

FAP: Recognizing the importance of family history and genetic testing

A young woman with a family history of abdominal scars presents with diarrhea accompanied by persistent hematochezia, diffuse abdominal pain, and anemia.

Mike Deeter, PA-C

CASE

An 18-year-old Hispanic female presented to the emergency department with a 4-day history of nausea, vomiting, diarrhea with persistent hematochezia, and diffuse abdominal pain. The patient also reported decreased appetite beginning 2 days before the onset of her current symptoms. She described the abdominal pain as waxing and waning, with episodes of greatest intensity lasting from 10 to 30 minutes. She denied any previous history of abdominal illness.

Results of GU and gynecologic assessments were negative.

Evaluation On the medical and family history questionnaire she completed at check-in, the patient reported no significant personal or family history of GI disorders. When asked specifically about GI problems during history-taking, she noted that several family members on her mother's side had large scars on their abdomens. She was unaware of the reasons for the scars but believed that her relatives had undergone surgery in their home country of Mexico. She further stated that her family did not discuss such matters.

Vital signs were within normal limits: BP was 121/75 mm Hg; heart rate, 74 beats per minute; and respiration rate, 18 breaths per minute. The patient was afebrile. Physical examination revealed hypoactive bowel sounds in all four quadrants and diffuse tenderness to palpation without guarding or rebound. There was no evidence of organomegaly, pulsations, bruits, or flank pain. Findings on ophthalmologic and gynecologic examinations were unremarkable; there was no evidence of lipomas, osteomas, dental abnormalities, or thyroid nodules.

Laboratory studies A CBC with differential revealed low hemoglobin, low hematocrit, and normal RBC indices, findings indicative of a normocytic, normochromic anemia (Table 1). A comprehensive metabolic panel showed electrolyte levels to be within normal range, as were the results of urinalysis and tests for amylase, lipase, and alpha-fetoprotein. Prothrombin time and partial thromboplastin time were unremarkable. A carcinoembryonic antigen (CEA) level was elevated, and results of a fecal occult blood test were positive for gross blood in the stool. The elevated

CEA level along with occult blood in the stool raised the suspicion for colon cancer. The patient's blood was typed, and a crossmatch was ordered. She was then admitted to the hospital's surgical service for further evaluation.

Colonoscopy and biopsy At colonoscopy the following morning, the patient had more than 100 polyps in her colon. No hemorrhoids or rectal masses were visible. Tissue samples from the polyps were sent to pathology for further analysis. The biopsy results were consistent with tubular adenoma and adenocarcinoma, confirming the diagnosis of familial adenomatous polyposis (FAP). The patient was advised to undergo total proctocolectomy with ileal pouch-anal anastomosis (IPAA). After the risks, benefits, and complications of the procedure were explained, the patient consented to the surgery. She was given an oral solution to prepare her bowel and scheduled for surgery the following day.

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Colonic polyps are a precursor to colon cancer.

DISCUSSION

FAP is an autosomal dominant syndrome that results from a germline mutation of the adenomatous polyposis coli (*APC*) tumor suppressor gene located on chromosome 5. The mutation often results in the truncation of a protein responsible for the control of cell adhesion, signaling, and apoptosis.¹ More than 300 pathogenic mutations of the *APC* gene have been recorded in the Human Genome Mutation Database.¹

Worldwide, FAP affects up to 1 in every 22,000 live births, with an equal distribution between males and females.² The mean age for the development of adenomatous polyps is 15 years; as many as 100 adenomas may develop in patients with FAP in their second decade.¹ Close to 100% of patients with FAP will develop polyps by the time they are 35 years old; without prophylactic polypectomy, colorectal cancer is a near certainty by age 50.³ FAP accounts for approximately 1% of all colon cancers in the United States.⁴

Diagnosis of FAP is based on endoscopic findings of more than 100 colonic polyps and a family history.⁴ However, up to 30% of patients with FAP present without any family history of the disorder.⁴ In these instances, genetic screening is helpful to confirm the diagnosis.⁴ Genetic screening is also recommended in children 10 years or older who have a family history of FAP.⁴ The protein truncation assay is a useful tool, but its sensitivity for FAP is only 80%.⁴ Another tool for genetic screening of FAP is the fecal DNA test, which uses polymerase chain reaction of DNA that is recovered from stool samples to detect mutations in the *APC* gene.⁵

Extraintestinal manifestations of FAP are variable and depend on the site of *APC* gene mutations.⁶ Gardner's syndrome is the presence of FAP with lipomas, desmoid tumors, osteomas, congenital hypertrophy of the retinal pigment, and dental abnormalities.⁶ Turcot's syndrome is the presence of FAP with malignancies of the CNS, papillary thyroid carcinoma, hepatoblastomas, or medulloblastoma.⁶

Treatment The standard treatment modality for patients with FAP is prophylactic proctocolectomy with IPAA because it offers decreased morbidity rates, increased functionality, and favorable quality of life (QoL) compared with other procedures.⁷ Total colectomy with ileorectal anastomosis (IRA) has been used for patients with FAP, but it does not

