

Sickle Cell–Induced Ischemic Colitis

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Sickle cell–induced ischemic colitis is a rare yet potentially fatal complication of sickle cell anemia. Frequent pain crises with heavy analgesia may obscure and prolong this important diagnosis. Our patient was a 29-year-old female with sickle cell disease who was admitted with left lower quadrant abdominal pain. A diagnostic workup, including chemistries, complete blood count, blood cultures, chest x-ray, computerized tomography scanning, and colonoscopy, was performed to identify the etiology of her symptoms. This case highlights the importance of differentiating simple pain crisis from more serious and life-threatening ischemic bowel. A review of the literature compares this case to others reported and gives a method for diagnosing and treating this complication of sickle cell disease.

Keywords: sickle cell anemia ■ ischemia

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INTRODUCTION

Sickle cell disease affects approximately 70 000 people in the United States, often with debilitating symptoms and a limited life expectancy. The most common symptom in adult patients is sickle cell pain crisis, which can mimic acute abdomen when affecting the abdominal area. It is often difficult for practitioners to distinguish between pain crisis and the etiologies of acute abdomen. Our case illustrates the importance of distinguishing pain crises from sickle cell–induced ischemic colitis, a rare yet potentially life-threatening complication of sickle cell disease. We also present a review of the literature and discuss management options.

CASE

A 29-year-old African American female presented to the emergency department with left lower quadrant abdominal pain of 1 day's duration. She also complained of constipation, lower-back pain, and leg pain of 4 days' duration. Her history was significant for sickle cell dis-

ease, with frequent pain crises, including 21 hospital admissions in the past year. She rated her abdominal pain 8 out of 10, and reported that her usual analgesic medications were not effective in alleviating this pain. She had been given lactulose 3 days earlier at the sickle cell day clinic, and reported that her last bowel movement was the previous day. It was scant and watery, with "some clots."

Physical exam revealed an afebrile patient with normal vital signs. Examination of her head, eyes, ears, nose, and throat was unremarkable. Cardiovascular exam showed regular rate and rhythm, and lungs were clear to auscultation without rales or wheezes. The abdomen was slightly distended and tender to palpation diffusely, but especially in the left lower quadrant. No masses were palpated, and bowel sounds were present. Vaginal exam revealed a normal vagina with scant discharge; gonorrhea and chlamydia cultures were taken and were both negative. Rectal exam was negative for gross blood, and no impaction was detected. Stool was sent in triplicate for *Clostridium difficile* cytotoxin testing, which came back negative. The patient's extremities were tender to palpation, but no clubbing, cyanosis, or edema was noted.

Laboratory data were unremarkable on presentation with normal complete blood count, electrolytes, and liver function tests. A computed tomography (CT) scan of the abdomen and pelvis showed a large amount of stool in the colon but was otherwise not revealing; therefore, the patient was given hydromorphone patient-controlled-analgesia (PCA), intravenous fluid hydration with normal saline, and lactulose for sickle cell crises with opiate-induced constipation. After 2 days of failed lactulose therapy, the patient was given an enema to induce a bowel movement, which only resulted in scant watery diarrhea. The patient reported that she was passing gas, but that her abdominal pain remained 8 out of 10 and was localized to the left lower quadrant.

On hospital day 5, the patient spiked a fever of 39°C, and her white blood cell count increased to 19 000/ml. She was started on intravenous piperacillin/tazobactam and vancomycin, and a repeat chest x-ray and abdominal CT were obtained. The abdominal CT showed thickening of the left descending colon, indicating possible ischemic colitis (Figure 1). The patient received 10 units of packed red blood cells in an exchange transfusion,

and subsequently went for colonoscopy with biopsy. Colonoscopy showed a 10-cm segment of colon beginning at the splenic flexure with ulceration and a friable cobblestone appearance. Biopsy revealed fragments of ischemic bowel with inflammatory infiltrate and pseudomembrane formation. Intravascular spaces revealed marked sickling of erythrocytes (Figure 2), leading to a diagnosis of sickle cell–induced ischemic colitis.

The patient continued to be aggressively hydrated and was kept on intravenous vancomycin and piperacillin/tazobactam. Her pain was significantly improved after exchange transfusion, and she began having normal bowel movements shortly thereafter. All studies for infectious organisms returned as negative. She had an uneventful recovery and was discharged home 7 days later.

Disease Process and Review of Case

Sickle cell disease is an autosomal recessive hemoglobinopathy in which hemoglobin S aggregates into large polymers under low oxygen tension, leading to erythrocyte distortion and decreased deformability. Affected patients suffer from recurrent vascular occlusions that lead to ischemia and distal tissue infarction in multiple organs. These vascular occlusions manifest as sickle cell pain crises.¹ Abdominal pain is common in sickle cell pain crises, with an incidence of 30% to 57% in patients presenting with pain. It is attributed to vaso-occlusion or infarcts in the mesenteric vasculature, and has been termed “girdle syndrome” because it causes pain in a girdle-like distribution.² While it may mimic a surgical emergency, such as intestinal obstruction, acute cholecystitis, pancreatitis, or appendicitis, some patients have relative absence of abdominal signs, with normal

bowel sounds and minimal rebound. Conservative management with standard rehydration and analgesia usually leads to resolution within 48 to 96 hours.

