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Case 10-2017: A 6-Month-Old Boy with Gastrointestinal Bleeding and Abdominal Pain

Lauren M. Allister, M.D., Ruth Lim, M.D., Allan M. Goldstein, M.D., and Jochen K. Lennerz, M.D.

PRESENTATION OF CASE

Dr. Akash Gupta (Medicine and Pediatrics): A 6-month-old boy was seen in the emergency department of this hospital because of gastrointestinal bleeding and abdominal pain.

The patient had been in his usual state of health until 2 days before presentation, when his parents noted that he began to have intermittent episodes of abdominal pain. During these episodes, some of which woke the patient from sleep, he cried and pulled his legs up toward his chest while lying on his back. His parents reported that they palpated his abdomen during some of the episodes and it felt rigid; they suspected that he might be having discomfort related to excessive intestinal gas. He continued to eat and drink normally without vomiting. The next day, the patient had two bowel movements, and the stools had reddish discoloration. With the first bowel movement, the redness seemed to be present in a small amount and only on the outside of the stool; with the second bowel movement, the amount of redness increased. The patient's mother attributed the stool discoloration to beet consumption, since bowel movements with reddish stools had also occurred in the past after the patient had eaten beets. Intermittent episodes of apparent abdominal pain continued, and between the episodes, the patient behaved normally. On the morning of presentation, he had a third bowel movement with reddish stools. His parents took him to day care, where he continued to have occasional periods of crying and pain, followed by a bowel movement that appeared to consist almost entirely of blood, including a large clot. After this bowel movement, he was reportedly pale and diaphoretic. The day care provider called the patient's mother, who picked him up and took him to the emergency department of another hospital.

On examination at the other hospital, the temperature was 36.5°C, the pulse 178 beats per minute, the blood pressure 95/52 mm Hg, the respiratory rate 24 breaths per minute, and the oxygen saturation 100% while the patient was breathing am-

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Table 1. Laboratory Data.*

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Variable	Reference Range, Age-Adjusted†	On Presentation, This Hospital
Hematocrit (%)	33.0-39.0	17.5
Hemoglobin (g/dl)	10.5-13.5	5.7
Reticulocyte count (%)	0.5-2.5	7.6
White-cell count (per mm ³)	6000–17,500	22,200
Differential count (%)		
Neutrophils	17–49	38
Lymphocytes	67–77	59
Monocytes	4–11	3
Red-cell count (per mm ³)	3,700,000-5,300,000	2,070,000
Prothrombin time (sec)	11.0–14.0	12.4
Prothrombin-time international normalized ratio	0.9–1.1	1.0
Activated partial thromboplastin time (sec)	22.1–37.0	19.4
Total protein (g/dl)	6.0-8.3	5.4
Albumin (g/dl)	3.3-5.0	4.1
Globulin (g/dl)	1.9–4.1	1.3
Iron (µg/dl)	45–160	19
Iron-binding capacity (µg/dl)	230–404	351

* 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.

> bient air. The weight was 9.1 kg. On palpation of the abdomen, there was diffuse tenderness, which was greater on the right side than on the left, and no masses. There were no external anal fissures, and the remainder of the physical examination was normal. Two hours after arrival at the other hospital, the patient passed a dark-red stool that was described as resembling currant jelly. Intravenous normal saline (5 ml per kilogram) was administered, and he was brought by ambulance to the emergency department of this hospital for further evaluation and treatment.

> The patient had a history of infantile colic and gastroesophageal reflux, which had previously been treated with ranitidine. He received a lowlactose cow milk–based formula. Pureed fruits and vegetables had recently been introduced into his diet, after which constipation developed, his

stools became more firm, and daily bowel movements were associated with straining. He received cholecalciferol, and he had begun using an unspecified over-the-counter teething gel and unspecified homeopathic teething tablets 1 week earlier. Immunizations were current through 4 months of age; vaccines (including the second dose of live, oral human-bovine reassortant pentavalent rotavirus vaccine) had been administered 6 weeks earlier. There were no known allergies. The patient lived with his parents, attended day care, and had no known sick contacts. His parents were from Brazil; he was born in the United States and had not traveled outside the country. There was no family history of bleeding disorders.

On examination, the temperature was 36.3°C, the pulse 160 beats per minute, the blood pressure 98/47 mm Hg, the respiratory rate 32 breaths per minute, and the oxygen saturation 99% while the patient was breathing ambient air. He appeared well. Bowel sounds were present; the abdominal examination was otherwise limited because the patient was crying. The diaper contained melena and a small amount of stool. The remainder of the examination was normal.

