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Acute Mesenteric Ischemia: The Challenge of Gastroenterology

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Abstract
Intestinal ischemia has been classified into three major categories based on its clinical features, namely, acute mesenteric ischemia (AMI), chronic mesenteric ischemia (intestinal angina), and colonic ischemia (ischemic colitis). Acute mesenteric ischemia is not an isolated clinical entity, but a complex of diseases, including acute mesenteric arterial embolus and thrombus, mesenteric venous thrombus, and nonocclusive mesenteric ischemia (NOMI). These diseases have common clinical features caused by impaired blood perfusion to the intestine, bacterial translocation, and systemic inflammatory response syndrome. Reperfusion injury, which exacerbates the ischemic damage of the intestinal microcirculation, is another important feature of AMI. There is substantial evidence that the mortality associated with AMI varies according to its cause. Nonocclusive mesenteric ischemia is the most lethal form of AMI because of the poor understanding of its pathophysiology and its mild and nonspecific symptoms, which often delay its diagnosis. Mesenteric venous thrombosis is much less lethal than acute thromboembolism of the superior mesenteric artery and NOMI. We present an overview of the current understanding of AMI based on reported evidence. Although AMI is still lethal and in-hospital mortality rates have remained high over the last few decades, accumulated knowledge on this condition is expected to improve its prognosis.

Key words Mesenteric ischemia · Nonocclusive mesenteric ischemia · Thrombus · Superior mesenteric artery

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Introduction

Acute intestinal ischemia is an abdominal emergency, which should be distinguished from other critical conditions such as panperitonitis caused by perforation of the digestive tract. Above all, acute mesenteric ischemia (AMI) is often lethal and in-hospital mortality rates have remained high over the last 20 years, at 60%–80%.[1–12] Although AMI accounts for only about 1%–2% of gastrointestinal illnesses,[10] the incidence has been increasing considerably.[13,14]

It is paradoxical that cardiovascular surgeons[15] and nephrologists[16] are more familiar with this emergency abdominal condition than gastroenterologists, but they are very likely to encounter AMI in patients undergoing major vascular surgery and those on hemodialysis. Because of its relative infrequency, the incidence of AMI has been underestimated and there are no established guidelines for its diagnosis and treatment based on the evidence of randomized controlled trials.[11]

There is another drawback in establishing a general consensus for the treatment of AMI, apart from its low incidence. The pathophysiology of AMI, particularly nonocclusive mesenteric ischemia (NOMI), is poorly understood. Although recent studies have shed light on the unique aspect of systemic influences secondary to acute intestinal ischemia, such as bacterial translocation and systemic inflammatory response syndrome (SIRS), many predisposing factors for AMI, such as advanced atherosclerosis or severely impaired cardiac function, remain unclear. Thus, we review the literature on AMI to present an overview on the current understanding of this life-threatening condition.

Classification of Acute Intestinal Ischemia

There is still some confusion surrounding the terminology related to intestinal ischemia. Some investigators

Table 1. Classification of intestinal ischemia according to the obstructive mechanism

1. Occlusive intestinal ischemia
a. Arterial occlusion (thrombus and embolus)
1. Acute ischemia
2. Chronic ischemia
b. Ischemic colitis
c. Venous occlusion
2. Nonocclusive intestinal ischemia

Table 2. Classification of intestinal ischemia proposed by the American Gastroenterological Association in 2000

1. Acute mesenteric ischemia
a. Major arterial occlusion
b. Minor arterial occlusion
c. Major embolus
d. Mesenteric venous thrombosis
e. Splanchnic vasoconstriction (nonocclusive mesenteric ischemia)
2. Chronic mesenteric ischemia or intestinal angina
3. Ischemic colitis

classify intestinal ischemia according to the mechanisms of vessel obstruction (Table 1), whereas others are more concerned with its pathogenesis, and are indifferent to whether the clinical onset of the disease is acute or chronic. Venous mesenteric thrombosis is distinct from arterial thromboembolism with respect to underlying diseases such as coagulopathy or atherosclerosis. More recently, the American Gastroenterological Association (AGA) published an article classifying intestinal ischemia into three major categories, focusing on the clinical features: acute mesenteric ischemia (AMI), chronic mesenteric ischemia (CMI), also known as intestinal angina, and colonic ischemia (CI), also known as ischemic colitis (Table 2).[11] Acute mesenteric ischemia has several categories in the AGA classification, including arterial thromboembolism, venous thrombosis, and splanchnic vasoconstriction (see *Nonocclusive Mesenteric Ischemia*). We discuss AMI as an abdominal emergency.

