Chapter 25
Clinical Presentation and Diagnosis

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Nonocclusive mesenteric ischemia (NOMI), a condition in which blood supply to the splanchnic circulation is hampered by a non-obstructive cause, accounts for approximately 20 % of all causes of acute mesenteric ischemia [1, 2]. Prevalence is highest in the intensive care setting in patients suffering from either cardiogenic or septic shock in which mesenteric circulation is compromised by hypotension and decreased cardiac output and with the subsequent use of vasopressors [1]. As a result, a lowered mesenteric flow causes intestinal hypoxia with watershed areas of critical mesenteric circulation. Early and adequate diagnosis is essential to prevent intestinal ischemia, necrosis, sepsis, and death. Although the widespread use of invasive hemodynamic monitoring has reduced the mortality of NOMI from almost 100 to 70 % [3–5], increased awareness of clinical symptoms in combination with novel diagnostic modalities may help us further reduce these dramatic mortality rates.

In this chapter an overview of etiology, clinical presentation, and diagnostic considerations of NOMI will be presented, after which treatment will be discussed in Chap. 26.

Etiology

Splanchnic hypoperfusion can be caused by different mechanisms but is primarily the result of a homeostatic mechanism to preserve cardiac and cerebral blood flow at the cost of mesenteric and peripheral circulation via disproportionate vasoconstriction. Intestinal mucosal damage is initiated at the villous tips because of their

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relatively high oxygen requirement and results in irreversible necrosis after 2–3 h of hypoperfusion. Particularly elderly people are at risk because of limited compensatory hemodynamic strategies. Besides age, also pre-existing myocardial infarction, congestive heart failure, hypotension following dialysis, and recent major cardiovascular or abdominal surgery in combination with extensive enteric feeding have been described as risk factors for the development of NOMI [3, 6–8]. Furthermore, administration of pharmacological agents such as alpha-adrenergic agonists is responsible for an increased vasoconstriction and thus an increased resistance in peripheral splanchnic vessels.

Clinical Manifestation

Compared to the acute and severe abdominal pain in occlusive mesenteric ischemia, severity and location of abdominal pain in NOMI is more variable. Peritoneal signs of inflammation are often absent in the early phase; however, when ischemia progresses, bowel distension, rebound tenderness and guarding of abdominal musculature, hypotension, fever, decreased bowel sounds, nausea, vomiting, diarrhea, and anorexia are likely to be observed [9]. However, these symptoms may take days to develop and are not seldom precluded by intestinal perforation [10]. Conversely, 20–30 % of patients with NOMI do not report any abdominal pain at all. The clinical condition of these patients is often dominated by extensive comorbidities. Under these circumstances, intestinal ischemia may not be clinically evident until hours or days after the initial hemodynamic insult [8].

Diagnostic Considerations

According to the ACC/AHA Guideline for the management of patients with peripheral artery disease, NOMI should be suspected in (1) patients with low flow states or shock of any origin who develop abdominal pain, (2) patients receiving vasoconstrictor substances and medications (e.g., cocaine, vasopressin, norepinephrine) who develop abdominal pain, or (3) patients who develop abdominal pain after coarctation repair or after surgical revascularization for intestinal ischemia caused by arterial obstruction [10].

Rapid diagnosis of mesenteric ischemia is crucial in order to avoid intestinal necrosis and its sequela. Therefore, priority should be given to resuscitation when suspecting NOMI by improving cardiac output and correcting hypotension, hypovolemia, and cardiac arrhythmias. Subsequently, diagnostic procedures need to be performed as soon as possible to confirm or reject clinical suspicion. Nonetheless, early symptoms of NOMI are nonspecific and often result in delayed diagnosis. Several diagnostic tools are available in the workup of mesenteric ischemia, and in many cases a combination of the outcome of several diagnostic modalities confirms the diagnosis.

Laboratory Assays

Although laboratory findings are nonspecific for the detection of mesenteric ischemia, several tests have been investigated in the context of NOMI. Firstly, following intestinal dehydration, hematocrit increases. Secondly, the anaerobic glycolysis during hypoxia leads to lactate acidosis. Thirdly, due to intestinal cell death, lactate dehydrogenase (LDH) and creatine kinase will be released into the circulation. Moreover, leukocytosis can be considered another nonspecific associated reaction [11].