Dr. Ruth Lim: Thirty-five minutes after the patient's arrival in the emergency department, an ultrasound examination of the abdomen was performed. There was no evidence of intussusception, appendicitis, a focal lesion, or abnormally dilated bowel loops. Bowel peristalsis was present.

Dr. Gupta: On examination after ultrasonography, the pulse was 168 beats per minute, and the blood pressure 94/36 mm Hg. The patient appeared pale. The abdomen was soft, without distention, tenderness, or masses, and bowel sounds were present. Results of the physical examination were otherwise unchanged. Blood levels of electrolytes, glucose, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, total bilirubin, direct bilirubin, and C-reactive protein were normal, as were the anion gap, platelet count, red-cell indexes, and results of renal-function tests. The results of other laboratory tests are shown in Table 1. Packed red cells were transfused, and pantoprazole and famotidine were administered intravenously.

A diagnosis was made.

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DIFFERENTIAL DIAGNOSIS

Dr. Lauren M. Allister: This 6-month-old boy presented with gastrointestinal bleeding manifested by hematochezia, along with intermittent abdominal pain and one episode of melena. He appeared ill and had tachycardia. Pertinent features of the history include gastroesophageal reflux, a possible milk-protein allergy (since he was receiving a low-lactose formula), and exposure to unspecified teething tablets and a homeopathic teething medication. It is important to note the absence of fever, forceful vomiting, and hematemesis. Because care in the emergency department is more process-driven than outcomedriven, the evaluation in this case can be condensed into the following steps: rapid assessment, stabilization, and diagnostic evaluation.

RAPID ASSESSMENT

This ill patient had tachycardia, pallor, profound anemia with ongoing blood loss, and intermittently abnormal findings on abdominal examination. He presented with gastrointestinal bleeding manifested by hematochezia and melena. My initial diagnostic considerations include causes of lower gastrointestinal bleeding, although the description of melena gives me reason to think that this patient could have bleeding from both upper and lower gastrointestinal sources. Less likely is an isolated, massive upper gastrointestinal bleed with rapid transit time through the infant's gastrointestinal tract.

STABILIZATION

The patient's airway was intact, and his breathing was unlabored. However, his circulation was compromised; he was pale and had tachycardia, and the hematocrit was 17.5% with ongoing blood loss. He required volume resuscitation with the administration of isotonic fluids and the transfusion of packed red cells, which was performed in the emergency department.

The patient was neurologically intact. A bedside glucose measurement may have been useful in determining whether poor feeding with resultant hypoglycemia contributed to his unwell appearance. The reported use of homeopathic and unspecified teething medications raises concerns about an unintentional toxic exposure. Could the teething tablets or medications have contained acetaminophen, which can cause an overdose that leads to liver failure and gastrointestinal bleeding, or nonsteroidal antiinflammatory drugs, which can cause irritation of the gastric mucosa and subsequent gastrointestinal bleeding? Although these exposures are unlikely underlying causes of this patient's illness, they warrant further consideration and, possibly, toxicologic testing.

DIAGNOSTIC EVALUATION

My diagnostic considerations fall into three broad categories: common, less common, and potentially life-threatening. Among the common diagnoses, ileocolic intussusception seems to be the most likely possibility; the patient presented at a typical age (since intussusception most commonly occurs during infancy or early childhood) and had colicky abdominal pain and worsening gastrointestinal bleeding, with stool described as resembling currant jelly. Meckel's diverticulum is the most common congenital malformation of the gastrointestinal tract, and if the diverticulum contains ectopic or heterotopic mucosa, it can cause gastrointestinal bleeding.^{1,2} Of the clinical findings associated with Meckel's diverticulum, bleeding is one of the most common in children.^{1,3,4} Since Meckel's diverticulum is classically associated with painless bleeding, this patient's apparent abdominal pain is difficult to reconcile with this diagnosis.^{5,6} However, if Meckel's diverticulum is associated with obstruction caused by intussusception, volvulus, or perforation, then pain can be a complicating feature.³ I would also consider an inflammatory or allergic gastritis or colitis, because these are common causes of lower gastrointestinal bleeding among children who present to the emergency department.⁷ The presence of mild gastritis plus colitis related to a milk-protein allergy could explain both the hematochezia and melena (mixed upper and lower gastrointestinal bleeding), as well as the associated pain. Infectious colitis seems unlikely, given the absence of fever, sick contacts, and travel. Other common causes of lower gastrointestinal bleeding, such as a fissure or polyp, are not typically associated with such a severe presentation, so these diagnoses are easily ruled out in this case.