Pathophysiology of Acute Intestinal Ischemia

The intestinal circulation is controlled by systemic blood pressure as well as local autonomic mechanisms. Circulating native and exogenous catecholamines primarily induce vasoconstriction of the mesenteric postcapillary venules and regulate the splanchnic vascular volume. Autonomic factors include the opposing effects of α- and β-adrenergic stimuli, producing vasoconstriction and vasodilation, respectively. Intense persistent vasoconstriction, induced by rennin, angiotensin, vasopressin, thromboxanes, or leukotrienes, is considered to cause intestinal necrosis, as in NOMI (see *Nonocclusive Mesenteric Ischemia*).

Normal intestinal circulation can be maintained even with low blood flow and perfusion pressure, without severe injury for several hours, because only 20%–25% of the mesenteric capillaries remain patent for oxygenation in the fasting condition.[17] The other capillaries are recruited once intestinal ischemia develops.

In moderate ischemia, increased oxygen extraction by the ischemic tissue compensates the impaired oxygen supply; however, once the blood flow falls below 30 ml/min per 100 g tissue[18] or the systemic blood pressure falls below 40–70 mmHg,[19] the oxygen uptake becomes flow dependent. Irreversible ischemia may develop even in moderate ischemia of the intestine, because of the reduction in blood flow caused by the stretched intestinal well, as in "obstructive colitis."

The relative imbalance in oxygen consumption and supply also results in acute intestinal ischemia combined with decreased oxygen supply. An experimental study showed that the lipid component in enteral formulas may cause intestinal ischemia by increasing metabolic demands and mucosal oxygen uptake more than other nutritional elements after ischemia reperfusion.[20]

The clinical features of AMI originate from local and systemic responses, which are induced by the impaired microcirculation through the activation of a variety of cells such as endothelium, monocytes, leukocytes, and platelets (Fig. 1). Damage to the microcirculation leads to irreversible intestinal necrosis locally, and disseminated intravascular coagulation (DIC) or systemic inflammatory response syndrome (SIRS) in the whole body or in remote organs systemically. Activated neutrophils, endothelium, monocytes, and platelets in the ischemic intestine produce inflammatory cytokines, such as tumor necrosis factor (TNF), interleukins, platelet-activating factor (PAF), and leukotrienes, through leukocyte–endothelial interactions. Endothelial adhesion molecules such as E-selectin are upregulated in the reperfused intestine.[21] The associated DIC disturbs the intestinal microcirculation through obstruction caused by leukocyte adhesion and platelet aggregation.[22] Organ injury is also exacerbated by vasoconstriction of the mesenteric vessels caused by impaired production of nitric oxide by the damaged endothelial cells.[23,24]

Reperfusion injury is a feature of AMI. During ischemia, xanthine dehydrogenase, which exists predominantly in nonischemic tissue, is irreversibly converted to xanthine oxidase. Reoxygenation of the ischemic intestine converts a large amount of intracellular hypoxanthine to uric acid, which is catalyzed by xanthine oxidase. Activated neutrophils in the reperfused intestine release superoxide, catalyzed by nicotinamide

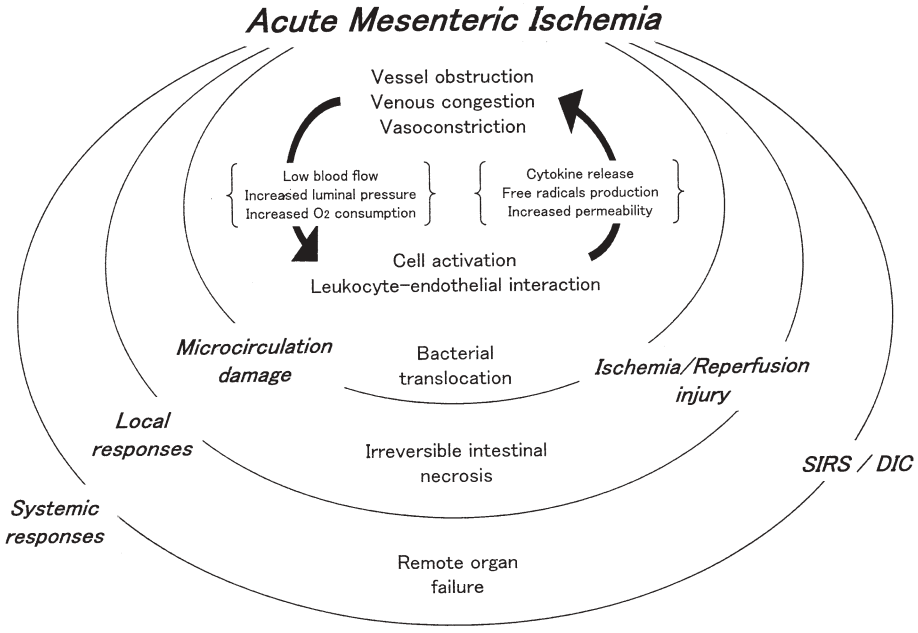

Fig. 1. Local and systemic responses in acute mesenteric ischemia. *SIRS*, systemic inflammatory response syndrome; *DIC*, disseminated intravascular coagulation

