A 64-year-old Man with Postprandial Epigastric Pain

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A 64-year-old man with a history of type 2 diabetes mellitus and tobacco use presented to the emergency department for evaluation of abdominal pain of six-months duration. He initially reported to his primary care physician six months earlier with a complaint of postprandial abdominal pain localized to the epigastrum. He was started on a proton-pump inhibitor but experienced only limited relief of symptoms. He described his abdominal pain as non-radiating and dull, usually occurring after meals and lasting approximately twenty minutes. He denied dysphagia, nausea, vomiting, fever, chills, diarrhea, dizziness, syncope, chest pain, shortness of breath, hematemesis, melena, chronic heartburn, or a history of peptic ulcer disease. He reported bright red blood per rectum which he attributed to hemorrhoids. He smoked a pack of cigarettes daily for the past 50 years. His history of alcohol consumption was significant. He was taking non-steroidal anti-inflammatory agents once or twice a week but was not receiving any prescribed medications.

Vital signs upon presentation included a temperature of 98.4° Fahrenheit, pulse of 72 beats per minute, blood pressure of 130/73 mmHg, and a respiratory rate of 18 breaths per minute. Pertinent physical findings included bilateral temporal wasting and bilateral carotid bruits with normal cardiac and pulmonary exams. His abdomen was nondistended without scars and demonstrated normoactive bowel sounds without tenderness to palpation. The liver measured twelve centimeters in the right midclavicular line and no spleen was palpated. His skin examination revealed chest wall telangectasias, but no palmar erythema or tattoos. The rectal examination revealed heme-positive brown stool with no evidence of gross blood.

His admission laboratory values revealed normal electrolytes, a serum blood glucose of 149 mg/dL (65-99mg/dL), a white-cell count of $14.9 \times 10^3/\mu L$ ($4.5-11 \times 10^3/\mu L$) with 74 percent neutrophils, a platelet count of $245 \times 10^3/\mu L$ ($134-400 \times 10^3/\mu L$), and a hemoglobin and hematocrit of 16.4 gm/dL (13.5-17.5 gm/dL) and 49.3 percent (40-51 percent), respectively. Coagulation studies were within normal ranges.

He was admitted to the hospital for further evaluation of abdominal pain and hematochezia. He received

CME INFORMATION

TARGET AUDIENCE

The July/August Clinical Case of the Month is intended for primary care physicians, general internists, surgeons, radiologists, and gastroenterologists.

EDUCATIONAL OBJECTIVES

After reading the article, the healthcare provider should be able to discuss the epidemiology, clincial manifestations, diagnosis, and treatment of chronic mesenteric ischemia.

CREDIT

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DISCLOSURE

Dr. Richert has nothing to disclose.
Dr. Masri has nothing to disclose.
Dr. Wardlaw has nothing to disclose.
Dr. Lopez discloses that he is a member of the *Journal* Board of Trustees and the *Journal* Editorial Board.

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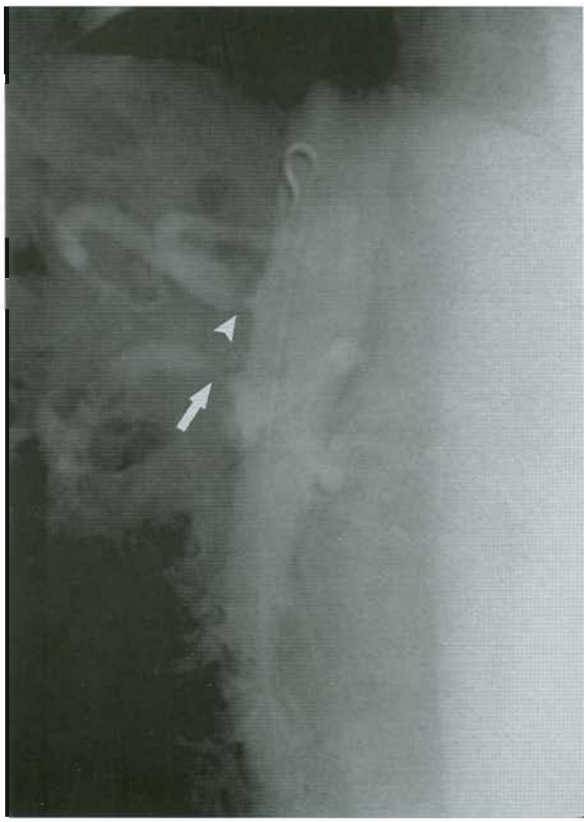

Figure 1. Patient's abdominal aortogram demonstrating severe narrowing of both the proximal celiac artery (arrowhead) and the proximal superior mesenteric artery (arrow).

