we present two cases of FAP in a single 10 members family. Out of the four male

siblings, one case presented here with Adenocarcinoma of sigmoid colon in familial adenomatous polyposis, later underwent abdominoperineal resection. Other case presented with multiple polyps throughout colon and underwent colonoscopic biopsy. The four female siblings and remaining family members were all subjected to the screening and follow up as recommended for FAP patients. It revealed that all were at various stages of polyposis. Genetic test and follow up was advised.

Case 1: Adenocarcinoma of the sigmoid colon

A 34-year-old man presented with abdominal pain, loss of appetite, and bleeding per rectum. On proctoscopy, there were numerous polyps of variable sizes. His blood investigations were within normal limits. Colonoscopy showed a stricture at the sigmoid colon and multiple polyps throughout the colon. The patient underwent abdominoperineal resection.

We received a specimen consisting of a sigmoid colon with the rectum and anal canal measuring 25x4x2 cm. (Fig.1 A) The external surface showed a stricture in the sigmoid colon and taenia coli attached. The cut section from stricture shows napkin ring with heaped-up margins and ulceration in the center measuring 2.5 cm in diameter. (Fig.1 B) Multiple polyps of variable sizes sessile and pedunculated seen along the whole length of the colon. Largest polyp measuring 1.3cm and smallest measuring 0.3 cm. Rectum shows multiple grey-brown polyps largest measuring 2x1x0.5 cm. 2 lymph nodes were isolated from the specimen. Taenia coli show satellite nodules largest measuring 0.5 x 0.3cm.

Microscopically sections studied from tumor proper of the sigmoid colon show mucosa lined by tumor cells arranged in solid and closely packed glandular pattern. They are infiltrating into lamina propria, muscularis propria, and serosa. The tumor cells are columnar having vesicular nucleus, prominent nucleoli, and moderate cytoplasm. (Fig.2 A, B & C)

Sections studied from multiple polyps show hyperplastic to dysplastic changes of mucosa.

Section studied from satellite nodules of taenia coli shows tumor deposits. Sections from lymph nodes show no metastasis. It was reported as well-differentiated adenocarcinoma of sigmoid colon and rectum with satellite nodules in taenia coli. The TNM classification and staging as follows - T3 N0 M0 and Stage IIA of the tumor.

Case 2: Adenomatous Polyps

A 32-year old younger brother presented with abdominal pain and loss of appetite. On colonoscopy showed multiple polyps throughout the colon. Numerous biopsies from caecum, transverse colon, sigmoid colon, and rectum were received.

Microscopically sections from the caecum, transverse colon, sigmoid colon, and rectum show polyps lined by mucosa with tall columnar cells with basal placed hyperchromatic nuclei, eosinophilic cytoplasm. It was reported as adenomatous polyps. (Fig.3)

Discussion

Diagnosis of FAP is based on suggestive family history, clinical findings, and large bowel endoscopy or full colonoscopy. Whenever possible, the clinical diagnosis

should be confirmed by genetic testing. When the *APC* mutation in the family has been identified, genetic testing of all first-degree relatives is advocated. Pre symptomatic and prenatal (amniocentesis and chorionic villous sampling), and even preimplantation genetic testing is possible. Referral to a geneticist or genetic counselling is mandatory in such cases.

Differential diagnosis of FAP includes other disorders causing multiple polyps (such as Peutz-Jeghers syndrome, familial juvenile polyps or hyperplastic polyposis, hereditary mixed polyposis syndromes, and Lynch syndrome). Cancer prevention and maintaining a good quality of life are the main goals of management. Regular and systematic follow-up and supportive care should be offered to all patients of FAP. By the late teens or early twenties, colorectal cancer prophylactic surgery is advocated. The recommended alternatives are total proctocolectomy and ileoanal pouch or ileorectal anastomosis for AFAP. Duodenal carcinoma and desmoids are the two leading causes of mortality after total colectomy. Hence, they need to be identified early and treated as early as possible.

Upper endoscopy is necessary for surveillance to reduce the risk of ampullary and duodenal cancer. Patients with progressive tumors and unresectable disease may respond or stabilize with a combination of cytotoxic chemotherapy and surgery (when possible to perform). Adjunctive therapy with celecoxib has been approved by the US Food and Drug Administration and the European Medicines Agency in patients with FAP.⁵ Individuals with FAP carry a 100% risk of colorectal carcinoma; however, this risk is reduced significantly when patients enter a screening-treatment program. The colorectal cancer mortality rate is lower in FAP patients who choose to be screened than those who present with symptoms^[14].

There are three main surgical options for patients with FAP: (1) total proctocolectomy with Brooke ileostomy, (2) subtotal colectomy with ileorectal anastomosis and (3) restorative proctocolectomy with the formation of an ileal reservoir and ileoanal anastomosis^[4,6].

The decision to remove the rectum is influenced by the number of polyps in the rectum and the family history. If there are only a few polyps in the rectum, total colectomy with ileorectal anastomosis may be recommended. If the rectum is involved, then restorative proctocolectomy with ileal pouch-anal anastomosis is the treatment of choice.¹² Prophylactic surgery significantly improves the outcome of patients with FAP.

In conclusion, his case reported a rare occurrence of FAP affecting all the family accounting individuals accounting for ten members. Wherever genetic testing is not possible, at least the first-degree relatives should undergo colonoscopic surveillance at the earliest. The index case developed adenocarcinoma of the sigmoid colon after ignoring his symptoms for a prolonged time.

Strict compliance with regular follow-up is an important factor while deciding on the optimal type of preventive surgery. Patients who are not adherent to surveillance should undergo proctocolectomy with ileal pouch-anal anastomosis. Timing and type of preventive surgery and compliance with preventive strategies, and strict follow-up, are essential for minimizing cancer development in patients with FAP.



