

# Chronic Ischemic Colitis Mimicking Crohn's Disease: A Case Report

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## Abstract

Ischemic colitis can present a wide spectrum of severity; most patients are mild to moderate in clinical course and can be treated supportively and expected to recover fully, while a minority with severe ischemia may develop long term complication such as stricture or chronic ischemic colitis. Chronic ischemic colitis may lead to chronic ulcerations in segments of colon and separated by normal-appearing mucosa, mimicking Crohn's disease. Here we present a case of 59-year-old female who has multiple comorbid presented with progressive abdominal pain associated with diarrhea and rectal bleeding. Colonoscopy showed severely inflamed severe stricture at the hepatic flexure. Right hemicolectomy was performed and surgical pathology confirmed chronic ischemic colitis. Raising awareness of this disease entity and having a high index of suspicion, especially in the setting of elder patients presenting with abdominal pain, rectal bleeding, and existence of comorbid status is crucial to establish an early diagnosis. (J Intern Med Taiwan 2017; 28: 298-303)

**Key Words: Ischemic colitis, Crohn's disease**

## Introduction

Ischemic colitis (IC) results when blood flow to the colon is reduced and the normal cellular metabolic function cannot be maintained. Colonic ischemia with following reperfusion can cause reperfusion injury and this combined injury may create more damage than just reduction of blood flow alone<sup>1</sup>. Ischemic colitis can clinically present a wide spectrum of severity; most patients are mild to moderate in clinical course and can be treated supportively and expected to recover fully, while a minority with severe ischemia may develop long term complication such as stricture or chronic ischemic colitis<sup>2,3</sup>. About 20% of patients with acute

ischemic colitis may develop a long-term complication known as chronic ischemic colitis<sup>2</sup>. With the non-specific clinical presentation, such as abdominal pain and rectal bleeding, ischemic colitis must be differentiated from the other causes (for example, infection, inflammatory bowel disease, diverticulosis, or colon cancer). Biopsies via endoscopy can provide more information in the differential diagnosis. Here we present a patient with history of pancreas and kidney transplantation for type I diabetes mellitus (DM) and chronic renal failure, who subsequently presented with progressive abdominal pain, rectal bleeding, and colonic ulcerations with stenosis mimicking Crohn's disease (CD).

## Case Report

A 59-year-old Caucasian female was referred to our tertiary medical facility for a 15 months history of progressive abdominal pain associated with diarrhea and intermittent bright red blood per rectum. The frequency of bowel movements varied from three to six times per day. No fever, night sweating, or weight loss was noticed. Her medical history was remarkable for type 1 DM diagnosed since the age of 25, hyperlipidemia, chronic renal failure status post pancreas and kidney transplantation at the age of 44; however, the transplanted kidney failed in 8 days. She received the second kidney transplantation at the age of 56 and unfortunately the graft failed again. She was on anti-rejection medications, tacrolimus and mycophenolate mofetil, but discontinued 2 years ago. Other medications included insulin, atorvastatin, gabapentin, darpoetin, duloxetine, paracalcitol, sevelamer, low dose prednisone (5mg per day), and levothyroxine. Her prior screening colonoscopy, which was done 8 years ago, was reported unremarkable. Physical examination revealed stable vital signs and otherwise unremarkable except multiple scars in the abdomen from previous abdominal surgeries.

Remarkable laboratory findings included: chronic anemia with hemoglobin 9.4 g/dL, elevated blood urea nitrogen 38 mg/dL, and elevated creatinine 5.6 mg/dL. Stool infectious work up was negative. Quantiferon tuberculosis blood test was negative. Colonoscopy was performed and revealed a 5 cm in length segmental lesion, characterized with circumferential ulcerated, stricturing, and congested mucosa, at hepatic flexure and proximal transverse colon (Figure 1). Additional scattered small ulcers were found in sigmoid colon. The mucosa between ulcerated mucosal lesions appeared normal. Histopathology from the biopsies obtained at hepatic flexure and proximal transverse colon displayed moderate chronic active

inflammation without granulomas, cytopathic viral inclusion, and dysplasia. Immuno-histochemical stain for cytomegalovirus was negative. Under the initial impression of CD, an empirical course of budesonide (9mg/day) was prescribed by referring primary health facility but no improvement. After one week, patient was transferred to our tertiary

