Updates in Ischemic Colitis

Eden A. Nohra∗
Ghattas Khoury†

Walid Faraj†
Samer Deeba∗∗

∗American University of Beirut, en11@aub.edu.lb
†American University of Beirut
‡American University of Beirut
∗∗American University of Beirut, sd08@aub.edu.lb
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Abstract

Purpose: The purpose is to provide an understanding of diagnosis and management schemes of ischemic colitis to positively influence outcome.

Methods: A review of the literature using keywords on pubmed and manual searching of references.

Results: A synopsis of the etiology, diagnosis, management, and outcome of ischemic colitis.

Conclusions: We are presenting a thorough review of the literature to provide the current updated guidelines for the diagnosis and management of ischemic colitis to medical practitioners.

KEYWORDS: Ischemic colitis, pathophysiology, diagnosis, treatment, prognosis, gangrenous ischemic colitis, non-gangrenous ischemic colitis
Background

Ischemic colitis (IC) is an emergency clinical condition that is worrisome to general surgeons and associated with an increased rate in mortality and morbidity of patients, not to mention the burden it puts on the physician and on the healthcare system.

Etiology and pathogenesis

Blood supply of the colon is regulated by several factors, of which local auto-regulatory mechanisms, extrinsic influences, oxygen demand of the tissue according to needs such as motility and metabolism, and circulating as well as local humoral agents. The physiologic state of ischemia of the colon is a mismatch between the supply of blood bringing in oxygen and nutrients and demand of these by the tissue. The balance between supply and demand can be affected by changes in the systemic circulation, and anatomic or functional changes in the mesenteric blood flow such as states of hypoperfusion, anatomic artery occlusion, or generalized states of artery vasospasm leading to decreased blood flow to the tissues. Unfortunately, the colon and its mucosa are not resistant to ischemia and changes in the mucosa are seen within few minutes of the ischemic insult.\(^1\)

Disruption of the blood supply of the colon can be attributed to numerous pathologic processes such as trauma, thrombosis and embolization of the mesenteric arteries. Certain operations are associated with an increased risk of IC such as abdominal aortic repair operations where the risk can range from 5-9% in elective cases and up to 60% in emergency cases.\(^2\) The extent of the ischemia in the affected segments depends on the proximity of the occlusion to the takeoff of the vessel. Lesions closer to the inferior mesenteric artery (IMA) origin will manifest clinically with descending/sigmoid colon necrosis, while distal lesions in the branches of the main arteries may manifest with patchy necrosis. If there is adequate blood collaterals supplying the colon, distal occlusions might go unnoticed. Venous outflow obstruction is uncommon and is more commonly associated with pelvic trauma/surgical patients and with hypercoagulable states such as malignancy, portal hypertension, and pancreatitis. Vasospasm can lead to ischemia because profound systemic insults cause intense vasoconstriction of the mesenteric feeding vessels as
a compensatory mechanism to increase the vascular resistance and shift the remaining blood supply to more vital organs, occasionally at the expense of needed blood supply to the bowel. Certain medications can precipitate mesenteric vasoconstriction with ischemic consequences such as diuretics, digitalis, catecholamines, and cocaine. Large bowel obstruction can also predispose to ischemia as in the case of tumors, fecal impaction, adhesions, volvulus, and diverticular disease.\[3\]

Several regional factors predispose the colon to ischemia. The colon has less blood perfusion per 100 gram of tissue than the rest of the gastrointestinal tract\[4\] and hence has less reserve blood flow to mobilize in situations of need. The presence of an extensive network of capillary anastomoses in the muscularis and submucosal layers, which is less developed in the large bowel than in the small bowel, contributes to the attenuation of collateral flow. The right colon is more susceptible to ischemia because it runs on longer vasa recta (small terminal blood vessels) which are more predisposed to vasospasm than the short left colon vasa recta. Furthermore, the decrease in blood flow to the colon during contraction, in contrast to the exact opposite phenomenon in the small bowel during digestion, is experimentally shown to render the colon more susceptible to ischemia. Patients using non-steroidal anti-inflammatory drugs are more prone to develop IC because of the inhibition of the cyclooxygenase pathway and the diversion of the metabolism of arachidonic acid into the production of vasoconstrictor leukotrienes.\[5\] Vasoconstrictor inflammatory mediators, along with free radicals formed during their metabolism, can cause vascular insufficiency and ulceration of the mucosa.\[6\]

