CASE RECORDS of the MASSACHUSETTS GENERAL HOSPITAL

Case 6-2016: A 10-Year-Old Boy with Abdominal Cramping and Fevers

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N Engl J Med 2016;374:772-81.
DOI: 10.1056/NEJMcpc1408597

PRESENTATION OF CASE

Dr. Hasan Merali (Pediatrics): A 10-year-old boy was seen in the gastroenterology clinic of this hospital because of intermittent abdominal cramping and fevers.

The patient had been well until approximately 3 weeks before this presentation, when intermittent fevers to a temperature of 39.7°C occurred, followed by episodes of cramping in the periumbilical and subumbilical abdominal regions, without vomiting. He had one or two bowel movements daily; the stools were formed, and hematochezia had occurred on one or two occasions. He had reportedly been unable to attend school for 2.5 weeks. Two days before this presentation, he was seen in the emergency department of another hospital. Blood levels of electrolytes, glucose, albumin, amylase, lipase, and urea nitrogen were normal, as were urinalysis and results of liver-function tests. Screening tests for celiac disease and Epstein–Barr virus infection were negative; other test results are shown in Table 1.

Dr. S. Reha Butros: Computed tomography (CT) of the abdomen and pelvis (Fig. 1A and 1B), performed after the administration of contrast material, revealed circumferential, moderate thickening of a long segment of the colonic wall at the hepatic flexure and adjacent mesenteric lymphadenopathy (with the largest lymph node measuring 1.2 cm in diameter), with no surrounding fat stranding. No dilated loops of bowel were present to suggest bowel obstruction or any other areas of bowel-wall thickening. The appendix was normal, and there was no abscess formation.

Dr. Merali: The patient was referred to the gastroenterology clinic of this hospital. He reportedly had had intermittent, mild, self-resolving abdominal pain throughout childhood that was associated with diarrhea and was thought to be caused by lactose intolerance. He reported having a stable weight while he was consuming a regular diet (which included dairy) and occasional headaches but no joint pains or mouth sores. He had had frequent bouts of acute pharyngitis ("strep throat") during early childhood and had undergone a tonsillectomy at 19 months of age and sinus surgery in the past. His immunizations were current; he took no medications and had no known allergies. He was a student and lived with his parents.

Table 1. Laboratory Data.*

Variable	Reference Range, Age-Adjusted†	2 Days before Presentation, Other Hospital	2 Wk after Presentation, This Hospital
Hematocrit (%)	35.0–45.0	31.2 (ref 28–43)	33.2
Hemoglobin (g/dl)	11.5–15.5	10.0 (ref 9.0–14.0)	10.3
White-cell count (per mm^3)	4500–13,500	8400 (ref 4500–13,500)	7600
Differential count (%)			
Neutrophils	40–59	70.9 (ref 23–66)	66
Lymphocytes	33–48	16.6 (ref 24–57)	24
Monocytes	4–11	11.4 (ref 4.7–12.5)	7
Eosinophils	0–8	0.7 (ref 0.7–7.0)	2
Basophils	0–3	0.2 (ref 0.1–1.2)	1
Platelet count (per mm^3)	150,000–450,000	368,000 (ref 150,000–400,000)	471,000
Erythrocyte count (mm^3)	4,000,000–5,200,000	4,540,000 (ref 3,900,000–5,300,000)	4,940,000
Mean corpuscular volume (μm^3)	77–95	68.7 (ref 80–100)	67
Mean corpuscular hemoglobin (pg/red cell)	25.0–33.0	22.0 (ref 24–30)	20.8
Mean corpuscular hemoglobin concentration (g/dl)	31.0–37.0	32.1 (ref 32.2–35.5)	31.0
Peripheral-blood smear			3+ hypochromasia, 3+ microcytosis
Erythrocyte sedimentation rate (mm/hr)	0–13	35 (ref 0–15)	34
Creatinine (mg/dl)	0.60–1.50	0.4 (ref 0.7–1.4)	0.52
Phosphorus (mg/dl)	4.5–5.5		4.1
C-reactive protein (mg/liter)	<8.0 (for inflammation)	28	56.9
Iron (μg/dl)	45–160	13	12
Iron-binding capacity (μg/dl)	230–404		386
Ferritin (ng/ml)	30–300		18
Carcinoembryonic antigen (ng/ml)	<3.4		2.1

* The term ref denotes the reference range at the other hospital. To convert the values for creatinine to micromoles per liter, multiply by 88.4. To convert the values for phosphorus to millimoles per liter, multiply by 0.3229. To convert the values for iron and iron-binding capacity to micromoles per liter, multiply by 0.1791.

