Acute Mesenteric Ischemia: A Diagnostic Challenge in Clinical Practice

by Mamata Ravipati, Srikanth Katragadda, Betty Go, Edwin J. Zarling

Mesenteric ischemia remains a difficult condition to diagnose clinically. It can be classified as occlusive and non-occlusive, depending on the presence or absence of vascular occlusion. Occlusion due to embolic clot is the most common form, and accounts for nearly half the cases of acute mesenteric ischemia (AMI). Early diagnosis is essential as delay in diagnosis can result in bowel infarction and irreversible damage. The clinical presentation, serum markers and plain films may be non-specific in mesenteric ischemia. Angiography, ultrasonography and CT/MRI imaging are being increasingly used in its diagnosis. Although pharmacological therapy can be helpful, especially in the initial hours, surgery is usually advised. Despite new diagnostic and therapeutic modalities, the mortality and morbidity have remained high. This article reviews the anatomy, pathophysiology and clinical presentation of acute mesenteric ischemia, with a note on various diagnostic and therapeutic modalities.

INTRODUCTION

Mesenteric ischemia is a morbid abdominal illness that poses a diagnostic challenge and a high rate of mortality. The term denotes a wide array of clinical symptoms ranging from mild abdominal pain to severe rigidity and guarding, depending on the visceral vascular compromise. In the past three decades, AMI has been diagnosed more frequently perhaps due to enhanced radiologic tools.

ANATOMY

Mesenteric blood flow is derived from the celiac artery (which supplies the foregut, hepatobiliary system and spleen); the superior mesenteric artery (which supplies the small intestine and proximal mid-colon) (Figure 1) and the inferior mesenteric artery (which supplies the distal colon and rectum) (Figure 2).

Anatomically, there are rich collateral flow pathways between the superior and inferior mesenteric arteries. The gastroduodenal branch of the celiac artery and the pancreaticoduodenal artery of the superior mesenteric artery provide a potential source of collateral blood flow between mesenteric and non-mesenteric vessels. Due to this collateral blood flow in the intestine, at least two of the three major vessels have to be occluded to create mesenteric ischemia.
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PATHOPHYSIOLOGY

General Factors

Intestinal blood flow may be reduced as result of decreased circulating blood volume and poor systemic perfusion (hypovolemic, cardiogenic, or neurogenic shock). The intestinal mucosa has a narrow range of oxygen tension and the low oxygen availability in the setting of intestinal ischemia may not be sufficient to meet needs of basal metabolism. Several theories have been proposed to explain tissue injury in intestinal ischemia: neutrophil mediated injury to visceral organs; reperfusion injury resulting in free radicals which cause disruption of cell membranes and thus damage the mucosal barrier; increased flux of fluid into the lumen due to increased mucosal permeability; and proliferation of intestinal bacteria. Intestinal ischemia can progress in a transmural fashion from mucosa to serosa.

These autonomic, humoral and local factors can collectively affect the clinical outcome in a patient with mesenteric ischemia: alpha adrenergic stimuli causing vasoconstriction, and beta adrenergic stimuli causing vasodilatation with altered bowel absorption, secretion and motility; systemic hypotension from any cause stimulating the release of vasopressin which can further exacerbate the splanchnic vasoconstriction. Factors that can affect splanchnic circulation include angiotensin II, generated by the renin-angiotensin system, arachidonic acid metabolites and cAMP. Substances such as papaverine, prostaglandin E1 and glucagon can potentiate the vasodilating action of cAMP.

Specific Factors

Acute mesenteric ischemia is more common than chronic ischemia. On analysis of various causes for AMI, superior mesenteric embolism accounts for 40–50%, superior mesenteric artery thrombosis for 18–25%, non-occlusive mesenteric ischemia for 20% and mesenteric venous thrombosis accounts for 5% of all cases.
Acute Mesenteric Arterial Embolism: Nearly half the cases of AMI are attributed to an embolism, usually in the superior mesenteric artery. Emboli most commonly originate from cardiac abnormalities such as atrial fibrillation, myocardial infarction, left ventricular aneurysm with mural thrombus and mitral stenosis. Untreated acute occlusion of the superior mesenteric artery carries a poor prognosis in patients with no pre-existing visceral artery occlusive disease.

Acute Mesenteric Arterial Thrombosis: Patients having acute thrombosis of the mesenteric vessels usually have an underlying atherosclerotic disease. Most of them have a history of symptoms suggestive of chronic mesenteric ischemia, including pain after food intake, weight loss and early satiety. In contrast to embolic mesenteric ischemia, patients with acute mesenteric thrombosis often have delayed attention and diagnosis due to slow onset of symptoms.

