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Case Report

Familial Adenomatous Polyposis of Colon- A Case Report with Review of Literature

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ABSTRACT

Familial adenomatous polyposis (FAP) accounts for 1% of large intestinal tumor diagnosis. It is associated with mutation in tumor suppressor APC gene which is located on Chromosome 5q21. It is an autosomal dominant condition and is has high risk of colorectal cancer. The disease may occur following spontaneous mutation in 20% - 30% of the patients, who show a negative family history. The occurrence of a single case of the disease does not rule out high hereditary predisposition because, given patient may be first carrier of the mutation and thorough investigations among family members need to be carried out. We present a case of familial adenomatous polyposis coli in 17 years old male with no family history.

Key Words: Familial adenomatous polyposis (FAP,) APC gene, colorectal cancer.

INTRODUCTION

Familial adenomatous polyposis (FAP) is an autosomal dominant disease that results from mutation in adenomatous polyposis coli (APC) gene located on chromosome 5q21-22. Approximately 75 % are inherited, while remaining appears to be caused by de novo mutations. [1] The diagnosis of FAP is based on detection of more than 100 adenomatous colorectal polyps, but as many as several thousand may be present. Colorectal adenocarcinoma develops in 100% of untreated FAP patients, often before age 30 and nearly always by age 50. [1] As a result prophylactic colectomy is the standard therapy for individuals carrying APC mutations.

CASE REPORT

17 year old male presented and admitted for complaints of pain in abdomen, loose stools and haematochezia since 3 months. No other positive finding seen on systemic examination. CT scan of abdomen & pelvis showed multiple polyps more than 100 in entire colon from caecum to rectum; suggestive of polyposis syndrome. No family history of the disease in any of the family members. Colonoscopy done 6 months back showed colonic polyps; one was resected and histopath report was benign adenomatous polyp. The patient was operated and underwent pancolectomy with ileostomy.

Gross examination: Colon altogether of length 25 cm along with ileocaecal junction and appendix was received. Cut section showed mucosal surface studded with multiple polyps, both sessile and pedunculated of sizes varying from 0.5 cm x 0.5 cm to 3x 2 x1 cm. The serosal surface was smooth. Caecum along with appendix was received. Cut section of caecum also showed multiple polyps of sizes 0.5 cm to 2 cm. Appendix was unremarkable on gross.

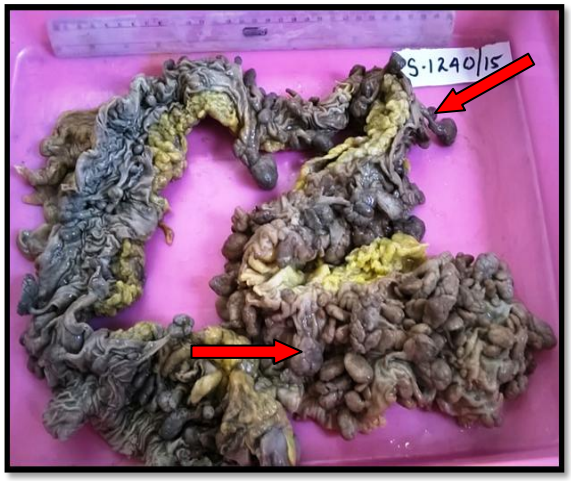

Fig 1.Gross specimen showing multiple polps in colon (Arrow showing polyps)

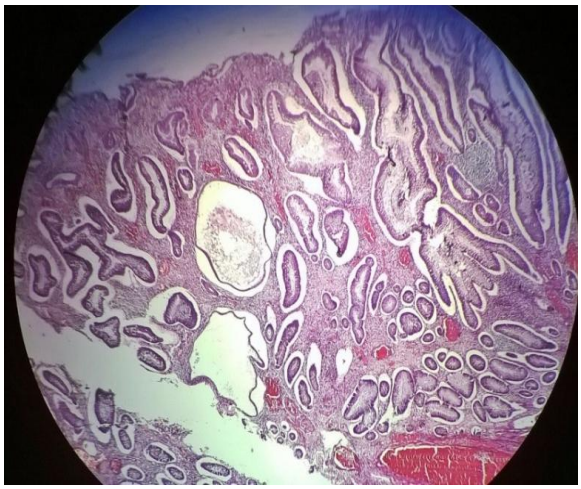

Fig 2.H& E – 4X Scanner view showing irregular and cystically dilated glands in adenomatous polyp.