† Reference values are affected by many variables, including the patient population and the laboratory methods used. The ranges used at Massachusetts General Hospital are age-adjusted for patients who are not pregnant and do not have medical conditions that could affect the results. They may therefore not be appropriate for all patients.

His father had hypertension and hypercholesterolemia, his father's cousin had Crohn's disease, and a paternal uncle and great-grandfather had had colon cancer at 60 and 65 years of age, respectively. Both grandmothers had diabetes mellitus, and other relatives had heart disease.

On examination, the patient appeared to be healthy and was in no distress. The blood pressure was 136/76 mm Hg, the pulse 84 beats per minute, the weight 48.6 kg, and the height 151.4 cm; his weight and height were both at the 96th percentile for his age. The abdomen was soft and nontender, with no organomegaly.

Dr. Butros: An abdominal radiograph, obtained with the patient in an upright position, showed a normal bowel-gas pattern, and no dilated

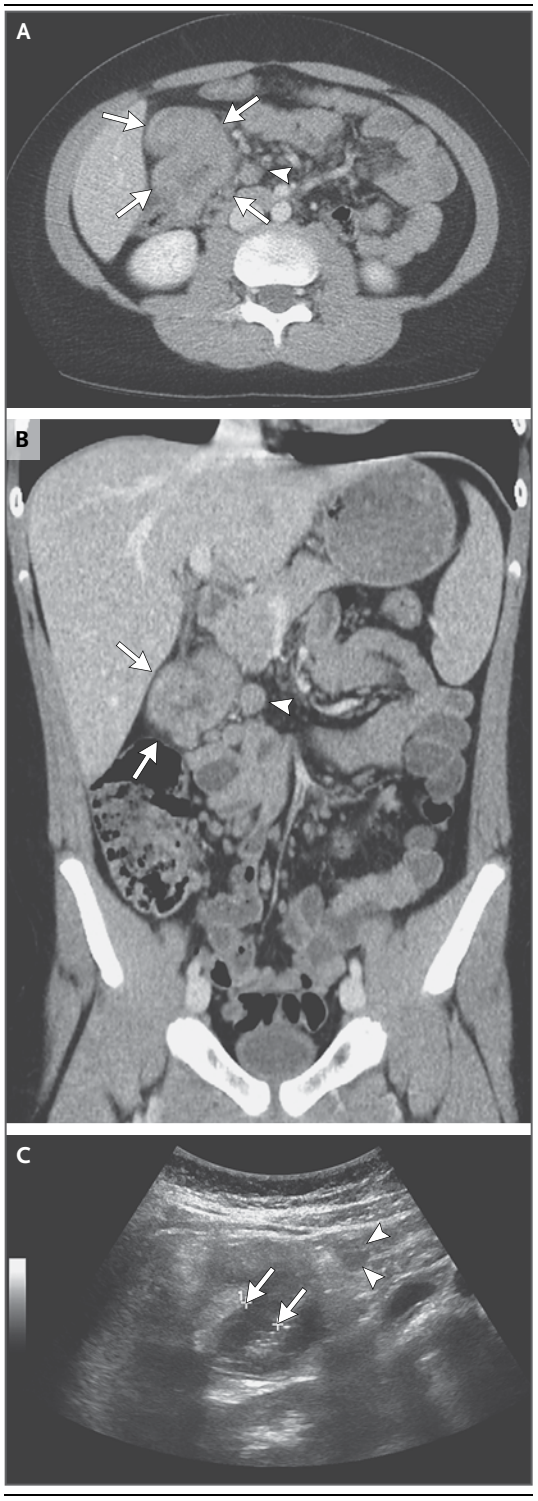

Figure 1. Abdominal Imaging Studies.
Contrast-enhanced axial and coronal CT scans (Panels A and B, respectively) show circumferential, moderate thickening of a long segment of the colonic wall at the hepatic flexure (arrows) and adjacent mesenteric lymphadenopathy (arrowheads). An ultrasound image (Panel C) shows circumferential, marked thickening of the colonic wall at the hepatic flexure (arrows) and adjacent mesenteric lymphadenopathy (arrowheads).

loops of bowel were present to suggest obstruction. Ultrasonography of the abdomen (Fig. 1C) revealed circumferential, marked thickening of a long segment of the colonic wall at the hepatic flexure and adjacent mesenteric lymphadenopathy. Color Doppler imaging studies showed increased blood flow in the affected segment of the colon.

