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Case Report

Familial Adenomatous Polyposis with Synchronous Invasive Malignancy: A Case Study with Review of Literature

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ABSTRACT

Familial adenomatous polyposis (FAP) is a rare autosomal dominant condition characterized by diffuse intestinal polyposis, specific gene mutation, and predilection for developing colon cancer. Left untreated, patients with FAP usually develop colorectal carcinoma during early adulthood. A patient affected with FAP and synchronous colorectal cancer was studied and the case study presented here with a review of literature.

Key words: Familial adenomatous polyposis, synchronous, malignancy.

INTRODUCTION

Familial adenomatous polyposis is defined as an inheritable disorder in which the large bowel contains multiple adenomatous polyps (typically more than 100). [1] It is an autosomal dominant inherited cancer-predisposition syndrome that is caused by genetic mutation of adenomatous polyposis coli (APC) gene located on chromosome5q21. [1] The incidence of the disease ranges from 1 in 5,000 to 1 in 17,000 live births per year. [1] The polyps in this condition are initially benign but in the absence of proper surgical intervention, inevitably progresses to malignancy around the mean age range of 34-43 years. [2]

CASE REPORT

A 43 year old male presented with abdominal pain of 15 years duration which aggravated since 6 months and on and off passage of loose stools alternating with episodes of constipation. Family history revealed his brother, father and son suffering from similar abdominal pain. Colonoscopy revealed multiple polyps of varying sizes throughout the entire large bowel extending from caecum to rectum along with a mass in hepatic flexure (figure 1 A). Upper GI scopy revealed polyps in pharynx and second part of duodenum (figure 1 B). A diagnosis of familial adenomatous polyposis was rendered and patient underwent total colectomy. Gross examination (figure 2) revealed that the entire colonic as well as rectal mucosa was laden with numerous polyps (n>100) of varying sizes ranging in size from 1.5 to 0.3 cm. Most of these polyps were sessile with few pedunculated forms, grey brown in appearance and firm in consistency. The hepatic flexure of colon revealed an infiltrative mass of size 5 x 3 x 0.6cms (figure 4 A). Histopathological examination of the polyps revealed tubular adenoma with moderate to severe dysplasia (figure 3). The hepatic flexure mass showed features of moderately differentiated adenocarcinoma with subserosal fat invasion (figure 4 B). The lymph nodes around the colon were free of any metastasis.

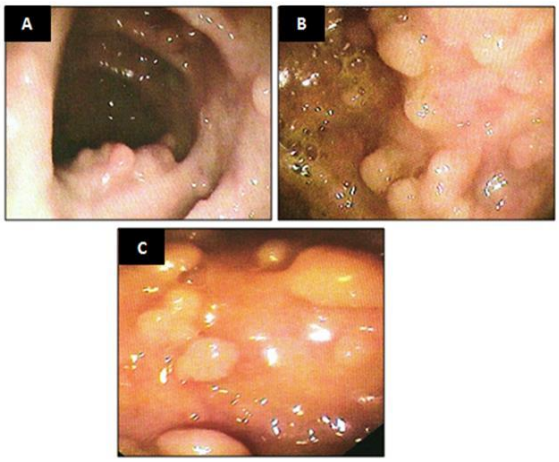

Figure 1(A,B): Colonoscopy revealed multiple polyps of varying sizes throughout the entire large bowel.
C: Upper GI scopy revealed polyps in second part of duodenum.

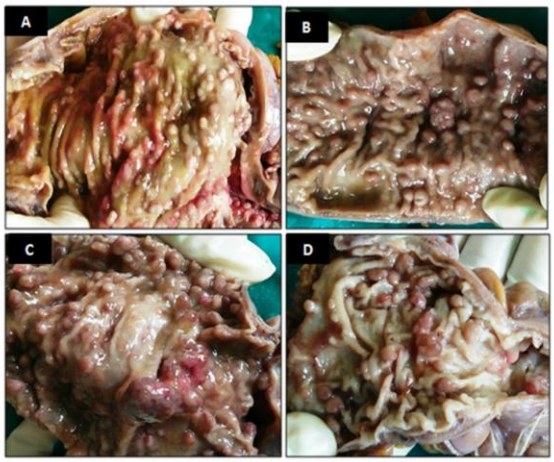

Figure 2(A-D): Gross examination revealed that the entire colonic as well as rectal mucosa was laden with numerous polyps (n >100) of varying sizes ranging in size from 1.5 to 0.3 cm.
Most of these polyps were sessile with few pedunculated forms, grey brown in appearance and firm in consistency

