CASE RECORDS of the MASSACHUSETTS GENERAL HOSPITAL

Case 3-2016: A 9-Year-Old Girl with Intermittent Abdominal Pain

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PRESENTATION OF CASE

Dr. Patricia M. Guglietta: A 9.5-year-old girl with chronic constipation was seen in the gastroenterology clinic of this hospital because of recurrent episodes of abdominal pain with associated nonbilious vomiting.

The patient had been generally well until she was 4 years of age, when occasional episodes of abdominal pain began to occur. These episodes, which occurred a few times per year and were separated by asymptomatic periods, were sometimes associated with constipation or nonbloody, nonbilious vomiting. Neither fevers nor diarrhea occurred. The patient's family reported the symptoms during routine annual examinations or other scheduled or urgent appointments at a health center affiliated with this hospital. Polyethylene glycol was administered intermittently for constipation, with improvement.

When the patient was 8 years of age, a sudden episode of sharp pain on the left side of the chest occurred, with associated tachycardia and nausea, in the absence of precipitating factors. On examination at school, the pulse was 150 beats per minute; at the health center, the temperature and the remainder of the physical examination were normal, as were a chest radiograph and an electrocardiogram. The patient returned home. Results of a cardiologic evaluation that was performed 2 months later were normal.

During the next 18 months, the episodes of abdominal pain became more frequent (up to three or four times weekly) and occurred more often when the patient was at school than during weekends. The pain was typically epigastric and associated with vomiting. On evaluation when the patient was 8 years 7 months of age, a urine culture was sterile, serologic testing for *Helicobacter pylori* infection was negative, and an abdominal radiograph showed no evidence of obstruction. Polyethylene glycol and omeprazole were administered; the constipation transiently diminished when the medications were taken regularly.

When the patient was 9 years 4 months of age, she was seen at an urgent care clinic because of sharp, crampy epigastric pain. Examination revealed a normal temperature, mild diffuse abdominal tenderness, fullness in the left lower quad-

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N Engl J Med 2016;374:373-82.
DOI: 10.1056/NEJMcpc1413305

rant that was consistent with the presence of stool, and no abdominal guarding or rebound tenderness. Therapy with the laxative was resumed, and constipation diminished; however, abdominal pain recurred intermittently thereafter, along with vomiting, which gave partial pain relief.

One month later, a physical examination was normal. A complete blood count and white-cell differential count were normal, as were blood levels of electrolytes, calcium, glucose, total protein, albumin, globulin, free thyroxine, and thyrotropin and results of renal- and liver-function tests; testing for *H. pylori* infection and celiac disease was negative. Abdominal radiography was performed.

Dr. Pallavi Sagar: The abdominal radiograph (Fig. 1) showed a nonobstructive bowel-gas pattern and a moderate-to-abundant amount of stool distributed in the colon, particularly in the ascending colon; these findings are consistent with the clinical history of constipation. There was a normal distribution of bowel gas and no evidence of abnormal mass effect or intraabdominal calcifications.

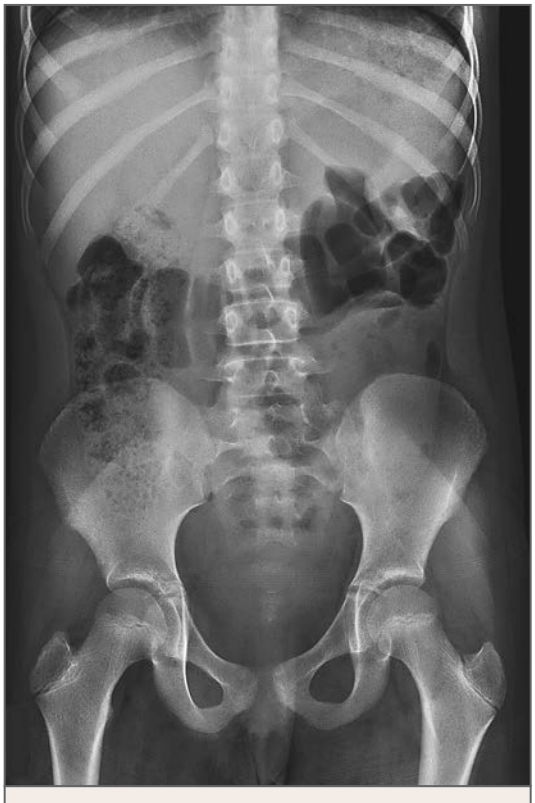

Figure 1. Abdominal Radiograph.
An abdominal radiograph shows a moderate-to-abundant amount of stool in the ascending colon, a finding suggestive of constipation.

