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Delayed Diagnosis of Mesenteric Ischemia

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Patrick Romano, MD; MPH, Debra Bakerjian, PhD, APRN, RN; Garth Utter, MD, MSc; Anamaria Robles, MD; Ulfat Shaikh, MD for this Spotlight Case and Commentary have disclosed no relevant financial relationships with commercial interests related to this CME activity.

Learning Objectives

At the conclusion of this educational activity, participants should be able to:

- Describe the symptoms, physical examination findings, and laboratory findings of mesenteric ischemia
- List the three major causes/mechanisms of intestinal ischemia, and risk factors for each cause/mechanism
- Explain how the differential diagnosis and work-up of acute abdominal pain differs between people assigned male at birth and people assigned female at birth
- Identify several prevention strategies to mitigate diagnostic error that address systems causes and individual cognitive root causes

The Case

A 49-year-old married mother of two children saw her primary care physician (PCP) for recurrent bouts of post-prandial abdominal pain, occasional vomiting, and diarrhea. She was referred to a gastroenterologist who ordered an upper gastrointestinal (GI) series of x-rays and performed both esophagogastroduodenoscopy (EGD) and colonoscopy. All three studies were interpreted as normal, and the patient was reassured that her symptoms should abate. (Note: subsequent medicolegal review by experts revealed that there were scattered petechial hemorrhages and mucosal thickening on both the EGD and colonoscopy.)

The patient's pain continued, sometimes leaving her writhing on the floor, and was unrelieved by opioids. Her weight decreased from 100 pounds to 65 pounds. She was seen by her PCP three times over the subsequent six months, each time following an Emergency Department (ED) visit every 6-8 weeks. At each ED visit, routine laboratory tests, including a complete blood count, liver function tests, urinalysis, and amylase and lipase, were normal. No imaging was performed. Finally, another gastroenterologist covering for the patient's primary gastroenterologist suggested the diagnosis of intestinal ischemia to the patient, his colleague (the primary gastroenterologist), the patient's PCP, and her endocrinologist. None of these physicians followed up on the possibility of mesenteric ischemia, reportedly because they felt it was too unlikely to pursue.

On another ED visit, the covering gastroenterologist consulted a surgeon, and a mesenteric angiogram was performed. The diagnosis of mesenteric ischemia was confirmed, but the intestines were now almost entirely gangrenous. The patient underwent near-total intestinal resection, developed post-operative infections requiring additional operations, experienced cachexia despite parenteral nutrition, and died of sepsis 3 months later.

The Commentary

By Anamaria Robles, MD, and Garth Utter, MD, MSc

Background: Mesenteric Ischemia

Mesenteric ischemia occurs when there is reduced blood flow to the small or large intestines from multiple potential etiologies involving interruptions of either the arterial or venous systems. This condition is classified by the time to onset of symptoms (acute vs chronic), the affected portion of bowel (small intestine vs colon) and the degree of ischemic compromise (occlusive vs nonocclusive). This disease can result from several different pathophysiological processes, be challenging to diagnose, and have high morbidity and mortality if unrecognized, particularly in the acute setting.

Acute mesenteric, or intestinal, ischemia occurs when perfusion abruptly decreases, with or without vascular occlusion. In general, the intestines are protected by an extensive collateral vasculature; as such, an ischemic insult develops when there is inadequate flow through either direct or collateral vessels.[1] A sudden occlusive arterial obstruction is often due to thromboembolism—frequently from a cardiac source—that blocks the superior mesenteric artery (SMA), but it can also occur from thrombosis of an atherosclerotic plaque of the SMA. Nonocclusive mesenteric ischemia is the result of a "low flow state" often due to vasoconstriction in the setting of hypovolemia, vasopressor use, or poor cardiac output.

Obstruction of the venous mesenteric outflow occurs as a result of venous thrombosis of the superior (SMV) or inferior mesenteric veins (IMV). Lastly, chronic mesenteric ischemia most often arises in the setting of atherosclerosis of at least two of the three main visceral arteries (celiac artery, SMA, and inferior mesenteric artery) and is associated with insufficient mesenteric perfusion after meals and oral intake. The pain is thought to be due to an inability to meet the increased blood flow demands of the postprandial intestines.

The frequency of these major causes of mesenteric ischemia among all patients is estimated as: 50% mesenteric arterial embolism, 15-25% mesenteric arterial thrombosis, 5% mesenteric venous thrombosis, and 20-30% nonocclusive mesenteric ischemia.[2] Risk factors for developing mesenteric ischemia vary by etiology but include any process that results in mesenteric hypoperfusion or increases the likelihood of intestinal embolism, thrombosis, or vasoconstriction. Most arterial emboli are cardiac in origin – risk factors include severe cardiac disease such as arrythmias or valve dysfunction. Acute arterial thrombosis is most common in patients with a history of chronic mesenteric ischemia due to atherosclerosis and peripheral artery disease.[3,4] Risk factors for venous thrombosis include infection, inflammation, and hypercoagulable states. Finally, nonocclusive ischemia can result from hypovolemia, poor cardiac function, and vasoconstrictive medications including vasopressors and illicit drug use[5] leading to relative hypoperfusion.