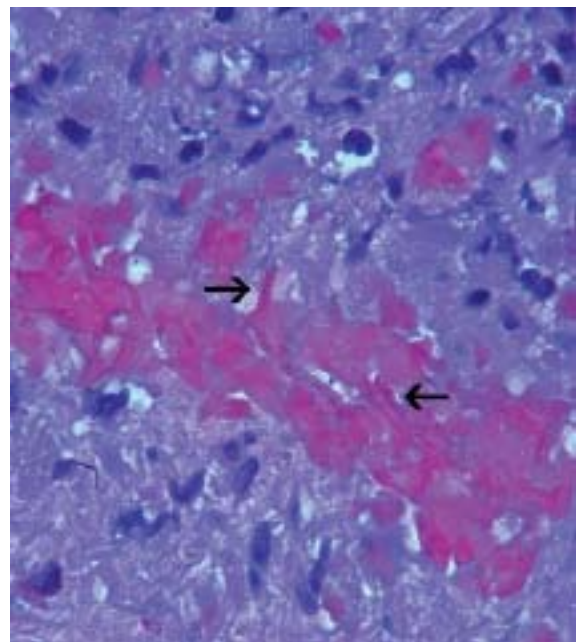
Progression to significant ischemic damage of the intestine despite adequate analgesia and fluids is rare in sickle cell disease. Only 7 cases have been described in the literature previously.³⁻⁹ This is likely because the colon has an abundant collateral blood supply and low oxygen extraction. In fact, the bowel can tolerate up to a 75% reduction of mesenteric blood flow for up to 12 hours with no ischemic changes.¹⁰ However, low perfusion pressure may increase the likelihood of erythrocyte sickling, vascular obstruction, and ischemic injury.^{4,5} The diagnosis of ischemic colitis can be delayed—and ischemic damage allowed to progress—in patients with sickle cell disease because traditional signs of intestinal ischemia and perforation are masked by opiate analgesia. In addition, multiple reports deny these patients having characteristic bright red or maroon stool with ischemic colitis.⁶ This diagnosis should be considered in every patient with sickle cell disease or trait with “girdle syndrome” that does not resolve rapidly, as failure to do so can result in significant morbidity and mortality.^{2,7}

A review of previous reports clearly demonstrates that abdominal CT is most effective for diagnostic imaging, demonstrating thickening of the intestinal wall. Additional noninvasive testing may show elevated serum lactic acid levels, and blood in the stool, which was present in 3 of 7 reported cases. If bowel infarction is suspected, a colonoscopy should be performed. Character-

Figure 1. Thickening of the Left Descending Colon, Consistent With a Diagnosis of Ischemic Colitis



Figure 2. Colonic Biopsy Viewed Under High Power with Hemotoxin and Eosin Staining



Arrows point to sickled erythrocytes within intravascular spaces.

istic findings of colonoscopy include segmental distribution of disease, abrupt transition between injured and uninjured mucosa, and rectal sparing.⁶ Colonic biopsies in several cases, including ours, clearly demonstrated sickling within the vasculature of the diseased colonic segment; however, pathology may be nonspecific, showing submucosal hemorrhage, edema, and loss of crypt architecture.⁵ Angiography cannot reliably image smaller vessels that are involved in colonic vascular injury, and colonic blood flow usually has returned to normal by the time of symptom onset in patients. The single case in which angiography was attempted was unrevealing, and it is believed that this test does not contribute to diagnosis or treatment.^{6,7,9}

Colonic resection in these patients can be avoided by attempting to optimize colonic perfusion, using exchange transfusions, several days of bowel rest, and broad spectrum intravenous antibiotics. This therapy was successful in 4 of 7 reported cases, and has led to resolution in as little as a week. However, 1 case reported needed up to 7 weeks to resolve, with total parenteral nutrition for a 5-year-old child.⁸ Patients who do not respond to therapy in 10 to 14 days are at greater risk for perforation, which must be weighed against the risks of surgery.⁵

Patients whose clinical condition deteriorates despite conservative management and those with signs of peritoneal irritation, sepsis, or gangrene at endoscopy should undergo laparotomy with resection of the involved bowel. Patients with sickle cell disease have a high frequency of serious postoperative complications. This can be decreased by transfusion regimens that decrease the hemoglobin S level below 30% or increase hemoglobin levels to 100 g/L. Hemoglobin concentrations should not be raised above 100 g/L due to increased viscosity and worsening of vaso-occlusion.¹

In conclusion, sickle cell-induced ischemic colitis is a rare yet serious complication of sickle cell disease. Symptoms range from mild abdominal pain to characteristics of acute abdomen, and masking of symptoms by analgesia may allow the disease process to progress. Ischemic colitis should be considered in all sickle cell patients with abdominal pain when symptoms persist beyond 4 days with conservative management. An abdominal CT demonstrating colonic thickening should prompt the start of exchange transfusions, broad spectrum antibiotics, and close monitoring for further deterioration and the need for surgery.

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