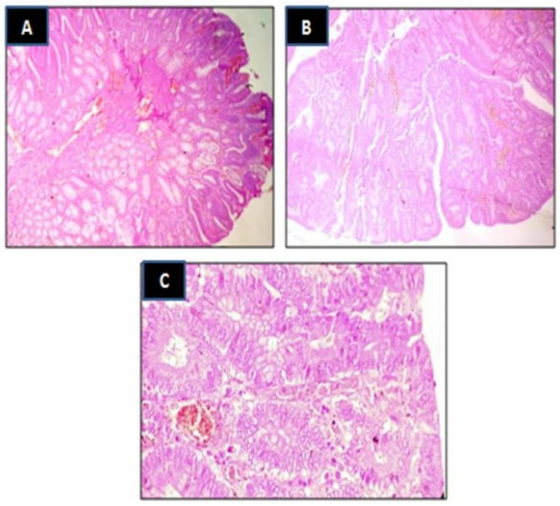

Figure 3 (A-C) Histopathologicalexamination of the polyps revealed tubular adenoma with moderate to severe dysplasia, H&E,100X(A,B),400X(C).

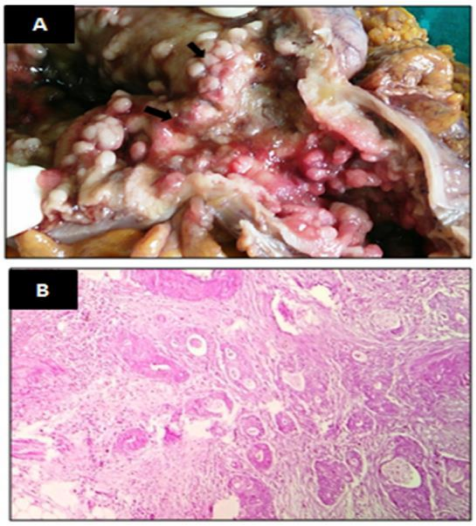

Figure 4-A: On gross examination -The hepatic flexure of colon revealed an infiltrative mass of size 5 x 3 x 0.6cms(marked by arrows). **B:** Microscopic examination of the hepatic flexure mass revealed features of moderately differentiated adenocarcinoma with subserosal fat invasion

DISCUSSION

Colorectal carcinomas are mostly sporadic, only 25% are hereditary. FAP and Hereditary Non Polyposis Colorectal Carcinomas (HNPCC) account for 5% among inherited cases. [1] Only 1% cases of colorectal carcinoma have an origin from FAP. [3] Estimates of the prevalence of FAP range from 1 in 6,850 to 1 in 31,250 live births (2.29 to 3.2 cases per 100,000 individuals) with equal incidence in men and women. [4] The first description of FAP was rendered by Chargelaigne in 1859 and its mendelian dominant trait was documented by Harrison Cripps in 1882. The association of intestinal cancers with FAP was revealed in 1890 by Handford. [5]

Three variants are known to occur-classic FAP, attenuated FAP and autosomal recessive FAP (or MYH-associated polyposis). Classic FAP and attenuated FAP (originally called hereditary flat adenoma syndrome) are initiated by APC gene defects on chromosome 5 while autosomal recessive FAP is caused by faults in the MUTYH gene on chromosome 1. [6] While classic FAP presents with >100 adenomas arising in late teens or early twenties , AFAP is defined by <100 adenomas at presentation and arising in an older age

group, typically between 40 and 70 years old. [1,4]

The molecular basis of FAP is the mutation of adenomatous polyposis coli (APC) gene of the Wnt signalling pathway. APC gene is located in 5q21 comprising of 15 exons coding for 310 k Damultidomain protein. APC is a tumour suppressor protein which regulates transcription of a number of cell proliferation genes, through its interaction with β-catenin. Germline mutations in the APC gene, mostly nonsense or frameshift mutations resulting in a truncated protein product with abnormal function have been detected in most (80%) FAP patients while in 20% of cases it occurs as a spontaneous mutation without prior family history. [7,8] In the present case, the patient gave a family history of pain abdomen in his brother; father as well as son, none of which was investigated further but it highly suggested a hereditary origin.