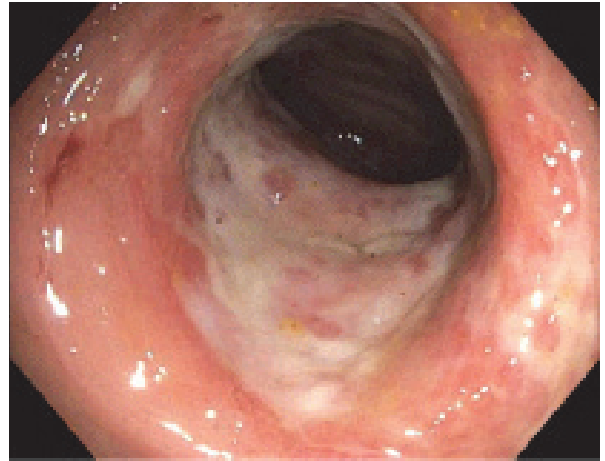


Figure 1. Colonoscopy showed a 5cm in length segmental ulcerated, narrowing, and congested mucosa at hepatic flexure.

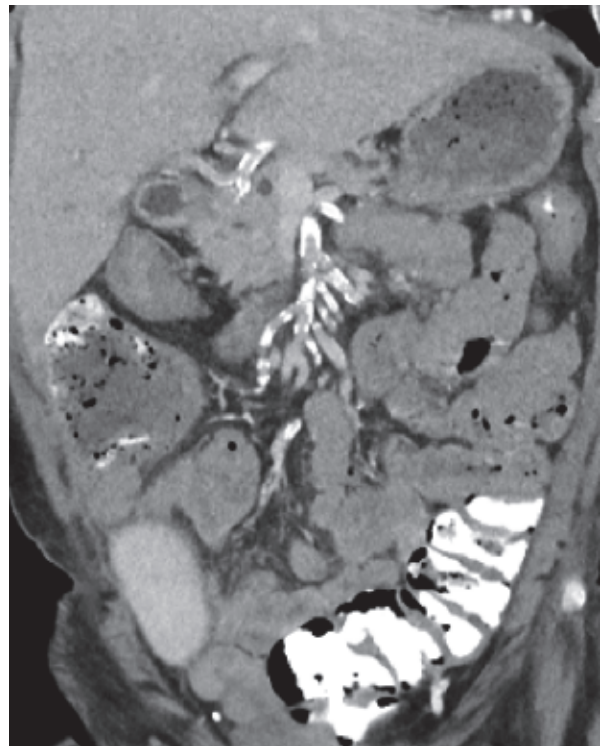


Figure 2. CT scan of abdomen and pelvis showed diffusely significant atherosclerosis of celiac and mesenteric vessels.

medical center and was hospitalized for the progressive severe abdominal pain and diarrhea. CT scan of abdomen and pelvis revealed abnormally segmental colonic wall thickening in hepatic flexure and focal colonic thickening in the splenic flexure. Colonoscopy was performed and revealed severely inflamed non-traversable stricture at the hepatic flexure and several ulcers at the splenic flexure. Under the differential diagnosis of chronic IC, CT angiography was performed and revealed diffusely significant atherosclerosis of celiac and mesenteric vessels although no acute mesenteric ischemia (Figure 2). With the high-degree colonic stricture and progressive severe abdominal pain, the decision of surgical abdominal exploration was made and identified an obstructing hepatic flexure non-malignant mass. Right hemi-colectomy with Hartmann procedure and end ileostomy was performed.

Histopathology from the right hemi-colectomy specimen displayed extensive mucosal and submucosal hyalinization with ulceration and chronic inflammation, which is consistent with chronic IC (Figure 3). No malignancy was seen and Congo red stain for amyloidosis was negative. No characteristic histopathological feature of inflammatory bowel disease (IBD) was identified. In addition, vascular segments with Monckeberg calcifications in the specimen were identified (Figure 4). Patient recovered well after the surgery. Patient recovered well post-operatively and was able to tolerate diet orally with gradual advancement.