Microscopic examination: Section from the polyps from different areas of colon show hyperplastic colonic mucosal glands arranged compactly with intervening fibrovascular stromas which show chronic inflammatory infiltrate. No evidence of dysplasia or malignancy.

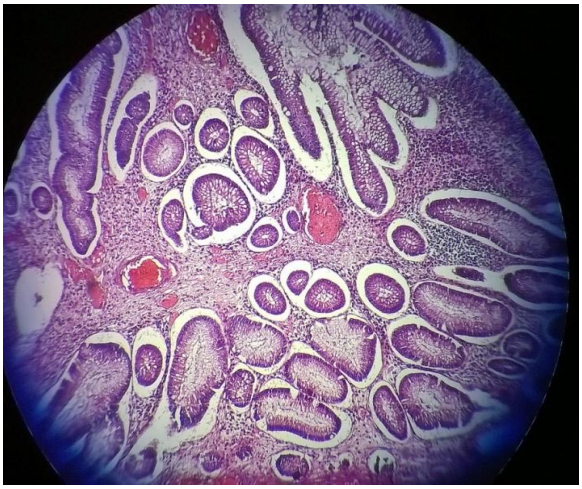

Fig 3.H & E- 10X Low power view showing irregular tubular shaped glands in adenomatous polyp.

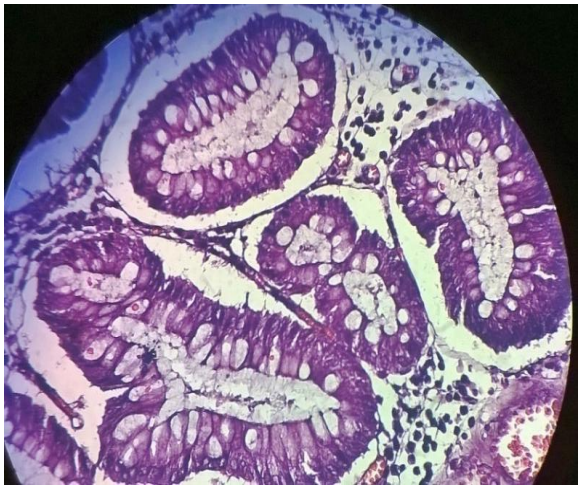

Fig 4. 40X High power showing benign nature of the glands, no evidence of dysplasia.

DISCUSSION

The initial clinical description of multiple polyps of large bowel is given by Menzelio who published his data in 1721. [2] The familial nature of multiple colonic polyposis was not recognised till 100 years; later when Cripps gave his findings in 1882. [3]

FAP and variants of this gene arise from the APC gene on chromosome 5.Males

and females are equally affected, and new mutations occur in approximately one third of new cases of FAP. [4] The prevalence of FAP is approximately one in 10,000 births and accounts for less than 0.5% of cases of colon cancer. These polyps occur in younger patients, around the age of 16 years. Almost all patients who carry the FAP gene develop polyps by age of 35 years and approximately 7% of these patients develop colon cancer by age 21 years. [5] Due to these reasons, physicians should be highly suspicious of FAP in a patient with any colonic malignancy that occurs at an early age.

