Ischemic Colitis

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Abstract

Keywords

- ischemic colitis
- colectomy
- colonoscopy
- lower gastrointestinal bleed

Most clinicians associate ischemic colitis with elderly patients who have underlying cardiovascular comorbidities. While the majority of cases probably occur in this population, the disease can present in younger patients as a result of different risk factors, making the diagnosis challenging. While a majority of patients respond to medical management, surgery is required in approximately 20% of the cases and is associated with high morbidity and mortality.

As the name implies, ischemic colitis is thought to be an injury to the colon as a result of reduced blood flow. The insult can range from inflammation and superficial injury to full thickness necrosis. While this simplified explanation accounts for a portion of the cases, ischemic injury to the colon has been attributed to multiple other causes, and the pathophysiology is undoubtedly more complex. This article will present the etiology, presentation, and risk factors associated with ischemic colitis. It will then review the workup and evaluation of these patients. Finally, it will discuss the long-term outcome of this disease.

History and Nomenclature

Ischemic colitis as a disease entity has been referenced in the medical literature as early as 1966 by Marston et al.¹ It has commonly come to be classified in two groups, gangrenous and partial thickness. However, historically, it had been classified as gangrenous, stricturing, and transient. Despite different nomenclature it remains the most common form of gastrointestinal ischemia, accounting for 50 to 60% of the cases.²

Etiology and Presentation

The condition is commonly seen in older patients in their sixties to seventies. Most of these patients have previous history of atherosclerotic disease. Because patients can present with a wide spectrum of symptoms from vague abdominal discomfort to complete abdominal catastrophe,

the diagnosis of ischemic colitis is sometimes challenging to make.

The classic presentation of ischemic colitis is an elderly patient presenting with bloody bowel movements, abdominal pain, and leukocytosis. Patients typically present with the acute onset of crampy abdominal pain and usually pass blood mixed with stool within 24 hours. The episode is usually preceded by an episode of transient hypoperfusion. The vasculature of the colon is thought to play an integral part in the disease.

The superior mesenteric artery provides blood flow to the gastrointestinal tract from the duodenum to the mid transverse colon. The inferior mesenteric artery (IMA) supplies blood to the remaining part of the colon and the superior aspect of the rectum. The internal iliac arteries communicate with the IMA via the superior and middle hemorrhoidal arteries.

As illustrated in ►Fig. 1, the collateral flow through the mesenteric branches is provided via the marginal artery of Drummond and the meandering mesenteric artery, also known as the Arc of Riolo. The marginal artery runs parallel to the colon to give branches to the vasa recta.

The marginal artery runs along the splenic flexure, but is absent or underdeveloped in 5% of the population. Injury to the colon is believed to typically occur in the “watershed” areas of the splenic flexure (Griffith point) and sigmoid colon (Sudeck point).³

The pathophysiology of ischemic colitis is more often an acute, self-limited decrease in blood supply rather than a specific vascular lesion or embolic event. Angiography, when

Fig. 1 Vascular anatomy of the large intestine. Adapted with permission from Gordon PH, Nivatvongs S. *Principles and Practice of Surgery for the Colon, Rectum and Anus*. 2nd ed. St. Louis, MO: Quality Medical Publishing, Inc.; 1999.

abnormal, shows narrowing of the small vessels and tortuosity of the long colonic arteries.⁴

While earlier studies suggested a preponderance of left-sided cases, more recent literature has questioned this “classic” presentation. A review of 49 patients presenting with clinically documented ischemic colitis found that multiple sites were affected in 55% of the patients. In addition, there was no significantly preferred location of the disease.⁵

Risk Factors

Ischemic colitis is typically associated with abdominal pain and blood in the stool. A large, prospective, population-based study from Iceland looked at all patients requiring hospitalization for lower gastrointestinal bleeding who underwent colonoscopy. A total of 16% of the cases were a result of ischemic colitis.⁶ Another case-control study looked at patients presenting with lower abdominal pain with or without bleeding. The investigators found that age greater than 60 years, hemodialysis, diabetes mellitus, hypertension, hypoalbuminemia, and use of constipation-inducing medications were associated with having ischemic colitis.⁷

