A 54-year-old woman was transferred to our medical center with altered mental status, abdominal pain, and hypotension. Her medical history included type 2 diabetes mellitus, hypertension, hyperlipidemia, active tobacco use, prior cholecystectomy, and a recent stroke. One month earlier, she presented to an outside facility with right-sided facial weakness and numbness. Brain magnetic resonance imaging (MRI) at that time revealed multiple small lacunar-type infarcts. Computed tomography (CT) angiography of the head and neck, 48-hour Holter monitoring, and transesophageal echocardiography did not reveal an embolic source. She was discharged on aspirin and clopidogrel for secondary prevention.

On the current presentation, the patient had a syncopal episode with subsequent confusion, transient episodes of unresponsiveness, and garbled speech, prompting evaluation in her local emergency department. Initial vital signs were as follows: blood pressure, 70/50 mm Hg; heart rate, 108 beats/min; respiratory rate, 20 breaths/min; oxygen saturation, 95% on room air; and temperature, 36.3°C. Physical examination revealed tachycardia and clear lung fields, and her abdomen was soft and non-tender with normoactive bowel sounds. The patient was oriented only to person without focal neurologic deficits.

Initial laboratory studies were as follows (Mayo Clinic reference ranges for an adult woman are provided parenthetically): white blood cell count, 40.6 × 10⁹/L (3.4 to 9.6 × 10⁹/L); hematocrit, 48.7% (35.5% to 44.9%); platelets, 226 × 10⁹/L (157 to 371 × 10⁹/L); sodium, 127 mEq/L (135 to 145 mEq/L); creatinine, 1.35 mg/dL (0.59 to 1.04 mg/dL); blood urea nitrogen, 53 mg/dL (6 to 21 mg/dL); bicarbonate, 13 mmol/L (22 to 29 mmol/L); anion gap, 23 (7 to 15); glucose, 343 mg/dL (70 to 140 mg/dL); aspartate aminotransferase, 18 U/L (8 to 48 U/L); alanine aminotransferase, 16 U/L (7 to 45 U/L); total bilirubin, 0.5 mg/dL (≤1.2 mg/dL); lipase, 55 U/L (13 to 60 U/L); and lactate, 10.0 mmol/L (0.5 to 2.2 mmol/L).

Computed tomography of the head did not demonstrate acute hemorrhage or infarction. Brain MRI again demonstrated multiple foci of restricted diffusion, suggestive of multiple infarcts in an embolic distribution. Electrocardiography showed sinus tachycardia. She was subsequently transferred to our medical center for further management.

On arrival, the patient endorsed abdominal pain. Examination revealed diffuse tenderness to palpation without rebound or guarding and hypoactive bowel sounds.

1. Which one of the following is the most likely cause of this patient’s abdominal pain?
   a. Gastrointestinal perforation
   b. Pancreatitis
   c. Appendicitis
   d. Gastroenteritis
   e. Acute mesenteric ischemia

Gastrointestinal perforation is an important cause of diffuse abdominal pain. Classically, one would expect peritoneal signs in the acute setting because of intraperitoneal gastrointestinal contents causing peritoneal irritation. Our patient did not have peritoneal signs on examination.

Acute pancreatitis is manifested with abdominal pain, typically in the epigastric region. Diagnosis requires 2 of the following: epigastric abdominal pain, serum amylase or
lipase activity more than 3 times the upper limit of normal, and CT or MRI findings consistent with pancreatitis.\textsuperscript{1} By this criterion, our patient does not meet the diagnosis of acute pancreatitis.

Appendicitis is classically manifested with anorexia and central abdominal pain migrating to the right lower quadrant with localized tenderness in that region.\textsuperscript{2} Our patient’s history and examination findings make the diagnosis of appendicitis less likely.

Gastroenteritis is defined as diarrheal illness of rapid onset, often with associated abdominal pain, nausea, vomiting, or fever. Our patient did not have diarrhea or vomiting, making this diagnosis less likely.

Acute mesenteric ischemia is caused by insufficient blood flow to the mesenteric organs, most commonly due to arterial obstruction.\textsuperscript{3} Four distinct pathophysiologic mechanisms of acute mesenteric ischemia have been described: arterial embolism (50%), arterial thrombus (20%), nonocclusive pathologic processes (20%), and mesenteric venous thrombus (10%).\textsuperscript{4} Most cases of acute mesenteric ischemia are due to occlusion of the superior mesenteric artery (SMA); acute mesenteric ischemia due to occlusion of the inferior mesenteric artery (IMA) is less common. Patients may present with classic “pain out of proportion to examination” with severe abdominal pain despite a benign examination finding; many patients will have tenderness to palpation on examination, but peritoneal signs are not present initially. Patients typically have marked third spacing into the ischemic bowel, leading to fluid-responsive hypotension that may require substantial fluid resuscitation. Elevated serum lactate concentration can serve as an indicator of tissue (intestinal) hypoperfusion.\textsuperscript{5} In patients with a history of vascular disease or thromboembolism, presentation with acute abdominal pain should suggest the diagnosis of acute mesenteric ischemia. In our patient with abdominal pain of acute onset, evidence of embolic cerebrovascular disease, and marked elevation in serum lactate concentration, acute mesenteric ischemia is the most likely diagnosis.