Dr. Guglietta: Therapy with omeprazole was initiated. The patient was referred to the pediatric gastroenterology clinic of this hospital.

The patient and her family reported that the sharp, intermittent epigastric pain was sometimes associated with and partly relieved by nonbloody, nonbilious emesis and was not associated with or relieved by defecation. The patient had chronic constipation; the stools were hard and passed with straining, without blood, mucus, grease, tenesmus, urgency, cramping, or diarrhea. Constipation had resolved with the regular administration of polyethylene glycol and lactulose, and epigastric pain had diminished with omeprazole therapy. The patient had a history of asthma and had had pneumonia at 2 years of age. She had no mouth sores, fevers, or joint pains. Her growth was normal. She had no known allergies. Her diet was relatively low in fiber, with few vegetables and fruits. She lived with her parents and attended school; she was an excellent student. She was of South American ancestry and had traveled to South America when she was 8 years of age. Her father had gastroesophageal reflux disease, a sister had hyperthyroidism, and her maternal grandmother and aunts had migraines; there was no family history of celiac disease, Crohn's disease, ulcerative colitis, or the irritable bowel syndrome.

On examination, the patient had a shy and somewhat anxious demeanor. The blood pressure was normal, the height 130.3 cm (19th percentile), and the weight 28.6 kg (28th percentile). The epigastrium was tender, without abdominal guarding, rebound tenderness, or stool loading; the remainder of the examination was normal. Analysis of the stool for *H. pylori* antigen was negative. Omeprazole therapy was stopped after a 2-month course.

At a follow-up visit in the gastroenterology clinic 6 weeks after the initial visit, the patient and her family reported that the epigastric pain had recurred approximately weekly, despite the omeprazole therapy; the pain was associated with vomiting and appeared to be unrelated to stress or defecation. The patient passed stools once or twice per day that were formed, with mucus and

without blood. She had no nocturnal pain, headaches, or morning nausea. On examination, there was epigastric tenderness just beneath the xiphoid process; the abdomen was otherwise soft and nontender, with no mass in the left lower quadrant to suggest stool loading. The remainder of the examination was normal.

One month later, an abdominal ultrasound image was normal. Esophagogastroduodenoscopy was performed; although there was suspicion for duodenitis, pathological examination of biopsy specimens of the esophagus, stomach, and duodenum was normal. Blood levels of electrolytes, glucose, calcium, total protein, globulin, amylase, and lipase and results of renal- and liver-function tests were normal. All medications were discontinued. A diagnosis of abdominal migraine was considered, and the patient was referred to a neurologist; an appointment was scheduled for 4 months later.

During the next 2 months, the frequency of abdominal pain increased, and the patient began to have "fits of pain" at school and at home, during which she was pale, had diaphoresis, and fell on the floor. Her symptoms partially improved when she bent over and held her abdomen. Results of an examination by her pediatrician were unchanged. Therapy with omeprazole and polyethylene glycol was reinitiated, and amitriptyline therapy for abdominal migraine was begun.

At 9 years 11 months of age, an episode of unrelenting severe abdominal pain occurred that began in the left upper and left lower quadrants and radiated to the back. On the third day of the episode, the patient was seen by her pediatrician at the health center. The examination was normal; the abdomen was soft and nontender. There was a lack of response to the initial dosage of amitriptyline, so the dosage was increased. The patient was referred to a mental health consultant for instruction regarding biofeedback and relaxation techniques. An additional study was performed at the request of the patient's parents, and a diagnosis was made.

DIFFERENTIAL DIAGNOSIS

Dr. Guglietta: I was involved in the care of this patient, and all discussants are aware of the diagnosis. This 9-year-old girl presented on numerous occasions with the acute onset of abdominal pain. Although the differential diagnosis of abdominal pain in children is quite broad, several notable features of her presentation initially influenced my working diagnosis.