A recent retrospective, case-control study sought to examine the role of cardiovascular disease, cardiovascular risk factors, and treatment on the development of ischemic colitis. A total of 161 cases of ischemic colitis presenting from 1998 to 2003 were matched with 322 controls. Diabetes, dyslipidemia, heart failure, peripheral vascular disease, and use of aspirin or digoxin were associated with the development of ischemic colitis.⁸ While this profile matches the typical presentation of ischemic colitis, certain behaviors may put other subsets of the population at risk and warrant mention. Surgery for aortic aneurysm repair often compromises colonic blood flow and can lead to ischemia. In addition,

constipation, coagulopathy, illicit and prescription drug use, and extreme exertion have shown to be risk factors in young adults.

Abdominal Aortic Aneurysm Repair

Ischemic colitis is a rare but morbid complication of aortic aneurysm surgery. Utilizing the Nationwide Inpatient Sample database, Perry et al identified 89,967 patients undergoing surgery for abdominal aortic aneurysm repair over a 2-year period. The overall incidence of ischemic colitis was 2.2%. As expected, the incidence was much higher (8.9%) for repair of a ruptured aneurysm. Interestingly, it was also higher for open repair (1.9%) than endovascular repair (0.5%). Regardless of the approach, colonic ischemia was associated with increased morbidity and a two to fourfold increase in mortality.⁹ Because of this, several articles have advocated for routine endoscopic examinations in patients following repair of ruptured aneurysms. While it seems to reliably detect ischemic injury,¹⁰ its ability to impact mortality is questionable.¹¹

Constipation

A retrospective review compared the clinical features of 16 patients with ischemic colitis younger than 45 years with those older than 70 years. Constipation before the onset of symptoms was more frequently found in younger patients.¹² To evaluate the clinical features of the disease, Habu et al looked at 68 patients with ischemic colitis whose age ranged from 22 to 98 years. They found that chronic constipation was commonly associated with ischemic colitis in both young and old patients.¹³ Finally, using a research database, investigators found that the relative risk for ischemic colitis was 2.78 times higher for patients with constipation.¹⁴ While the exact mechanism has not been determined, it is speculated that increased intraluminal pressure results in decreased blood flow to the mucosa, and predisposes these patients to ischemic attacks.

Coagulopathy

Coagulopathy may predispose patients to ischemic colitis as well. A total of 18 patients with a history of ischemic colitis underwent an extensive hypercoagulability evaluation. Five patients, or 28%, tested positive for one or more clotting abnormalities, compared with a prevalence of 8.4% in the general population.¹⁵

Illicit and Prescription Drugs

Numerous studies have shown that illicit drug use can result in ischemic colitis in otherwise healthy patients. A retrospective review of 18 patients with documented cocaine-associated enterocolitis found patients typically presenting within 3 days of cocaine use. Inflammatory changes were most often found on the right side. While the majority of cases responded to nonoperative management, the need for laparotomy was found to have a 50% mortality.¹⁶ A case-control study conducted over a 9-year period compared 19 patients with cocaine-associated ischemic colitis to 78 patients with ischemic colitis without cocaine use. Patients with cocaine use were younger but had a significantly higher mortality than

other patients with ischemic colitis (26 vs. 7.7%).¹⁷ Methamphetamines are synthetic sympathomimetic drugs that may cause vasoconstriction and end organ damage. Their use has also been reported to result in colonic ischemia.¹⁸

In addition to these illicit substances, numerous prescription drugs have been associated with the development of ischemic colitis (► **Table 1**). The exact mechanism for many of these is not completely understood.

Endurance Athletes

A total of 27% of recreational triathletes, 20% of marathon runners, and 87% of 100-mile ultramarathon runners test positive for fecal occult blood.¹⁹ While there are a myriad of causes of occult bleeding, numerous accounts of ischemic colitis developing in high endurance athletes have been reported.²⁰ The authors recommended ensuring adequate hydration, avoiding nonsteroidal anti-inflammatory medications, and avoiding caffeine, alcohol, and high energy or hypertonic food and drink during exercise.