Our patient was treated initially with intravenous fluid resuscitation and broad-spectrum antibiotics.

2. Which one of the patient’s laboratory values most bolsters the suggestion of acute mesenteric ischemia?
   a. Anion gap  
   b. White blood cell count  
   c. Hemoglobin  
   d. Creatinine  
   e. Lipase

Central to the pathophysiologic mechanism of acute mesenteric ischemia is the reduction in mesenteric blood flow and resultant tissue hypoperfusion.\textsuperscript{5} Necrotic cells of the gut release lactate dehydrogenase into the blood, although lactate dehydrogenase elevation can occur from lysis of other cells and is nonspecific. High levels of plasma lactate released as a result of loss of aerobic metabolism in ischemic tissues will produce an anion gap metabolic acidosis, as seen in our patient. A useful clinical guideline is that any patient with acute abdominal pain and metabolic acidosis has intestinal ischemia until proven otherwise, and a lactate level should be obtained for any patient with a significant anion gap acidosis.

Laboratory evaluation may also reveal marked leukocytosis, hemoconcentration (a rise in the hemoglobin and hematocrit values from baseline), and elevation in creatinine and blood urea nitrogen concentrations. However, these findings are nonspecific and may be seen in a variety of pathologic processes. Lipase is not typically elevated in cases of acute mesenteric ischemia.

Many laboratory studies are nonspecific, and although abnormal laboratory values may be helpful in bolstering suspicion for acute mesenteric ischemia, normal laboratory values do not exclude the diagnosis. For example, a normal or declining lactate level does not exclude the diagnosis of acute mesenteric ischemia as a complete lack of bowel perfusion can preclude the locally accumulated lactate from entering the systemic circulation.
Our patient’s laboratory findings of anion gap metabolic acidosis (lactic acidosis) in conjunction with her acute abdominal pain necessitate exclusion of intestinal ischemia.

3. Which one of the following tests would provide the highest diagnostic yield for this patient?
   a. Abdominal radiography
   b. Abdominal Doppler ultrasound
   c. Abdominal CT with intravenous contrast enhancement
   d. Abdominal CT without oral or intravenous contrast enhancement
   e. Abdominal CT with oral contrast enhancement

   Plain abdominal radiographs can be useful in cases of acute abdominal pain to rapidly identify intraperitoneal free air. However, in this patient with a nonfocal abdominal examination and absent peritoneal signs, this test would be of limited value in identifying the cause of her pain and is known to have limited sensitivity.

   Abdominal Doppler ultrasound can assess for compromise of intestinal blood flow. However, because of its dependance on both operator skill and patient factors, this imaging test is not typically used in initial evaluation of acutely ill patients with suspected intestinal ischemia.

   Computed tomography with intravenous administration of contrast material is a preferred imaging technique in the evaluation of patients with abdominal pain of unclear etiology because it has high sensitivity, can be performed quickly, and is less dependent than other imaging modalities on operator skill and patient factors. Contrast-enhanced CT can assess nonvascular findings and also affords exquisite visualization of the bowel, which is useful to detect abnormalities consistent with ischemia or infarct. Specific CT imaging findings that suggest acute mesenteric ischemia include absence of wall enhancement, indicating cessation of arterial flow; paper-thin wall caused by volume loss of the tissues and vessels; and pneumatosis, portomesenteric venous gas, and free peritoneal gas, indicating a transmural infarction.

   Most imaging signs of bowel ischemia, such as vascular filling defects and decreased bowel wall enhancement, rely on intravenous administration of contrast material for visualization. Thus, a CT examination without oral or intravenous contrast enhancement and CT performed with oral administration of contrast material have reduced sensitivity and are of limited utility when bowel ischemia must be excluded.

   Our patient underwent a CT examination of the abdomen and pelvis without oral or intravenous administration of contrast material at the outside facility, which showed no acute intra-abdominal findings. Repeated CT of the abdomen and pelvis with intravenous contrast enhancement was obtained on transfer. This revealed an acute occlusion of the SMA and IMA with significantly decreased distal flow and resultant diffusely hypoperfused small and large bowel with ischemic changes.

4. Which one of the following interventions should be performed next in the management of this patient’s condition?
   a. Emergent laparotomy
   b. Catheter-based mesenteric thrombectomy
   c. CT angiography
   d. Thrombolysis with tissue plasminogen activator (alteplase)
   e. Supportive management alone

   Immediate laparotomy is indicated for patients with acute mesenteric ischemia and clinical symptoms or signs of advanced ischemia (eg, peritonitis, sepsis, radiographic features of advanced ischemia). Our patient’s radiologic features of advanced bowel ischemia (acute SMA and IMA occlusion with resultant ischemic changes throughout the bowel) and septic shock necessitate emergent laparotomy.