Given the potential for devastating outcomes when not diagnosed in a timely fashion, as in the presented case, mesenteric ischemia is an important diagnosis to consider in all patients with severe abdominal pain. Its chronic form most commonly affects women; more than 70% of patients with this disease are female.[6] The most common universal presenting symptom is abdominal pain; for acute ischemia this is classically described as “pain out of proportion to exam” with an abdominal bruit on auscultation,[7] although this is not present in all patients. In patients with acute abdominal pain, it is important to assess for atherosclerotic risk factors and arrythmias, potential sources of embolus, and/or hypoperfusion, as this would increase clinical suspicion for this disorder.[8] Accompanying symptoms include nausea and vomiting. Patients with chronic mesenteric ischemia complain of recurrent episodic post-prandial abdominal pain (“intestinal angina”) and often develop “food fear” with an associated significant weight loss.[8] Symptoms of weight loss and dietary changes in the setting of atherosclerosis should increase suspicion for chronic mesenteric ischemia until proven otherwise.

Physical exam and laboratory studies can be relatively unrevealing early in the disease process, until frank bowel ischemia progresses to intestinal infarction and acute abdominal pain develops. There are no laboratory studies that are sufficient or accurate enough to diagnose bowel ischemia or infarction, although elevated lactate or d-dimer levels might be helpful.[9] Once bowel ischemia has developed, one would expect worsening markers of infection and end-organ perfusion, including leukocytosis and lactic acidosis. However, these are late findings, and lactate levels are insensitive because they can be completely normal if the ischemic tissue has no ongoing blood flow. A definitive diagnosis for acute ischemia requires either exploration in the operating room or, more commonly, computed tomographic (CT) angiography of the abdomen to evaluate the mesenteric vessels and bowel viability.[10] In the setting of chronic mesenteric ischemia, abdominal duplex ultrasound of the mesenteric vasculature can be used for monitoring and surveillance.

Once diagnosed, initial management consists of fluid resuscitation, broad spectrum antibiotics, anticoagulation in most cases, and urgent surgical consultation to General Surgery and Vascular Surgery for abdominal exploration.[9] Surgery includes prompt laparotomy to establish mesenteric blood supply via either open or endovascular techniques and assessment of bowel viability with resection of non-viable bowel. Damage control surgery is commonly performed with planned repeat laparotomy to reassess bowel viability in most patients. Outcomes of this disease process depend on the etiology, with higher mortality in arterial (50-70%) compared to venous ischemia (30%).[11] Unfortunately, mortality rates exceed 60% in acute mesenteric ischemia[4] and these high mortality rates have been unchanged in recent series.[12]

Importance of Keeping a Broad Differential Diagnosis

In addition to mesenteric ischemia, there are other important diagnoses that do not appear to have been given sufficient consideration in this case. For her workup, this patient underwent an upper GI series, EGD, and colonoscopy that did not elucidate the cause of her symptoms. The finding of mucosal petechiae is nonspecific and could have been due to multiple causes of inflammation or infection, although it is an abnormal finding that should have prompted further imaging workup and evaluation.

Cross-sectional imaging, usually in the form of an abdominal CT scan, can be very helpful to evaluate for structural causes of diffuse abdominal pain, such as hollow viscous perforation, obstruction, or mass. With post-prandial abdominal pain, it is important to consider a pancreatic or biliary etiology such as recurrent cholecystitis and/or pancreatitis, and an abdominal ultrasound can be helpful in this setting to evaluate for cholelithiasis. It is also important to consider a pelvic etiology in female patients including genitourinary and gynecologic disease processes; all female patients of childbearing age should have a pregnancy test, and pelvic ultrasound can be helpful in evaluation. Extraintestinal causes of diffuse abdominal pain are also important to consider and can include cardiac disease, diabetic ketoacidosis, adrenal insufficiency, lead poisoning, and electrolyte derangements such as hypercalcemia. As such, mesenteric ischemia is one of several potentially life-threatening diagnoses that were not considered in this case.

Identifying Risks to Patient Safety

The PCP, gastroenterologist, and endocrinologist did not fully consider their patient's symptoms or the recommendations of the one gastroenterologist who included the correct diagnosis in their differential. The history of severe post-prandial pain is a concerning symptom for mesenteric ischemia, especially when accompanied by vomiting, diarrhea, and weight loss. An earlier mesenteric angiogram likely would have saved this patient’s life. Being overconfident, anchoring to an initial diagnosis, allowing negative tests to confirm one's opinions, and failing to re-assess one's impression in the face of worsening symptoms can have devastating consequences. Humbly listening to one's patients and colleagues is a necessary and valuable skill, but sometimes one that is hard to maintain in practice.