adenine dinucleotide phosphate (NADPH) oxidase as well as elastase and collagenase. Furthermore, myeloperoxidase from neutrophils produces chloride ions from peroxide.[25] These reactions generate toxic oxygen free radicals, such as superoxide (O_2^-), peroxide (H_2O^2), and hydroxyl radicals($^{\cdot}OH$),[26] which damage the cell membrane through lipid peroxidation. These oxygen metabolites and enzymes of neutrophils also cause serious damage to the surrounding tissue and distant organs by direct and indirect injury to the vascular endothelium. It has been postulated that a high concentration of xanthine dehydrogenase in the mesenteric endothelium may be one of the reasons for the susceptibility of the intestine to reperfusion injury.

Reperfusion induces interstitial edema and luminal fluid accumulation through increased capillary permeability.[27] The damaged intestinal microcirculation loses its resistance to bacteria as well as to water, which leads to endotoxemia[28] or bacteremia.[29,30] This bacterial translocation may play an important role in the development of SIRS, adult respiratory distress syndrome (ARDS),[31] and cardiac dysfunction.[32] There is also substantial evidence that the poor prognosis associated with acute intestinal ischemia is strongly related to the multiple organ failure caused by these sepsis-like systemic responses.[33]

Common Clinical Features and Diagnosis of AMI

Acute mesenteric ischemia caused by obstruction of the superior mesenteric artery (SMA) is sometimes referred to as "acute mesenteric arterial syndrome,"[10] because of the common clinical features. The major symptom of acute mesenteric ischemia is sudden and severe abdominal pain out of proportion to the physical findings. However, it should be noted that many elderly patients have obscure symptoms and sometimes even no early findings. Boley et al.[34] reported that patients who present with abdominal pain and are at risk of AMI are older than 50 years with congestive heart failure, cardiac arrhythmias, recent myocardial infarction, hypovolemia, hypotension, or sepsis. According to another study, mesenteric arterial disease was found in 18% of patients aged over 65 years[35] and 70% of those undergoing aortofemoral bypass.[36] Patients with AMI may have a history of deep vein thromboses, arterial embolism, collagen disease, or chronic postprandial pain.

There is substantial evidence that the mortality varies with the cause of AMI. Mesenteric venous thrombosis (MVT) is much less lethal than acute thromboembolism of the superior mesenteric artery and NOMI. In general, survivors of AMI are younger, with less extensive bowel infarction and a shorter clinical history.[37] Several retrospective studies have shown that prompt diagnosis improves the survival rate significantly. Another study found that the intestine was viable in over 90% of patients if the duration of symptoms was less than 12 h.[6]

The plain X-ray findings suggestive of AMI include a thickened bowel wall and a "ground-glass appearance" in the abdomen.[38] However, as these findings are nonspecific and the condition is associated with a high

mortality rate, plain X-ray films are considered to be useful only for excluding other possible causes of acute abdominal pain, such as a perforated peptic ulcer.

The role of current radiographic and noninvasive modalities is limited in the early diagnosis of AMI. Computed tomography (CT) scans may reveal bowel wall thickening, ascites, or occlusion of the mesenteric arterial trunk. However, most of those abnormal signs are nonspecific and found only in the late stage of acute intestinal ischemia.[39,40] One study found that a correct diagnosis was obtained by CT scans in only 26% of suspected cases.[41] Another retrospective comparison of plain X-ray films and CT scans in patients with proven intestinal infarction demonstrated low specificity in both examinations, of 30% and 39%, respectively.[42] Multislice spiral CT and magnetic resonance angiography (MRA) are promising diagnostic modalities and may be more useful than conventional CT scans because they provide high-resolution functional images indicating low oxygen satruation.[43] However, clinical evidence of the superiority of these diagnostic modalities over CT is not yet available.[44]

Duplex sonography is also a potentially useful diagnostic modality for acute intestinal ischemia, although it is highly user-dependent and diminished blood flow can only be confirmed in the mesenteric trunks.[45,46] Moreover, these recent imaging devices have only limited value in the diagnosis of NOMI.[45,46]