PRIMARY CARE PERSPECTIVE

Constipation

The intermittent nature of this child's symptoms and the history of hard infrequent stools, a low-fiber diet, and relief after the administration of osmotic laxatives made constipation the working diagnosis for much of her clinical course. However, despite adequate treatment for constipation, acute episodes of abdominal pain recurred.

Functional Abdominal Pain

The patient's episodes of pain were more frequent at school; this factor is suggestive of functional abdominal pain, a diagnosis that is commonly seen in a general pediatrics practice. Some studies have reported that functional abdominal pain has an overall prevalence of up to 19%; the prevalence is highest among female patients, and the most common age at onset is between 4 and 6 years[1] (the age range in which this patient's episodes of abdominal pain began). There were several features of this child's presentation that suggested the diagnosis of functional pain, but the severity, quality, increasing frequency, and epigastric location of the pain prompted the consideration of alternative diagnoses (Table 1), and consultation with a pediatric gastroenterologist was required.

GASTROENTEROLOGY PERSPECTIVE

Dr. Christopher J. Moran: When evaluating a pediatric patient with chronic abdominal pain in the outpatient setting, several important "alarm" symptoms and signs should be considered. These include weight loss, pain located away from the umbilicus, nighttime awakenings due to pain, and loss of functional status.

Constipation

This patient initially presented with abdominal pain in the context of hard, infrequent stools. I agree that constipation seemed to be the most likely cause of these symptoms, and this impression is strengthened by the improvement seen with the administration of polyethylene glycol.

Table 1. Differential Diagnosis of Abdominal Pain in This Patient.

Cause	Findings in This Patient
Gastritis	Pain became localized to the left upper quadrant and epigastrium; vomiting occurred
Intermittent obstruction	Episodes of abdominal pain were severe, abrupt in onset, and relatively brief in duration
Biliary obstruction	Episodes of abdominal pain were severe, abrupt in onset, and relatively brief in duration; pain became localized to the epigastrium; abdominal pain was sometimes associated with eating and relieved in part by vomiting
Functional abdominal pain	Abdominal pain occurred more often during school than at home; the patient was a high achieving student with an anxious personality; laboratory test results and abdominal radiographs were normal throughout the clinical course
Abdominal migraine	Acute episodes of abdominal pain were treated in the emergency department with analgesic agents, with improvement over time

Although many cases of constipation require a self-limited course of osmotic laxative therapy, some cases require long-term laxative use.[2] When abdominal symptoms recur (as they did in this patient), possible causes include poor adherence to therapy, as well as the possibility that constipation might coexist with an additional underlying cause of abdominal pain. In patients without alarm symptoms, it is reasonable to administer treatment for constipation under close observation.

Gastroesophageal Reflux Disease

This patient had abdominal pain that was sometimes epigastric in location, intermittent vomiting, and a history of an episode of chest pain. Peptic injury could cause these symptoms and could be exacerbated by a large stool burden. Gastroesophageal reflux disease is typically thought to cause heartburn, but vomiting and abdominal pain may be more prevalent among children with this condition.[3] Gastroesophageal reflux disease is often diagnosed clinically, and pH monitoring is reserved for atypical cases.[4] Upper endoscopy with biopsy plays a helpful role in evaluating for other diseases, such as eosinophilic esophagitis, celiac disease, gastric ulcers associated with *H. pylori*, and inflammatory bowel disease; however, the absence of evidence of esophagitis on upper endoscopy does not rule out the possibility of uncomplicated gastroesophageal reflux disease. Empirical treatment with an acid-blocking medication, such as the proton-pump inhibitor that was prescribed to this patient, was appropriate.

Helicobacter pylori Infection

Disease associated with *H. pylori* is often considered in the differential diagnosis of abdominal pain, because infection with this bacterium can cause gastritis or peptic ulcer disease.[5] However, a causative role for *H. pylori* in pediatric chronic abdominal pain has been difficult to prove.[6] Current guidelines for screening pediatric patients for *H. pylori*–associated disease focus on patients with recalcitrant iron-deficiency anemia, a family history of gastric cancer, or the presence of a peptic ulcer on endoscopic examination.[5] This patient did not meet these criteria, and therefore *H. pylori*–associated disease is an unlikely diagnosis.