   Catheter-based arteriography and endovascular treatment can be considered only for patients with acute mesenteric ischemia who are hemodynamically stable and who do not have clinical or imaging signs of
advanced ischemia. Thus, this intervention would not be appropriate for our patient.

Computed tomography angiography (as opposed to standard CT with intravenous administration of contrast material) has 95% to 100% accuracy and is considered the “gold standard” imaging modality for the diagnosis of visceral ischemic syndromes. Our patient’s CT imaging provided sufficient diagnostic information, and pursuing additional diagnostic testing would only delay critical therapeutic intervention.

Whereas catheter-directed thrombolysis can be considered in cases of incomplete percutaneous embolectomy or distal mesenteric embolization in patients without signs of advanced ischemia, thrombolysis with alteplase alone is not indicated for acute mesenteric ischemia.

Supportive management, including aggressive fluid resuscitation, broad-spectrum antibiotics, and immediate initiation of intravenous heparin, is important but does not address the underlying cause or provide definitive treatment. Therefore, supportive management alone is insufficient.

Our patient went for emergent laparotomy. Extensive ischemia of the entire small bowel, cecum, and ascending and transverse colon was identified.

5. Which one of the following is true of this patient’s prognosis?
   a. Time to diagnosis does not influence survival
   b. Mortality rate is high
   c. An arterial cause confers a better prognosis
   d. Perioperative mortality remains low
   e. Risk of rethrombosis is low

Time to diagnosis and treatment is paramount to survival for patients with acute mesenteric ischemia. Mortality remains high, with rates exceeding 60% despite aggressive treatment, regardless of approach. Patients with an arterial cause of acute mesenteric ischemia have worse survival compared with those with a venous cause. In cases of successful surgical revascularization, perioperative mortality remains high. For those patients who do survive, the risk of recurrent thrombosis is high.

Unfortunately, the extent of ischemic bowel changes seen intraoperatively in our patient was not amenable to repair or resection, and her condition was not compatible with survival. Therefore, the surgical team proceeded with abdominal closure without intervention. The patient transitioned to comfort care and died peacefully.

DISCUSSION

Although acute mesenteric ischemia remains one of the less common life-threatening causes of abdominal pain, its nonspecific signs and the gravity of a missed or delayed diagnosis make it one of the most important differential diagnoses to consider in the acute care setting.

A high index of suspicion based on the patient’s history and physical examination findings is essential for timely diagnosis and treatment. Clinicians should assess the patient’s medical history for evidence of vascular disease or diagnoses predisposing to thromboembolic disease (eg, atrial fibrillation). More than 70% of persons with acute mesenteric ischemia are female, which contrasts with other vascular disorders. The classically described pain out of proportion to physical examination findings is present in one-third to one-half of patients; although this should raise clinical suspicion, its absence should not exclude the diagnosis. Patients often have tenderness to palpation, bowel emptying, nausea, and vomiting. Clinical sepsis, fluid-responsive hypotension or shock, and mottled skin may be present in advanced cases.

Laboratory investigation may show marked leukocytosis, elevated hematocrit (hemoconcentration), and metabolic (anion gap/lactic) acidosis. Computed tomography angiography is the gold standard imaging modality for the diagnosis of mesenteric ischemic syndromes.

Fluid resuscitation, broad-spectrum antibiotics, and initiation of heparin infusion are critical first steps. However, these interventions should not delay time to revascularization. The treatment of choice for arterial
embolism or other causes with signs of advanced ischemia is open surgical therapy to revascularize the occluded vessel, to assess the viability of the bowel, and to resect the necrotic bowel. Endovascular revascularization techniques are becoming more common for patients without advanced bowel ischemia, but these approaches remain controversial.\(^3,4\) Regardless of treatment approach, mortality among patients with this condition is 60% to 80%, emphasizing the need for early diagnosis and emergent intervention.\(^3\) Clinicians should always maintain a high index of suspicion for acute mesenteric ischemia in critically ill patients with abdominal pain, particularly in the absence of another explanation or in the presence of warning signs such as marked anion gap/lactic metabolic acidosis, to ensure a timely and potentially lifesaving diagnosis.

**POTENTIAL COMPETING INTERESTS**
The authors report no competing interests.

**Correspondence.** Address to Jacob C. Jentzer, MD, Department of Cardiovascular Medicine, Mayo Clinic, 200 First St SW, Rochester, MN 55905 (jentzer.jacob@mayo.edu).

**ORCID**
Caroline L. Matchett. [https://orcid.org/0000-0003-0663-826X](https://orcid.org/0000-0003-0663-826X)

**REFERENCES**

**CORRECT ANSWERS:** 1. e. 2. a. 3. c. 4. a. 5. b.