TABLE 1. Patient's pertinent laboratory values

Parameter	Result	Reference range
Carcinoembryonic antigen	12 ng/mL	<5 ng/mL
Hematocrit	30%	37%-47%
Hemoglobin	8 g/dL	12-16 g/dL
Mean corpuscular hemoglobin	26 pg	27-31 pg
Mean corpuscular hemoglobin concentration	34%	32%-36%
Mean corpuscular volume	82 μm^3	80-95 μm^3

eliminate the risk of rectal cancer. Risk of rectal cancer 10 years after IRA is 4.5%; 30% of patients develop rectal cancer by age 60 years.⁸ The 5-year survival after IRA is only 68%; the primary cause of death is rectal cancer.⁸

QoL for patients remains favorable after proctocolectomy with IPAA. Delaney and colleagues followed 1,895 patients over a 10-year period to assess the QoL of those who had proctocolectomy with IPAA. Determination of QoL was established using the Cleveland Global Quality of Life score. Overall, 96% of study participants were satisfied with the results of the procedure, and only 4.1% of patients required excision or permanent diversion of the pouch because of pouch failure.⁹ Patients younger than 45 years had a slightly higher QoL because they were less likely to experience incontinence and nocturnal seepage.⁹

As with any surgical procedure, proctocolectomy with IPAA can be followed by complications. The most common complications are anastomotic leakage, pouchitis, small-bowel obstruction, and pouch failure.⁸⁻¹¹ Other associated morbidities include pouch-anal fistula, incisional hernia, and pelvic cysts.⁸

Anastomotic leakage is a rare but serious complication that can be fatal if not recognized promptly. A study conducted by Walker and colleagues determined survival rates in patients with anastomotic leakage following resection of the colon. Of the 1,722 patients evaluated, 5.1% developed anastomotic leakage, and the 5-year survival rate with leakage

TEACHING POINTS

- Familial adenomatous polyposis (FAP) is an autosomal dominant syndrome that results from a germline mutation of the adenomatous polyposis coli (*APC*) tumor suppressor gene. As many as 100 adenomas may develop in patients with FAP in their second decade. Nearly 100% of patients with FAP will develop polyps by the time they are 35 years old; without prophylactic polypectomy, colorectal cancer is a near certainty by age 50 years.
- Diagnosis of FAP is based on endoscopic findings of more than 100 colonic polyps and a family history. However, up to 30% of patients with FAP present without any family history of the disorder.
- The standard treatment for patients with FAP is prophylactic proctocolectomy with ileal pouch-anal anastomosis because it offers decreased morbidity rates, increased functionality, and favorable quality of life compared with other procedures. Total colectomy with ileorectal anastomosis has been used for patients with FAP, but it does not eliminate the risk of rectal cancer.
- The postoperative treatment plan for FAP patients should always include genetic counseling in order to avoid missed diagnoses and untreated FAP in future generations.

“Pouchitis, another postoperative complication of proctocolectomy with IPAA, occurs most commonly within 2 years after surgery.”

was 44.3%.¹⁰ Leakage has also led to metastasis beyond the intestinal lumen.¹⁰

The manifestations of anastomotic leakage are similar to those of generalized peritonitis, but a subclinical leak may only be recognized by abdominal CT with contrast.¹⁰ Subclinical leaks have a favorable outcome and usually require only percutaneous drainage and frequent follow-up.¹⁰ General anastomotic leaks, however, are much more serious and require urgent abdominal closure of the dehiscence.¹⁰

Pouchitis, another postoperative complication of proctocolectomy with IPAA, occurs most commonly within 2 years after surgery and more often in patients with ulcerative colitis who have undergone the procedure. Clinical symptoms of pouchitis are stool frequency and urgency, rectal bleeding, abdominal cramping, and pelvic discomfort.¹¹ Definitive diagnosis of pouchitis is made through endoscopic findings.

Metronidazole (MTZ, Flagyl) is the treatment of choice in acute pouchitis (duration less than 4 weeks), while MTZ plus ciprofloxacin (Cipro) is the standard therapy in chronic cases.¹¹ Some sources suggest using probiotics, such as lactobacilli, but this has so far been ineffective as primary treatment in pouchitis.¹¹ Overall, pouchitis has a good prognosis and is an infrequent cause of pouch failure.

Conclusion At her 30-day postoperative evaluation, our patient reported that she was tolerating the procedure well, with only limited pain at the incision site. A postoperative CT revealed no signs of pouch failure. The patient was

attending regular physical therapy sessions and said her QoL had returned to its preoperative level. She and the members of her immediate family have an appointment with a genetic counselor.

Because the patient lacked a complete family history at presentation, the likelihood that her FAP would be missed was high. If the condition had been left undiagnosed, she stood a 100% chance of developing colon cancer by age 50 years. FAP is a devastating disease that requires prophylactic proctocolectomy with IPAA to avoid untimely colon cancer and possible death. With continued postoperative follow-up, the prognosis in this case is very good. The postoperative treatment plan for FAP patients should always include genetic counseling in order to avoid missed diagnoses and untreated FAP in future generations. **JAAPA**

Mike Deeter works at NextCare Urgent Care in Phoenix, Arizona. He has indicated no relationships to disclose relating to the content of this article.

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