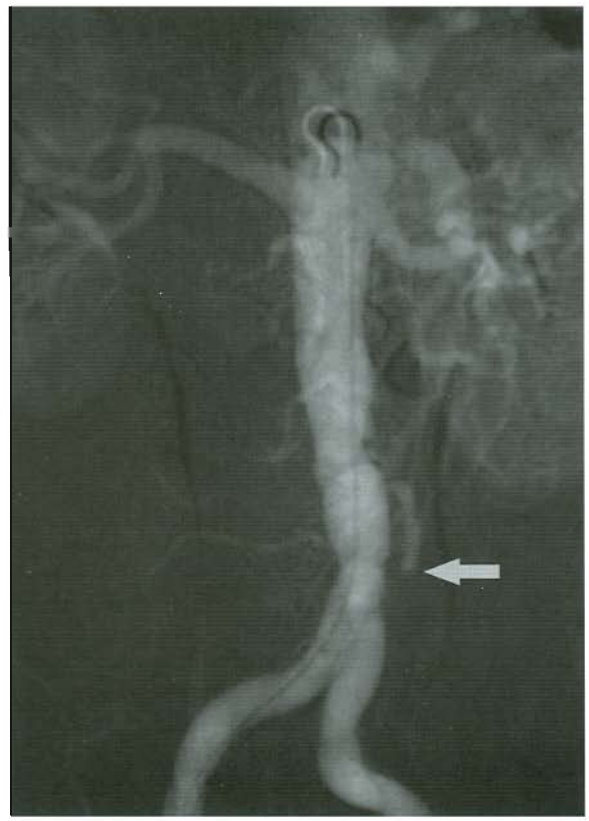

Figure 2. Patient's abdominal aortogram showing the complete occlusion of the inferior mesenteric artery (arrow).

intravenous fluids, and his hemoglobin and hematocrit were monitored with serial complete blood counts. Esophogastroduodenal endoscopy revealed a small esophageal polyp, a small hiatal hernia, antral gastritis, and a 3-mm pyloric ulceration without visible signs of bleeding. Colonoscopy revealed external and internal hemorrhoids, a hyperplastic rectal polyp, evidence of diverticulosis in the sigmoid and descending colon, an adenomatous polyp in the sigmoid colon, and a white 3-centimeter ulceration at the hepatic flexure that was worrisome for ischemia. An abdominal aortogram revealed atherosclerotic changes in the aorta, 95% stenosis of the celiac artery, 95% stenosis of the superior mesenteric artery (SMA), and 100% occlusion of the inferior mesenteric artery (Figures 1,2). A diagnosis of chronic mesenteric ischemia was established, and he underwent percutaneous transluminal angioplasty and stent placement in both the celiac trunk and the SMA (Figure 3). After the procedure, the patient reported great relief from his abdominal pain and tolerated a regular diet without difficulty.

INTRODUCTION

The spectrum of ischemic bowel diseases includes acute mesenteric ischemia, chronic mesenteric ischemia (CMI) and colonic ischemia. Colonic ischemia is the most common intestinal vascular disorder in the elderly.[1] Colonic ischemia and its clinical presentations, including mild abdominal pain with tenderness and guarding and lower gastrointestinal bleeding, are usually due to a secondary cause of decreased mesenteric perfusion such as shock, congestive heart failure, cardiac arrhythmias, vasculitis, or collagen vascular diseases.[1] The second most common intestinal vascular disorder is acute mesenteric ischemia (AMI).[1] AMI results from hypoperfusion of the gastrointestinal tract either from occlusive or nonocclusive obstruction of the arterial or venous vasculature, typically resulting in bowel necrosis. If not addressed early in its course, AMI results in a high mortality rate.[2] The third type of intestinal vascular disorder is chronic mesenteric ischemia. CMI, also known as intestinal angina, occurs when the intestinal blood supply is not able to meet the physiologic needs of the gastrointestinal tract.[1,3] Our patient represents a case of chronic mesenteric ischemia, and this article will focus on the epidemiology, vascular anatomy, physiology, clinical presentation, diagnostic procedures, and treatment of this disease process.