**Types and distribution of ischemic colitis**

There are two distinct types of IC, the nongangrenous (85%) and the gangrenous type (15%).\[4\] The nongangrenous type involves the mucosa, submucosa, and even the muscularis; whereas the gangrenous type is transmural. If ischemia involves the first two inner layers of the bowel wall, then it heals with no consequence. If the muscularis is involved, then it heals with stricture formation. If the ischemia is transmural, then surgical excision is mandatory.\[7, 8\]
In IC, the left colon and/or rectum, splenic flexure, and right colon are affected in around 70-75%, 20 %, and 10% respectively. Ligation of the IMA leads to IC in the descending colon and the sigmoid, while systemic low flow states present as IC in the retroperitoneal part of the right colon. Non-occlusive ischemia normally affects watershed areas such as the splenic flexure and the rectosigmoid junction.\cite{4,9}

**Clinical Presentation**

The clinical presentation is a spectrum of symptoms ranging from nonspecific abdominal pain for the nongangrenous mucosal ischemia to full-blown sepsis and acute surgical abdomen for the gangrenous type because of colon wall perforation. The extent of the ischemia varies according to severity, magnitude, and rapidity of the insult. Ischemic insults resulting from embolic phenomena have a quicker and more intense clinical presentation than those resulting from chronic atherosclerotic vascular insufficiency, the latter having a more insidious onset as the colon usually develops vascular collaterals by the time atherosclerosis totally obstructs its main supply, as is the case of IMA obstruction.

Self-limiting nongangrenous IC is the most common presentation. Typically, the patients are above 60 years of age with no previous abdominal complaints.\cite{7, 9, 10} The predisposing risk factors were identified by Park et. al in a study that included 467 patients.\cite{11} He concluded that old age, hemodialysis, hypertension, diabetes mellitus, hypoalbuminemia, and the use of constipation-inducing medications are risk factors for the diagnosis of IC in patients presenting with lower abdominal pain with or without bloody diarrhea.\cite{11}

Usual presenting symptoms include abdominal pain, diarrhea, change in bowel habits, and blood per rectum. If bleeding is profuse then the diagnosis of IC should be questioned and other diagnoses should be entertained. In typical cases of IC, the pain is sudden in onset and localizes to the left lower quadrant. It is crampy in nature and is often associated with tenesmus, nausea, vomiting, and loss of appetite. Examination reveals stable cardiovascular parameters with low grade fever, mild abdominal distention and tenderness localized to left lower quadrant. Digital rectal examination often reveals blood per rectum. Laboratory results reveal leukocytosis with a shift to the left. The symptoms
are usually self-limiting and resolve spontaneously. In this group of patients, those who progress to the chronic form of the disease are usually in the older age group, have longer time to resolution, and longer time to laboratory value normalization.\[^3\]

As for the patients presenting with full thickness gangrenous IC, the presentation is that of an abdominal catastrophe with full-blown sepsis and shock. The presentation is much more acute than the previous group. The patient usually has higher fevers and has cardiovascular instability with tachycardia and hypotension. The abdominal examination reveals a board-like abdomen, which is tender in all quadrants, and signs of peritonitis. Gangrenous IC often manifests in chronically hospitalized patients, especially in high dependency units, and may be missed because of the debilitated state of the patient due to the original illness. Therefore, the physician must always keep a high index of suspicion in susceptible patients and should always question bowel viability when other causes of sepsis are ruled out.\[^12\]

Both gangrenous and non gangrenous types are being seen more frequently in young patients and a high index of suspicion should be present in the context of coagulopathies\[^7\], sickle cell disease\[^{13}\], vasculitis\[^{14}\], use of vasoactive medications\[^{15}\], marathon runners\[^{16}\], and cocaine abuse\[^{17}\].

### Diagnosis

The physicians’ high index of suspicion in the appropriate clinical presentation remains the best adjunct to early diagnosis and management of IC. Serial physical examination complemented with serial radiologic and endoscopic studies is the mainstay of diagnosis. For a patient suspected of nongangrenous IC with no signs of systemic sepsis, negative findings on abdominal films, and a physical examination showing localized signs in the left lower quadrant, it is best to investigate the potential diagnosis of IC by colonoscopy. On the other hand, patients are suspected of gangrenous forms of the disease if they have a septic presentation, abdominal films showing air under the diaphragm (perforation of the colon), air within the bowel wall, or portal venous air, and a physical examination suggestive of an acute abdomen. These patients usually have an infarcted colon wall and must undergo exploratory laparotomy straight away.\[^{18}\] Imaging is an option for patients with borderline presentations before the decision to
operate is contemplated (Figure 1). Serum markers like lactate and lactate dehydrogenase levels are non-specific but can be used for follow up after the diagnosis is confirmed using other modalities. \[19\] Plain abdominal films or contrast films using barium enema can be used but have fallen out of favor since CT scans became readily available. The physician should bear in mind that the use of barium as a contrast may cause further contamination in the abdominal cavity in patients who have a perforation or may even cause an iatrogenic perforation. \[20\] Abdominal ultrasound may help in the diagnosis although it relies on nonspecific findings such as a thickened bowel wall; it may also identify collections in the paracolic area similar to a CT scan. \[21, 22\]