The most common clinical symptoms in FAP are bleeding per rectum, abdominal pain, tenesmus and diarrhoea. [1] Anaemia resulting from blood loss may be present. The present patient suffered from long standing on and off pain abdomen along with irregular bowel habits. Diagnosing FAP before the development of CRC is important for the patient as well as his family members who may be affected and colonoscopy /sigmoidoscopy is a helpful means in doing so. In addition to numerous colonic polyps, the phenotype of FAP includes benign and malignant neoplasms in other organs. Other organs commonly involved include the stomach (fundic polyps), thyroid (with papillary thyroid cancer), adrenal (non-functioning adenomas), the small intestine (adenomas or carcinoma), bones (osteomas), retina (congenital hypertrophy of the retinal pigmented epithelium), and skin (epidermoid cysts). However, the most frequent causes of death in FAP after CRC are duodenal or ampullary cancer and desmoid disease. [4,9] Our patient, in addition to colorectal polyps had polyps in pharynx and second part of duodenum, but did not show any extra intestinal manifestations.

Similar to cases reported by Osuagwu, et al, Nzegwu, et al, Lakatos, et al, Sameer, et al, Srinivasamurthy M, et al ;in our case synchronous invasive colorectal cancer was present along with polyposis. [7,8,10-12]

In FAP, adenomatous polyps are usually strewn evenly throughout the colon, with a slight distal colonic excess. The size of the polyps is variable, 90% of adenomas are <0.5 cm in diameter, and <1% of polyps are >1 cm. [4] In the present case, only 3 polyps were > 1 cm in size, others ranged in size from 0.3 cm-1 cm. Morphologically these polyps are mostly tubular adenomas, as in our case; indistinguishable from common or sporadic adenomas, less commonly villous and tubulovillous adenoma. [4] A unique histologic feature of FAP not observed in the general population is dysplastic or adenomatous epithelial cells in single crypts or even portions of single crypts designated as microadenoma. [4]

Most common surgical intervention for FAP is proctocolectomy with ileoanal anastamosis. If FAP is associated with adenocarcinoma the treatment is surgical resection with chemotherapy and radiotherapy depending upon the stage of the disease. [1] Adenomas may develop in the ileal pouch after colectomy or small segment of remaining rectal epithelium/anal transition zone after restorative proctocolectomy and studies reveal a minor risk for cancer in these sites. [4] So, even after surgery, endoscopic surveillance of the rectum or ileal pouch should continue yearly.

The generally accepted colon screening guideline for children at risk for classic FAP is every 1- to 2-year sigmoidoscopy beginning at 10 to 12 years of age. [4] However nowadays genetic tests have been developed where genomic DNA is isolated from the tissue/ blood of the potential high risk patients (relatives of a known case of FAP) which is then subjected to analysis of APC gene

mutations. [7] Studies are being carried out on the role of chemopreventive drugs like Celecoxib and Sulindac for helping in regression and prevention of colonic and rectal adenomas. [4,13]

CONCLUSION

Hereditary cancer syndromes like FAP are rare events affecting few unfortunate families. However, early diagnosis through active surveillance in high risk cases and timely treatment can help in avoiding subsequent complications as exemplified by our case and reducing morbidity.

Abbreviations:
FAP: Familial adenomatous polyposis
APC: Adenomatous polyposis coli
GI: Gastrointestinal
AFAP: Attenuated familial adenomatous polyposis
CRC: Colorectal cancer
DNA: Deoxyribonucleic acid

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