Inflammatory Bowel Disease

Inflammatory bowel disease can cause chronic intermittent abdominal pain and is a plausible consideration in this patient, although her normal growth and initial improvement with laxative therapy argue against this diagnosis. The normal complete blood count, serum albumin level, and erythrocyte sedimentation rate are also inconsistent with this diagnosis; however, 9 to 19% of children with inflammatory bowel disease have similar results at the time of initial presentation.[7] In this case, if the suspicion for inflammatory bowel disease had been higher, screening for fecal occult blood and potentially for inflammatory markers (e.g., calprotectin or lactoferrin) might have been helpful in the evaluation.

Food-Specific Disorders

Food-specific disorders may also cause abdominal pain and gastrointestinal symptoms and should be considered in this patient. These disorders are typically categorized as allergic disorders, nonallergic immune-related disorders (e.g., celiac disease), and food intolerances.

Allergic Disorders

A severe allergic reaction to food may cause gastrointestinal symptoms, but it would be unusual for abdominal pain and vomiting to be the sole clinical manifestations of anaphylaxis. Patients with eosinophilic esophagitis can present with vomiting and abdominal pain, as well as

feeding difficulties and dysphagia.[8] Eosinophilic gastroenteritis is another allergic condition that causes abdominal pain, along with characteristic clinical manifestations that depend on the layer of the gastrointestinal tract (mucosal, serosal, or muscular) that is involved.[9] Mucosal eosinophilic gastroenteritis often causes diarrhea and can be identified by means of endoscopic biopsy. Serosal eosinophilic gastroenteritis is usually manifested by eosinophilic ascites and is diagnosed through a combination of imaging studies and paracentesis. Muscular eosinophilic gastroenteritis often results in obstructive symptoms. This patient had normal results of an upper endoscopic examination and of abdominal ultrasonography, thus ruling out the diagnoses of eosinophilic esophagitis and mucosal and serosal eosinophilic gastroenteritis. Muscular eosinophilic gastroenteritis is not a likely cause of this patient's symptoms, but it is difficult to obtain the tissue-based diagnosis, and therefore this condition cannot be definitively ruled out.

Celiac Disease

Celiac disease is characterized by the triad of abdominal pain, diarrhea, and weight loss; not all these symptoms were present in this patient, but the triad is not seen in all affected patients. Pediatric guidelines for chronic constipation include consideration of celiac disease, because 18% of patients with this disorder have constipation.[10] The guidelines recommend against routine screening for celiac disease in the absence of alarm symptoms, but the chronic and intense nature of the symptoms present in this patient warranted evaluation for this disorder.[11] Serologic testing for celiac disease, which has greater than 95% sensitivity, was negative in this patient, and histopathological examination of a duodenal-biopsy specimen revealed no findings suggestive of this diagnosis.[12]

Food Intolerances

Food intolerance is a common cause of abdominal pain and would have been a reasonable consideration in this patient. Lactose intolerance is present in 70% of the overall world population; the prevalence varies widely among different ethnic groups.[13] Approximately one in five children of Hispanic, Asian, or African heritage suffers from some degree of lactose intolerance by 5 years of age.[14] Although empirical lactose restriction can be diagnostically informative, breath testing is also available and fairly reliable. On breath testing, persons with lactose intolerance have an elevated concentration of hydrogen in expired air after consuming a standardized amount of lactose, a finding that indicates fermentative metabolism of the unabsorbed carbohydrate by intestinal bacterial flora.[15] A partial response to lactose restriction should prompt consideration of secondary forms of lactose intolerance, such as those associated with celiac disease, inflammatory bowel disease, and other enteritides. Dietary exclusion of a wide number of poorly absorbed, fermentable carbohydrates has recently been shown to be effective for decreasing abdominal symptoms in adults with the irritable bowel syndrome.[16] Although lactose or carbohydrate intolerance might have explained this child's crampy abdominal pain, this diagnosis is unlikely because of the absence of diarrhea and because of long symptom-free periods without lactose restriction.