In a 6-month-old infant, the less common diagnoses that cause lower gastrointestinal bleeding include vascular malformations of the gastrointestinal tract, atypical lymphonodular hyperpla-

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sia, the hemolytic–uremic syndrome, inflammatory bowel disease, toxin-mediated processes, and underlying bleeding diatheses. I would give these causes careful consideration only after the common diagnoses have been ruled out.

In this case, several diagnoses must be considered because they are potentially life-threatening if missed. These diagnoses can be consequences of either the common or the less common conditions and include a perforated viscus, an acute abdomen, obstruction, hemorrhagic shock, septic shock, and the presence of associated upper gastrointestinal bleeding while the patient is being evaluated for lower gastrointestinal bleeding. Serial physical examinations and diagnostic testing are critical in identifying any of these potentially life-threatening processes.

DIAGNOSTIC TESTING

The findings ascertained through diagnostic testing that are the most important in developing a differential diagnosis in this case are the hematocrit of 17.5%, the elevated white-cell count of 22,200 per cubic millimeter (which is nonspecific but worrisome), and the absence of intussusception and other notable findings on ultrasonography. The normal electrolyte levels, liver profile, and coagulation indexes are reassuring, and they argue against some systemic disease processes that would typically be associated with abnormalities in one or more of these measures. However, a few additional studies would help to narrow the differential diagnosis. Because of the possibility of a toxic exposure, I would perform a serum toxicology screen. In addition, I would perform blood and stool cultures to evaluate for infection, as well as abdominal radiography to assess for bowel perforation, given the multiple days of gastrointestinal symptoms and the worsening clinical appearance. To rule out upper gastrointestinal bleeding, I would consider performing gastric aspiration.

In view of the available test results, the absence of intussusception on abdominal ultrasonography, and the patient's ongoing blood loss, two diagnoses from my list of common diagnoses remain most likely: Meckel's diverticulum and gastritis plus allergic colitis. Many other diagnoses have been effectively ruled out through diagnostic testing, and several less common causes would not be seriously considered until these two common diagnoses are ruled out. In addition, I am worried about the possibility of potentially life-threatening hemorrhagic shock, given the patient's continued blood loss and profound anemia.

In the emergency department, emphasis is placed on providing the best possible systematic care during the period leading up to the diagnosis rather than conclusively determining the diagnosis; nevertheless, I think the diagnosis in this case is Meckel's diverticulum. In an infant who has massive lower gastrointestinal bleeding with resultant hemodynamic compromise and for whom intussusception has been ruled out on the basis of ultrasonographic findings, the most likely diagnosis is Meckel's diverticulum, and this possibility needs to be investigated before other diagnoses can be considered.⁷ The abdominal pain is one aspect of this patient's clinical presentation that does not totally fit with the diagnosis of Meckel's diverticulum, although an obstruction or perforation could introduce pain into the clinical picture. The description of melena is not consistent with Meckel's diverticulum but could be explained if the bleeding mucosa from the diverticulum was proximal enough for resultant blood to undergo partial digestion.6 It is also possible that the single stool described as melena was not truly melena but stool with darker or maroon blood that originated from a lower, rather than an upper, gastrointestinal source. Mixed gastritis and colitis is less likely than Meckel's diverticulum overall, and bleeding related to allergic gastrointestinal disease is unlikely to be as acute and severe as the bleeding seen in this case.⁸ In the emergency department, it is more straightforward to obtain a scan to assess for Meckel's diverticulum than to perform upper and lower endoscopy; the scan mandates coordination of fewer hospital resources, does not require the administration of anesthesia, and is noninvasive. If a scan were nondiagnostic, I would consider other studies, such as endoscopy or abdominal computed tomography.

Dr. Virginia M. Pierce (Pathology): Dr. Baldwin, what was your impression when you evaluated this patient?

Dr. Katherine R. Baldwin (Pediatric Gastroenterology): Our first step was to localize the source of blood loss. Melena is classically thought to reflect upper gastrointestinal bleeding (proximal to the ligament of Treitz), but it can also be

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caused by more distal lesions, such as lesions in the small bowel and right colon.⁹ We considered both upper gastrointestinal sources (including variceal bleeding, vascular malformations, and ulcer) and lower gastrointestinal sources (including colitis, Meckel's diverticulum, and vascular malformations). We thought that the subacute tempo of this patient's clinical presentation, the large volume of blood loss, and his age were most consistent with Meckel's diverticulum. Although Meckel's diverticulum is commonly thought to be a painless lesion, pain can result from intussusception (with the diverticulum serving as the lead point), intermittent volvulus around associated fibrous bands, or torsion.

