Acute Abdomen in a Patient with Systemic Lupus Erythematosus

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Systemic lupus erythematosus (SLE) is a multisystem inflammatory disorder that manifests with a variety of symptoms. Systems affected include integumentary, genitourinary, cardiovascular, musculoskeletal, hematologic, and neurologic. Mesenteric vasculitis is a serious but underrecognized gastrointestinal complication of SLE and carries a high mortality rate.[1] This article describes a patient with a history of end-stage renal disease due to SLE who presented with progressive abdominal pain. He was found to have lupus enteritis, or gastrointestinal vasculitis. The diagnosis and treatment of lupus enteritis are discussed.

CASE PRESENTATION

Patient Presentation and History

A 31-year-old man presented to the emergency department with a 1-week history of abdominal pain. His past history was significant for end-stage renal disease, SLE, pericarditis, hypertension, right atrial thrombus, and colitis associated with cyclophosphamide. He had been seen in the emergency department 4 days earlier with similar complaints of right periumbilical pain, radiating diffusely throughout the abdomen. Pain increased with movement, cough, and deep inspiration. There was associated anorexia, nausea, and vomiting. The patient was not currently taking any medications; he had, however, been treated with prednisone and hydroxychloroquine in the past. His lupus flares consisted of rash, lymphadenopathy, and nonspecific arthralgias. In addition, his history documented cardiovascular, renal, and hematologic system involvement. Mucocutaneous and gastrointestinal involvement were not evident in the spectrum of his disease. Cyclophosphamide had been tried for his renal disease (biopsy-proven World Health Organization Class IV lupus nephritis) but was not tolerated. He subsequently developed progressive renal failure requiring hemodialysis. He had a long history of noncompliance with his dialysis and with taking medications, including prednisone, hydroxychloroquine, antihypertensive agents, and an anticoagulant.

Physical Examination and Laboratory Studies

Physical examination showed a man in moderate distress secondary to pain. Oral temperature was 97.8°F. He was hypertensive (blood pressure, 225/159 mm Hg) and tachycardic (pulse, 118 bpm). He had diffuse lymphadenopathy, excoriations, and a papular rash on the upper and lower extremities bilaterally. His abdomen was distended and tympanitic to percussion, with hypoactive bowel sounds. Diffuse abdominal tenderness was elicited by light palpation. Rebound tenderness and voluntary guarding were noted. Leukocyte count was $9.4 \times 10^3/mm^3$ with left shift, a notable change from baseline leukopenia. Platelet count was low at $45 \times 10^3/mm^3$. Bicarbonate level was 19 mEq/L, blood urea nitrogen level was 86 mg/dL, and creatinine level was 5.7 mg/dL. Liver function test results and lipase and lactate levels were normal. The patient's temperature rose to 101.6°F on hospital day 2; subsequent blood cultures, urinalysis, chest radiograph, and assay for fecal leukocytes were negative. Further evaluation on day 2 revealed the following: erythrocyte sedimentation rate, 63 mm/h; antinuclear antibody >10 by enzyme-linked immunosorbent assay; anti–dsDNA 1:1280; low complement C3 (45 mg/dL; normal, 88–201 mg/dL) and C4 (13 mg/dL; normal, 16–47 mg/dL).

Imaging Studies

Abdominal radiographs showed a nonspecific gas pattern without signs of free air or bowel dilatation. Trauma

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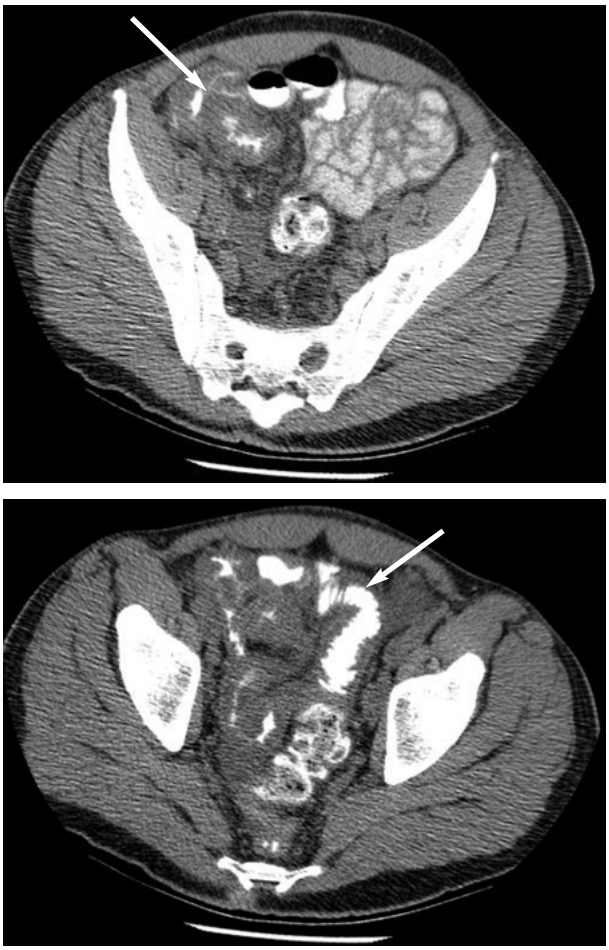