Migraine Variants

Abdominal migraine is a cause of recurrent abdominal pain that is often periumbilical and can be associated with nausea and vomiting. The cyclic vomiting syndrome is a condition that is similar to abdominal migraine, except the vomiting is a more prominent finding. The average age at symptom onset for abdominal migraine is 7 years, although it varies widely. The likelihood that a migraine headache will occur in 1 year in a patient with abdominal migraine is only 24%, so the absence of headaches in this patient did not preclude this diagnosis, and she was appropriately referred to a neurologist for further evaluation.

Biliary Obstruction

Biliary obstruction has a prevalence of 5 to 15% among adults and occurs far less frequently in school-age children, but the condition merits consideration in this patient with intermittent yet recurrent episodes of upper abdominal pain. Especially in an otherwise healthy child, the most likely type of gallstone is cholesterol-based, and ultrasonography of the right upper quadrant has greater than 90% sensitivity for the diagnosis of this entity. Gallstones were not observed on this patient's abdominal ultrasound image, thus making the diagnosis of biliary obstruction unlikely.

Intestinal Malrotation with Volvulus

The escalating frequency and severity of this patient's episodic, acute-onset abdominal pain and vomiting raise the possibility of an intermittent process originating from a congenital disorder that might require surgical intervention, such as intestinal malrotation with volvulus. Malrotation, which is due to incomplete rotation of the intestine in utero, is estimated to have a prevalence of between 1 in 200 and 1 in 6000 live births, with 75% of cases occurring during the first year of life.[17] In affected patients, abdominal pain and vomiting can be caused either by volvulus around a thin mesenteric pedicle containing the intestinal blood supply or by obstruction due to Ladd's bands, which are peritoneal attachments of the abnormally positioned cecum that extrinsically compress the duodenum as they cross to the abdominal wall. The majority of children who have intestinal malrotation outside of infancy have had symptoms lasting longer than a year by the time of diagnosis,[18] so the duration of symptoms present in this patient is compatible with this disorder.

Dr. Guglietta: Because most of the other diagnoses under consideration in this patient were ruled out through the evaluations performed by her primary care and gastroenterology physicians, it seemed likely that the diagnosis in this patient would be functional abdominal pain or abdominal migraine. Neither of these is a particularly satisfying or easily treatable diagnosis, and parents and medical providers understandably feel a great degree of frustration when they are unable to relieve chronic pain in a child. Some evidence suggests that mind–body therapies (e.g., biofeedback and relaxation techniques) are effective for the management of chronic abdominal pain and headache in children,[19] and a trial of such therapies was the planned next step for this patient.

As the pain became more severe and frequent, I met with the patient and her family regularly. Her parents expressed that the diagnosis of abdominal migraine did not make sense for their child and requested additional testing; I thought this was a reasonable request and ordered an abdominal computed tomographic (CT) scan, which in fact ultimately led to the diagnosis. The patient–doctor relationship in longitudinal primary care was what led to the diagnosis in this patient.[20]

CLINICAL DIAGNOSIS

Abdominal migraine.

RADIOLOGY STUDIES

Dr. Sagar: CT of the abdomen, performed after the administration of intravenous and oral contrast material, revealed a well-defined, homogeneously hyperenhancing, round mass in the left upper quadrant, anteroinferior to the normal spleen (Fig. 2). The overall pattern of enhancement was similar to that seen in the spleen, and the mass did not have calcifications, fatty components, or any areas of decreased enhancement that would be suggestive of necrosis. The appearance of the mass was unlike that of a lymph-node mass, a primary intraabdominal cancer, or metastatic disease; rather, the findings were most consistent with a relatively large accessory spleen, without evidence of complications such as necrosis or infarction.

DISCUSSION OF MANAGEMENT

Dr. Daniel P. Ryan: Accessory spleens, which can be multiple, are a common finding. A recent single-institution analysis of consecutive abdominal CT scans showed a prevalence of accessory spleens of approximately 11%, whereas autopsy studies suggest that they are present in as many as 30% of persons.[21] During normal embryologic development, clusters of mesenchymal cells in the area of the left dorsal mesogastrium join together to form the spleen; incomplete fusion results in an accessory spleen.