Diagnostic Evaluation

As with any patient presenting with abdominal complaints, a complete history and physical examination is essential. Because of the nonspecific and vague nature of the symptoms, clinicians must maintain a high index of suspicion and actively inquire about comorbidities, medications, and drug use that may predispose patients to ischemic colitis. While other studies may be obtained to evaluate the extent of the disease, the physical examination findings will drive the treatment algorithm. Patients with peritonitis and sepsis should be aggressively resuscitated and taken to the operating room. As ischemic colitis can be very similar to other cases of colitis (i.e., ulcerative, infectious, diverticulitis, or malignancy), additional confirmatory tests are needed.

Laboratory Tests

A complete blood count, metabolic panel, and liver function studies are helpful to evaluate the extent of physiologic impairment. In addition to these routine laboratory tests, specific markers for lactate, lactate dehydrogenase, creatine kinase, or amylase should be obtained. It is important to realize that there is no specific laboratory test for ischemic colitis, and that elevated levels of these markers suggest inadequate global perfusion or nonspecific tissue injury.

Infectious etiologies should be investigated. Stool studies should be performed for *Salmonella*, *Shigella*, *Campylobacter*, and *Escherichia coli* (O157:H7) as well as *Clostridium difficile*. Testing for parasites including *Entamoeba histolytica* and *Angiostrongylus costaricensis*, and viruses such as cytomegalovirus should also be considered.

Imaging Studies

Early in the course of the disease, abdominal X-rays are likely to show a nonspecific gas pattern or ileus. As the disease progresses, submucosal hemorrhage or edema can result in focal mural thickening, often described as “thumbprinting.”

Table 1 Drugs potentially associated with ischemic colitis

- Digoxin
- Aspirin
- Naratriptan
- Ma huang (herbal food supplement)
- Phentermine (weight loss medication)
- Oral contraceptives
- Pseudoephedrine
- Phenobarbital
- Nasal decongestants
- Dextroamphetamine
- Type I interferons (IFN- α and IFN- β)
- Tumor necrosis factor α
- Antipsychotics
 - Clozapine
- Serotonergic medications
 - Alosetron
 - Tegaserod
- Vasopressors
- Cocaine
- Methamphetamine

Perforation and pneumatosis are consistent with severe injury to the colon.²¹

A computed tomographic (CT) scan may appear normal in early or mild cases of ischemic colitis, but may be useful to rule out other causes of abdominal pain or sepsis. Segmental thickening of the colon wall or pericolic stranding may be seen later in the course of the disease as illustrated in ► **Fig. 2**. However, these findings are not specific and can be seen in other conditions, such as inflammatory bowel disease or infection. Pneumatosis or portal venous gas, when seen, are a late finding and suggest bowel infarction.²²

Other imaging studies have been evaluated in the management of patients with ischemic colitis. A small prospective group of seven patients with documented ischemic colitis underwent serial abdominal magnetic resonance imaging (MRI) examinations, colonoscopy, and CT scans. While the timing of the studies made direct comparisons difficult to interpret, the authors concluded that MRI may be used as a substitute to invasive procedures to diagnose and follow patients with ischemic colitis.²³ Tc-99m nuclear medicine studies have been evaluated in a small number of patients and were not considered useful.²⁴

Colonoscopy

In the absence of peritoneal signs, colonoscopy is the diagnostic test of choice to evaluate the degree of ischemia. Colonoscopy remains the most sensitive and specific study available for the diagnosis of ischemic colitis because it allows for detection of mucosal changes by directly visualizing the mucosa. Endoscopic findings consistent with ischemic colitis include petechial hemorrhages, edematous and fragile mucosa, mucosal bleeding, segmental erythema, scattered erosions, and longitudinal ulcerations. More severe findings include loss of haustral markings, cyanosis, and gangrene (► **Figs. 3** and **4**). Biopsies can be helpful to rule out other disease processes, but the pathological findings are relatively nonspecific. Histology often reveals erosion, granulation

Fig. 2 Computerized tomographic scan of coronal sections of the abdomen showing thickening of the splenic flexure, descending colon, and proximal sigmoid colon in a patient with documented ischemic colitis.

tissue hyperplasia, gland atrophy, lamina propria hemorrhage, and macrophages with hemosiderin pigmentation in the submucosa²⁵ (► **Fig. 5**). As the ischemia progresses, evidence of submucosal edema and hemorrhage can be seen as bluish-black blebs protruding into the lumen of the bowel. These lesions are responsible for the characteristic thumb-printing sign on radiographic studies.²⁶

Colonoscopy, when undertaken, should be performed with caution to prevent perforation. Minimal air insufflation and gentle maneuvering should be practiced. Many endoscopists caution that colonoscopy in the setting of suspected ischemic disease should proceed to, but not past, the area of injury.