Dr. Merali: Additional follow-up was scheduled. During the next 10 days, the pain became more constant; the patient reported pain that waxed and waned between 5 and 10 on a scale of 0 to 10 (with 10 indicating the most severe pain) and occasional, brief pain-free intervals that lasted minutes. The pain varied in quality between cramping and sharp and was located below the umbilicus in both lower quadrants, with occasional radiation to the epigastrium and lower back. Eating increased the pain, and the patient lost approximately 3 kg of weight over several weeks. Hematochezia became more frequent. Intermittent fevers and associated night sweats occurred. There was no improvement with ibuprofen or acetaminophen; the combination of acetaminophen and codeine caused increased stomach distress, and a cold pack occasionally helped to decrease this discomfort.

Eleven days after the patient presented to the gastroenterology clinic, his family called because of another episode of abdominal pain and associated low-grade fever. The family declined to have the patient seen urgently in the clinic. Diphenhydramine was prescribed, and the patient's family was advised to contact the clinician if symptoms worsened.

Two weeks after the patient's initial presentation, he was seen at a scheduled follow-up appointment. Results of liver-function tests and blood levels of electrolytes, glucose, urea nitrogen, calcium, magnesium, total protein, albumin, and globulin were normal; other test results are shown in Table 1.

A diagnostic procedure was performed.

DIFFERENTIAL DIAGNOSIS

Dr. Jeffrey A. Biller: I was involved in the care of this patient, and all discussants are aware of the diagnosis. This 10-year-old boy presented with

the acute onset of abdominal pain. The differential diagnosis of acute abdominal pain in a 10-year-old boy with intermittent fevers and weight loss is quite broad. Disorders such as hepatitis, pancreatitis, and the hemolytic–uremic syndrome can be ruled out on the basis of the examination and laboratory data. The location of his pain, normal urinalysis, and findings on CT and ultrasonography make a peptic process, urologic disorder, and cholecystitis unlikely. Appendicitis should be considered, but the normal appearance of the appendix on imaging studies and the absence of adjacent inflammation and fluid collection rule out this diagnosis. Henoch–Schönlein purpura (IgA-associated vasculitis) should also be considered in this child. Although the abdominal pain of Henoch–Schönlein purpura is often associated with a purpuric rash, arthritis, and nephritis (findings that were not present in this patient), abdominal pain precedes the rash in as many as 30% of cases, and Henoch–Schönlein purpura without a rash has been reported.[1] Persons with symptomatic Meckel's diverticulum often present with painless rectal bleeding, but acute inflammation of the diverticulum develops in a subset of patients and results in symptoms similar to those of acute appendicitis; therefore, this diagnosis should also be considered in this case.

The findings on abdominal imaging studies help to narrow the differential diagnosis. CT and ultrasonography reveal localized colonic-wall thickening with a masslike effect in the region of the hepatic flexure and associated lymphadenopathy. Causes that could explain both the symptoms and the findings on imaging studies include Crohn's disease, intussusception, infection, and cancer.

CROHN'S DISEASE

Approximately one quarter of all persons with Crohn's disease receive the diagnosis by 18 years of age; most of those cases occur in older children and adolescents.[2] Persons with Crohn's disease can present with localized areas of inflammation anywhere in the bowel, but only 10% of affected persons have disease that is restricted to the colon. On imaging studies, the bowel often appears thickened (as was noted in this patient) because of the presence of transmural inflammation. Fistulas and phlegmonous masses can also develop, and patients may present with acute or chronic symptoms of abdominal pain and obstruction. In this patient, the abdominal pain, bowel-wall thickening with enlarged adjacent mesenteric nodes, and elevated inflammatory markers would be consistent with Crohn's disease, but the presence of an isolated area of colonic-wall thickening in the region of the hepatic flexure would be unusual in the absence of the luminal narrowing and fat stranding that are typically seen in persons with Crohn's disease.

