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Mesenteric ischemia: Recognizing an uncommon disorder and distinguishing among its causes

ABSTRACT

Mesenteric ischemia occurs because of inadequate intestinal blood flow. Its severity depends on the vessels involved and whether collateral blood vessels are available to prevent malperfusion. Mesenteric ischemia is an uncommon cause of abdominal pain, but it is associated with high mortality and often poses a diagnostic challenge to clinicians because its symptoms are nonspecific. Early recognition and treatment are imperative to improve patient outcomes.

KEY POINTS

Mesenteric ischemia is classified into acute or chronic subtypes according to the timing of vessel occlusion and onset of symptoms.

Diagnosis requires a high index of suspicion with focused evaluation.

Early recognition and intervention are key to preventing morbidity and mortality.

MESENTERIC ISCHEMIA is an uncommon cause of abdominal pain that occurs from inadequate intestinal blood flow. It is associated with high mortality owing to the challenge of diagnosis. Mesenteric ischemia is classified as acute or chronic based on the timing of vessel occlusion and onset of symptoms. Early recognition and treatment are imperative to improve patient outcomes. This article reviews key features of common and uncommon causes of mesenteric ischemia.

■ MESENTERIC CIRCULATION

The mesenteric circulation is a complex vascular network supplied by 3 primary vessels: the celiac artery, superior mesenteric artery (SMA), and inferior mesenteric artery. The celiac artery perfuses the gastric, splenic, and hepatic organs, as well as the intestines through the gastroduodenal artery; the SMA supplies the midgut organs from the duodenal papillae to the proximal two-thirds of the colon; and the inferior mesenteric artery perfuses the distal one-third of the transverse colon, descending colon, and proximal two-thirds of the rectum. The celiac artery and SMA are primarily connected through the pancreaticoduodenal arcades, and the SMA and inferior mesenteric artery are connected by the marginal artery of Drummond and the arc of Riolan. Such collateral pathways ensure that the intestines are protected from transient periods of malperfusion.

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TABLE 1
Causes and clinical features of acute mesenteric ischemia

Cause	Incidence (%)	Clinical features	Risk factors
Arterial embolism	49	Acute, severe abdominal pain Peritonitis Bloody bowel movements	Atrial fibrillation Left ventricular dysfunction Aortic atherosclerosis Endocarditis
Arterial thrombosis	29	Postprandial pain Weight loss Food aversion	Atherosclerosis (acute-on-chronic mesenteric ischemia) Abdominal trauma Dissection Vasculitis
Nonocclusive mesenteric ischemia	20	Peritonitis Sepsis	Critical illness Vasoconstrictive medications
Venous thrombosis	10	Vague, colicky abdominal pain	Surgery Inflammatory bowel disease Cirrhosis Sepsis Malignancy Hypercoagulability

Based on information from references 6 and 8.

TYPES OF MESENTERIC ISCHEMIA

Mesenteric ischemia can be classified as acute or chronic according to the timing of blood flow compromise and symptom onset. Acute mesenteric ischemia is a potentially fatal vascular emergency characterized by sudden intestinal hypoperfusion after abrupt obstruction of arterial or venous blood flow.¹ Symptoms of acute mesenteric ischemia are typically profound owing to a lack of available collateral blood vessels. Chronic mesenteric ischemia refers to episodic intestinal hypoperfusion caused by multivessel stenosis or occlusion, usually due to atherosclerosis. Symptomatic patients typically present with abdominal angina, characterized by postprandial pain, weight loss, and food aversion.²⁻⁴

ACUTE MESENTERIC ISCHEMIA: CLINICAL RECOGNITION

Acute mesenteric ischemia is uncommon, accounting for less than 1.5% of all emergency department visits for abdominal pain, but its overall mortality exceeds 60%, owing to complications of intestinal infarction and sepsis.⁵⁻⁷ Clinical presentation varies depending on the underlying pathologic process (Table 1).^{6,8} The classic clinical presentation involves severe abdominal pain that is “out of proportion” to the physical examination.⁷ However, patients may present with atypical

symptoms such as nausea, vomiting, and diarrhea, or complications such as peritonitis or sepsis, which often contribute to diagnostic delay.^{6,7}

The nonspecific nature of symptoms makes it difficult to differentiate acute mesenteric ischemia from other intra-abdominal pathologies such as acute cholecystitis, pancreatitis, and small-bowel obstruction. A high index of suspicion is critical to making the diagnosis and restoring blood flow, thereby improving patient outcomes. Morbidity depends on how long the vessel has been occluded and whether collateral circulation is present. Patients who present with sepsis are more likely to have poorer outcomes.⁷