Selective mesenteric angiography and digital subtraction angiography (DSA) are still the gold standard for the diagnosis of AMI[10,47–49] because they can identify NOMI and provide important preoperative information for mesenteric bypass surgery. Although routine angiography decreased the mortality rate without an apparent increase in complications in many series,[10,50,51] the role of preoperative angiography is still controversial in patients suspected of having AMI and those with peritoneal signs. Moreover, it is impossible to perform selective mesenteric angiography for every patient with suspected AMI in many hospitals. Some physicians even claim that performing angiography will delay surgical treatment for critically ill patients and, considering the low incidence of positive angiographic findings, they recommend taking the patient directly to surgery.[47]

Serum markers, such as amylase, arterial pH, and mucosal and seromuscular enzymes, frequently show abnormalities in AMI. However, these enzymes usually rise only after the development of a transmural intestinal infarction.[52] A Swedish group recently found that a D-dimer abnormality appears in the early stage of AMI and reported promising results using this examination.[12] Other research groups investigated the α subunit of glutathione *S*-transferase (α-GST), which is activated in the intestine and liver to maintain cellular homeostasis under oxidative stress, and found that α-GST is a better predictor of AMI than conventional biochemical tests.[53] However, experience with these serum markers is limited.

It is generally agreed that exploratory laparotomy and embolectomy with resection of the infarcted intestine is mandatory if patients present with obvious peritoneal signs and symptoms. Segmental acute intestinal ischemia can be treated by resection and primary anastomosis (see *Acute Mesenteric Arterial Embolus and Thrombus*). When blood perfusion of the anastomosis is not confirmed, osteomy or the creation of a mucus fistula should be done to monitor the viability of the intestine postoperatively. In general, a routine second-look procedure is done within 12–24 h postoperatively when the viability of the site of anastomosis cannot be confirmed at the initial operation.[54–56]

Intestinal viability can be assessed intraoperatively using a fluorescein method, Doppler ultrasound, or laser Doppler.[57] With the fluorescein method, sodium fluorescein is injected intravenously, and the dye leaks out of the microvasculature and is deposited in the interstitial tissue depending on the hypoxic damage. This leakage pattern of fluorescein visualized under a Wood's lamp should assess the intestinal viability.[58,59] According to Bulkley et al., the fluorescein method is more reliable for assessing intestinal viability than either clinical criteria such as color, peristalsis, and pulsations in the mesentery, or Doppler ultrasound.[60,61] However, this method is highly subjective and requires some experience to interpret the fluorescein pattern. A fiberoptic fluorometer, which was recently introduced to quantify the fluorescence concentration, has been shown to better evaluate bowel viability.[58] Laser Doppler and Doppler ultrasound may be more accurate for assessing intestinal viability, but their major drawback lies in the difficulty in achieving quick assessment of the whole length of intestine.

Acute Mesenteric Arterial Embolus and Thrombus

The abdominal pain caused by an SMA embolus is usually of acute onset and out of proportion to the physical findings. The embolus originates from the heart in most patients, some of whom have a history of emboli in an extremity or the brain. The abdominal pain associated with SMA thrombosis is typically insidious and gradually progressive. Other patients may have symptoms such as abdominal angina, consistent with chronic intestinal ischemia, or signs of progressive sepsis, such as dehydration, leukocytosis, bloody diarrhea, and eventually septic shock.

Angiography shows SMA thrombosis and embolus as an abrupt cutoff of contrast in the vicinity of its origin (Fig. 2). Although emboli to the SMA often appear as a