We recommended that the patient undergo prompt evaluation by a pediatric surgeon and that a scan to assess for Meckel's diverticulum be obtained after the administration of a histamine H₂-receptor antagonist to help retain radiotracer in the gastric mucosa. We did not think that endoscopy would be immediately useful; although the performance of upper gastrointestinal endoscopy is standard for a large volume of blood loss because of the potential for diagnostic and therapeutic intervention, most causes of lower gastrointestinal bleeding do not require colonoscopy. Furthermore, colonoscopy in a patient with acute severe bleeding may be technically challenging because of difficulty with visualization.10

CLINICAL DIAGNOSIS

Gastrointestinal bleeding due to Meckel's diverticulum.

DR. LAUREN M. ALLISTER'S DIAGNOSIS

Gastrointestinal bleeding due to Meckel's diverticulum.

IMAGING STUDIES

Dr. Lim: After the patient received premedication with intravenous famotidine, a technetium-99m pertechnetate scan was obtained to assess for the presence of a Meckel's diverticulum. Immediately after the intravenous injection of 0.97 mCi of radiotracer, anterior planar imaging was performed continuously for 1 hour. Additional imag-

ing was performed in a lateral view. An abnormal focus of radiotracer accumulation was seen in the right paramedian region of the abdomen that gradually increased in intensity over time (Fig. 1); this finding is consistent with ectopic gastric mucosa in a Meckel's diverticulum.

Technetium-99m pertechnetate normally accumulates in any gastric mucosa, including ectopic gastric mucosa; therefore, this radiotracer is useful in the evaluation of a suspected Meckel's diverticulum. False positive scans can occur. Technetium-99m pertechnetate is excreted by the urinary system, and activity is normally seen in the bladder and kidneys. Radiotracer activity in the stomach can pass distally into the duodenum and small bowel. Premedication with a histamine H₂-receptor antagonist can reduce the release of radiotracer from the stomach. Bowel or urinary activity is suggested by movement of focal radiotracer activity over time, whereas focal accumulation in a Meckel's diverticulum should remain fixed in position. A lateral view of the abdomen can be helpful in distinguishing urinary activity in the ureters, which are located in a posterior position. A false positive scan can also result from inflammation, intussusception, bowel obstruction, or vascular lesions.

A false negative scan can result from the presence of too little or no gastric mucosa in a Meckel's diverticulum; approximately 20% of Meckel's diverticula do not contain gastric mucosa. Other causes of false negative scans include recent ingestion of barium or perchlorate, movement of the Meckel's diverticulum, and brisk gastrointestinal bleeding.¹¹

DISCUSSION OF MANAGEMENT

Dr. Allan M. Goldstein: As a result of the clinical presentation and the findings on the scan, the infant was brought to the operating room. A short transverse incision was made in the right lower quadrant, and the diverticulum was identified (Fig. 2). Inflammation and scarring were present at its base; these findings are consistent with ulceration in the small intestine, at its junction with the diverticulum. A segmental smallbowel resection, which included the diverticulum and the presumed area of ulceration, was performed, followed by a hand-sewn end-to-end anastomosis.

A variety of operations can be performed to

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Figure 1 (facing page). Technetium-99m Pertechnetate Scan of the Abdomen.

A technetium-99m pertechnetate scan of the abdomen was performed to assess for Meckel's diverticulum. Anterior planar images (Panel A), which were obtained continuously for 1 hour, show an abnormal focus of radiotracer accumulation in the right paramedian region of the abdomen that gradually increases in intensity over time (black arrow). Physiological radiotracer accumulation is present in the stomach (white arrow), bowel (arrowhead), and bladder (asterisk). Lateral planar images (Panel B) confirm that the abnormal focus of radiotracer accumulation (arrow) is in a location that is compatible with bowel activity and is not consistent with urinary activity, which would be more posterior.

treat a Meckel's diverticulum that causes gastrointestinal bleeding. These include simple diverticulectomy, wedge resection of the diverticulum and the small cuff of adjacent ileum at its base, and segmental small-bowel resection, which was done in this case. The primary cause of bleeding is the presence of acid-producing ectopic gastric mucosa in the diverticulum, which leads to the development of an ulcer in adjacent normal mucosa. The ulcer can be present in the diverticulum itself but is usually located at the junction of the diverticulum and the ileum,¹² as appeared to be the case in this patient. Although removing both the ectopic mucosa and the ulcer would seem to be the best approach, removing the ectopic mucosa alone may be sufficient, since the ulcer would probably then heal. However, it is essential to remove all ectopic gastric mucosa, which cannot be reliably detected from the outside. Therefore, a reasonable approach is to perform a simple diverticulectomy for a diverticulum with a narrow base but to perform a wedge or segmental resection for a diverticulum with a broad base, since ectopic tissue may be left behind if the diverticular base is not fully excised. If the area of ulceration is apparent, as in this case, then resecting it with the diverticulum is also reasonable.