INTUSSUSCEPTION

Children with intussusception can present with colicky abdominal pain, hematochezia, and a mass effect in the intestine. Ileocecal intussusception is most common; however, more than 50% of persons with Henoch–Schönlein purpura and associated edema of the small-bowel wall have either jejunojejunal or ileoileal intussusception. This patient is older than the usual age at which intussusception manifests; approximately 80 to 90% of cases are diagnosed between the ages of 6 months and 36 months.[3] Among children in this typical age group, most cases are idiopathic, but intussusception can also occur after viral or bacterial enteritis and can occasionally occur in persons with celiac disease. Among children with intussusception who are younger than 6 months of age or older than 36 months, close consideration should be given to identification of a lead point (e.g., Meckel's diverticulum, polyp, small-intestine lymphoma, lipoma, or duplication cyst) or an underlying medical condition (e.g., Henoch–Schönlein purpura, cystic fibrosis, celiac disease, or Crohn's disease).[4] In this 10-year-old patient, intussusception is unlikely because of the findings on CT of isolated bowel-wall thickening at the hepatic flexure with a normal ileum and cecum, as well as the absence of colicky abdominal pain, of symptoms of obstruction, and of the typical target-sign finding on CT (in which concentric rings of compressed inner-bowel lumen, hypodense mesentery, and hyperdense outer-bowel wall are seen within one another).

INFECTION

Some gastrointestinal infections are associated with abdominal pain without diarrhea. Children with *Yersinia enterocolitica* infection, which is often acquired through the consumption of contaminated pork products, typically present with bloody diarrhea, abdominal pain, fever, and vomiting;

however, the presentation can be dominated by pain in the right lower quadrant and fever, and thus it can be difficult to differentiate this disease from acute appendicitis. Persons with amebiasis, which is caused by the protozoa *Entamoeba histolytica*, commonly present with abdominal pain, bloody diarrhea, and fever, but on rare occasions, patients may present with a palpable abdominal mass due to the development of granulation tissue in the colon (ameboma) and findings on imaging studies that are suggestive of cancer.[5] The presenting symptoms of tuberculous enteritis may include abdominal pain, fever, and fatigue, and patients may have an inflammatory mass in the ileocecal region.[6,7] This patient did not have obvious epidemiologic risk factors for any of these infections, and the localized thickening of the bowel wall at the hepatic flexure makes these diagnoses unlikely.

GASTROINTESTINAL CANCER

The gastrointestinal tract is a common site of extranodal involvement in adult patients with non-Hodgkin's lymphoma.[8] Primary non-Hodgkin's lymphoma of the colon is very rare in pediatric patients but can be manifested by ileocolonic intussusception.[9] CT may reveal a masslike effect in the right lower quadrant and adjacent lymphadenopathy, findings similar to those seen in this patient.

Colorectal carcinoma is extremely uncommon in children.[10,11] Ulcerative colitis, particularly with associated pancolitis, is a risk factor for cancer, but this patient was not known to have underlying ulcerative colitis. Hereditary cancer syndromes may confer a predisposition to colorectal carcinoma in children. The familial adenomatous polyposis syndrome is caused by a germline mutation of the adenomatous polyposis coli (*APC*) gene on chromosome 5 and is associated with numerous adenomatous polyps of the colon and intestine. The risk of colon adenocarcinoma among patients with the familial adenomatous polyposis syndrome approaches 90% by the time they are 50 years of age, and adenocarcinoma has been reported in affected children.[12,13] The Lynch syndrome (hereditary nonpolyposis colorectal cancer), which accounts for 3% of colorectal cancers in adults, is associated with a germline mutation in a DNA mismatch-repair gene. Patients with the Lynch syndrome often have a strong family history of cancers that occur at an early age, even during childhood or adolescence.[14,15] In addition, several gastrointestinal cancers, including colon cancer, have been reported in young children with homozygous germline mutations in the *MLH1* DNA mismatch-repair gene; such children have also had findings that are suggestive of neurofibromatosis type 1, including café au lait spots.[16,17] Patients who have inherited two mutations of DNA mismatch-repair genes are known to have the constitutional mismatch-repair deficiency (CMMRD) syndrome.[18]

In this patient, the increasingly severe abdominal pain, fever, weight loss, hematochezia, and localized thickening of the bowel wall at the hepatic flexure make a gastrointestinal cancer, such as non-Hodgkin's lymphoma or adenocarcinoma, the most likely diagnosis. In order to establish the diagnosis, we performed upper endoscopy and colonoscopy. Results of the upper endoscopy were normal. The colonoscopy revealed marked nodularity of the mucosa from the rectum to the middle of the transverse colon. A large, ulcerated mass that obstructed more than 50% of the lumen was found at the hepatic flexure; biopsies of the mass were performed.