Colonoscopy remains the gold standard for the diagnosis because it has the ability to visualize the mucosa and also to take tissue biopsy for histologic evaluation. \[23\] Hemorrhagic patches seen during colonoscopy represent bleeding into the submucosa and are analogous to the “thumb printing” we see in barium studies. The segmental distribution of these patches, with or without the presence of ulceration, strongly suggests IC. In the aftermath of the ischemic injury, serial colonoscopies and serial abdominal physical examination are necessary to determine outcome and to diagnose the clinical sequels, if any. The early diagnostic colonoscopy should be done within the first 48 hours of presentation \[24\] because, after that, the submucosal hemorrhages may be reabsorbed by the circulation or may slough into the lumen, at which point patches of ulceration may be seen instead of the more definitive signs described above. Colonoscopy is strictly contraindicated in the presence of peritonitis (these patients should have a laparotomy straight away). For patients in whom it is not contraindicated, caution is still advised as distension of the colon at room air to a pressure of 30 mmHg further diminishes colonic blood flow and may cause or potentiate ischemia. \[25, 26\] This may be alleviated by the use of carbon dioxide because of its vasodilator effect.
Figure 1. A cut from a CT of the abdomen of a patient presenting with surgical abdomen showing thickening of the large bowel at the splenic flexure and fluid around it.

The endoscopic and histologic examination of the colon in question depends on the stage of ischemia and on the intensity of the insult. \textsuperscript{[27]} Punctate ulcers interspersed among areas of alternating pale mucosa and hyperemic mucosa represent early ischemic changes. Biopsies from these pale areas will show submucosal hemorrhage and edema; whereas the hyperemic areas will show non-specific inflammatory infiltrates. \textsuperscript{[27]} Rare changes include the appearance of ghost cells. More commonly, examination will show vascular congestion, loss of mucin and surface epithelial cells, and degeneration of crypt architecture- the extent of each depends on the severity of the insult. At the early stages of ischemia, a moderate inflammatory cellular infiltrate is present in the lamina propria. \textsuperscript{[27]} When ischemia progresses from the described nongangrenous state to the fully infarcted gangrenous state, the changes will also progress to form extensive areas of gray-green to black mucosa and submucosa with small perforations seen in between. When ischemia becomes chronic and the initial insult was not enough to cause gangrenous colitis, the colon recovers partially according to the extent of the primary insult. Some atrophy is seen in the mucosa with dispersed areas of granulation tissue. In the state of scarring and stricture formation, the endoscopic image is that of a whitish narrowing in the lumen.
and biopsy reveals predominantly fibrosis, with minimal inflammation and some regenerating and damaged crypts.\textsuperscript{[27]}

The major mesenteric vessels like the IMA are usually patent in IC, with the occlusion being mainly at the arteriolar level. Thus, mesenteric angiography is of minimal benefit unless acute embolic phenomena to the IMA or the ileocecal artery are contemplated.\textsuperscript{[28]}

\textbf{Differential Diagnosis}

IC can be of different etiologies, each of which having a different pathophysiology. Acute mesenteric ischemia is the most serious, with sudden occlusion of the IMA due to an embolus originating in the proximal vascular system (heart or aorta). The patient presents with severe abdominal pain beyond physical findings.\textsuperscript{[29]} These patients are known to have vasculopathy elsewhere such as history of transient ischemic attacks in the brain or peripheral vascular disease with claudication, atherosclerosis of the aorta, or atrial fibrillation receiving treatment. The gold standard of diagnosis is mesenteric arteriography.

Mesenteric venous occlusion is another cause and is characterized by vague insidious onset abdominal pain crampy in nature, with distention and vomiting later in the course of the disease. Association with liver disease, inflammatory bowel disease, hematologic disease, hypercoagualopathies, and malignancies is common. CT scan may reveal an occlusion in the mesenteric veins or in the confluence of the mesenteric veins where they form the portal vein.

The diagnosis of diverticular disease should also be entertained, especially in patients who have documented previous attacks. Examination reveals peritonitis in the left lower quadrant with leukocytosis. CT scan with rectal contrast usually confirms the diagnosis.