Fig 1A: Resected sigmoid colon and rectum.

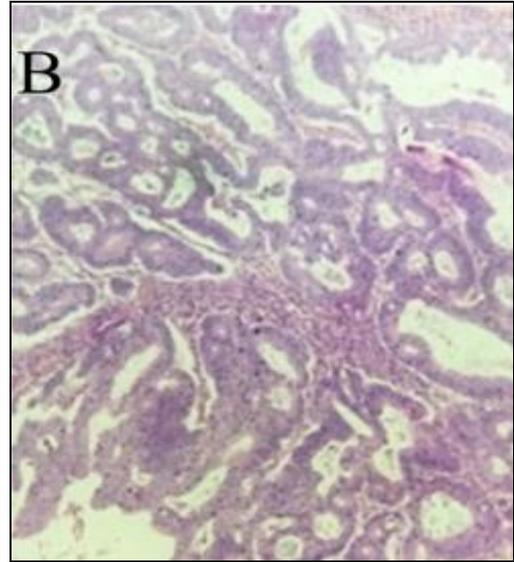


Fig 2B: High power view of tumor cells arranged in closely packed glandular pattern. (H&E 40X)

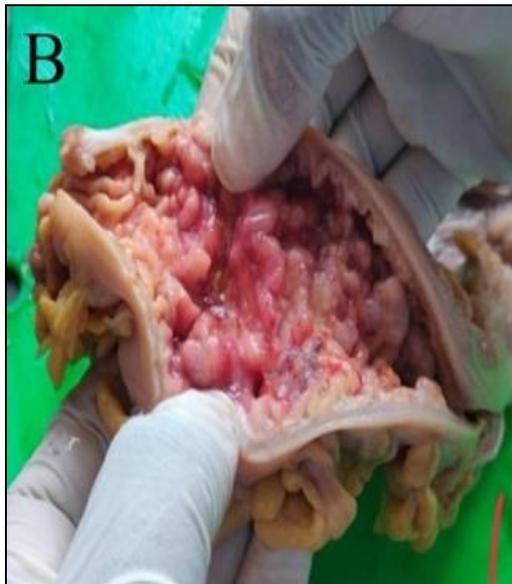


Fig 1B: The cut section of sigmoid colon showing multiple sessile, pedunculated polyps and napkin ring growth.

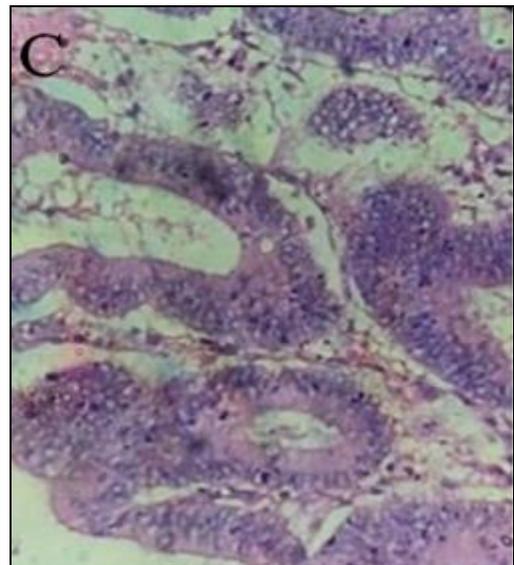


Fig 2C: Tumor cells showing hyperchromatic, cellular crowding, nuclear enlargement pseudo stratification, and mitotic activity. (H&E 40X)

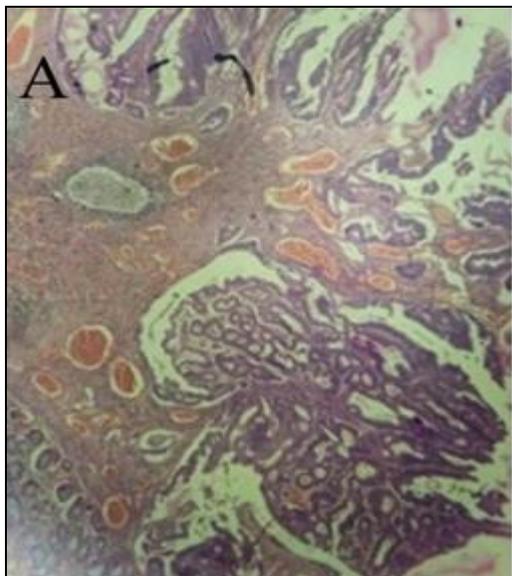


Fig 2A: Low power view of adenocarcinoma infiltrating into submucosa of sigmoid colon. (H&E 10X)

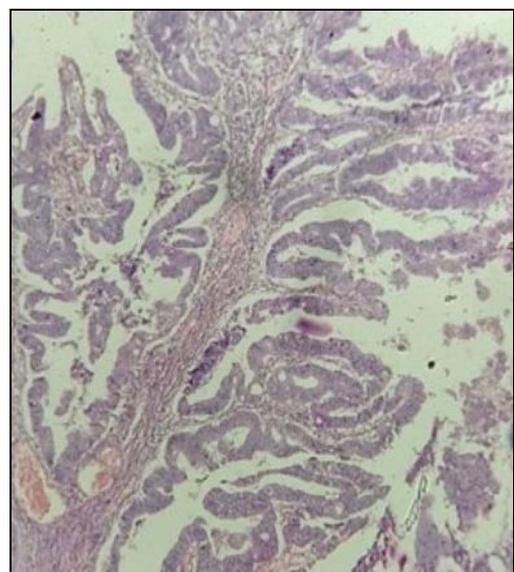


Fig 3: Low power view of adenomatous polyp with high grade epithelial dysplasia. (H&E 10X)

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