DR. JEFFREY A. BILLER'S DIAGNOSIS

Gastrointestinal cancer, most likely non-Hodgkin's lymphoma or adenocarcinoma of the colon.

PATHOLOGICAL DISCUSSION

Dr. Catherine E. Hagen: Examination of biopsy specimens of the mass revealed an invasive, poorly differentiated adenocarcinoma. An immunohistochemical stain for CDX2 was positive; this finding supported a primary gastrointestinal origin of the tumor.

Subsequently, a subtotal colectomy was performed, and gross examination of the colon revealed an exophytic, necrotic mass lesion, measuring 8.2 cm in greatest dimension (Fig. 2A). The tumor was histologically composed primarily of sheets of malignant, pleomorphic cells, with only focal glandular differentiation (Fig. 2B and 2C). One lymph node was positive for metastatic adenocarcinoma, and the tumor invaded the subserosal tissue; therefore, this adenocarcinoma of the colon was classified as stage III (pT3N1a) according to the American Joint Committee on Cancer staging system. In addition, 10

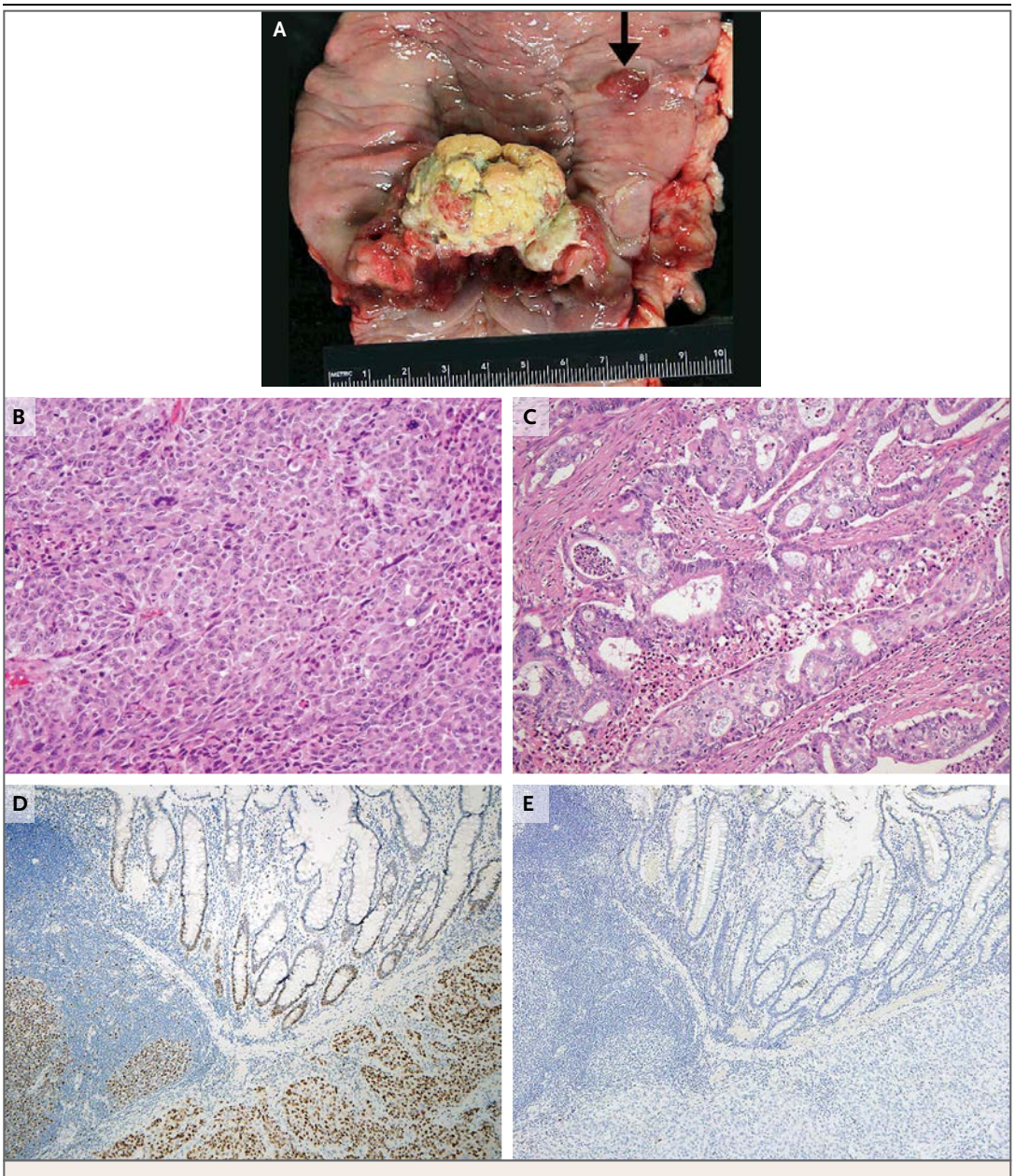

Figure 2. Colectomy Specimen.

On gross examination of the colectomy specimen (Panel A), a large tumor was visible centrally and a small tubular adenoma (arrow) was noted adjacent to the tumor. On hematoxylin and eosin staining, the tumor was histologically composed primarily of sheets of malignant, pleomorphic cells (Panel B), with only focal areas of discernible glandular formation (Panel C). On immunohistochemical staining, *MLH1* was intact in both the tumor tissue and the background normal tissue (Panel D), whereas *PMS2* was completely absent (Panel E).

small tubular adenomas were identified throughout the remaining colon.

Because adenocarcinoma of the colon is exceedingly rare in children, we must broaden our differential diagnosis to include the familial adenomatous polyposis syndrome, *MUTYH*-associated polyposis, and the Lynch syndrome, with possible biallelic mutations. We routinely screen pathological specimens of colorectal carcinoma for the Lynch syndrome.