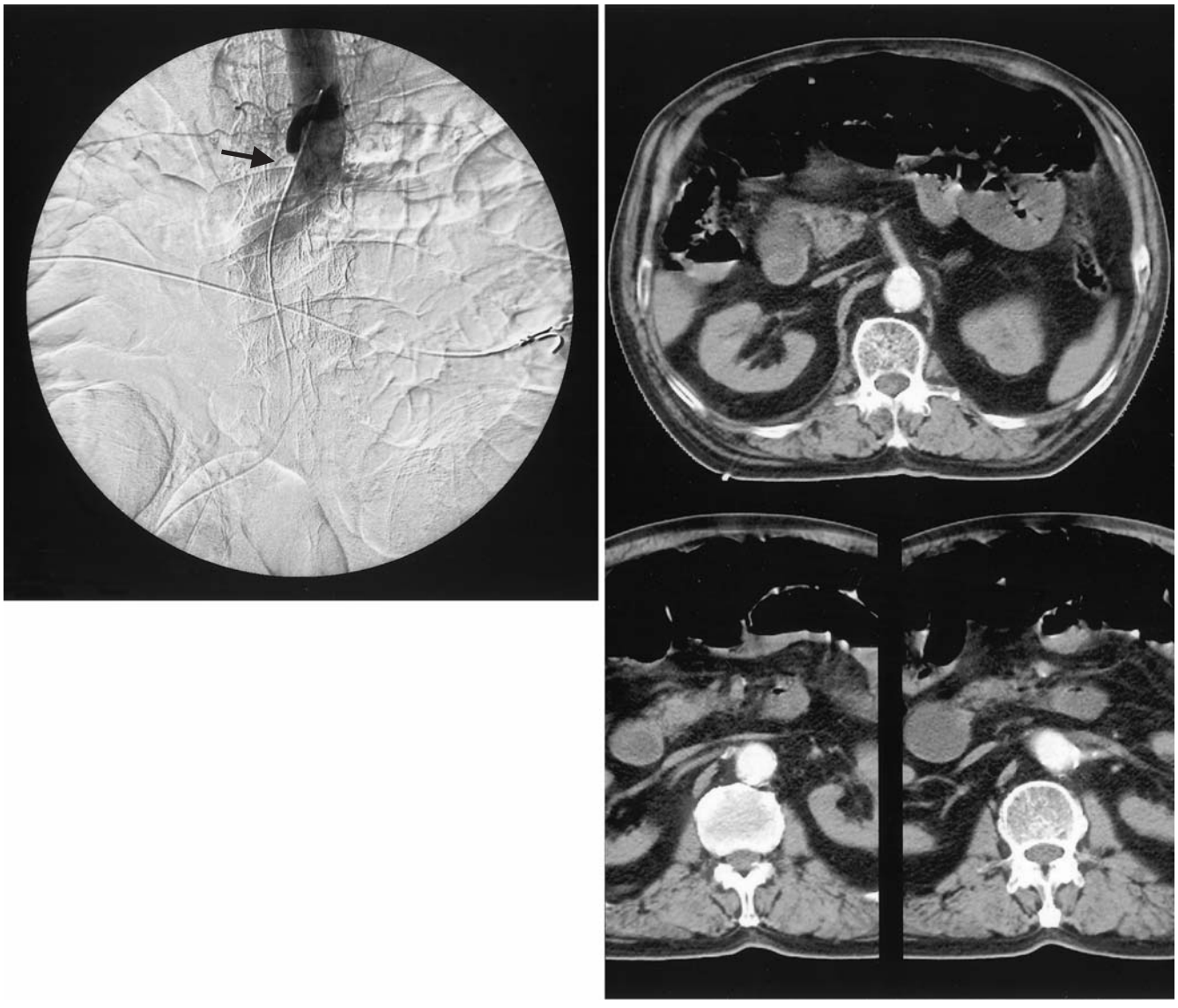

Fig. 2. **a** Typical abrupt cutoff sign of the superior mesenteric artery in a 72-year-old man with a thrombus caused by atrial fibrillation. **b** Abdominal computed tomography scan of the same patient. It is difficult to see the obstruction of the artery in this image

meniscus radiopaque sign within its lumen, the angiographic findings differentiating between embolus and thrombus are equivocal in many patients. It is important to assess the development of collateral vessels from the celiac axis or IMA connecting with distal branches when total occlusion of the SMA is seen. Enhanced collaterals may indicate chronic occlusion of the SMA, such as that caused by mesenteric thrombosis.

Once the diagnosis of embolus has been established, emergency embolectomy must be performed through an arteriotomy in the SMA, using a Fogarty catheter. It is important to establish if the ischemic lesion extends beyond the oral part of the ligament of Treitz in the SMA thrombus, although the proximal jejunum is usually unaffected by an SMA embolus.[10] When mesenteric thrombosis is diagnosed intraoperatively, an aortomesenteric bypass should be performed, using the saphenous vein as the conduit because of the risk of infection associated with a prosthetic graft in the setting of bowel ischemia or infarction. However, some surgeons prefer a prosthesis over the saphenous vein, to avoid kinking of the graft in the abdominal cavity.