Non-occlusive mesenteric ischemia (NOMI): Non-occlusive mesenteric injury usually occurs in systemic hypoperfusion resulting from cardiac failure, sepsis, or use of medications such as digitalis, ergotamine, cocaine and alpha adrenergic agents. These patients may not have the classic symptom of severe abdominal pain. The mortality is relatively high due to underlying systemic illness and delay in diagnosis.

Table 1. The Four Causes of Abdominal Ischemia

<table>
<thead>
<tr>
<th>Types of Mesenteric Ischemia</th>
<th>Acute mesenteric arterial embolism</th>
<th>Acute mesenteric arterial thrombosis</th>
<th>Non-occlusive mesenteric ischemia</th>
<th>Mesenteric venous thrombosis</th>
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<tbody>
<tr>
<td>Pathology</td>
<td>Atrial fibrillation, MI, valvular disease, left ventricular aneurysm</td>
<td>Atherosclerotic disease, superimposed on trauma, infection</td>
<td>Systemic hypoperfusion from cardiac failure, sepsis, medications</td>
<td>Hypercoagulable states, blunt trauma, infection, portal hypertension, pancreatitis, portal malignancy</td>
</tr>
<tr>
<td>Clinical Manifestation</td>
<td>Abrupt onset of abdominal pain; Minimal physical findings</td>
<td>Gradual onset of postprandial pain, nausea, bowel changes; Minimal physical findings</td>
<td>Gradual onset of malaise and abdominal discomfort; Minimal physical findings</td>
<td>Subacute onset of abdominal pain; Minimal physical findings</td>
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<tr>
<td>Diagnostic Study Treatment</td>
<td>Angiography</td>
<td>Angiography</td>
<td>Angiography</td>
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<td>All types</td>
<td>Superior mesenteric embolectomy; Chronic anticoagulation</td>
<td>Surgical revascularization</td>
<td>Vasodilator therapy (Papaverine)</td>
<td>Anticoagulant therapy (Heparin)</td>
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<td>Presence of Bowel Infarct</td>
<td>Surgery</td>
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Acute mesenteric venous thrombosis: Hypercoagulable states including anti-thrombin III, protein C and S deficiency, lupus anticoagulant, polycythemia vera and homocysteinemia increase the risk of venous thrombosis. Other risk factors include visceral infections and perforations, pancreatitis, portal hypertension, use of oral contraceptive pills, malignancy involving the portal system and nephritic syndrome.

**DIAGNOSIS OF MESENTRIC ISCHEMIA:**

**Clinical Symptoms**

To some extent, all types of acute mesenteric ischemia have similar clinical presentation. Differences for each type are discussed below, and summarized in Table 1. The most important finding is abdominal pain that is disproportionate to physical examination findings. The pain is typically moderate to severe, diffuse, non-localized, and constant and sometimes described as colicky; it may or may not respond to narcotics. Nausea and vomiting (75%), anorexia and diarrhea progressing to obstipation, abdominal distention and GI bleeding (25%) are also commonly associated symptoms. AMI should be highly suspected in any patient with abdominal pain disproportionate to physical findings, vomiting or diarrhea. Factors that make AMI more likely include oral contraceptive use, hypercoagulable states, atrial fibrillation, atherosclerosis, decreased cardiac output from myocardial infarction or congestive heart failure, volvulus, intussusception, tumor compression and aortic dissection.

**Clinical Signs**

Physical findings in patients with acute mesenteric ischemia are similar among the different etiologies. The clinical distinction is made based on time of presentation. Early in the course of the disease, in the absence of peritonitis, physical signs are few and non-specific. There is minimal or no tenderness and stool may contain occult or gross blood. Late in its course, when necrosis or perforation occurs, peritoneal signs develop: tenderness becomes severe, a palpable mass may be present, bowel sounds may be absent to hyperactive, voluntary and involuntary guarding appear. Fever, hypotension, tachycardia, tachypnea and altered mental status may be observed. Putrefaction of undigested alimentary material accumulated proximal to the pathologic site can cause foul breath. Risk factors for acute mesenteric ischemia may be noted, such as atrial fibrillation, heart murmurs, abdominal bruits, evidence of tumor, DVT or recent surgery. The differential diagnosis for AMI is listed in Table 2.