Figure 1. Enhanced computed tomography images of the abdomen and pelvis of the case patient show diffuse small bowel wall thickening and thumbprinting (*arrows*).

surgery was consulted on admission and recommended placing the patient on NPO status (nothing by mouth) and obtaining computed tomographic (CT) scans of the abdomen and pelvis with oral contrast. The CT scans showed diffuse mural thickening and thumbprinting of the distal small intestine and right colon (**Figure 1**). The cecal tip and appendix base appeared normal. There was a small amount of intraperitoneal fluid. Prominent retroperitoneal and small bowel mesenteric lymph nodes were detected. In the context of the patient's noncompliance, hypocomplementemia, and active skin disease, the thumbprinting suggested intestinal vasculitis. A colonoscopy was recommended, but the patient refused the prescribed bowel preparation.

Treatment

In consultation with the rheumatology service, the patient was placed on methylprednisolone 1 mg/kg daily intravenously (IV) for 2 days followed by oral prednisone 60 mg daily for 8 days (including 4 outpatient days) with a taper for an additional 14 days. The patient experienced prompt relief of abdominal pain on day 2 of therapy, and the abdominal examination results normalized. A repeated CT performed after 4 days of medical management showed a normal bowel wall and no evidence of thumbprinting or bowel ischemia (**Figure 2**). On day 6 of therapy, the patient was discharged home in good condition, with instructions to follow-up with his rheumatologist and hemodialysis center.

DISCUSSION

Epidemiology

Acute reversible ischemia of the small and large bowel has been previously described in SLE but is frequently misdiagnosed.[2] William Osler was the first to recognize the gastrointestinal manifestations of SLE and described 11 cases of acute abdominal crises associated with vomiting and diarrhea.[3] Lupus enteritis has a reported prevalence ranging from 0.2% (of patients with active SLE) to 53% (of patients with active SLE and abdominal pain).[4] A recent study of 175 patients admitted with active SLE showed that 38 patients (22%) presented with acute abdominal pain. Lupus enteritis was the most common cause of abdominal pain present in 17 (45%) of those patients.[5,6] Other causes of abdominal pain noted in this study included urinary tract infection in 6 patients (16%), acute gastroenteritis in 5 (13%), pancreatitis in 2 (5%), infectious diarrhea in 2 (5%), hemorrhagic gastritis in 2 (5%), serositis in 1 (3%), cholecystitis in 1 (3%), inferior vena cava thrombosis in 1 (3%), and gastric ulcer in 1 (3%).[5] With the improved diagnosis of SLE[7] and advent of more efficacious treatment modalities, physicians have been more successful in controlling SLE and its recurrences. Nevertheless, patients who present with abdominal pain and a history of SLE should be evaluated for lupus enteritis, whether undergoing treatment or not.

Pathophysiology

Vasculitis with histologic inflammation and necrosis of blood vessels can be seen in SLE.[8] Small vessels, both arteries and venules, are affected with thrombosis, inflammatory infiltrate, and fibrinoid necrosis of vessel walls. The tunica adventitia and the tunica media may also show immune complex and complement deposition.[4] As blood flow is diminished to the viscera, the bowel is particularly vulnerable to ischemia. The mucosa is the most sensitive to decreased blood flow followed by the muscular layers[2]; the submucosa and serosa are the

least affected. Once the muscular and submucosal layers are involved, radiographic evidence of ischemia may be clearly seen as bowel wall edema (thumbprinting). Disruption and ischemia of the muscular layer leads to ileus and dilatation.[6] Thrombocytopenia, a common finding in patients with gastrointestinal vasculitis, is theorized to occur from consumption of platelets in the process of microthrombi formation on injured vascular epithelium, as also seen in thrombotic microangiopathy.[9] Thrombocytopenia in SLE may also result from immune-mediated platelet destruction, antiphospholipid syndrome, or bone marrow suppression (in patients on immunosuppressant therapy).