Various other therapeutic approaches have been established for SMA thromboembolism, including intra-arterial perfusion with a thrombolytic agent and vasodilators with interventional radiology procedures. The indications for these treatments depend on whether

there are any signs of peritonitis, the extension of mesenteric occlusion, and if the mesenteric occlusion is in the distal or proximal area. Thrombolytic therapy is most likely to be successful if treatment is started within 12 h of the onset of symptoms and if the thrombus partially occludes the SMA trunk or occludes a single SMA branch distal to the ileocolic artery.[62–69] It was reported that a routine transcatheter infusion of papaverine improved survival in highly selected patients with major emboli of the SMA, although the experience is limited.[50,70]

Mesenteric Venous Thrombosis

Mesenteric venous thrombosis (MVT) is relatively rare and characterized by the insidious onset of abdominal discomfort. Some patients complain of diffuse intermittent abdominal pain lasting several days or weeks. The symptoms are usually less severe than those caused by an SMA embolus. Mesenteric venous thrombosis can be classified into acute and chronic types, depending on the duration of symptoms.[71] The acute type of MVT, in which symptoms last less than 4 weeks, accounts for only 5%–15% of patients with AMI.[72,73] Rhee et al. reported that only 9% of patients with MVT presented with symptoms of less than 24 h duration.[54]

Mesenteric venous thrombosis is also classified according to its etiology, into primary and secondary MVT. Primary MVT may be spontaneous or idiopathic, not associated with any other etiologic factor,[74] whereas patients with the following underlying conditions are classified as having secondary MVT: hypercoagulability, cirrhosis, splenomegaly, cancer, infection, trauma, pancreatitis, hematologic disease, inflammatory bowel disease, or diverticular disease.[54] According to some researchers, about 20% of cases are idiopathic and 80% are secondary.[75,76] The number of patients with secondary MVT has increased considerably over the last two decades because of the recognition of previously unknown factors, such as hematological disorders including protein C and S deficiency, antithrombin III deficiency, dysfibrinogenemia, abnormal plasminogen, polycythemia vera, thrombocytosis, sickle cell disease, and factor V Leiden mutation.[77–80] Thus, the MVT could be considered to be an analogy of deep venous thrombosis of the lower limb. In fact, both disease have many predisposing factors in common, including abnormal coagulopathy. Localized MVT can also develop secondary to volvulus, intussusception, or strangulation of the bowel.

Contrast-enhanced CT has been found to be more valuable for the diagnosis of MVT in contrast to its limited role in the diagnosis of AMI or NOMI.[81] Therefore, CT is done as the initial diagnostic examination in patients with severe abdominal pain and a history of deep vein thrombosis or a familial history of hypercoagulability.[82] Computed tomography can show thrombosis in the superior mesenteric vein, portal vein, and splenic vein, with or without bowel wall thickening or pneumatosis, in many asymptomatic patients (Figs. 3 and 4) Miller and Berland advocated duplex Doppler examination as the first diagnostic choice because it is as durable as CT scans.[83] Magnetic resonance imaging has

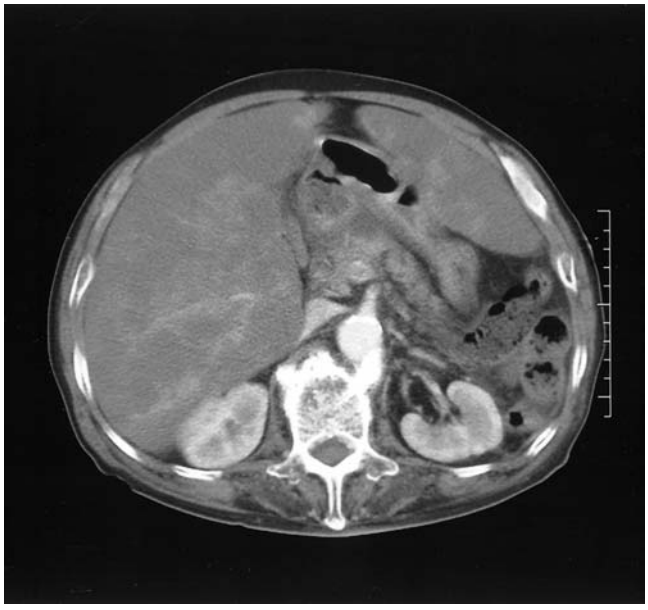

Fig. 3. Abdominal computed tomography scan showing portal vein thrombosis of 24 h duration associated with massive liver necrosis in a 67-year-old patient who died of multiple organ failure after massive intestinal necrosis