CAUSES OF ACUTE MESENTERIC ISCHEMIA

Mesenteric arterial occlusion from embolism or thrombosis is the most common cause of acute mesenteric ischemia (49% and 29%, respectively), followed by nonocclusive mesenteric ischemia (20%–22%) from splanchnic hypoperfusion and vasoconstriction and venous thrombosis (10%).^{6,8}

Arterial embolism

Acute arterial embolism causing partial or complete occlusion of the vessel lumen accounts for most (49%) cases of acute mesenteric ischemia.⁸ The SMA is often affected owing to its large diameter and oblique take-off

angle, with most emboli lodging distal to the origin of the middle colic artery.^{9,10} Most emboli originate from an intracardiac source of thrombus, such as the left atrium in atrial tachyarrhythmia or left ventricle in cardiomyopathy or myocardial ischemia.^{11,12} Less commonly, atheroembolism or thromboembolism originates from a proximal aortic segment.¹³ Rarely, mesenteric artery embolism has been described as a sequela of infective or nonbacterial thrombotic endocarditis.^{14,15}

The symptoms of embolic mesenteric artery occlusion are usually acute and dramatic because of a lack of collateral blood vessels. The typical patient is older, and women are more likely to be affected.⁹ Abdominal pain is the predominant symptom in 50% to 80% of patients and may be poorly localized.¹⁶ Nausea, vomiting, or diarrhea are observed in approximately 50% of patients.¹⁶ As bowel infarction develops, signs of peritonitis such as abdominal rebound and guarding may be seen on examination. Bloody bowel movements are uncommon until advanced stages of ischemia, and only one-third of patients present with the classic triad of abdominal pain, fever, and bloody stools.² Clinicians should be aware of more atypical presentations, such as mental status change in patients age 65 or older.¹⁷

Risk factors that should raise suspicion for acute arterial occlusion include history of cardiac arrhythmia, valvular disease, recent myocardial infarction, or aortic atherosclerosis. Roughly one-third of patients report a prior embolic event, and approximately 50% have a history of atrial fibrillation.⁷

Computed tomography angiography is 82% to 96% sensitive and 94% specific in the diagnosis of acute mesenteric ischemia and can additionally indicate a proximal source of embolus.^{12,18} Evaluation of these patients should also include prompt echocardiography. Select patients may benefit from ambulatory cardiac monitoring at a later time.

Arterial thrombosis

Mesenteric artery thrombosis accounts for 25% to 30% of acute mesenteric ischemia events.⁶ A majority occur at the origin of the SMA or celiac arteries in patients with preexisting atherosclerotic disease.

Acute thrombosis of a stenotic vessel results in symptoms like those of acute mesenteric embolism, also referred to as acute-on-chronic mesenteric ischemia.¹⁹ In some cases, however, progression from stenosis to occlusion and bowel infarction may be insidious owing to the ability of extensive collaterals to maintain gut viability.²⁰ This often leads to delays in seeking medical care. Many patients report prodromal symptoms of postprandial pain, weight loss, or food aversion suggestive of

chronic mesenteric ischemia.¹⁹ Acute abdominal pain in a patient who has a history of such symptoms should raise suspicion for acute mesenteric artery thrombosis.

Less commonly, mesenteric artery thrombosis may occur from vessel injury following abdominal trauma or dissection or an underlying hypercoagulable state from infection or malignancy.²¹ Hereditary or acquired thrombophilia are rare causes of mesenteric artery thrombosis. Vasculitis, typically of small to medium vessels, can infrequently result in acute mesenteric ischemia by way of arterial occlusion or vasospasm.^{22,23}

Nonocclusive ischemia

Nonocclusive mesenteric ischemia accounts for approximately 20% of acute mesenteric ischemia cases and has an in-hospital mortality of up to 50%.^{6,9,24} This form of mesenteric ischemia occurs in the setting of low blood flow states, such as low cardiac output, hypovolemia, or septic shock, leading to splanchnic arterial vasoconstriction, intestinal hypoxia, and necrosis.²⁵ The extent of ischemic injury is dependent on the number of vessels affected, collateral circulation available, and duration of hypoperfusion.