Differential Diagnosis

The diagnosis of lupus enteritis is challenging due to the broad differential of acute abdominal pain. Non–SLE-related abdominal pain may run the gamut of appendicitis, infectious enterocolitis, diverticulitis, pancreatitis, nonocclusive vasculopathy, or perforated viscus. Nonocclusive vasculopathy, which is typically caused by hypertension-induced splanchnic vasoconstriction, can cause up to 20% to 30% of mesenteric ischemia cases.[10] If not attended to early on, ischemia can rapidly progress to necrosis.

Patients with active SLE and abdominal pain may also have necrotizing pancreatitis, cholecystitis, or mesenteric thrombosis.[4] The presentation of these syndromes may mimic lupus enteritis but usually includes objective findings that help to exclude this diagnosis. Patients with necrotizing pancreatitis typically present with upper abdominal pain radiating to the back with associated nausea and vomiting. Lipase and amylase levels are elevated and CT scans may show peripancreatic inflammation, fluid collection, and air in the retroperitoneum. It must be remembered that patients with SLE may be on medications such as prednisone and azathioprine that can cause adverse reactions, including pancreatitis. In addition, lupus enteritis can also be the initial manifestation of SLE.[11]

Patients with cholecystitis typically present with right upper quadrant or epigastric pain that radiates to the back or shoulder. Alkaline phosphatase level, leukocyte count, and bilirubin levels are usually elevated, and CT scans may show wall edema and pericholecystic stranding and fluid.

Mesenteric thrombosis can present as acute mesenteric ischemia with severe periumbilical pain associated with nausea and vomiting. Its significance in those with active SLE is due to the predisposition of patients with the antiphospholipid antibody (APLA) syndrome to develop mesenteric thromboses. These patients tend to have both arterial and venous thromboembolic disease, including gastrointestinal involvement. Laboratory testing of patients with APLA syndrome reveals either positive lupus anticoagulant or antibodies to anticardiolipin or β2-glycoprotein I.

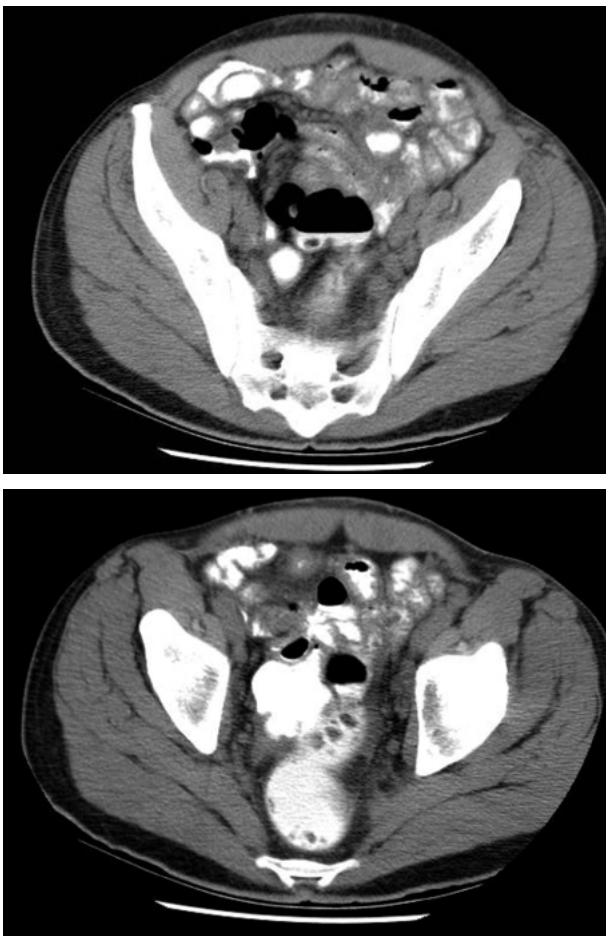

Figure 2. Enhanced computed tomography images of the abdomen and pelvis of the case patient 4 days after initiation of treatment with corticosteroids.