Although most accessory spleens are smaller than 2 cm in greatest dimension, this patient had a mass measuring 4.4 cm. Accessory spleens are most commonly located around the splenic hilum but may be present along the splenorenal ligament, the gastrosplenic ligament, the tail of the pancreas, or the omentum. The differential diagnosis for ectopic splenic tissue also includes splenosis, which generally occurs after trauma to the spleen, and polysplenia, a rare syndrome in which patients have multiple small spleens and often also have congenital cardiac abnormalities.[22]

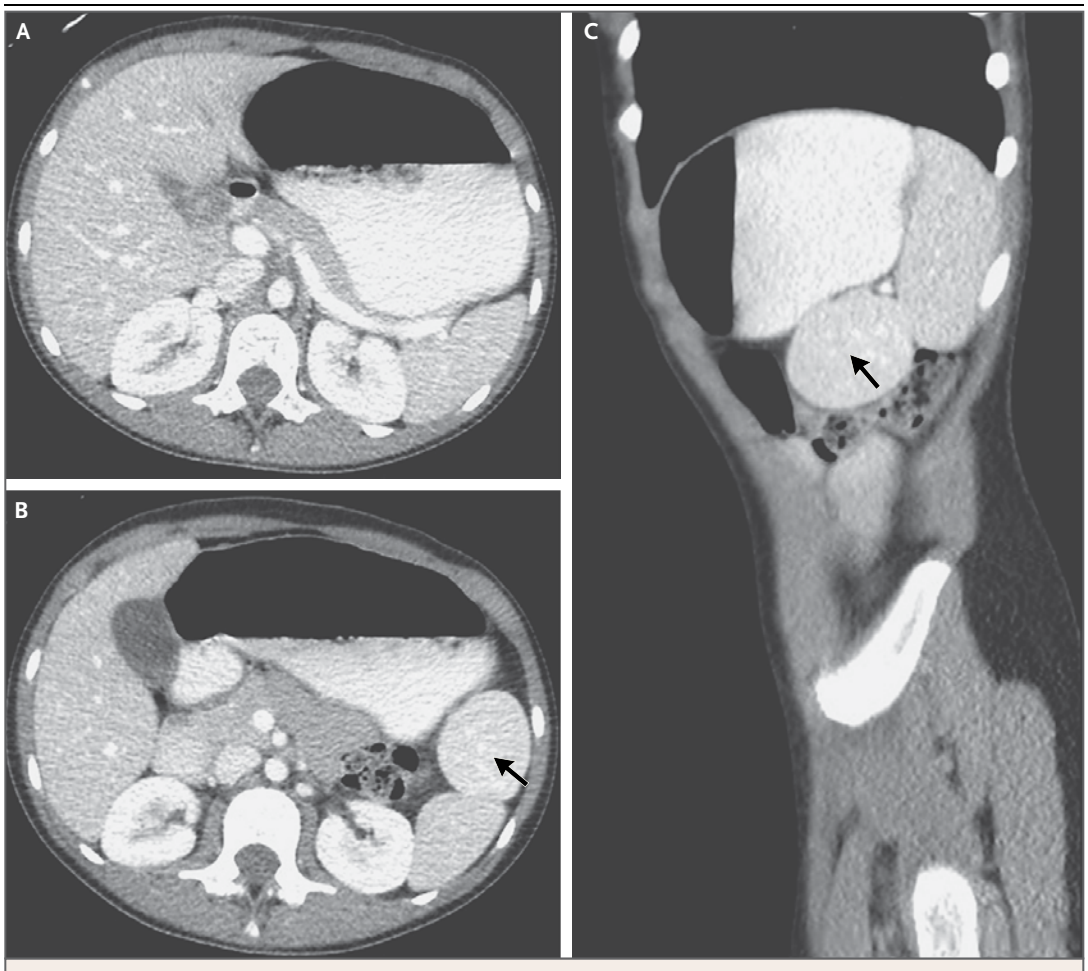

Figure 2. Contrast-Enhanced Abdominal CT Scan.
Axial (Panels A and B) and sagittal (Panel C) images show a well-defined, rounded, homogeneously enhancing mass anteroinferior to the spleen (arrows), a finding suggestive of an accessory spleen.