Nature of Diagnostic Errors

Diagnostic errors in healthcare are thought to be a widespread, but difficult to quantify, cause of medical error. In 2015, the National Academy of Medicine released “Improving Diagnosis in Health Care”, the report describing diagnostic error as a “blind spot in health care”, suggesting that most Americans will have

suffered a delayed or missed diagnosis at some point during their lifetimes.[13] It is estimated that diagnostic errors are responsible for 40,000-80,000 deaths yearly in U.S. hospitals[14] and impact almost 12 million individuals yearly;[15] moreover, these errors are leading contributors of significant preventable harm, morbidity, and mortality.

In its report, the National Academy of Medicine defines diagnostic errors as “the failure to (a) establish an accurate and timely explanation of the patient’s health problem(s) or (b) communicate that explanation to the patient”.[13] Based on a wide-ranging review of studies, the rate of diagnostic error in clinical medicine is thought to be approximately 15%,[16] although this varies significantly by specialty and practice setting.[17] Diagnostic errors have been historically underappreciated for many reasons – the data are limited, there are few reliable methods by which to quantify and measure these errors, and they are often only appreciated in retrospect, if at all. However, as in our presented case, inaccurate or delayed diagnoses can have catastrophic consequences for all involved.

Causes of Diagnostic Errors

Although the root causes of diagnostic errors have not been fully elucidated, research in the field suggests that both the individual clinician’s cognitive processes and system-related factors are responsible for most errors.[18] The most common cognitive problems in diagnosis were the result of faulty information synthesis, with the single most common cause due to premature closure, namely the failure to continue considering alternatives after reaching an initial diagnosis. Other cognitive processes found to lead to diagnostic error included faulty data gathering such as incomplete history or physical exam, lack of considering the correct diagnosis, and a heuristic bias towards a single explanation.[18] Importantly, relatively few errors were found to be the result of faulty or inadequate knowledge. The most common system-related problems were due to poor policies, processes, procedures, teamwork, and communication. Most notably, many diagnostic errors studied were the result of both system and cognitive problems occurring in the same case, and they likely both directly and indirectly contribute to one another, compounding the errors.

Moreover, subsequent study has demonstrated that physicians tend to underappreciate the likelihood of incorrect diagnosis, and that physician overconfidence is a major contributor to cognitive and system-related sources of diagnostic error.[17] This physician overconfidence stems from complex interrelated factors, including physician attitudes of complacency, failure to effectively utilize supportive decision-making resources, and cognitive errors, as above. Compounding the problem of overconfidence is lack of adequate feedback when errors are made, with physicians unaware of the frequency with which diagnostic errors are made.[17]

Systems Change Needed/Quality Improvement Approach

In our presented case, both cognitive and system-related causes are implicated; chiefly, the synthesis error of premature closure and overconfidence appears to have led to an inability to consider additional reasonable possible diagnoses in the face of worsening symptoms and clinical decompensation. In this case, an incomplete diagnostic workup failed to identify the source of the patient’s abdominal pain in a timely fashion. Moreover, when the consulting gastroenterologist suggested the possibility of what ultimately was the correct diagnosis, there was a failure of effective communication, teamwork, and

consideration by the associated providers. All in all, both system and cognitive causes of diagnostic error led to the tragic outcome presented.

As described by Graber and colleagues, prevention strategies to mitigate diagnostic error should address both the systems and individual cognitive root causes.[18] Firstly, better methodologies to quantify diagnostic errors need to be identified. System-related factors can be addressed on an institutional level through increased emphasis and training focused on improving teamwork, communication, and clinical reasoning. For providers, the healthcare system should better support the diagnostic process, with improved feedback via error reporting systems and health information technology reforms. For instance, investment in enhancements of the electronic medical record could assist in improving physician diagnostic processes and feedback.[19] Approaches to improve the cognitive aspect of diagnostic errors are more much challenging; some studies suggest that educating providers about errors of clinical reasoning and awareness of one's own cognitive processes ("metacognition") may be beneficial.[18] Additionally, the development of a robust patient review process that prioritizes critical discussion and feedback on diagnostic accuracy has shown improvements in provider learning and patient safety.[20]

Take Home Points

- Mesenteric ischemia is an uncommon but potentially life-threatening cause of abdominal pain that should be considered particularly in patients with either acute abdominal pain or weight loss, dietary changes, and recurrent episodic postprandial pain.
- Early diagnosis is critical in mesenteric ischemia and requires a mesenteric angiogram, usually by CT.
- Diagnostic errors are an underappreciated source of medical error and are thought to result from both poor health system coordination and physician cognitive errors.
- It is critical for providers to be aware of the potential and likelihood of diagnostic error.
- Creating a robust differential diagnosis, iteratively reassessing one's clinical reasoning, and humbly consulting one's colleagues, particularly in the setting of diagnostic uncertainty or worsening symptoms, are important steps to mitigate the potential for diagnostic error.

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