Diagnostic Evaluation

Although established criteria for lupus enteritis have not been developed, laboratory manifestations and radiographic findings have helped clinicians delineate which patients are more likely to have the diagnosis. The most prominent symptoms are nausea, vomiting, and abdominal pain. Diarrhea and malabsorption often are concurrent during the initial presentation.[12] In multiple studies, fever was present in all cases of gastrointestinal vasculitis.[13] Most patients present with lower quadrant cramping, anorexia, nausea, and vomiting. Concomitant features of active SLE, such as arthralgias, skin rash,

pleurisy, nephritis, and subcutaneous nodules, have also been seen in patients with lupus enteritis, suggesting that the abdominal symptoms are lupus related.[1]

There are no specific laboratory tests; however, several authors suggest that based on the physical examination combined with laboratory and radiographic findings, lupus enteritis can be diagnosed with some certainty.[2,4,5,14] Patients with active SLE presenting with acute abdominal pain should be thoroughly investigated for lupus enteritis or peritonitis unless an alternative diagnosis can be established. In those without active SLE, investigation for antineutrophil cytoplasmic antibody–positive vasculitides (eg, polyarteritis nodosa, Churg-Strauss syndrome) as a cause for abdominal pain may be warranted. Other vasculitides with multisystem involvement including Henoch-Schönlein purpura, APLA, Behçet's syndrome, and Takayasu's arteritis can also cause varying degrees of abdominal pain. Laboratory results such as elevated erythrocyte sedimentation rate, low complement levels, anemia, thrombocytopenia, anti-dsDNA, anti-Smith antibody, and anti-RNP antibodies have all been described in patients with abdominal pain due to lupus enteritis.[1,6]

Plain radiographs may show ileus, thumbprinting, and even pneumatosis intestinalis (ie, gas in the wall of the small or large intestine). The latter finding should prompt consideration of surgical exploration. Most often, however, radiographic findings are nonspecific, and other diagnoses must be considered. Although arteriography may demonstrate mesenteric arteritis, its utility in the diagnosis of lupus enteritis is still in question.[4,6,8,14]

With the increased use of CT scans, it has become easier to establish the diagnosis of lupus enteritis without endoscopic or surgical intervention. Common CT findings include bowel wall thickening, ring-like wall enhancement (target sign), prominent mesenteric vessels, and ascites.[14] In a recent study, jejunal and ileal segments seemed to be more commonly affected.[5] Other noninvasive techniques, such as ultrasound, magnetic resonance imaging, and leukocyte scans, may support the diagnosis.[4]

The case patient fulfilled the American College of Rheumatology classification criteria for SLE.[15] His presentation, CT findings, and exclusion of other abdominal pathology were consistent with lupus enteritis. The dramatic resolution of his symptoms, physical findings, and radiographic abnormalities following corticosteroid treatment further support the diagnosis of lupus enteritis.

Treatment

Owing to the paucity of patients, randomized prospective therapeutic trials of lupus enteritis have not been performed. Multiple case reports, however, indicate that corticosteroids are the first line of therapy. In addition, data suggest that the combination of prednisone and cyclophosphamide may reverse gastrointestinal vasculitis.[4] Currently, patients are treated with 1 mg/kg daily IV methylprednisolone and switched to oral prednisone as symptoms resolve, with the dosage tapered over a few weeks. IV cyclophosphamide may also be added to help suppress the inflammatory response.[5,16]

There is no definitive length of treatment; steroid regimens are therefore adjusted according to inflammatory markers, radiographic resolution, and patient symptoms. Patients should respond to steroid therapy within 12 to 48 hours of initiation.[6] If the patient does not improve within 48 hours, surgical intervention may be necessary. Extreme vigilance should be practiced on these patients during treatment with steroids. Steroids can mask the inflammatory process, including signs of peritonitis caused by intestinal leakage or bacterial translocation. Complicated lupus enteritis, defined as irreversible gastrointestinal vasculitis, should be treated with prompt surgical intervention. Late complications such as perforated viscus, bowel infarction or gangrene, and peritonitis require open laparotomy. These patients will frequently present with signs of septic shock (eg, fever, hypotension, leukocytosis, multi-organ failure).

CONCLUSION

The case patient presented with signs and symptoms consistent with lupus enteritis. This acute episode corresponded with his active SLE state. His noncompliance with medication and with appropriate follow-up clearly contributed to his disease progression. He quickly responded to corticosteroids, and interval resolution of his CT findings confirmed this.

Lupus enteritis is a recognized entity in patients with SLE. If the physician has a high clinical suspicion of this diagnosis, prompt treatment with corticosteroids is paramount. This approach may prevent the late sequelae of lupus enteritis and improve morbidity and mortality in this high-risk patient population. **HP**

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