A recessive form of familial adenomatous polyposis is caused by mutation in the base excision repair gene-MUTYH. The MUTYH gene is involved in repairing DNA lesions as a result of oxidative DNA damage. MUTYH associated polyposis (MAP) is a predisposition to the development of polyps of colon but the number of polyps is lower in comparison to classic FAP. [6]

Clinical features: FAP is associated with gastric and small intestinal polyp formation, but the malignant potential of the gastric fundal polyp is low and most gastric fundal polpys are hyperplastic. The prevalence of gallbladder, bile duct, thyroid adrenal, hepatoblastoma and pancreatic cancer is increased in patients with FAP. [5]
Extracolonic features of FAP vary **considerably and can include:** Retinal pigment discolouration of the eye fundus (congenital hypertrophy of retinal pigment epithelium)
Changes in dentition commonly the appearance of supernumery teeth as well as osteomas and changes in tooth structure.

Polyps in upper segments of gastrointestinal tract. Stomach polyps in FAP patients do not have potential to form neoplasms. Adenomas observed in 6% of cases form neoplasms even less frequently than polyps of stomach fundus. [7]

Desmoid tumors are observed in about 10% FAP patients and it arises commonly after surgical operation. [8] In comparison with general population, desmoids tumors are observed at significantly increased rates in FAP patients. [8,9]

Thyroid gland tumors are observed in FAP with more than 94% of cases being diagnosed in women. [10-12]

CNS neoplasms occur with low frequency of about 1% and most commonly are gliomas. The occurence of these tumors along with FAP symptoms in intestine is described as Turcot`s syndrome. [13]
The patient in this case report did not show any symptoms of extracolonic malignancy.

Differential diagnosis: FAP must be differentiated from other polyposis syndromes. Clinical and histology is the key to diagnosis. Variants of FAP include Gardner`s syndrome, Turcot`s syndrome and attenuated adenomatous polyposis.

Gardner`s syndrome is an autosomal dominant form of adenomatous polyp. The risk of cancer following diagnosis with this syndrome is 100%. It includes features of FAP and desmoids tumors, osteoma, fibroma, dental anomalies and congenital hypertrophy of retinal epithelium. The histology of Gardner`s syndrome is same as that of FAP adenoma.

Turcot`s syndrome is a hereditary disease in which colonic adenomatous polyps are associated with primary brain tumors, especially gliomas, glioblastomas and astrocytomas. This syndrome occurs in first and second decades of life. The most common type is mutation of APC gene with subsequent development of medulloblastoma. The second type involves the mutation of DNA mismatch repair genes with formation of glioblastoma multiforme. [14]

Attenuated adenomatous polyposis presents with the most adenomas in

proximal colon. In this variant, the mutation of APC gene occurs at the 5` end proximal portion. [15] In addition to clinical features, the key to diagnosis of FAP is age at the onset of disease. The mean age for attenuated FAP is approximately 55 years, a later age as compared to FAP. In addition, patients with attenuated adenomatous polyposis develop fundic, duodenal and periampullary tumors. [16]

Genetic testing for FAP is an in vitro protein synthesis test using peripheral blood. The test detects abnormal protein produced by the APC mutation and involves obtaining DNA from peripheral blood and in vitro synthesis of protein from APC gene. This test can diagnose more than 95% of persons at risk with more than 98% accuracy; however other forms of mutations occur in 10 to 20% of families of FAP. The index case is tested first and if positive, family screening is then performed. [17]

The effectiveness of screening for FAP is well established and should be performed in following types of patients: children of affected parents, members of extended family who are at risk and patients with suspected hereditary colorectal cancer for confirmation. [18] Yearly screening should begin at age of 10 to 12 years and if the patient tests are negative for polyps, repeat screening can be performed every 3 years. If the initial screening is positive for polyps, then repeat screening every 1 to 2 years should be performed until the patient reaches age 35 to 40 years, after which, if the test results are persistently negative, a repeat screening be performed every 3 years. [18]

CONCLUSION

Surgery is the mainstay therapy for patients with FAP. Prophylactic colectomy is required for patients of FAP in order to prevent development of invasive colon cancer. The patient in this case underwent pancolectomy. The patient does well postoperatively with minimal obstructive symptoms. The patients' family members are advised for screening and counseling is done.

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