An important scenario to consider is whether this patient would have received different treatment if the scan had been negative, which could have easily occurred, given the imperfect sensitivity of the test.^{13,14} Meckel's diverticulum needs to be included in the differential diagnosis for any child being evaluated for hematochezia. If a technetium-99m pertechnetate scan is negative



Figure 2. Intraoperative Photograph.

After a short transverse incision was made in the right lower quadrant, the diverticulum was identified. Inflammation and scarring are present at the base of the diverticulum; these findings are consistent with ulceration in the small intestine, at its junction with the diverticulum. Photograph courtesy of Dr. David Lawlor.

and other causes of bleeding have been ruled out, laparoscopy should be considered to assess for Meckel's diverticulum.

PATHOLOGICAL DISCUSSION

Dr. Jochen K. Lennerz: We received a segment of small bowel (1.7 cm by 1.5 cm by 1.5 cm) with an attached intact, blind-ending diverticulum (2.5 cm by 0.8 cm by 0.8 cm) for pathological examination. The serosa near the small intestine showed patchy fibrinous inflammation (Fig. 2) and was otherwise mildly hyperemic; the tip of the diverticulum had no attached bands. The sections showed an average wall thickness of 0.2 cm and normally folded mucosa with red discoloration toward the small bowel. In contrast to the mucosal herniation through the bowel wall that is present in diverticular disease, this diverticulum contained all three layers of bowel wall. Given the anatomical location of the diverticulum on the antimesenteric surface of the mid-ileum, these findings represent persistence of a proximal part of the vitelline duct (omphalomesenteric duct), or Meckel's diverticulum.

A histotopogram allowed us to perform a

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Figure 3. Histotopogram.

A histologic section of the diverticulum shows all three layers of bowel wall (Panel A); serosal fibrinous exudate is present (white arrow). The intestinal mucosa at the opening of the diverticulum shows mucosal erosion, acute inflammation, and underlying granulation tissue, findings consistent with an ulceration (Panel B). The gastric mucosa lines the entire diverticulum and is composed of surface foveolar cells, mucous neck cells, parietal cells, and basal chief cells (Panel C). The heterotopic gastric mucosa secretes hydro-chloric acid, which causes peptic ulceration in the adjacent intestinal mucosa (Panel A, black arrow).

histologic examination in the spatial context of the entire diverticulum (Fig. 3A). There were two key mucosal findings. First, the intestinal mucosa at the opening of the diverticulum showed epithelial erosion and underlying granulation tissue, findings consistent with mucosal ulceration (Fig. 3B). The acute inflammation extended through the muscularis propria and was associated with fibrinous serositis. Second, this diverticulum was remarkable because the mucosa of the entire diverticulum was made up of at least four distinct cell types: surface foveolar cells, mucous neck cells, parietal cells, and basal chief cells (Fig. 3C). This composition is diagnostic of a Meckel's diverticulum containing a large amount of terminally differentiated, heterotopic gastric mucosa of the body (fundic type). There was no evidence of heterotopic pancreatic tissue, dysplasia, or cancer.

It is unusual for a Meckel's diverticulum in a 6-month-old patient to be completely lined by gastric mucosa that is most likely secreting a large amount of acid into the small intestine. The mucin-secreting surface foveolar epithelial cells in this Meckel's diverticulum protected the underlying diverticular mucosa from the acid secreted by the underlying parietal cells. Thus, the pathophysiological cascade in this patient can be described as follows: the secreted, nonneutralized acid produced by the heterotopic gastric mucosa and the secreted chief-cell-derived enzymes in the diverticulum led to peptic ulceration in the adjacent intestinal mucosa, which caused gastrointestinal bleeding. The conversion of the hemoglobin in the gastrointestinal bleed into melena was presumably related to the large load of digestive chemicals secreted by the Meckel's diverticulum. The serosal fibrinous adhesions may have caused the pain.

Dr. Gupta: After surgery, the patient's course was briefly complicated by ileus, but by the third postoperative day, his diet was regular and he was discharged home. Nine days later, he was seen for follow-up by the pediatric surgeon and was doing well; he had no pain, hematochezia, or melena, and the abdominal examination was normal.

ANATOMICAL DIAGNOSIS

Meckel's diverticulum with heterotopic gastric mucosa and associated peptic ulceration in the intestinal mucosa.

This case was presented at Pediatric Grand Rounds.

Dr. Allister reports receiving consulting fees from Medscape Consult. 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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