Screening can be accomplished through either immunohistochemical staining for DNA mis-

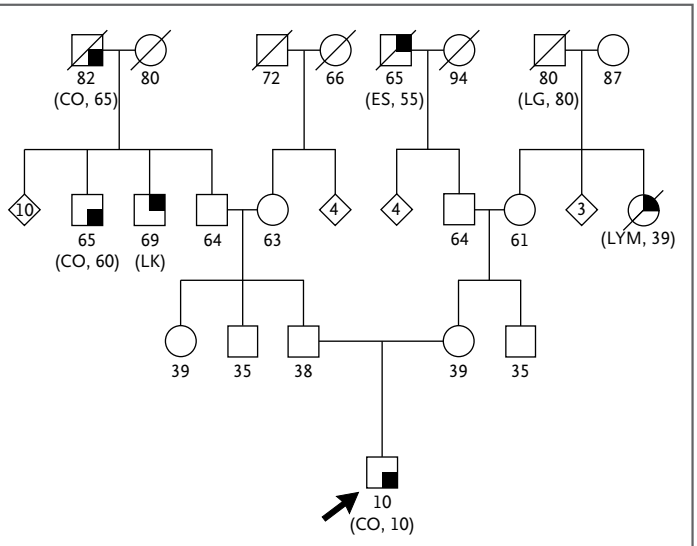

Figure 3. Family Pedigree.

A multigenerational family history of cancer was obtained. The patient's parents are of French-Canadian descent. Squares represent male sex, and circles female sex. The number below each circle or square reflects the current age in years; for family members who have died (indicated by a slash), the number reflects the age at death, when available. Diamonds represent family members whose sex was not recorded, and the numbers inside the diamonds represent the number of persons. Black shading in the right lower quadrant of a square or circle indicates that the family member had colon cancer; black shading in the right upper quadrant of a square or circle indicates that the family member had another type of cancer. In parentheses, the abbreviation and the number indicate the type of cancer and the age at diagnosis, when available. The arrow points to the patient under discussion. CO denotes colon cancer, ES esophageal cancer, LG lung cancer, LK leukemia, and LYM lymphoma.

match-repair proteins[19] or a polymerase-chain-reaction (PCR) assay for microsatellite instability. Immunohistochemical staining is performed for the four major DNA mismatch-repair proteins: *MLH1*, *PMS2*, *MSH2*, and *MSH6*. These proteins form heterodimer complexes, so when there is a mutation in one protein, there is usually also functional loss of the partner protein. In this patient, immunohistochemical staining revealed intact staining in tumor tissue for *MSH2*, *MSH6*, and *MLH1* but a complete absence of staining for *PMS2* in both the tumor tissue and the normal tissue (Fig. 2D and 2E). Normal tissue typically retains staining for the DNA mismatch-repair proteins and serves as an internal control for the staining process, so it was initially thought that the immunostaining for *PMS2* had failed.