**Acute mesenteric arterial embolism:** Acute mesenteric ischemia from an embolic cause usually occurs in patients over 50 years of age with a history of cardiac disease. The presence of sudden abdominal pain in patients with history of atrial fibrillation, recent MI, or previous embolic disease should raise the suspicion of acute mesenteric ischemia. Increasing abdominal pain, guarding and rigidity may point to underlying loss of intestinal viability and transmural infarction. Absence of peritoneal signs early on in mesenteric ischemia may mislead to an alternative diagnosis.

**Mesenteric artery thrombosis:** Patients with thrombosis of mesenteric vessels usually present with less clinical intensity. They have a history of postprandial pain, nausea and change in bowel frequency, symptoms more suggestive of chronic mesenteric ischemia. Symptoms gradually progress over 12–24 hours of onset and as the bowel becomes more...

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<th>Table 2. Differential Diagnosis for Acute Mesenteric Ischemia</th>
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<td>Abdominal Abscess</td>
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<td>Abdominal Angina</td>
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<td>Abdominal Aortic Aneurysm</td>
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<td>Acute Abdomen</td>
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<td>Acute Pancreatitis</td>
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<td>Acute Pyelonephritis</td>
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<td>Aortic Dissection</td>
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<td>Appendicitis</td>
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<td>Bacterial Pneumonia</td>
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<td>Biliary Colic</td>
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<td>Biliary Obstruction</td>
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<td>Boerhaave Syndrome</td>
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<td>Cholangitis</td>
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ischemic, rectal bleeding and sepsis (i.e. tachycardia, tachypnea, hypotension, fever, and altered mental status) develop. Catastrophic outcome results if not properly and rapidly identified and treated.

**Non-occlusive mesenteric ischemia:** Patients with NOMI usually have gradual onset of symptoms. Usage of drugs such as digitalis, alpha adrenergic agents, ergot alkaloids or episodes of hypotension can help in making a provisional diagnosis of non-occlusive mesenteric ischemia. Nearly a quarter of patients with NOMI do not have abdominal pain initially, but if infarction occurs, patients develop increased pain associated with vomiting, hypotension and tachycardia. When these signs develop, bowel injury may be severe and irreversible.[11]

**Mesenteric venous thrombosis:** Patients with mesenteric venous thrombosis usually have subacute onset of symptoms and nonspecific laboratory findings. Patients may complain of intermittent episodes of abdominal pain over a period of few days or prolonged period with gradual worsening. The chronic form may manifest as esophageal variceal bleeding. Many patients have risk factors for hypercoagulability i.e. oral contraceptive use, congenital hypercoagulable states, deep venous thrombosis, liver disease, tumor or postcaval surgery.

**DIAGNOSTIC STUDIES**

**Laboratory**

Laboratory indices may be helpful in ruling out or supporting the diagnosis of mesenteric ischemia, but only in late stages. Elevated levels of amylase, total leukocytic count, hemoglobin or phosphate in the blood and also metabolic acidosis are some of the non-specific indicators of mesenteric ischemia. Studies have shown that low lactate levels may help in ruling out the diagnosis of intestinal ischemia and avoid unnecessary laparotomies, especially in the elderly.[12,13,14] Enzymes such as creatine kinase (CPK), lactate dehydrogenase (LDH), and alkaline phosphatase may be helpful in diagnosis of transmural infarction, but are insensitive in early stages of ischemia. Currently, the role of laboratory markers in visceral ischemia is limited and the quest for a more definitive marker is still on.

**Radiography**

Plain radiographs of the abdomen are commonly ordered in patients presenting with acute abdominal pain to rule out visceral pathologies like perforation that may require emergent intervention. Plain films are usually normal in intestinal ischemia until the infarcted bowel undergoes irreversible ischemic changes. Common radiographic findings include air-fluid levels, distended adynamic ileus, and fixed dilated loops on repeated films. Presence of gas in the portal vein and intestines (pneumatosis intestinalis) are poor prognostic signs in mesenteric ischemia. Superior mesenteric artery occlusions usually take 12 hrs before the radiographic signs are elicited, whereas non-occlusive mesenteric ischemia may take several days for such radiographic changes.[15] Classic findings in barium studies of ischemic bowel include “thumbprinting” (due to mucosal edema) and delayed passage of contrast material through the paralytic segment. Barium studies should be avoided in patients having a clear diagnosis of intestinal perforation or ischemia and those in whom angiography is planned.

