CASE REPORT

Familial Adenomatous Polyposis

Mansoor-ul-Haq and Nabiha Faisal

ABSTRACT

Familial adenomatous polyposis represents approximately 1% of all colorectal tumours and is caused by germline mutations in the adenomatous polyposis coli (APC) gene. A 38-year-old lady presented with abdominal pain, diarrhoea and iron deficiency anemia. There was no history of colorectal cancer in the family. Colonoscopy showed hundreds of polyps throughout the colon sparing the rectum, and an ulcerative tumour of the sigmoid colon. The diagnosis was familial adenomatous polyposis (FAP) and adenocarcinoma of the sigmoid colon. Colectomy with ileorectal anastomosis was performed and later on she was given chemotherapy and advice life long surveillance. The patient had one brother and one sister, without clinical symptoms. The brother had a single hyperplastic rectal polyp, while the sister refused colonoscopy. The patient has 2 sons, the elder son had normal colonoscopic findings, and the younger son was also diagnosed as a patient of FAP and referred for colectomy.

Key words: *Familial adenomatous polyposis. Management. Surveillance. Colorectal cancer. Adenocarcinoma. Hyperplastic rectal polyp.*

INTRODUCTION

Familial adenomatous polyposis (FAP) is also known as adenomatous polyposis coli (APC). The syndrome is inherited as an autosomal dominant trait and caused by mutations in the APC gene. It is one of two well described forms of hereditary colorectal cancer, which is responsible for 1% or less of all colorectal cancer (CRC) cases.[1] This syndrome is characterized by the development of hundreds to thousands of adenomas in the colorectum as well as several extra colonic manifestations. Almost all patients will develop CRC if they are not identified and treated at an early stage.[2] Screening by genetic testing and endoscopy in concert with prophylactic surgery has significantly improved the overall survival of FAP. However, less well appreciated is duodenal adenocarcinoma, the second leading cause of death in patients with FAP.[3]

A possible way to improve the prognosis of patients with FAP further is early detection and treatment of the less common extra-intestinal cancers which are seen with increased frequency in individuals with FAP. Genetic analysis is now becoming available to diagnose such mutations which predispose to inherited cancer diseases.[4] Screening and prophylactic surgery are effective to prevent colorectal cancer in patients with FAP. Lifelong surveillance is necessary to detect and manage extra-colonic lesions. This report describes the occurrence of FAP in a familial way.

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CASE REPORT

A 38 years old lady presented in the outpatient clinic with the complaints of loose motions for the last 3 months and easy fatigability for the last 2 months. She had small loose stools with no blood or mucus, although she complained of small amount of fresh bleeding per rectum twice 2 months back. She had no history of abdominal pain, tenesmus, urgency, fever, or weight loss. She had a history of asthma, well controlled on inhalers. She was diagnosed as having iron deficiency anemia one year back and was kept on oral and parenteral iron therapy intermittently. She had a good appetite and had no addiction. Her father died of adenocarcinoma of the lung and her mother had multiple myeloma. She had no family history of colonic cancers.

On clinical examination, she appeared pale, with no signs of jaundice, clubbing, koilonychia or pedal edema. JVP was not raised, no lymphadenopathy was noted and thyroid was not enlarged. Abdomen was soft and non tender, there was no organomegaly; genital and rectal examination was normal.

Biochemical examination showed that she had microcytic hypochromic anemia, her hemoglobin was 6.7 gm/dl and ESR was 113 mm after 1st hour. Her liver profile, renal parameters, thyroid function tests, and random blood sugar were within normal range. Stool detail report was normal and culture did not yield any growth; stool for occult blood was positive. Ultrasound of abdomen was unremarkable. Colonoscopy showed hundreds of adenomatous polyps throughout the colon (Figures 1 and 2), sparing the rectum and an ulcerated tumour in sigmoid (Figure 3). The diagnosis established was FAP.