Nonocclusive mesenteric ischemia is typically seen in patients with severe preexisting disease such as heart failure, aortic insufficiency, and renal impairment, or in patients who are critically ill and receiving vasoconstrictive medications.²⁵ Symptoms may be absent, as these patients are usually intubated and sedated, and diagnosis is often further delayed by other overshadowing conditions such as hypovolemia and hypotension. As a result, the diagnosis may not be established until complications such as peritonitis or sepsis have developed.²⁶ Unexplained clinical deterioration with biomarkers of tissue ischemia should raise suspicion for nonocclusive mesenteric ischemia.²⁷ Computed tomography angiography is used for initial screening and to exclude other causes of acute mesenteric ischemia, and the diagnosis is confirmed on catheter-directed angiography or surgical exploration.²⁸

Treatment is focused on hemodynamic support and correcting the underlying cause. Transcatheter infusion of vasodilators such as papaverine and nitroglycerin may be used to relieve mesenteric vasoconstriction in cases where bowel necrosis has not occurred, and laparotomy is indicated when acute peritoneal signs are present.²⁴

Venous thrombosis

Mesenteric venous thrombosis is the least common cause of acute mesenteric ischemia, accounting for 10% of cases, with the superior mesenteric vein affected in approximately 95% of cases.^{6,29} Other factors that

can impact blood flow include inflammation caused by pancreatitis, inflammatory bowel disease, infection, or trauma including surgery.^{2,30} Malignancy is present in up to 16% of patients diagnosed with acute mesenteric venous thrombosis.²⁹ Cirrhosis and hereditary or acquired thrombophilia can also increase the risk for mesenteric venous thrombosis.³⁰ Approximately 20% of cases are idiopathic.^{2,30}

Mean age at presentation is 40 to 60 years, and mesenteric venous thrombosis is slightly more common in men.³¹ The severity of ischemic symptoms depends on the timing of thrombotic occlusion, with acute thrombotic venous occlusion resulting in more profound symptoms because collateral circulation has not developed. Patients may describe middle abdominal pain that is vague and colicky. The onset of pain is usually less abrupt than with acute arterial mesenteric ischemia, and patients typically present with nausea, vomiting, diarrhea, and abdominal cramping. Approximately 75% of patients have symptoms for at least 48 hours before seeking medical attention, and up to 29% of patients are hemodynamically unstable on presentation.³¹

Computed tomography with and without oral contrast is an appropriate initial screening test, and computed tomography or magnetic resonance angiography may be pursued if the initial computed tomography is nondiagnostic and clinical suspicion remains high.^{2,30} Doppler ultrasonography is highly specific but less sensitive for mesenteric venous thrombosis, and assessment of the smaller vessels is limited.²⁹ All patients should be assessed for history of malignancy, liver disease, and recent surgery. Anticoagulation is recommended in cases of acute mesenteric venous thrombosis; the duration of anticoagulation is 6 months or longer depending on the underlying cause.²⁹

CAUSES OF CHRONIC MESENTERIC ISCHEMIA

Chronic mesenteric ischemia describes intermittent or continuous intestinal hypoperfusion caused by occlusive disease of the mesenteric vessels. Most cases of chronic mesenteric ischemia are due to atherosclerosis. Less common causes include fibromuscular dysplasia, vasculitis, and retroperitoneal fibrosis.

Atherosclerosis

More than 90% of cases of chronic mesenteric ischemia result from atherosclerotic disease affecting the proximal segments of the visceral vessels.^{4,9} Risk factors include smoking, hypertension, diabetes, and the presence of atherosclerosis in other arterial beds. Most patients with chronic mesenteric ischemia are female.³ The reason is not entirely clear but appears to

be related to more acutely angulated mesenteric vessels in women compared with men.³²

Mesenteric artery stenosis is common, with post-mortem and duplex ultrasonography studies reporting an overall prevalence of 6% to 29% and as high as 67% in patients older than 80.⁴ Despite this, clinical manifestations of chronic mesenteric ischemia are rare because extensive collateral vessels develop over time, protecting against visceral malperfusion. Because of these collateral networks, symptoms and the need for revascularization are often delayed until at least 2 of the mesenteric vessels are stenosed.³³ The likelihood of mesenteric artery stenosis progressing to symptomatic chronic mesenteric ischemia is higher in multivessel disease.⁴ In a retrospective analysis of 77 patients with asymptomatic SMA stenosis, patients with stenosis of 2 or more mesenteric vessels had a higher incidence of chronic mesenteric ischemia compared with patients with single-vessel disease (15.1% vs 0%).³⁴ Approximately 20% to 50% of cases of symptomatic chronic mesenteric ischemia will progress to acute mesenteric ischemia, or acute-on-chronic mesenteric ischemia.³⁵