**Ultrasonography**

Doppler ultrasonography has emerged as a useful alternative to angiography in screening and diagnosis of visceral ischemia. This non-invasive diagnostic modality can detect arterial narrowing and blood flow velocity to identify stenotic lesions in the visceral vasculature. Normal blood flow observed in all visceral vessels may be sufficient to rule out mesenteric ischemia. Obesity, vessel wall calcifications and intestinal gas can sometimes hinder proper visualization of visceral vasculature. Ultrasonography is a fine non-invasive imaging modality that can greatly help in reducing the latent period between the symptom onset and therapeutic intervention.[16]

**Angiography**

Angiography has become a very important diagnostic and therapeutic intervention in intestinal ischemia. The classic angiographic finding in superior mesenteric artery embolus is the mercury meniscus sign seen
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approximately 3–8 cm distal to the origin of the superior mesenteric artery, best seen in anterio-posterior view. The embolus appears as the shape of a crescent that is convex on the surface much like the meniscus formed by mercury. However, lateral angiographic views are more helpful in superior mesenteric artery thrombosis, which classically show occlusion just distal to the origin of the superior mesenteric artery. Angiography can be used preoperatively in embolic or thrombotic occlusions of the mesenteric artery.

The role of angiography in mesenteric venous thrombosis is unclear and evidence from most recent studies emphasized the need of laparotomy in venous thrombosis. Angiography has a definite diagnostic and therapeutic role (infusion of Papaverine and thrombolytics through the angiogram catheter) in non-occlusive mesenteric ischemia. Papaverine is the only treatment of non-occlusive mesenteric ischemia other than resection of gangrenous bowel. Angiographic findings in non-occlusive mesenteric ischemia include diffuse or focal narrowing of mesenteric vessels, showing alternating segments of narrowing and dilatation, sometimes referred to as the classic “sausage sign.”

Angiography can sometimes precipitate embolization and worsen ischemia. Opting for angiography in case of severe acute occlusion can sometimes lead to delayed diagnosis and resulting in worsening of ischemia. Laparoscopy is a better option whenever angiography is precluded.

CT/MRI

In addition to helping establish the diagnosis of intestinal ischemia, CT and/or MRI imaging have the ability to rule out other causes of acute abdomen. CT imaging with IV and oral contrast could be a valuable diagnostic modality and predictor of outcome in acute mesenteric ischemia. Similarly, the findings on MRI imaging could include edema and increased thickness of the bowel wall, free fluid in the abdomen, or presence of collateral vessels. MRI imaging is being increasingly used in the diagnosis of chronic mesenteric ischemia. MRI angiography is rapid and non-invasive, and may supplant traditional angiography in the future.

MANAGEMENT OF ACUTE MESENTERIC ISCHEMIA

Acute arterial mesenteric ischemia: (thrombotic or embolic): In patients presenting with acute mesenteric ischemia, hypovolemia and hypotension need to be corrected first by appropriate administration of IV fluids and supportive care. Broad spectrum antibiotics, nasogastric tube decompression, Foley catheter and supplemental oxygen should also be considered.

Transcatheter administration of papaverine during angiography has been shown to be effective in both occlusive and non-occlusive mesenteric ischemia. Higher survival rates have been observed when vasodilators have been added to the treatment plan. Papaverine inhibits the phosphodiesterase enzyme and thus increases the tissue levels of C-AMP, a vascular smooth muscle relaxant. Clinically and angiographically guided papaverine therapy is generally given for a period of 24–48 hours, through angiographic catheter at a rate of 30–60 mg/hour. Repeat angiograms are advised every 24 hours until patient improves clinically. Surgical intervention should be undertaken in patients who exhibit any signs of clinical deterioration.

Necrotic bowel is surgically removed and primary anastomosis is preferred in uncomplicated cases. Intestines appearing marginally viable at initial operation should be allowed to remain, with the intent of undertaking a “second-look operation” 24–36 hours later. A second-look operation is indicated whenever bowel of questionable viability is resected. In case of large embolus in the SMA, embolectomy should follow papaverine to maintain the intestinal viability. Some studies have shown that management of acute mesenteric ischemia with revascularization and open surgical techniques may result in improved survival rates. Although percutaneous angioplasty may be successfully tried in acute mesenteric ischemia, is usually not recommended due to high risk of thromboembolus.

Thrombolytic therapy with streptokinase, urokinase or recombinant tissue plasminogen activator in acute arterial mesenteric ischemia is still in experimental phase and is limited to patients with contraindication to surgery and who present in the early phase of ischemia before infarction of bowel develops.

There is no role for heparin in acute management of bowel ischemia. It is not compatible with papaver-
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Summary
Ischemic injury to the intestines can occur when blood flow is compromised by a variety of mechanisms. Symptoms are often nonspecific, so clinicians must maintain a high degree of suspicion in order to identify and treat this potentially fatal condition.

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