Infectious colitis can also mimic the presentation of ischemic colitis, and is characterized by watery diarrhea, crampy abdominal pain, and generalized fatigue. A history of recent travel is common in these patients. Antibiotic use usually precedes the presentation of pseudomembranous colitis, which is due to \textit{C. difficile} infection. A rigid sigmoidoscopy may show the membranes and the edema associated with the latter.
Management

The management is strongly dependent on the presentation. If the signs and symptoms of intestinal ischemia are compatible with non gangrenous ischemia, then the patient is treated conservatively. Usually the patient is put on intravenous hydration with broad spectrum antibiotics covering for intestinal flora and the bowel is put to rest by keeping the patient nothing per os. If there is an associated ileus, a nasogastric tube is inserted to deflate the stomach and help in resolving the ileus. The patient is optimized hemodynamically and any medication that can precipitate or augment the ischemia is withheld. The patient is subjected to serial abdominal examinations looking for emergent signs of peritonitis, or any hemodynamic instability. This is complimented with serial radiologic examinations and endoscopic visualization along with serial monitoring of serum inflammatory markers like lactate, C-reactive protein (CRP), and LDH. Medications that are known to improve colonic blood flow in vivo such as histamine, serotonin, vasoactive intestinal peptide, and papaverine are not part of the routine management of IC, but have shown some benefit in experimental models. \[9\]

Patients presenting with septic hemodynamic status and an abdominal examination of an acute board-like abdomen with generalized peritonitis have very little chance of recovering if treated conservatively and must undergo an urgent laparotomy for prompt resection of the ischemic segment (Figure 2). No bowel preparation is administered because it may worsen a fecal peritonitis.
Of those diagnosed with IC, about 80% of patients respond to medical therapy and their symptoms start improving within the first two days after presentation while the endoscopic findings lag behind because the edema and submucosal hemorrhage requires a few weeks to resolve. Patients who have partial wall necrosis might heal into a stricture or an ulcer, but may be asymptomatic despite abnormal endoscopic and radiologic findings. These patients should be followed up closely to document healing, the presence of strictures, or persistent colitis. Persistent colitis is treated with topical steroid enemas not systemic steroids. Patients presenting with repetitive attacks of sepsis, or forming strictures with symptoms of pseudo-obstruction, are offered elective segmental resection.

The remaining 20% of patients present with an acute illness, hemodynamic instability, and sepsis, and require a
laparotomy for resection. These include the patients who deteriorate clinically from the conservative management group, develop sepsis, have peritonitis on presentation, have free air in the abdomen, or have extensive gangrene visualized by colonoscopy. The extent of the resection should be delineated preoperatively because the serosa may look normal although the mucosa may be severely ischemic. Any resected specimen should be examined intraoperatively to check for viable mucosa, additional resection should be undertaken so that the specimen has viable edges; only then is an anastomosis constructed with a covering reversible ileostomy to protect it. Adjuncts to intraoperative assessment of bowel viability include hand-held Doppler, measurement of tonometric (mucosal) intramural pH, pulse oximetry for colonic oxygen saturation, and intravenous fluorescein. All these have limited clinical acceptance and the surgeon usually relies on gross subjective examination of the mucosa looking for a healthy pink color, absence of edema and ulcers, as well as absence of skip areas of degenerated mucosa. Emerging technologies to assist in the assessment of blood flow exist via endoscopy ‘Novadaq Spy/ Pinpoint fluorescence imaging’ and via the Da Vinci Robot ‘Firefly fluorescence imaging’; the latter is FDA cleared to help visualize blood vessels and biliary structures in gallbladder surgery. The development of similar technology for application in laparotomy, and particularly in an emergency setting such as for ischemic colitis, is probably worth investigating.

In patients with right-sided ischemia, who have grossly viable terminal ileum and transverse colon, no gross abdominal contamination, and no sign of hemodynamic instability, an ileocolic anastomosis is constructed. If the ischemia has targeted the left colon, then invariably a Hartmann’s procedure is undertaken, or a terminal colostomy is exteriorized along with a mucous fistula of the distal segment, if the length of the distal segment permits. Construction of an anastomosis on the left is contraindicated according to several studies because the degree of contamination from a colon perforation is overwhelming and will cause the anastomosis to fail.

**Prognosis**

Mortality and morbidity of IC varies according to presentation, severity, co-morbidity of patients, and treatment...
modalities. Most mildly affected patients are asymptomatic after medical treatment. Severely affected patients and those who have strictures need to undergo surgery and have a higher morbidity and mortality rate. Establishing prognostic factors promptly is of great importance in deciding the best therapeutic strategy for each case. The main risk factors are high blood pressure, cardiovascular diseases, diabetes, chronic obstructive pulmonary disease, and chronic renal insufficiency. Surgical postoperative complications (which include bleeding and wound infections) occur in up to 21%, and surgical re-exploration may be mandated in cases of anastomotic leakage with consecutive peritonitis, bleeding, abscess formation, or fascial dehiscence. In this subgroup, post-operative mortality reaches as high as 47% to 60% as reported in the literature. This underscores the importance of this topic and the need for the attention to proper decision making in light of the presented principles of etiology and management.

References

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