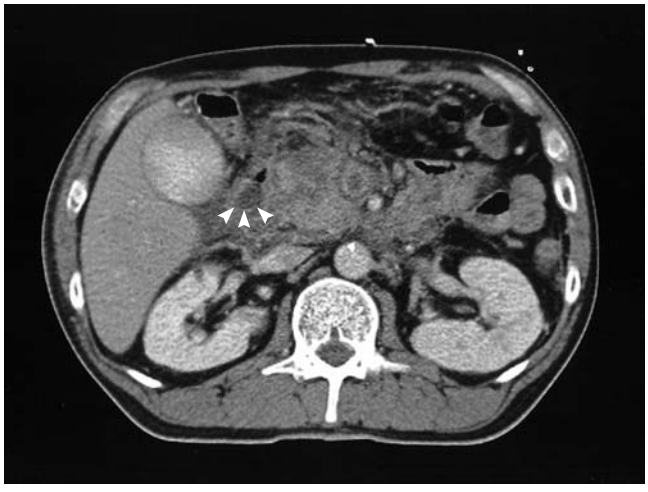

Fig. 4. Mesenteric venous thrombosis associated with acute pancreatitis. Computed tomography scan showing radiopaque image in the superior mesenteric vein and a swollen pancreatic head

also been reported to be sensitive for diagnosing MVT,[84] although it costs more than almost any other diagnostic modality.

Serum laboratory test findings, such as leukocytosis, and elevated serum levels of lactate and amylase, are not useful for the diagnosis of acute MVT. The diagnostic value of D-dimer, which is used extensively for the diagnosis of venous thromboembolism of the extremities, remains controversial.[85]

In symptomatic patients with acute MVT, the choice of treatment is determined by the severity of peritoneal signs. In the absence of peritoneal signs, anticoagulant therapy should be started immediately. Patients are first treated with heparin for 7–10 days, then an oral regimen of Coumadin or warfarin sodium for 3–6 months.[86] Thrombolysis is also a treatment of choice. The thrombolytic agents can be infused using several approaches, such as via the SMA,[86,87] via the internal jugular vein,[88] or transhepatically via the portal vein.[89,90]

Exploratory laparotomy should be performed immediately for all patients with peritoneal signs. Normal laboratory test results should not preclude exploration and the patient should receive continuous heparin infusion regardless of the risk of bleeding. Perioperative anticoagulation therapy decreases the risk of recurrence of thrombosis and ultimately improves survival.[71] Venous thrombectomy is not usually recommended for acute MVT because thrombosis often recurs and results in distal diffuse extention.[71]

For asymptomatic patients with an incidental diagnosis based on CT scan findings, either no therapy or 3–6 months' systemic anticoagulant administration is recommended, although there is no available evidence supporting this therapeutic decision.

The rate of recurrence for acute MVT, which generally occurs within 30 days, is high.[10] The long-term survival of patients with chronic MVT depends on their underlying diseases and appears to be better than that of patients with acute MVT.[77] All patients who have suffered recurrent MVT should be kept on warfarin sodium for the rest of their life.

Nonocclusive Mesenteric Ischemia

Nonocclusive mesenteric ischemia is defined as "intestinal necrosis with a patent arterial tree" and has also been termed "hemorrhagic enteropathy," "hemorrhagic necrosis of gastrointestinal tract," "intestinal infarction without mesenteric vascular occlusion," and "hemorrhagic necrotizing enteropathy."[91] Nonocclusive mesenteric ischemia is the most lethal form of AMI, with mortality rates of up to 70%–100%. Nonocclusive mesenteric ischemia was previously thought to be rare, but its frequency is increasing,[13] and its overall incidence is estimated at about 1 in every 5000 hospital admissions,[48] which accounts for 25%–60% of all bowel infarctions.

The frequency of NOMI among patients undergoing cardiac surgery[15] and those on hemodialysis[16,92–94] has dramatically increased over the last few decades. In fact, 9%–20% of deaths among patients on hemodialysis are attributable to NOMI. Newman and colleagues also noted that 22% of patients with bowel infarction had renal failure as comorbidity.[95] It was also reported that hemodialysis-induced hypotension triggers NOMI in patients with signs of atherosclerosis.[92]

Colonic ischemia (CI) is another important comorbidity involved in the pathogenesis of NOMI. Colonic ischemia frequently occurs after cardiac function has been optimized and the presumed cause of mesenteric vasoconstriction has been corrected,[96] for example, after major cardiovascular surgery or a hypotensive episode caused by rupture of an abdominal aortic aneurysm. Colonic ischemia is often associated with systemic conditions, such as vasculitis; the use of various medications that can induce intense vasospasm, such as oral contraceptives, β-blockers, diuretics, and digitalis; and colonic obstructive lesions, such as carcinoma. Therefore, some investigators suggest that reperfusion after NOMI could induce CI and it is reasonable to assume that reperfusion injury may explain the high incidence of CI.