Her esophagogastroduodenoscopy was normal. The next week she underwent colectomy with ileorectal

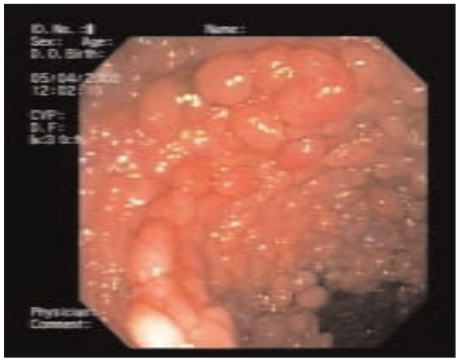

Figure 1: Multiple polyps in ascending colon.

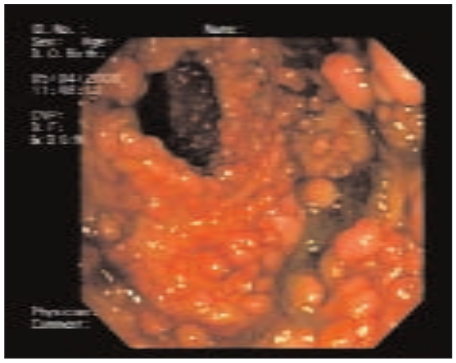

Figure 2: Multiple polyps in transverse colon.

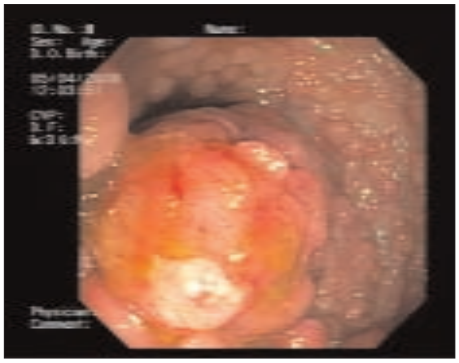

Figure 3: Ulcerated growth in sigmoid colon.

anastomosis. The histopathological examination of the sigmoid tumour showed adenocarcinoma, Dukes B2. She recovered from surgery uneventfully. Genetic counselling and mutation analysis for APC gene was not available in Pakistan so it could not be done. Post operatively she was given chemotherapy and advised for lifelong surveillance.

She had 2 sons, the elder son had normal colonoscopic findings, while the younger son was also diagnosed with FAP and referred for surgery. She had one sister and one brother; her brother was found to have a single hyperplastic rectal polyp on colonoscopy while her sister refused to undergo colonoscopy.

DISCUSSION

FAP is characterized by the development of multiple (> 100) adenomas in the colorectum. Colorectal polyposis develops by the age of 15 years in 50% and age 35 years in 95% of patients. The lifetime risk of colorectal carcinoma is virtually 100% if patients are not treated by colectomy.[5]

Patients with FAP can also develop a wide variety of extra-intestinal findings. These include cutaneous lesions (lipomas, fibromas, and sebaceous and epidermoid cysts), desmoid tumours, osteomas, occult radio-opaque jaw lesions, dental abnormalities, congenital hypertrophy of the retinal pigment epithelium, and nasopharyngeal angiofibroma.[5] In addition, FAP patients are at increased risk for several malignancies, such as hepatoblastoma and pancreatic, thyroid, biliary-tree, and brain tumours.[5]

Once the diagnosis of FAP is established, the high risk relatives should be notified and surveillance measures should be instituted. All patients with clinical evidence of multiple colorectal adenomas need genetic counseling. Since in Pakistan these facilities are not available and financial support was lacking in this patient to get these tests done abroad, therefore, genetic testing for APC gene could not be done in this case.

Periampullary carcinoma is the second leading cause of death after colorectal cancer in these individuals.[6] Therefore, esophagogastroduodenoscopy (EGD), including side-viewing endoscopy, should be performed at diagnosis, and periodic surveillance should be continued indefinitely. Desmoid fibromatosis, a benign but locally invasive mass or infiltrative process, is the third most common cause of death in patients with FAP.[7] Fibromatosis usually affects the abdominal wall or intra-abdominal vasculature, and its incidence peaks within a few years immediately after proctocolectomy. Periodic clinical surveillance and surveillance with computed tomography or magnetic resonance imaging are recommended, although long-term data on surveillance duration are lacking. Papillary thyroid carcinoma is rarely encountered but is more common in the setting of FAP than sporadic disease.[7] Patients with APC gene mutations should be followed with clinical evaluation and imaging studies (for example, ultrasonography).