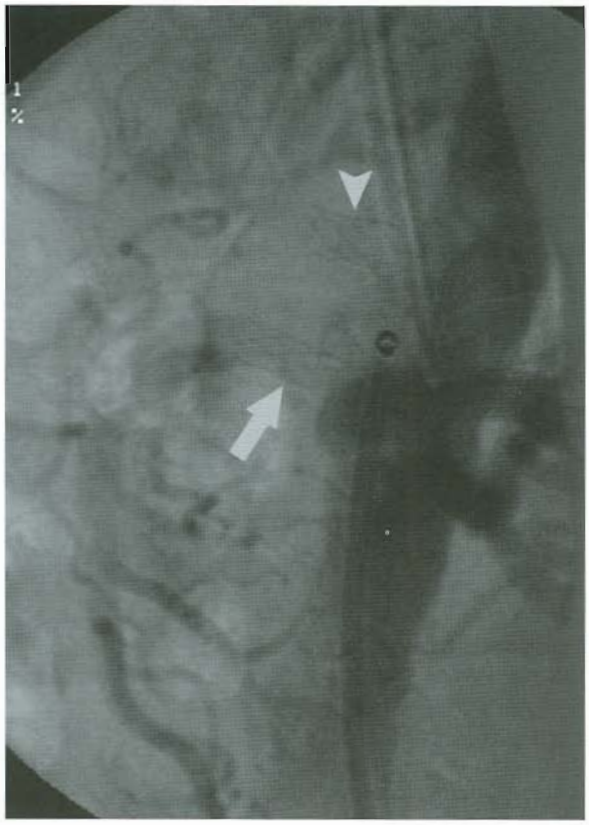

Figure 3. Patient's abdominal aortogram after stent placement in the proximal celiac artery (arrowhead) and the superior mesenteric artery (arrow).

EPIDEMIOLOGY

CMI has been estimated to have an annual incidence of 1 in 100,000 of the general population. Although a mesenteric artery stenosis of greater than fifty percent is found in eighteen percent of the population over the age of sixty-five years, very few of these patients are symptomatic.[4] CMI is found more often in women than men, classically in a three-to-one ratio.[1] The mean age at presentation is approximately fifty-eight years.[5] Significant risk factors for developing CMI include a history of tobacco use, hypertension, and hyperlipidemia.[5] Atherosclerosis is the most common cause of CMI, but other miscellaneous etiologies include, though are not limited to, median arcuate ligament compression, polyarteritis, inflammatory bowel disease, radiation, diabetes mellitus, and Buerger's disease.[6]

ANATOMY

The abdominal aorta supplies the mesenteric system via the celiac, superior mesenteric (SMA), and the inferior mesenteric arteries. The celiac artery (CA) comes off the abdominal aorta to give rise to the left gastric, splenic, and common hepatic arteries. Collectively, these vessels supply the foregut which is comprised of the stomach, proximal duodenum, pancreas, and liver. The SMA arises from the aorta approximately 1 centimeter below the celiac trunk. The SMA gives rise to the middle colic, ileocolic, right colic, and the inferior pancreaticoduodenal arteries as well as 4-6 branches which supply the jejunum. The arteries branching from the SMA supply the midgut, which includes the distal duodenum, pancreas, jejunum, ileum, cecum, and colon. The last major artery to branch off the abdominal aorta to supply the gastrointestinal tract is the IMA. The origin of the IMA is approximately 6 centimeters below the SMA trunk, and its branches are the left colic, sigmoid, and hemorrhoidal arteries. These arteries supply the distal transverse colon, descending colon, sigmoid colon, and the rectum, which collectively are known as the hindgut.[7]

PATHOPHYSIOLOGY

The mechanism of CMI involves a gradual reduction in perfusion of the intestines. As the stomach begins the digestive process, blood is shunted from less metabolically active areas such as the midgut and hindgut to the stomach. This occurs because the stomach requires more tissue perfusion due to its increased metabolic demands. The shunting of blood away from the SMA and IMA circulation to the celiac artery potentially results in adverse effects on the midgut and hindgut regions. This steal phenomenon could lead to inadequate tissue perfusion in the presence of intrinsic SMA or IMA sclerosis with subsequent postprandial abdominal pain known as "intestinal angina".[3] In order for intestinal angina to occur, two of the three major arteries need to be occluded, or partially occluded, since the splanchnic circulation is essentially one large vascular bed with a rich vascular supply of arterial and collateral blood flows.[8]