There is no uniformly accepted classification system for the endoscopic findings of ischemic colitis. However, one study of 85 patients with ischemic colitis compared patients with longitudinal and circumferential ulcers on colonoscopy to those with redness and erosions. They found that patients with ulcers were more likely to present with abdominal pain and had a higher baseline C reactive protein. In addition, they had a significantly longer hospital stay than those with redness or erosions.²⁷

Medical Treatment

Once the diagnosis of ischemic colitis has been made, patients should be aggressively resuscitated and receive broad-spectrum intravenous antibiotics. If the patients are hemodynamically stable and do not have signs of peritonitis, they should undergo urgent colonoscopy. The treatment is dictated by the findings of physical examination and the appearance of the colonic mucosa on endoscopy. Patients with peritoneal signs or nonviable bowel on endoscopy need immediate operative intervention; otherwise they can be managed medically.

Medical management consists of bowel rest, intravenous fluids, and broad-spectrum antibiotics. Nasogastric tubes should be used selectively in patients with distention or ileus. A “splanchnic focused” resuscitation with avoidance of vaso-

constrictive medications should be implemented. Mental status, abdominal pain, and urine output should be monitored to assess for signs of adequate end organ perfusion. Additional endpoints of resuscitation, including lactate levels and mixed venous oxygen saturation, may be indicated, depending upon the severity of the attack.

Surgical Treatment

In the acute setting, the operative procedure is dictated by the extent of injury to the bowel and the overall condition of the patient. All nonviable bowels must be resected. A damage-control approach may be indicated if intraoperative monitoring reveals hypothermia, coagulopathy, and acidosis. Second look operations may be useful if there are areas of questionable perfusion. The decision to perform an anastomosis should be based on the immediate condition of the patients as well as an assessment of their comorbidities and nutritional status.

After resolution of the acute attack, a small number of patients will develop strictures in the colon. Colonoscopy with biopsy is recommended to evaluate for malignancy or other pathology. Depending upon the severity of the symptoms and the degree of stenosis, dilation or surgical resection may be indicated.

Fig. 3 Endoscopic photograph of colonic mucosa demonstrating: (A) mucosal bleeding, erythema, and intraluminal blood consistent with mild ischemic colitis; (B) ulceration, scattered erosions, and intraluminal clot consistent with severe colonic ischemia.

Fig. 4 Photograph from colonoscopy which demonstrates: (A) gangrenous mucosa and (B) a transition point, distally, to normal mucosa.

Outcomes

Acute ischemic colitis usually resolves with medical care but morbidity and mortality rates remain high for patients requiring surgery. A recent meta-analysis revealed that 80.3% of the patients were managed medically with a mortality rate of 6.2%. Surgery was associated with a 39.3% mortality rate.²⁸ This is consistent with a retrospective review of 49 patients with ischemic colitis looking at the outcome of surgical intervention. Emergency colectomy was performed in 81.6%. The authors reported a morbidity rate of 85.7% and a mortality rate of 44.9%. Preoperative hypotension was a significant risk factor for mortality.²⁹

The long-term prognosis for these patients is more favorable. A retrospective review of 135 patients with ischemic colitis reported that recurrence rates were 2.9 and 9.7% at 1 and 5 years, respectively. Five-year survival was 69%, but most patients died because of other causes.³⁰

Conclusion

The combination of vague symptoms and physical findings, and nonspecific laboratory and radiographic results can make the diagnosis of ischemic colitis challenging to even the most seasoned clinicians. Recognizing risk factors in younger pa-

Fig. 5 Histologic photograph from a biopsy specimen of a patient with ischemic colitis which shows ulceration with fibrinous exudate, vascular congestion, and hemorrhage with associated acute inflammation and granulation tissue reaction.

tients and maintaining a high index of suspicion is essential to institute timely care. The majority of patients respond to medical management. Surgery (colectomy), when required, is associated with a high morbidity and mortality rate.

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