Given that mesenteric ischemia starts from the intestinal mucosa, two promising mucosal biomarkers have been identified: intestinal fatty-acid binding protein (I-FABP) and alpha-glutathione S-transferase (alpha-GST) [12]. I-FABP comprises a class of low molecular weight cytosolic proteins and can be found in tissues involved in uptake and consumption of fatty acids. It is highly expressed in cells on the luminal side of small intestinal villi and released into the circulation upon enterocyte membrane integrity loss. Urinary and plasma I-FABP levels are significantly elevated in patients with intestinal ischemia compared to healthy controls [13]. I-FABP has been reported as a specific and sensitive marker for postoperative intestinal necrosis [14]. A clinical trial demonstrated a high sensitivity (0.90) and specificity (0.89) for urinary I-FABP [15]. Alpha-GST is released by a variety of cells following cell membrane damage [16] and is known to be highly active both in the liver and the small intestine mucosa [17]. Alpha-GST has pooled sensitivity and specificity for diagnosing mesenteric ischemia of 0.68 and 0.85, respectively.

Angiography

The American Gastroenterological Association guideline of 2000 states that mesenteric angiography is the standard of reference for diagnosing mesenteric ischemia [18]. When a clinician is aware of possible mesenteric ischemia, angiography is accurate and increases survival [19]. In patients with NOMI, selective angiography can exclude a significant arterial lesion while demonstrating areas of narrowing and irregularity in major branches, decreased or absent flow in the smaller vessels, and an absent submucosal blush [1].

Moreover, the major benefit of performing a digital subtraction angiography (DSA) in patients suspected of NOMI is that immediate treatment by infusion of vasodilators through the angiographic catheter can be initiated to reverse the underlying condition causing the mesenteric vasoconstriction. Nevertheless, intra-arterial angiography is invasive and time consuming, and the unavailability of this diagnostic modality in some hospitals may lead to a critical delay in diagnosis. Therefore, over the last decade there has been a major shift toward computed tomography angiography (CTA) because it is less invasive, less time- and resource consuming, and more readily available.

Computed Tomography

CTA has replaced angiography as the standard of reference in diagnosing mesenteric ischemia with a sensitivity and specificity of 0.96 and 0.94, respectively [20, 21]. With a short examination time and the ability to rule out several other causes of acute abdominal pain, CTA provides a noninvasive method to adequately depict the abdominal aorta, the origin of the splanchnic arteries, their central parts, and its branches in diagnostic quality. During the examination vascular enhancement is achieved by administration of iodinated contrast agents in bolus techniques after which luminal narrowing of the splanchnic vasculature can be assessed and graded. Besides evaluation of contrast distribution during bolus injection, thickening of the bowel wall, absence of bowel wall enhancement, intramural hemorrhage, focal or diffuse intraperitoneal fluid collections, intestinal pneumatosis, portal venous gas collections, edematous wall thickening, or inhomogeneous contrast enhancement of the mucosa may be observed and have been associated with mesenteric ischemia. Unfortunately, all of the above have been considered nonspecific and are present in only 20–60 % of patients with mesenteric ischemia [22, 23].

Magnetic Resonance Imaging

Contrast-enhanced magnetic resonance angiography (CE-MRA) is considered a novel approach in the identification of mesenteric ischemia. CE-MRA of the splanchnic vessels is appealing because of its noninvasive character, and moreover it avoids the nephrotoxicity and allergic risks associated with iodinated contrast agents [21]. Although, to our knowledge, CE-MRA has not been used to evaluate NOMI in humans, non-occlusive emboli have been adequately visualized as filling defects, and it yielded a sensitivity and specificity of 0.95 and 1.00, respectively, in a clinical trial designed to diagnose severe stenosis or occlusion of the origins of the celiac axes and superior mesenteric artery [24]. Unfortunately, the use of CE-MRA is limited to identification of more proximal located occlusions and does not have the same spatial resolution and acquisition time as CTA [25]. If better spatial resolution becomes available in the future, CE-MRA has the potential to become the diagnostic modality of choice.

Summary

Considering the potential lethal consequences of non-occlusive mesenteric ischemia, timely and adequate diagnosis is of the utmost importance. Although elevated levels of hematocrit, LDH, lactate, and creatine kinase have been associated with the presence of NOMI, lack of specificity hampers routine clinical implementation.

Novel markers (I-FABP and alpha-GST) are currently investigated for their early diagnostic power and their feasibility for diagnosing mesenteric ischemia in an early stage. Angiography by means of either CTA or DSA for detection of arterial vasoconstriction is still considered the standard of reference for evaluation of NOMI. Future improvements in spatial resolution and acquisition time may result in MRA being the superior, noninvasive modality.

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