CLINICAL PRESENTATION

Patients generally present with CMI in their sixth to seventh decade and usually only after symptoms have been present for fourteen to eighteen months.[1] Often the patient has already undergone an extensive evaluation for long-standing weight loss and abdominal pain. Acalculous cholecystitis, ischemic gastritis, peptic ulcer disease, peripheral vascular disease, and coronary artery disease are commonly found in patients suffering from CMI.[8] Patients are typically malnourished, volume contracted, and anemic at initial evaluation and present with complaints of postprandial, upper abdominal pain which occurs within the first hour after eating.[5] The abdominal pain increases in severity only to plateau and slowly resolve within one to three hours.[1] Unintentional weight loss of ten to fifteen kilograms, sitophobia (fear of eating), bloating, flatulence, constipation, and diarrhea are other common complaints of patients with CMI.[1,8]

DIAGNOSIS

The diagnosis of chronic mesenteric ischemia requires a high index of clinical suspicion. Initial diagnostic studies are often nonspecific and used to exclude other causes of postprandial abdominal pain. Laboratory findings are usually not helpful but will often show findings consistent with malnutrition including hypoalbuminemia, lymphopenia, and a low hematocrit.[5] Abdominal plain films are used to rule out bowel obstruction or perforation. Findings on plain film that suggest mesenteric ischemia include bowel wall edema and calcification of the mesenteric vessels.[10] EGD and colonoscopy are sometimes performed to evaluate for peptic ulcer disease and occult malignancy. Biopsies done at the time of colonoscopy may occasionally show nonspecific changes associated with ischemia, including chronic inflammation, villous atrophy, or epithelial cell flattening.[5]

The abdominal computed tomographic (CT) scan has traditionally been used to assess patients with abdominal pain. Bowel wall thickening, submucosal edema, or portal vein gas are indirect clues to the diagnosis of mesenteric ischemia.[2] Pneumatosis, which occurs when intraluminal gas dissects into the diseased bowel wall, is a nonspecific finding in mesenteric ischemia that can also be seen in other conditions such as steroid use or collagen vascular diseases.[2]

Recent studies have focused on the use of CT and magnetic resonance imaging (MRI) angiography in the diagnosis of mesenteric ischemia. The use of three-dimensional enhanced reconstruction of the mesenteric vasculature has added another non-invasive modalitity for diagnosing this disorder.[11] However, the limitations of angiography include the inability to delineate accurately distal mesenteric disease as well as inferior mesenteric artery stenosis. It is ideally suited, however, for proximal celiac and superior mesenteric arterial occlusive disease. Because magnetic resonance (MR) can measure the postprandial flow changes in mesenteric vessels, current studies are evaluating its use to document the lack of postprandial hyperaemia in patients with chronic mesenteric ischemia.[11]

Duplex ultrasonography has been used as a diagnostic tool for chronic mesenteric ischemia for over twenty years. Doppler waveforms obtained at several sites along each mesenteric vessel in the fasting patient allow for the evaluation of individual blood flow velocities. Based on the available literature, a peak systolic velocity in the superior mesenteric artery of greater than 275 cm/sec is indicative of at least a seventy percent stenosis with an 89% sensitivity, 92% specificity, 85% positive predictive value, and a 96% negative predictive value.[12] A celiac artery peak systolic velocity of greater than 200 cm/sec reflects a greater than 70% stenosis (75% sensitivity, 89% specificity, 85% positive predictive value, and 80% negative predictive value).[12] Limitations in the use of mesenteric sonography include respiratory variation, obesity, abdominal gas, and prior abdominal surgery. Just as in CT and MRI angiography, the inferior mesenteric artery is difficult to evaluate accurately and is not routinely measured.[12] In addition to its role in diagnosis, duplex ultrasonography is now being employed in the postoperative surveillance of patients who have undergone previous mesenteric revascularization.[5]

