

Gastrointestinal Perforation in Childhood Lupus: A Case Report and Discussion

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Abstract

Perforation from intestinal vasculitis in systemic lupus erythematosus (SLE) is a rare but high mortality complication. It is a challenging condition both to identify and manage. We present a case report of a 13-year-old female child with SLE complicated with small bowel perforations. The child failed to respond to a regimen of high dose steroid therapy and required repeated surgical intervention. The patient subsequently responded to cyclophosphamide showing regression of clinical symptoms including closure of fistulae. We therefore encourage clinicians to aggressively utilize this emerging management option for SLE bowel vasculitis.

Introduction

Bowel vasculitis is one of the most devastating complications of systemic lupus erythematosus (SLE). Secondary complications from bowel wall vasculitis and mesenteric arteritis include bowel hemorrhage, infarction and perforation (1, 2). Amongst these consequences of bowel vasculitis, perforation is the most ominous and has been shown in the past to be a leading cause of death in SLE patients with acute abdominal events (3, 4). The mortality rate in the largest published series of bowel wall perforation in SLE was greater than 50 percent (5). Figure 1 is an example of severe small intestinal vasculitis.

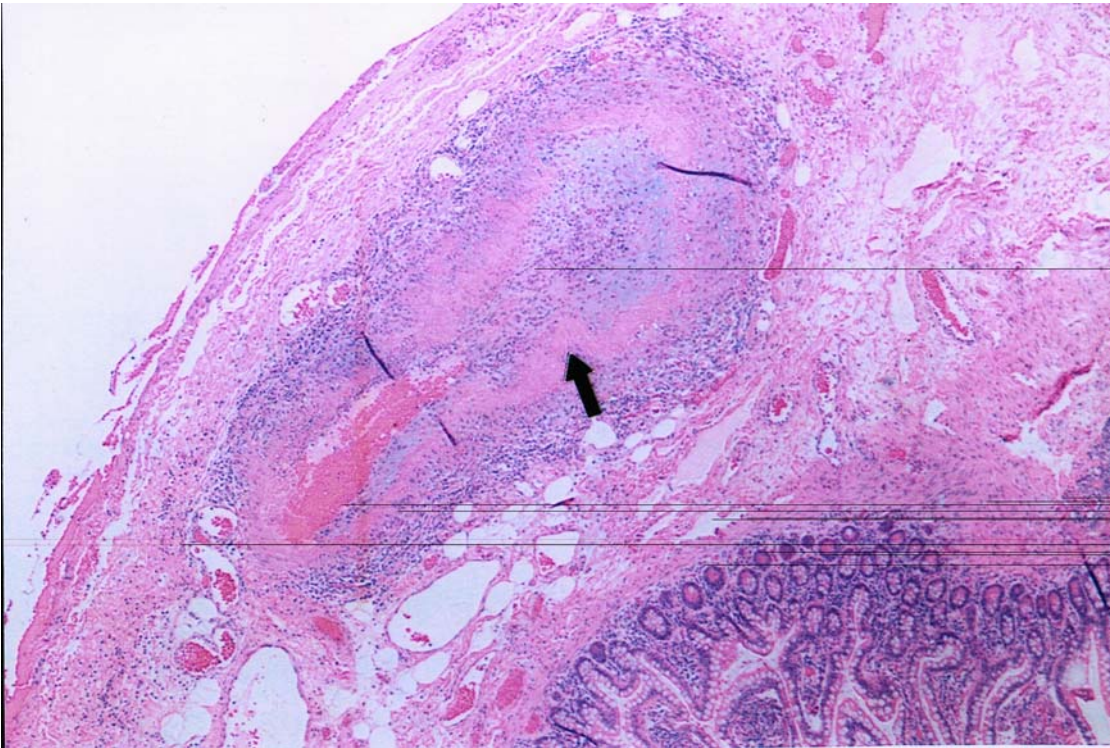


Figure 1: Vasculitis of the small intestine in a child with SLE

Hematoxylin and eosin medium power (200 x) view of small intestine.

Endarteritis obliterans and periadventitial inflammation in submucosal vessel.

Arrow at fibrinoid necrosis.

The most commonly used treatment for bowel vasculitis is a high dose steroid regimen (2, 6). If high dose steroids fail to control the progression of symptomatology, early recognition of the regimen's failure and prompt initiation of other aggressive disease modifying agents is necessary to prevent the more morbid complications of bowel vasculitis including perforation (7).

We report a case of repeated bowel perforations in a pediatric patient with SLE who responded well to pulse cyclophosphamide therapy.

Case Report

A 13-year-old African-American girl was diagnosed with SLE associated with nephritis, hypertension and depression. The patient achieved remission with oral prednisone 60 mg daily and was maintained on prednisone 40 mg every other day and hydroxychloroquine 200mg twice daily. The patient also received fluoxetine 20 mg a day and enalapril 2.5 mg a day.

The patient presented four months after diagnosis to the pediatric rheumatology clinic with a one week history of incapacitating generalized muscle aches, severe arthralgias, low-grade fevers, malar erythema and multiple mucosal oral and labial ulcers. The patient denied any gastrointestinal symptoms at that time. Laboratory analysis revealed a normal white blood cell and platelet count. The patient's hemoglobin 9.5 gm/dl was low and serum creatinine was 0.9 mg/dl (0.3-0.6 mg/dl). A rheumatologic work up revealed elevated antinuclear antibody (ANA) (>1: 640) and anti DNA (>1: 80) titers. The patient's C3 {36mg/dl (80-175mg/dl)} and C4 {6.6 mg/dl (15-45 mg/dl)} levels were low.