The high mortality rates associated with NOMI are frequently attributed to a delay in diagnosis because of its mild and nonspecific symptoms compared with other types of AMI. An abrupt onset of severe abdominal pain may be less common. The most common symptom is a gradual onset of crampy, periumbilical abdominal pain, which progresses to constant pain. Some patients may not complain of any apparent symptoms because of their severe underlying illness and many patients have experienced a recent episode of hemorrhagic shock or sepsis. Abdominal distension and feeding intolerance may be the early manifestations of NOMI, and in its late stage, fever metabolic acidosis or hypovolemic shock can develop in patients receiving enteral feeding.

Reinus et al.[97] reviewed the symptomatology of NOMI and concluded that it most often develops in patients older than 60 years with associated underlying cardiovascular disease, and frequently abdominal pain, distension, and leukocytosis. The patients at highest risk include those with disorders predisposing to atherosclerosis, such as diabetes mellitus, advanced age, hypertension, dyslipidemia, a history of smoking, and arterial occlusive disease.[98]

Several hypotheses have been proposed to explain the pathogenesis of NOMI, among which persistent and irreversible vasoconstriction is thought to be the most important. Previous experimental and clinical studies have demonstrated that long-standing vasoconstriction

can become persistent and irreversible.[96] Vasoconstriction of the splanchnic resistance vessels occurs during cardiogenic/hemorrhagic shock or sepsis. Although the intestine can tolerate a short period of hypoxia (see *Pathophysiology of Acute Intestinal Ischemia*), persistent vasoconstriction may induce critical intestinal ischemia.[99] This persistent vasoconstriction is also likely to induce NOMI after the restoration of blood flow following embolectomy of the SMA.

Experimental studies suggest that persistent vasoconstriction is primarily mediated by angiotensin II and vasopressin derived from the kidney and pituitary gland.[100,101] (see *Pathophysiology of Acute Intestinal Ischemia.*) The histological findings of NOMI resemble those induced by angiotensin II in animals.[102,103] Angiotensin II is generated via the renin-angiotensin system, which is stimulated by the hypoperfused kidney. A disproportionate distribution of angiotensin II receptors on splanchnic vascular smooth muscle cells may induce mesenteric vasoconstriction.[104]

Intestinal mucosal damage in NOMI begins at the villous tip,[105] which is characterized by the features of mucosal circulation. In vasoconstriction severe enough to reduce intestinal blood flow by 30%–50% in experimental animals, the volume of blood supplying the intestinal villi remains unchanged, but blood flow velocity to the villus tip is reduced. The reduced velocity of blood flow in the villus increases oxygen shunting from artery to vein via a "countercurrent exchange" mechanism. This is why the villous tip is susceptible to vasoconstriction.

Angiography must be performed to diagnose NOMI before intestinal infarction occurs.[70,98] The classic angiographic finding of NOMI is spasming and narrowing of multiple branches of the mesenteric arteries. Irregularities in the branches, spasm of the arcades, or impaired filling of intramural vessels may also be seen.[106] Although some physicians are skeptical about the usefulness of angiography to improve the short-term prognosis,[94] it may prevent unnecessary dissection around the SMA, which could exacerbate vasoconstriction. One of the advantages of preoperative angiography is that pharmacoangiographic treatment (see below) can be initiated simultaneously when the diagnosis of NOMI is made. Early diagnosis by angiography followed by intra-arterial papaverine infusion may be the best option for improving survival and maintaining intestinal integrity.

The therapeutic options for NOMI vary according to the interval between the onset of symptoms and the start of treatment. Initial treatment should include correction of any underlying causes, such as congestive heart failure, arrhythmia, or hypovolemia. When the diagnosis of NOMI has been made, pharmacoangiographic procedures are utilized. Papaverine hydrochloride (30–60 mg/h) is infused through a catheter in the SMA to relieve the vasoconstriction and prevent it being persistent.[70,93,98,107] The presence of peritoneal signs or an ischemic time of longer than 12 h may indicate the need for urgent laparotomy. Papaverine infusion should be continued during and after surgery. When the diagnosis of peritonitis is made intraoperatively, large segments of intestine must be resected, which often leads to short bowel syndrome. However, intestinal resection must be done in areas of questionable viability to preserve a longer segment of intestine. A second-look exploration is necessary to confirm the viability of the remaining intestine. Sheridan et al. reported that the accuracy of prediction of intestinal viability using clinical criteria, such as intestinal color, arterial pulsation, and peristalsis, was only 58%.[108]

Conclusions

Acute mesenteric ischemia is not a single clinical entity but rather a complex of diseases with many clinical features caused by impaired blood perfusion to the intestine. Despite advanced diagnostic modalities, AMI is still a life-threatening condition, and although many predisposing factors, such as aging and atherosclerosis, are beyond the physician's control, accumulated knowledge on this condition is expected to improve its prognosis through a multidisciplinary approach.

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