Most persons with accessory spleens are asymptomatic, but abdominal pain can occur with torsion, which was the suspected diagnosis in this patient. Torsion of an accessory spleen is most commonly reported in children but can also occur in adults.[23,24] Patients with torsion may present with acute abdominal pain, but intermittent or chronic pain has also been described, and infarction or rupture leading to acute abdominal hemorrhage can occur. Removal of the accessory spleen results in rapid resolution of the pain; however, more conservative management can be successful.

In this patient, laparoscopic removal of the accessory spleen was performed. During surgery, the mass that had been identified on CT

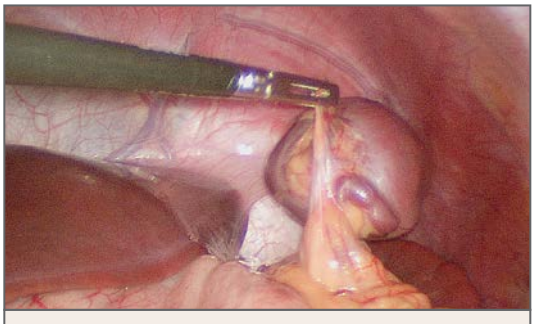

Figure 3. Surgical Photograph.
During laparoscopic surgery, the gastrocolic omentum was opened to reveal a large accessory spleen in the lesser sac. The vascular supply of the accessory spleen was contained in a very narrow pedicle.