## Discussion

The combination of the acuteness of ischemic event, degree of preexisting vascular collateralization, and the length of time the reduced blood flow persists determine the manifestation of IC to be reversible or irreversible injury. Reversible injury may present with subepithelial hemorrhage or edema, colitis, and ulcerations. Irreversible injury may present with gangrene, fulminant colitis, stric-

ture formation, chronic ischemic colitis, and recurrent sepsis due to bacterial translocation<sup>1</sup>. The risk factors for IC may include comorbid history (e.g. cardiovascular disease, hypertension, chronic kidney disease, DM, irritable bowel syndrome with constipation, and chronic obstructive pulmonary disease), coagulopathy (e.g. thrombophilia, especially in young patients with IC), and surgical history (e.g. abdominal aortic aneurysm repair with inferior mesenteric artery sacrificed and other abdominal operations). Patient's drug history is inevitably relevant while searching for the underlying contributory factor of IC; for examples, constipation inducing medications, immunomodulators, vasoconstrictors

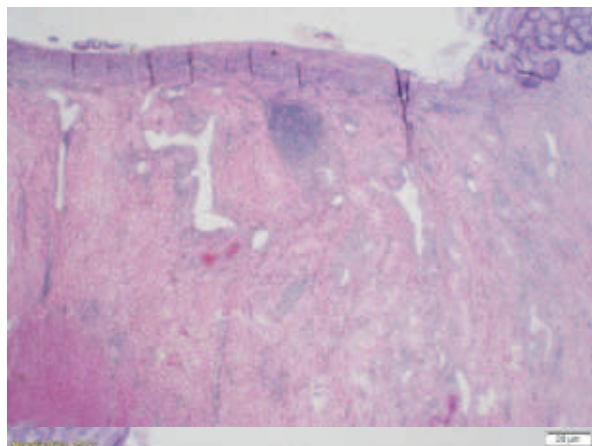


Figure 3. Histopathology from the right hemi-colectomy specimen displayed extensive mucosal and submucosal hyalinization with ulceration and chronic inflammation.

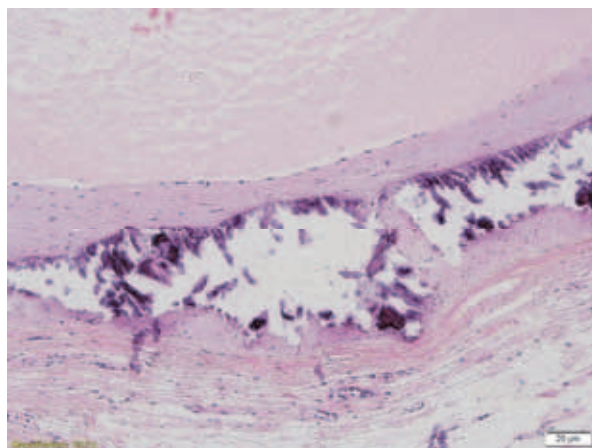


Figure 4. Vascular segments with Monckeberg calcifications in the specimen were identified.

(dopamine), illicit drugs (cocaine), over-the-counter drugs such as pseudoephedrine, laxatives, nonsteroidal anti-inflammatory drugs, and promotion of thrombosis (estrogen). In some case reports<sup>4,5</sup>, systemic steroid has been concerned as a risk factor for IC, possibly through its induced hypercoagulative state. Although budesonide is generally considered as a non-absorbable steroid, its effect on hypercoagulative state and IC remains unclear.

In a large retrospective study<sup>6</sup>, the most common clinical symptoms of presentation were abdominal pain (87%), rectal bleeding (84%), diarrhea (56%), and nausea (30%). Most episodes of IC are mild to moderate (mucosal and submucosal hemorrhage and edema, with or without mucosal ulceration; reportedly 3.3% to 9.4% of cases with muscularis propria replaced by fibrous tissue forming a stricture<sup>7,8</sup> and only a minority of cases are severe (for example, gangrenous colitis and fulminant colitis were reported in 9.9% and 2.5% of cases, respectively<sup>9</sup>).

Although the left colon is most commonly affected (32.6%), other parts of colon can be involved as well (distal colon (24.6%), right colon (25.2%), and entire colon (7.3%))<sup>10</sup>. Interestingly, isolated right colon ischemia (IRCI) has been associated with higher mortality rates compared with other patterns of IC<sup>1</sup>. In addition, IRCI was associated more frequently in patients with sepsis, coronary artery disease and chronic kidney disease on hemodialysis just like our case. In a previous study, the combination of IRCI or pancolonic patterns of ischemia was associated with a hazard ratio of 14.6 for need of surgery or mortality<sup>6</sup>. The percentage of chronic and recurrent IC reportedly ranges from 6.8% to 16%<sup>6,11,12</sup>. Chronic and recurrent IC may lead to chronic ulcerations in segments of colon and separated by normal-appearing mucosa, mimicking IBD or CD. Crypt abscesses and pseudopolyps may also be found in IC. Endoscopic presentation of the mucosa may not always allow a final diag-

nosis to be made, but endoscopic biopsy of the mucosa may be helpful in differentiating between infectious disease, IBD or IC. Furthermore, it has been postulated that small multifocal gastrointestinal infarction and repetitive thrombotic mesenteric microvascular occlusion may lead to IBD. A vascular etiology for IBD is supported further by studies showing that IBD occurs less frequently in patients with inherited disorders of coagulation (e.g., hemophilia or von Willebrand's disease) and that smoking has a deleterious effect on the progression of Crohn's disease<sup>13,14</sup>.