However, there can be exceptions to the typical immunohistochemical staining patterns for DNA mismatch-repair proteins. Mutations that result in false negative and false positive staining have been reported. Mutations in *PMS2* may not result in an absence of staining for *MLH1*, because *MLH1* can be stabilized by other proteins.[20] Finally, biallelic mutations can result in the complete absence of staining. Although the absence of staining for *PMS2* in both the tumor tissue and the normal tissue was initially thought to indicate failure of the staining process, this result also raised the possibility of a biallelic mutation, particularly given this patient's young age.[14,21]

Because the results of immunohistochemical staining were believed to be inconclusive, testing for microsatellite instability was also performed. DNA was extracted from both tumor and nontumor tissue, and PCR assay was performed with the use of 10 microsatellite loci. Alteration of the size of repeat microsatellites in tumor tissue, as compared with the size of those in normal tissue, is indicative of instability. In this patient, 5 of the 10 evaluated loci were found to be unstable; tumors with 30% or more unstable microsatellites are considered to have high microsatellite instability,[22] and thus these results confirmed a mismatch-repair abnormality that conferred a predisposition to adenocarcinoma of the colon.

Ms. Gayun Chan-Smutko: The patient was referred for genetic counseling and risk assessment. A multigenerational family history was obtained (Fig. 3). The patient was an only child of nonconsanguineous parents. When the patient's mother was asked about skin lesions in the patient, she reported that he had two brown spots on the back and thigh; a skin examination was declined. The mother's family had no history of colon cancer. In the father's family, the patient's paternal uncle and great-grandfather had had colon cancer at 60 and 65 years of age, respectively.

The patient presented with colon cancer and 10 adenomas at a young age, and closely related family members were not affected by the same condition. These factors are suggestive of a de novo presentation of the familial adenomatous polyposis syndrome or the Li–Fraumeni syndrome or of an autosomal recessive inherited disorder such as *MUTYH*-associated polyposis or the CMMRD syndrome, which involves biallelic mutations of one of the DNA mismatch-repair genes.

Genetic testing and its role in guiding long-

Table 2. Results of Genetic Testing.

Hereditary Cancer Syndrome	Gene	Patient's Result	Mother's Result	Father's Result
Familial adenomatous polyposis syndrome	*APC*	No mutation detected	Not tested	Not tested
Li–Fraumeni syndrome	*p53*	No mutation detected	Not tested	Not tested
MUTYH-associated polyposis	*MUTYH*	Negative for Y179C and G396D mutations	Not tested	Not tested
Lynch syndrome and CMMRD syndrome*	*PMS2*	Mutation 1: c.2117delA (deletion of one nucleotide causing a translational frameshift predicted to produce a premature or alternate stop codon) Mutation 2: EX9_15del (gross deletion spanning exons 9 through 15)	EX9_15del mutation	c.2117delA mutation

* CMMRD denotes constitutional mismatch-repair deficiency.

term surveillance for the patient and his family members were discussed. With the informed consent of the patient's parents, testing for mutations associated with the possible diagnoses was performed (Table 2). Analysis of *PMS2* was prioritized over the other DNA mismatch-repair genes because of the results of immunohistochemical staining. The identification of mutations in both inherited copies of the *PMS2* gene confirmed a diagnosis of the CMMRD syndrome.

MANAGEMENT AND FOLLOW-UP

Dr. Annah N. Abrams: Children with new diagnoses of cancer at this hospital are routinely seen for psychological assessment. The first thing we do as part of this evaluation is try to understand what the child knows about the diagnosis and treatment plan. This patient told us that he knew that he had colon cancer and that the treatment plan was chemotherapy, which would get rid of the cancer cells that still remained in his body. He also said that he liked knowing what was going on and what the plan was going to be. This is a developmentally on-target response for a child of this age. In children with medical illnesses, establishing mastery over what is going on in the hospital setting improves their coping ability.