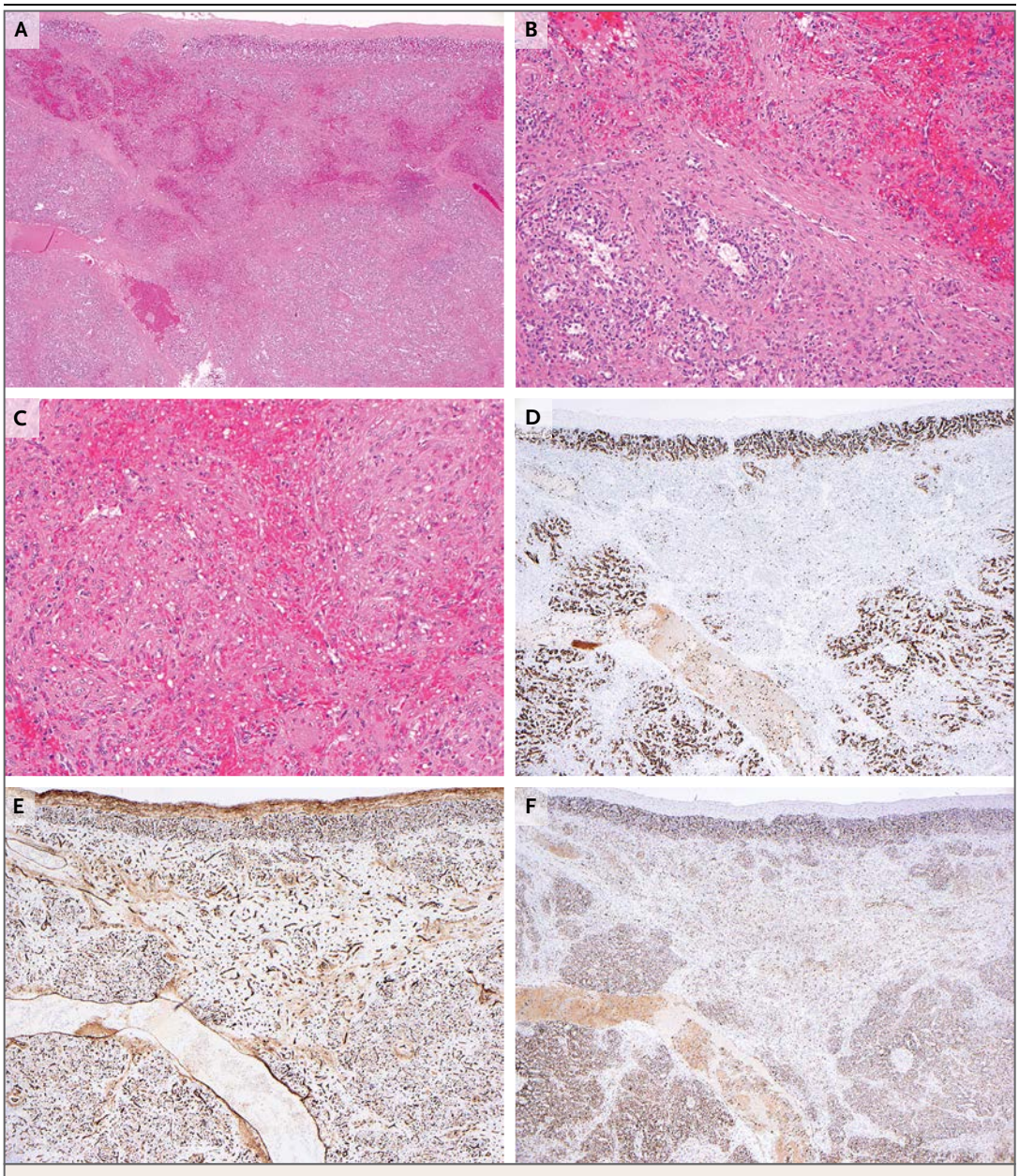

Figure 4. Specimen of the Accessory Spleen.

Hematoxylin and eosin staining of the accessory spleen shows a subcapsular focus of hemorrhage with fibrosis (Panel A). At a higher magnification, this area contrasts with the surrounding spleen (Panel B) and shows neovascularization (Panel C). Immunohistochemical staining for CD8 is positive in the surrounding splenic sinuses but negative in the endothelial cells lining the vessels in the focus (Panel D); staining for CD34 is positive in the focus (Panel E). Staining for CD68 is positive in macrophages of splenic cords in the surrounding spleen but not in the focus (Panel F). These findings are consistent with a reparative process.

was found to be in the lesser sac; the mass was noted to have a very narrow vascular pedicle (a feature that is consistent with torsion) but did not appear to be infarcted (Fig. 3). The accessory spleen was extracted in pieces through the insertion site of an umbilical trocar. The appendix was also extracted and appeared to be moderately dilated. The surgery was un-

eventful, and the patient had a normal recovery after the procedure.

PATHOLOGICAL DISCUSSION

Dr. Amelia E. Huck: Two specimens were received for pathological examination. The first was an appendix, which was essentially normal, with mild luminal dilatation. The second was composed of multiple fragments of splenic tissue that aggregated to a measurement of 3.2 cm in greatest dimension. The tissue was predominantly unremarkable red and white pulp with an overlying capsule; the appearance was consistent with that of an accessory spleen. In one focus, there was a subcapsular, triangle-shaped area of fibrosis, hemorrhage, and increased vascularity (Fig. 4A, 4B, and 4C). Immunohistochemical staining for CD8 was positive in cells lining the splenic sinuses, and staining for CD68 was positive in frequent cells in the splenic cords; there was a decreased number of both CD8+ and CD68+ cells in the area of fibrosis. Immunohistochemical staining for CD34 was positive in endothelial cells throughout the splenic tissue, including some in the fibrotic area (Fig. 4D, 4E, and 4F). Taken together, these findings are consistent with a reparative process consisting of organizing hemorrhage and fibrosis, with neovascularization.

Dr. Nancy L. Harris (Pathology): Dr. Guglietta, how is the patient doing now?

Dr. Guglietta: The patient had an uneventful recovery from surgery. More than 3 years after removal of the accessory spleen, she continues to do well and has had no recurrence of abdominal pain, although she occasionally still uses an osmotic laxative for the treatment of constipation.

Dr. Chadi El Saleeby (Pediatrics): In retrospect, can the accessory spleen be seen on the ultrasound images?

Dr. Sagar: The ultrasound images did not show the accessory spleen. There are two possible explanations: the accessory spleen may have been obscured by overlying bowel gas, or it was not visible because of its location, since our routine protocol for abdominal ultrasonography focuses primarily on evaluating the solid intraabdominal organs and does not include imaging of the lower quadrants.

FINAL DIAGNOSIS

Chronic recurrent abdominal pain caused by intermittent torsion of an accessory spleen.

This case was presented at Pediatric Grand Rounds.

Dr. Moran reports receiving consulting fees from Janssen Scientific and grant support through his institution from Actavis Labs. No other 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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