The following fictional case is intended as a learning tool within the Pathology Competencies for Medical Education (PCME), a set of national standards for teaching pathology. These are divided into three basic competencies: Disease Mechanisms and Processes, Organ System Pathology, and Diagnostic Medicine and Therapeutic Pathology. For additional information, and a full list of learning objectives for all three competencies, see https://www.journals.elsevier.com/academic-pathology/news/pathology-competencies-for-medical-education-pcme.1

Keywords: Pathology competencies, Organ system pathology, Gastrointestinal tract, Mechanical disorders of bowel, Diverticulosis, Intestine, Gastrointestinal hemorrhage, Meckel diverticulum

Primary objective

Objective GT8.3: Diverticulosis. Describe the pathogenesis and complications of diverticulosis.

Competency 2: Organ System Pathology; Topic GT: Gastrointestinal tract; Learning Goal 8: Mechanical disorders of bowel

Patient presentation

A 60-year-old man visits his family medicine physician shortly after obtaining health insurance. He has not seen a primary care physician for the past 20 years. He expresses concerns regarding episodic hematochezia for the past year. He states that the episodes occur sporadically, often months apart without symptoms. He describes his stools as formed with swirls of frank blood in the toilet after bowel movements. He also reports intermittent nausea and constipation over the same period. He endorses a sedentary lifestyle and a low fiber diet. He reports no family history of colorectal cancer and has never had a screening colonoscopy. He does not take any medications including over the counter products, such as aspirin or nonsteroidal medications. He reports no fever, weight loss, abdominal pain, rectal pain, vomiting, or diarrhea.

Diagnostic findings, Part 1

The patient’s weight is 230 pounds and his height is 5 feet 7 inches. His body mass index (BMI) is 36 kg/m². On physical examination, his vital signs while seated are a blood pressure of 122/80 mmHg, heart rate of 86 beats per min, respiratory rate of 15 breaths per min, and an oxygen saturation of 99% on room air. The patient is afebrile with a temperature of 98.6 °F. Cardiac auscultation reveals a normal S1 and S2 and regular rate and rhythm without murmur or gallop. His lungs are clear on auscultation. The abdomen is soft and nontender with normal bowel sounds and no palpable masses. No hepatomegaly is palpated although this portion of the exam is limited by body habitus. Rectal exam reveals no masses or tenderness. Stool guaiac testing in of positive for occult blood.

Question/discussion points, Part 1

What are the causes of gastrointestinal bleeding?

Gastrointestinal (GI) bleeding has a broad differential diagnosis that consists of multiple pathologies within the GI tract. Bleeding can be classified by location broadly broken down into upper GI bleeding and lower GI bleeding. The upper GI tract encompasses the esophagus, stomach, and duodenum and the lower GI tract encompasses the jejunum, ileum, colon, and anorectal area. The ligament of Treitz, which suspends the junction of the duodenum and jejunum, is often used as a demarcation point between upper and lower GI structures. Pathologies affecting these areas include malignancy, inflammatory disorders, autoimmune conditions, mechanical disorders (intussusception), and vascular disease (Table 1).

Clinically, GI bleeding in stool presents in three forms, occult blood, melena, and hematochezia. Occult bleeding is defined as blood in the stool that is not readily visible. It is typically diagnosed with a positive fecal occult blood test that uses guaiac acid and hydrogen peroxide reagent to detect heme within stool. Occult bleeding is not a specific finding as it can occur at any point in the GI tract and can be caused by malignancy, infection,
bleeding allows time for gastric acid to convert hemoglobin to hematin, its appearance. Brisk GI bleeds typically result in hematemesis. Slower GI hematemesis, or granular dark vomit, known as coffee ground emesis due to and sporadic). Upper GI bleeding may also present in vomit as frank blood, intussusception, Meckel diverticulum, and juvenile polyps (both familial
atochezia relatively unique to the pediatric population include cerative colitis is most often associated with hematochezia and both

| Location     | Common conditions           | Bleeding presentation |
|--------------|-----------------------------|-----------------------|
| Upper GI     | Esophagus Esophagitis, Esophageal varices, Mallory-Weiss tear, Esophageal cancer | Melena, Occult bleeding, Hematemesis, Coffee ground emesis |
| Stomach      | Gastritis, Gastric ulcer, Gastric cancer | |
| Duodenum     | Duodenal ulcer, Arteriovenous malformation | |
| Lower GI     | Jejunum/Ileum Crohn disease, Meckel diverticulum | Hematochezia (with or without clots), Occult bleeding |
| Colon        | Ulcerative colitis, Crohn disease, Angiodysplasia, Diver ticulosis, Polyp, Colon cancer | |
| Anorectal    | Hemorrhoids, Anal fissure | Hematochezia |

Table 1
Sites of GI bleeding.

What is the differential diagnosis for hematochezia?