The patient was recommended to a very careful follow-up, with a surveillance pouchoscopy within 6 months postoperatively, which was normal and then at every 6 month interval. Screening EGD was also done along with side viewing (duodenoscope) that showed few sessile duodenal polyps, biopsy was negative for dysplasia. The patient was advised for surveillance EGD every 2-3 years.

Screening of family members of a patient with FAP using flexible sigmoidoscope should be done beginning at the age of 10 years. An interval of 2 years between normal sigmoidoscopies is appropriate. If adenomas are detected, colonoscopic investigations should be performed annually until colectomy is planned. In high risk members (first-degree relatives of affected patients) from families without an identified APC mutation, surveillance should be continued at 2-yearly intervals until the age of 40 years. After this age, the intervals between examinations may be longer - for example, every 3-5 years and surveillance may be discontinued at age 50.[8]

Various non-steroidal anti-inflammatory drugs, such as sulindac, indomethacin, and celecoxib, have been evaluated in preventing colonic polyp development, performing rectal-sparing surgery, and delaying the

need for surgical treatment. Increasing evidence shows that these agents may slow the development of upper gastrointestinal adenomatous polyps, potentially lowering risk particularly for duodenal cancer.[9] Risks of use of non-steroidal anti-inflammatory drugs include gastrointestinal bleeding, renal damage, and possibly cardiovascular events; these must be balanced against the potential benefits of long-term use, factoring in comorbid conditions and drug-drug interactions.[10] Currently none of these chemoprevention strategies will replace endoscopic surveillance and carefully timed surgery.

A dedicated FAP registry in the gastroenterology department is essential. It is the only way to assess the real changes in the management of colon cancer. The registry should offer education, counselling, genetic testing and surveillance recommendation. Registration of patients and families with FAP may lead to a very significant decrease in mortality.

Although FAP is a serious condition that may become life-threatening, if diagnosed early it can be treated successfully. Clinicians should investigate the family history and be prepared to consider much earlier intervention if symptoms occur in a patient with a family history of FAP.

REFERENCES

1. Drenick EJ, Ahmed AR, Greenway F. Cutaneous lesions after intestinal bypass. *Ann Intern Med* 1980; **93**:557-9
2. Cruz-Correa M, Giardiello FM. Familial adenomatous polyposis. *Gastrointest Endosc* 2003; **58**:885-94.
3. Brosens LAA, Keller JJ , Offerhaus GJA, Goggins M, Giardiello FM. Recent advances in clinical practice. Prevention and management of duodenal polyps in FAP. *Gut* 2005; **54**:1034-43.
4. Parvez T, Parvez B, Al-Taifi A. Psychosocial implications of cancer screening In genetic cancer syndromes. *Pak Armed Forces Med J* 2007; **57**:305-16.
5. Trimbath JD, Giardiello FM. Review article: genetic testing and counselling for hereditary colorectal cancer. *Aliment Pharmacol Ther* 2002; **16**:1843-57.
6. Griffioen G, Bus PJ, Vasen HF, Verspage HWt, Lamers CB. Extracolonic manifestations of familial adenomatous polyposis: desmoid tumours, and upper gastrointestinal adenomas and carcinomas. *Scand J Gastroenterol Suppl* 1998; **225**:85-91.
7. Cetta G, Montalto M, Gori MC, Curia A, Cama S, Olschwang S. Germline mutations of the APC gene in patients with familial adenomatous polyposis-associated thyroid carcinoma: results from a European cooperative study. *J Clin Endocrinol Metab* 2000; **85**:286-92. Comment in: *J Clin Endocrinol Metab* 2001; **86**:1429.
8. Vasen HFA, Möslein G, Alonso A, Aretz S, Bernstein I, Bertario L, *et al.* Guidelines for the clinical management of familial adenomatous polyposis, *Gut* 2008; **57**;704-13. Epub 2008 Jan 14.
9. Janne PA, Mayer RJ. Chemoprevention of colorectal cancer. *N Engl J Med* 2000; **342**:1960-8.
10. Mukherjee D, Nissen SE, Topol EJ. Risk of cardiovascular events associated with selective COX-2 inhibitors. *JAMA* 2001; **286**:954-9. Comment in: *Curr Gastroenterol Rep* 2002; **4**:445.