The adequate treatment and prognosis depend on the severity of IC. Mild disease is defined for those who have typical symptoms of IC with a segmental colitis not isolated to the right colon and with none of the commonly associated risk factors for poorer outcome (e.g., male gender, hypotension (systolic blood pressure <90 mm Hg), tachycardia (heart rate >100 beats/min), abdominal pain without rectal bleeding, blood urea nitrogen >20 mg/dl, Hb <12 g/dl, LDH >350 U/l, serum sodium <136 mEq/l, WBC >15×10<sup>9</sup> /l, or colonoscopically identified mucosal ulceration) that are usually seen in moderate disease. Moderate disease includes any patient with up to three of the above factors. Severe disease is defined by more than three of the previously listed criteria or any of the following: peritoneal signs on physical examination, pneumatosis on CT, gangrene on colonoscopy, and a pancolonic distribution or IRCI on CT or colonoscopy<sup>1</sup>. As most mild to moderate cases of IC resolve spontaneously after supportive care, surgical intervention should be considered in cases accompanied by hypotension, tachycardia, abdominal pain without rectal bleeding, IRCI and pancolonic IC, and in the presence of gangrene. Antibiotics have been widely used in clinical practice for the treatment of perianal CD; however, several controlled trials have not consistently demonstrated its efficacy in luminal CD<sup>15</sup>. For IC, although there is still no robust clinical evi-

dence antimicrobial therapy may be considered for patients with moderate or severe disease and believed to prevent poor outcome through decreased bacterial translocation in the setting of acute ischemia and reperfusion injury.

Colonoscopy has become the primary tool to diagnose IC, usually after CT scan has revealed a segment of colon that is thickened. Although the pathognomonic colonoscopic features like dusky, cyanotic hue of necrotic mucosa suggesting gangrene in minority of severe IC may be encountered, most cases' colonoscopic manifestations are non-specific (e.g. erythema, edema, and ulceration include aphthous ulcers, which may suggest Crohn's disease, pseudomembranes, which are more often seen with *C. difficile* infection, and pseudopolypoidosis, which may develop with healing). Pathognomonic histopathologic features, infarction and ghost cells (i.e., preserved individual cellular outlines without cell content), presented in biopsy specimens obtained colonoscopically are infrequently seen<sup>16</sup>. More commonly seen nonspecific histopathologic features in biopsy specimens include mucosal and submucosal hemorrhage and edema and capillary fibrin thrombi with neutrophilic infiltration that can support the diagnosis of IC.

In conclusion, chronic ischemic colitis is relatively uncommon and could be under recognized, due to its clinical features overlapped with other diseases (such as IBD), by healthcare professionals. Raising awareness of this disease entity and having a high index of suspicion, especially in the setting of elder patients presenting with abdominal pain, rectal bleeding, and existence of comorbid status (e.g. coronary artery disease, DM, chronic kidney disease, peripheral vascular disease) is crucial to establish an early diagnosis.

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# 慢性缺血性大腸炎：類似克隆式症的病例報告

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## 摘 要

缺血性大腸炎可以有相當不同嚴重性的臨床表現。大多數病人呈現出輕到中度臨床病程，而且通常可以完全復原。少數嚴重案例可以有長期合併症，譬如腸道狹窄或演變成慢性缺血性大腸炎。慢性缺血性大腸炎可以表現出腸道潰瘍，有時呈現非連續性腸炎間接穿插一些正常的腸道黏膜，因而可能看似克隆式症的內視鏡表徵。在這個病例報告中，是一位59歲女性，過去病史具有多重臨床合併症，主述腹痛腹瀉及血便，經大腸鏡檢發現嚴重大腸發炎及潰瘍，並且有合併狹窄。後來經過右側大腸部分切除術，術後病理學報告證實缺血性大腸炎。所以，對於年長病患同時具有多重臨床合併症，如果臨床主述腹痛及血便，臨床醫師如果具備高度警覺及即時鑑別診斷的準備，將有助於早期正確診斷缺血性大腸炎。