The differential diagnosis for hematochezia includes colorectal carcinoma, vascular disorders, anatomical disorders, anorectal disorders, and other abdominal disorders. One of the most serious causes of hematochezia in adults is colorectal cancer and this diagnosis must be considered when GI bleeding presents. Cancer may present insidiously with asymptomatic bleeding, vague symptoms such as fatigue, or weight loss. Colitis is an acute cause of hematochezia that often presents with abdominal pain among other symptoms. The three major etiologies of colitis are infectious, ischemic, and inflammatory. Differentiation between specific types of colitis is reliant on clinical context, colonoscopy findings, laboratory data, and histological findings. Relatively benign causes of hematochezia are hemorrhoids. Presentation of hemorrhoids is variable and largely dependent on location relative to the dentate line. Internal hemorrhoids proximal to the dentate line are typically less symptomatic due to visceral innervation and those distal typically cause pain and irritation due to somatic innervation. Causes of relatively asymptomatic gastrointestinal bleeding includes diverticulosis and angiodysplasia. Diverticulosis ranges widely in its presentation; often it is asymptomatic and found incidentally. Other common presentations include hematochezia, abdominal pain, constipation, or diarrhea. Angiodysplasia results from malformation of mucosal and submucosal vessels in the right colon. It is a less common diagnosis but is responsible for a significant portion of heavy GI bleeding. Other diagnoses to be considered are the inflammatory bowel diseases, Crohn disease, and ulcerative colitis. Ulcerative colitis is most often associated with hematochezia and both
diseases may present with greater symptoms such as abdominal pain, bloating, diarrhea, or fever.

Based on the clinical presentation, what diagnostic studies should be ordered?

Workup for this patient should include complete blood count, electrolytes, coagulation studies, and colonoscopy. A computed tomography scan would be ordered if diverticulitis is suspected.

![Fig. 1. Several diverticula (arrow) are present on colonoscopy.](image-url)
Diagnostic findings, Part 2

A CBC, C-reactive protein (CRP), electrolyte panel, and coagulation panel are ordered (Table 2).
A diagnostic colonoscopy is performed (Fig. 1).

Question/discussion points, Part 2

What is the interpretation of the laboratory results in Table 2?

The low Hb/Hct indicates that this patient is anemic. The anemia can be classified as microcytic based on the low MCV. This finding is consistent with iron deficiency anemia based on elevated RDW and decreased MCH and MCHC. Due to a normal white blood cell count (WBC) and CRP, infectious or inflammatory processes are unlikely. Electrolytes are within normal limits and coagulation studies do not indicate a coagulopathy.

Describe the colonoscopy findings in Fig. 1

Diagnostic colonoscopy shows multiple diverticula in the sigmoid colon. The background colonic mucosa shows normal vasculature pattern and is devoid of inflammatory changes. No polyps or mass lesions were seen. There were no internal hemorrhoids or anorectal disorders (The rectum and anus are not seen in Fig. 1 but were unremarkable.)

What is the final diagnosis?

Based on the colonoscopy, diverticulosis is the most likely cause for this patient’s clinical presentation.

Based on clinical presentation, colonoscopy and laboratory results, how should this patient be managed?

The patient should be instructed to switch to a high fiber diet or take fiber supplements to reduce symptoms and prevent complications, but the evidence supporting fiber has been found to be inconsistent and the data is controversial. Of note patients have previously been instructed to avoid foods, such as, popcorn, seeds, and nuts due to a theoretical risk of diverticular irritation and obstruction; however, there is no evidence to support this recommendation.

Fig. 2. Several diverticula (arrows) are present in this section of sigmoid colon. The arrows show where the mucosa and submucosa are herniated through the muscle layers.

Fig. 3. The large intestine gross image shows fecal debris trapped in a diverticulum (arrow).

Fig. 4. Two diverticula (*) extend through the muscularis externa toward the serosa. (H&E, low magnification).

Fig. 5. The colonic diverticulum contains only the mucosa and submucosal layers of the large intestine (arrow). There is no inflammation thus warranting the diagnosis of diverticulosis versus diverticulitis. (H&E, intermediate magnification).
Regarding the patient’s anemia, confirmatory testing for iron deficiency anemia would require measurement of serum iron, ferritin, and total iron-binding capacity (TIBC). Low levels of iron and ferritin would be expected while TIBC would be high. Management for this patient’s anemia would consist of oral iron supplementation. Cases of severe bleeding and symptoms such as light-headedness, shortness of breath, or fatigue with vital sign instability may require blood transfusion and surgery. The presence of significant abdominal pain and fever may indicate development of acute diverticulitis which is treated with antibiotics and surgery in severe cases.

Describe the findings seen in Figs. 2–4 from a resected colon from a patient with hematochezia

Gross Morphology: Several diverticula can be seen in areas where the mucosa and submucosa are herniated through the muscularis externa layer creating “pouches” (Fig. 2). Fecal debris can be seen trapped within diverticula (Fig. 3).