The patient was admitted and the dose of prednisone was increased to 40 mg daily with slow improvement of her musculoskeletal symptoms and mucosal ulcers. The patient further developed a painful erythematous bullous rash which on biopsy showed IgG and C1q linear staining of the basement membrane consistent with a diagnosis of bullous SLE.

The patient responded well to the pulse corticosteroid therapy of 1 gm methylprednisolone infusion daily for three consecutive days; as manifested by resolution of the rash and musculoskeletal symptoms.

Subsequently the patient complained of the onset of diarrhea and abdominal pain. Physical exam revealed marked abdominal guarding and distension with hypoactive bowel sounds. Roentological films (x-rays) showed both large and small bowel distension. An emergency exploratory laparotomy showed diffuse peritonitis and four distal ileal perforations. A 6-cm segment of the distal ileum was resected and ileostomy was performed. Histopathology of the resected bowel showed chronic lupus vasculitis as evidenced by endarteritis obliterans and periadventitial inflammation in submucosal vessels including areas of fibrinoid necrosis (Fig 1).

The patient was started with oral feeding on the sixth postoperative day but soon developed an acute exacerbation of musculoskeletal symptoms and an entero-cutaneous fistula. Additional imaging studies revealed bilateral pleural and pericardial effusions. The C3 and C4 as well as the ANA titers at this time remained unchanged. The enteral feedings were discontinued and a second pulse of steroids was initiated. The patient improved and underwent surgery for resection of the fistula, small bowel re-anastomosis and ileostomy closure.

The patient's second postoperative course was again complicated by two entero-cutaneous fistulae. Her C3 and C4 remained low and the ANA was 1:640. At this point the patient was started on intravenous cyclophosphamide (500 mg / m²) therapy which resulted in regression of musculoskeletal symptoms and improvement in C3 (62 mg/dl) and C4 (7.8 mg/dl) levels. The patient received six more monthly pulses of intravenous cyclophosphamide (750 mg / m²) and the entero-cutaneous fistulae closed after the third pulse. The patient did not require further surgical intervention and has been symptom free for the last eighteen months on low dose oral prednisone and intravenous cyclophosphamide pulse therapy every three months.

Discussion

Acute abdominal pain is a common feature of SLE and can be secondary to symptoms of gastro-esophageal reflux disease from esophageal dysmotility, pseudo-obstruction from gastric or intestinal dysmotility, mesenteric arteritis, peritonitis, acute pancreatitis, biliary tract disease, sterile serositis, intestinal perforation or other surgical causes. The acute abdomen in patients with SLE is thus a diagnostic challenge (3, 5, 8, 9). Intestinal vasculitis remains a relatively uncommon complication involving only 2% of all SLE patients (7) but is associated with a very high morbidity rate and mortality rate of up to 50% in cases of perforation (5). Other signs of lupus vasculitis, which may accompany patients with gut vasculitis, such as skin and peripheral nervous system involvement may be helpful in diagnosing intestinal vasculitis. This was demonstrated by our patient who presented with severe musculoskeletal and mucocutaneous vasculitis prior to clinically evident intestinal vasculitis (3).

A study by Zizic et al reported that the majority of patients with bowel perforation had gastrointestinal symptoms including diarrhea and all patients had fever prior to the abdominal crisis (5). Abdominal x-rays revealed evidence of small bowel perforation in only 25% of patients in the same study. Computerized tomography (CT) scans have been shown to offer direct observation of the thickness of the intestinal wall and Si-Hoe et al reported such small bowel wall thickening in 30 out of 54 SLE patients who underwent abdominal CT scans for various complaints. The characteristic finding in small bowel vasculitis has been reported as wall thickening with prominence of the mesenteric vessels though these findings are by no means specific to this condition(6). The abdominal ultrasound (US) has been previously reported as a useful

tool to make an early diagnosis of intestinal vasculitis, showing non-specific edema of the intestinal wall. It is of course a safe and non invasive modality and can be used repetitively without exposure to radiation, compared to CT scans and gastrointestinal contrast studies. US may also be helpful for follow up of patients after the initiation of treatment (7).

Treatment of lupus-induced abdominal vasculitis has been difficult; nearly all reported cases have been treated with high dose steroids and surgery. Despite these measures, symptoms usually recur when steroids are tapered (5, 8, 9). Our patient had bowel vasculitis which failed to respond to high dose steroid therapy and surgery.

Early trials of intravenous cyclophosphamide for lupus nephritis and cerebritis have been promising (11,12). Laing and Grimbacher have reported successful treatment of SLE induced gastrointestinal vasculitis with pulse intravenous cyclophosphamide while Eberhard reported a similar failed attempt in a 13 yr old girl (9,13,14). Our patient showed marked clinical improvement of gut vasculitis to intravenous cyclophosphamide pulse therapy as evidenced by closure of the enterocutaneous fistulae, resolution of her cutaneous and systemic symptoms of SLE, and improvement of her complement levels.

Conclusion

There exists a need to decrease the high morbidity and the mortality arising from bowel vasculitis induced by SLE and its secondary complications. There is no single definitive clinical, laboratory or imaging modality available for early detection of SLE induced bowel vasculitis. CT scans or US of the abdomen may be used as non invasive methods of evaluating for small bowel vasculitis in this population, but it is our belief that not tests and scans but a high index of suspicion towards SLE patients with gastrointestinal symptoms is the most important factor that may lead to early identification of bowel vasculitis.

The results of steroid therapy in bowel vasculitis are not very encouraging. The option of pulse cyclophosphamide therapy has been used successfully in adults and needs to be encouraged in the pediatric SLE population. We would recommend that pulse cyclophosphamide therapy be considered early in active SLE patients with gastrointestinal involvement, especially if the child is not responding to high dose parenteral steroid therapy.

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