Mesenteric angiography remains the gold standard for diagnosing chronic mesenteric ischemia.[4] A high index of suspicion or a positive preliminary screening test, such as duplex ultrasonography, in a symptomatic patient should warrant direct angiographic evaluation. Due to the extensive collateral circulation present in the splanchnic vasculature, most physicians adhere to Mickkelsen's rule which states that at least two of the primary mesenteric vessels must be significantly stenotic in order to cause symptoms of mesenteric ischemia. According to the 2000 American Gastrointestinal Association technical review on intestinal ischemia, the diagnosis of chronic mesenteric ischemia "is based upon clinical symptoms, arteriographic demonstration of an occlusive process of the splanchnic vessels, and, to a great measure, exclusion of other gastrointestinal disorders".[13]

TREATMENT

After making the diagnosis of symptomatic chronic mesenteric ischemia (CMI), it is important to refer the patient for treatment because the patient is at risk for developing acute mesenteric ischemia via embolism or thrombus formation. A review spanning ten years at the Mayo Clinic revealed that 43% of patients with acute mesenteric ischemia (AMI) had prior symptoms of untreated CMI.[14] Surgical intervention has been the mainstay of treatment for many years. However, angioplasty with or without stent placement has been gaining increased acceptance in certain patients over the last decade.

Several options for surgical revascularization have been used successfully. Since CMI is relatively uncommon, many surgeons have not performed the number of procedures needed to develop their own principles of management based on experience. In addition, there is a lack of randomized controlled studies to compare the different surgical interventions. Therefore, no consensus has been established regarding the appropriate surgical approach to CMI.[15] The choice of intervention should be individualized based on surgical experience and the patient's co-morbidities in order to minimize the potential complications and maximize the chance of surgical success. The three types of surgical interventions for CMI include bypass grafting, endarterectomy, and reimplantation.[16]

The most commonly utilized approach is bypass grafting.[15] There is some variability in the literature regarding specifics of the bypass procedures. Some surgeons favor single vessel revascularization whereas others feel that a multivessel procedure is superior. The pro-

ponents of single vessel revascularization to the SMA argue that this is the most important vessel supplying blood to the gut and that there are plenty of collateral vessels. Others argue that bypassing all diseased vessels with a multivessel approach reduces the risk of recurrence. Also, if graft occlusion should occur it would not necessarily be catastrophic. Regardless of the number of bypass vessels, the blood flow may be supplied from an antegrade reconstruction (supraceliac aorta) or a retrograde reconstruction (infrarenal aorta/common iliac artery). Proponents of an antegrade reconstruction argue that it provides a more durable procedure, whereas those favoring the retrograde approach argue that the anatomy is more familiar and that it avoids supra-renal clamping. Although there are studies in support of an antegrade approach, there are others that conclude that there are no significant differences between the two procedures.[14] Finally, there is a choice between the types of conduit, i.e., prosthetic or vein graft. The prosthetic material has the advantage of being able to deliver large volumes of blood with a reduced chance for developing an obstruction secondary to kinking;[16] however, studies comparing the two reveals no difference in graft failure.

Angioplasty with or without stent placement is an alternative treatment regimen that has been increasing in popularity over the last decade. Although an endarterectomy can be performed through the origin of the CA, SMA, or aorta with good results, the procedure comes with increased risks of complications including arterial dissection. Reimplantation has also been done in the past but is now used only as part of an aortic replacement.[16] Once reserved for patients who were not surgical candidates, angioplasty is now being considered by some to be an equivalent alternative treatment option.[17] Reported comparisons between angioplasty and bypass surgery have described similar complication and mortality rates, albeit with more durable results noted with bypass.[15]

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For each question, choose the one answer that is most correct.

1. All of the following are true about chronic mesenteric ischemia (CMI) except:
   a) CMI is found more often in women than men.
   b) The mean age at presentation is approximately 58 years.
   c) Significant risk factors for developing CMI include a history of tobacco use, hypertension, and hyperlipidemia.
   d) Inflammatory bowel disease is the most common cause of CMI.

2. True or False: The abdominal aorta supplies the mesenteric vasculature via the celiac, mesenteric, and inferior mesenteric arteries. In order for the "intestinal angina" of CMI to occur, only one of these three arteries needs to be occluded.

3. The typical patient with CMI may present with all of the following except:
   a) Complaints of postprandial pain and bloating
   b) Weight gain
   c) Lab abnormalities including anemia and hypoalbuminemia
   d) Fear of eating (sitophobia)

4. True or False: Mesenteric angiography remains the gold standard for diagnosing chronic mesenteric ischemia.