Histology: Herniation of the mucosal and submucosal layers through the muscularis externa layer to the serosa creating a diverticulum is seen (Figs. 4 and 5).

What is the pathophysiology of diverticulosis?

The exact pathophysiology of diverticulosis is currently unknown. Theories about genetics, gut motility, mechanical stress, and inflammation may all contribute to the development of a diverticulum within the colon. One leading theory implicates age related degeneration and weakening of the mucosal walls as a preceding event to diverticulosis. Weakness in the outer muscularis, alongside increased pressure within the colonic lumen, lead to diverticula formation at the insertion points of the vasa recta and nerves into the muscular layer. Neural degeneration of the gastric myenteric plexus may also contribute to the development of diverticula due to loss of gastric motility and subsequent increases in luminal pressure. Recent studies have also implicated inflammation as a factor influencing symptomatic presentation and complication of diverticular disease. Gross and microscopic inflammation is seen as a risk factor for recurrence of diverticulitis. Pro-inflammatory states, such as obesity, also pose increased risk for diverticular complications.

What are the complications of diverticulosis?

Diverticulosis is often asymptomatic, but due to its prevalence many patients experience complications that range in severity. One of the leading complications of diverticular disease is acute diverticulitis, inflammation of diverticula thought to be caused by micro-perforations and erosion of the bowel wall. Of those with diverticulitis, approximately 12% will develop further complications such as abscess, perforation, fistula, or obstruction. Abscess and perforation are associated with development of peritonitis with signs of acute abdomen on physical exam and associated with increased mortality. A study on older adults in the United Kingdom found that there was a 6-fold increase in risk of death for those with perforated diverticular disease compared to the general population. Uncomplicated diverticulitis is treated with oral or intravenous antibiotics depending on severity of infection. Peritonitis, colonic perforation, or recurrent episodes of diverticulitis may require surgery and resection of the affected area of colon. Diverticular bleeding is a common complication of diverticulosis, with or without diverticulitis. Severity of bleeding can range from painless hematochezia that spontaneously ceases to hemodynamic instability calling for immediate resuscitation and transfusion.
Compote diverticulosis with meckel diverticulum

Diverticulosis and Meckel diverticulum have numerous shared qualities as well as pertinent differences in pathophysiology and anatomy (Fig. 6). Diverticula are classified as “true” or “false” based on their anatomical make-up. False diverticula are created by the mucosa and submucosa layers of bowel protruding through weak points of the muscularis to create a pouch covered only by the external serosa; this is most commonly seen in diverticulosis.1,2 The true diverticulum seen in Meckel diverticulum is composed of the mucosa, submucosa, and muscularis externa layers of the bowel.1,3 As previously stated, false diverticula are thought to develop when pressure within the bowel lumen exceeds the strength of the muscular wall near the insertion of vasa recta. This most prominently affects the sigmoid colon of adults.5 Meckel diverticulum is a congenital abnormality that results from the incomplete obliteration of the omphalomesenteric (vitelline) duct in the small bowel.5,9,10 There are also differences in the patient population that each pathology affects. Because Meckel diverticulum is a congenital defect, its symptoms often present in children; however, it is possible for the condition to be asymptomatic until adulthood.5,6 Diverticulosis is much more prevalent in older age with an estimated half of the world population being affected by age 60 and even higher rates in industrialized countries including the United States.5,11 Most similarities between these disorders arise in symptomatic presentation. Both conditions are asymptomatic in many patients and are often found incidentally through imaging and screening colonoscopy. Symptomatic Meckel diverticulum may contain ectopic gastric or pancreatic tissue leading to abdominal pain (Fig. 7). Additionally, the complications associated with both conditions are similar, the most notable being bleeding and inflammation.

Teaching points

- The location of GI bleeding can be roughly differentiated based on visual characteristics of stool. Melena originates in upper GI structures while hematochezia originates in lower GI structures.
- Diverticulosis varies widely in presentation, from asymptomatic detection on imaging and screening colonoscopy to intrusive abdominal pain or GI bleeding and anemia.
- The pathophysiology of diverticulosis is uncertain. Mechanical stress, inflammation, and decreased gut motility are likely contributing factors to the development of diverticula.
- Complications of diverticulosis include bleeding, diverticulitis, abscess, perforation, fistula, and bowel obstruction.
- Diverticula found in diverticulosis are classified as “false diverticula” as they are made up of the mucosa and submucosal layers protruding through the muscularis of the bowel. This is in contrast to “true diverticula” which consist of mucosa, submucosa, and muscularis as seen in Meckel diverticulum.
- Diverticulosis is extremely common and prevalent in up to half of the population by the age of 60.
- The recommendation for first line treatment of uncomplicated diverticulosis is increased fiber intake, but evidence for this treatment is disputed. Patients do not need to remove food items that includes seeds or nuts from their diet.

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