More than 70% of patients with symptomatic chronic mesenteric ischemia report abdominal angina, a postprandial abdominal pain often described as dull and crampy that usually begins within 30 minutes of eating and lasts 1 to 2 hours.⁴ As abdominal pain progresses over time, many patients turn to adaptive eating patterns, eating smaller portions or, in advanced cases, avoiding food (ie, food fear).³⁵ Weight loss is a key feature and is present in more than 60% of patients.^{4,34} Less typical symptoms include nausea, vomiting, diarrhea, or constipation.³⁶

Physical examination is often nonspecific but may reveal signs of malnutrition or cachexia. An abdominal bruit may be present; however, the classic triad of abdominal bruit, postprandial pain, and weight loss is present in only approximately 22% of cases.⁴

The nonspecific nature of symptoms makes it challenging to differentiate chronic mesenteric ischemia from common abdominal pathologies such as gallstone disease and peptic ulcer disease. Again, a high index of suspicion is crucial to promptly establish the diagnosis. A careful patient history should aim to identify patients with atherosclerotic risk factors and those reporting weight loss. The diagnosis is further supported by radiographic findings of high-grade stenosis or occlusion of at least 2 mesenteric vessels. Computed tomography angiography is recommended as the initial study of choice for mesenteric ischemia by the Society for Vascular Surgery, American College of Radiology, and European Society of Vascular Surgery, with close to

100% sensitivity. However, duplex ultrasonography is an effective, low-cost alternative that is more than 90% sensitive and specific in detecting high-grade stenosis.³⁷

Fibromuscular dysplasia

Rarely, chronic mesenteric ischemia has been reported as a complication of fibromuscular dysplasia, a nonatherosclerotic, noninflammatory disorder leading to stenosis, aneurysm, dissection, or occlusion of arteries that predominantly occurs in young and middle-aged women.³⁸ The US Registry for Fibromuscular Dysplasia reported mesenteric involvement in 15.1% of cases; however, symptoms of mesenteric ischemia were rare (1.3%).^{39,40}

Symptomatic patients present with severe abdominal pain or signs of acute arterial dissection.^{41,42} Because fibromuscular dysplasia can affect nearly any vascular bed, many patients will have multivessel involvement, which can result in other signs and symptoms, including pulsatile tinnitus and hypertension.

The classic angiographic appearance of beading (medial fibroplasia) or focal stenosis (intimal fibroplasia) supports the diagnosis.³⁹ Histopathology has shown proliferation of the arterial smooth muscle cells and destruction of elastic fibers.⁴¹

Vasculitis

Mesenteric ischemia is a rare but severe, life-threatening manifestation of systemic vasculitis.⁴³ Chronic inflammation can cause arterial wall thickening leading to stenosis or occlusion, or can weaken the arterial media and lead to aneurysm formation.⁴⁴ Gastrointestinal involvement is mostly seen in vasculitis affecting the medium and large arteries, such as polyarteritis nodosa, giant cell arteritis, and Takayasu arteritis.⁴³ Cases of mesenteric vasculitis have also been reported in patients with systemic lupus erythematosus and Behçet disease.^{45,46} Inflammatory markers may be elevated but

can be nonspecific. Further serologic testing is often necessary, including a viral hepatitis panel, antineutrophil cytoplasmic antibodies, and antinuclear antibodies. Diagnosing the underlying condition is important, as these patients may require immunosuppression in addition to other therapies for ischemia.

Retroperitoneal fibrosis

Retroperitoneal fibrosis is a rare inflammatory disease of the retroperitoneum that occurs predominantly in middle-aged men. The fibrosis characteristically encases the infrarenal abdominal aorta and iliac arteries, and may compress visceral vessels, resulting in ischemia.^{47,48} More than 50% of cases are idiopathic; other causes include malignancy and infection.⁴⁹

Patients typically present with dull abdominal or low back pain. Other symptoms include diarrhea, weight loss, jaundice, and leg swelling. Renal impairment resulting from ureteral obstruction is seen in up to 25% of cases.⁵⁰ Diagnosis is made based on a high index of suspicion and computed tomography and magnetic resonance imaging showing retroperitoneal perivascular soft-tissue masses.

CONCLUSION

Mesenteric ischemia remains a diagnostic challenge to many clinicians because it is uncommon and its symptoms are nonspecific. Early recognition and focused evaluation are crucial for timely diagnosis and prevention of catastrophic complications.

DISCLOSURES

Dr. Wu reports no relevant financial relationships which, in the context of their contributions, could be perceived as a potential conflict of interest. Dr. Nanjundappa has disclosed teaching and speaking for Abbott, Medtronic, and Phillips Healthcare, consulting for Argon and Phillips Healthcare, and ownership interest (stock, stock options in a publicly owned company) for Zoll.

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