The patient did not describe symptoms of depression or anxiety and did not appear to be depressed or anxious on examination. Rather, he said that he felt relief at knowing why he had been in pain for more than a month. His mother shared that he had had separation anxiety in the past and that counseling had been very helpful. Children with a history of a psychiatric condition are at higher risk for having the same emotional challenges that they have had in the past, so we knew that we would need to be on the lookout for the reemergence of separation anxiety in this patient as he encountered various medical and psychosocial stressors during the course of his illness.

By nurturing children's strengths and competencies, we can help them to better manage the stresses of an illness. At the time of his psychological assessment, the patient was doing well in school, enjoyed playing hockey and video games, and identified very close relationships with each of his parents and with his grandparents. He had already shared his diagnosis with his friends and school and wanted to stay connected with everyone. By offering age-appropriate activities during hospitalizations and maintaining his connection with school, we were able to help him to continue functioning at an appropriate developmental level.

Dr. Daniel C. Chung: As compared with the Lynch syndrome, which is classically associated with a high risk of the development of colorectal and endometrial cancer in adulthood, the CMMRD syndrome (which was first described in 1999 as a pediatric cancer-susceptibility syndrome) is associated with a different spectrum of tumors and age range at onset.[23,24] In the largest reported series, which included 146 cases, cancers of the central nervous system arose in 81 patients (55%) at a median age of 9 years,

colorectal cancers in 59 patients (40%) at a median age of 16 years, and hematologic cancers in 48 patients (33%) at a median age of 6 years.[25] More than 60% of patients with the CMMRD syndrome have café au lait macules similar to those associated with neurofibromatosis type 1, and approximately one third of affected patients have multiple colonic adenomas, as did this patient.

The majority of cases of the Lynch syndrome are attributable to a germline mutation in either *MSH2* or *MLH1*; only approximately 10% of cases are associated with *PMS2* mutations. In contrast, more than half the patients with the CMMRD syndrome carry biallelic mutations in *PMS2*, as did this patient. This discrepancy may reflect the underrecognition of *PMS2* heterozygotes (such as this patient's parents) in the population, because they often have an attenuated clinical phenotype. In addition, consanguinity is not uncommon in many families with the CMMRD syndrome.

The available data have not permitted the establishment of evidence-based cancer-surveillance guidelines for persons with the CMMRD syndrome; however, recommendations have been proposed that are based on the current understanding of clinical features. These recommendations include magnetic resonance imaging of the head every 6 to 12 months starting at 2 years of age, annual colonoscopy starting at 8 years of age, annual upper endoscopy and small-bowel capsule endoscopy starting at 10 years of age, a complete blood count every 6 months starting at 1 year of age, and annual gynecologic evaluations starting at 20 years of age.[18] Close attention to any new symptoms is also essential. This patient is being followed with regular sigmoidoscopies and upper endoscopies, abdominal imaging studies (as part of the aftercare for colorectal cancer), annual complete blood counts, and regular physical examinations. The long-term effectiveness of such an intensive surveillance program and the impact of the program on the natural history of the disorder remain to be defined, but preliminary reports indicate that such protocols can lead to successful identification of resectable lesions.[26]

There is emerging evidence that regular use of aspirin may reduce the incidence of cancer and cancer-related deaths among patients with the Lynch syndrome, and it is reasonable to consider that this benefit might also apply to patients with the CMMRD syndrome. On the basis of this information, daily aspirin was prescribed for this patient.

Dr. Mary S. Huang (Pediatrics): As is often the case when we encounter cancers that are very rare in children but common in adults, we consulted with colleagues who specialize in adult oncology when planning this child's care. He received chemotherapy with a modified FOLFOX6 regimen, which includes 12 cycles of a combination of fluorouracil and oxaliplatin. The patient finished his planned chemotherapy regimen about 1.5 years ago and continues to do well.

When we first met this patient, his parents did not know much about their family history. As a direct result of this child's diagnosis, his maternal grandmother underwent screening; an abnormality was reportedly identified and she recently underwent a colectomy. This child's diagnosis has had clear repercussions for the rest of the family.

PATHOLOGICAL DIAGNOSIS

Invasive, poorly differentiated adenocarcinoma of the right colon with high microsatellite instability in a patient with the constitutional mismatch-repair deficiency syndrome with biallelic mutations in the *PMS2* gene.

FINAL DIAGNOSIS

The constitutional mismatch-repair deficiency syndrome and stage III adenocarcinoma of the colon.

This case was presented at Pediatric Grand Rounds.

No potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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