

Lupus intestinal pseudo-obstruction and hydronephrosis

Case report

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Abstract

Introduction: Intestinal pseudo-obstruction (IPO) is a rare and life-threatening complication of lupus.

Patient Concerns: A patient with long-standing lupus developed recurrent abdominal pain and distension as well as nausea and emesis.

Diagnosis: Imaging showed dilated small bowel loops with air-fluid levels and bowel wall thickening. She also had bilateral hydronephrosis.

Interventions : She was given high-doses of intravenous steroids and cyclophosphamide.

Outcomes: Her symptoms resolved within a week of starting immunosuppression. She was eventually transitioned to mycophenolate mofetil. She remained in remission and immunosuppression was successfully stopped after 1 year.

Conclusions: Intestinal pseudo-obstruction is a rare complication of lupus that is often seen in association with ureterohydronephrosis and interstitial cystitis. This clinical syndrome is thought to be because of smooth muscle dysmotility of the gastrointestinal and genitourinary tracts, although the exact mechanism of dysmotility remains unknown. This condition is often responsive to immunosuppression if recognized and treated promptly.

Abbreviations: CT = computed tomography, GI = gastrointestinal, GU = genitourinary, IPO = intestinal pseudo-obstruction, LMV = lupus mesenteric vasculitis, MRI = magnetic resonance imaging, SLE = systemic lupus erythematosus.

Keywords: dysmotility, hydronephrosis, lupus, pseudo-obstruction

1. Introduction

Intestinal pseudo-obstruction (IPO) is a rare complication of systemic lupus erythematosus (SLE) that is characterized by ineffective propulsion of the intestine resulting in obstructive symptoms without a mechanical cause.^[1] SLE-IPO is a relatively rare entity that is likely underdiagnosed. In one recent series of hospitalized patients with SLE, the prevalence of lupus intestinal pseudo-obstruction (SLE-IPO) was approximately 2%^[2] and SLE-IPO encompasses about 5% of all cases of SLE-induced

abdominal pain requiring admission to the hospital.^[3] SLE-IPO clinically manifests as abdominal pain and distension, nausea and emesis, constipation, and/or diarrhea.^[4] The small bowel is typically affected, although there are reports of involvement of the distal colon as well.^[5] Bowel perforation is a rare but serious complication.^[6]

There is a striking association between intestinal pseudo-obstruction in SLE and genitourinary (GU) complications including hydronephrosis, hydroureter, and cystitis.^[7] Approximately, 60% of SLE patients with IPO also have coinciding ureterohydronephrosis,^[2,8] and among these patients many have reduced bladder capacity and histologic evidence of interstitial cystitis.^[7,9-11] SLE-interstitial cystitis can often be distinguished histologically from idiopathic interstitial cystitis by the presence of immunofluorescent deposits in blood vessel walls of the urinary bladder.^[10,12] Gall bladder wall thickening, biliary and pancreatic duct dilation, and esophageal dysmotility are also associated findings with SLE-IPO.^[2,13-15] Concurrent involvement of the gastrointestinal (GI) and GU tracts in SLE should strongly raise suspicion for intestinal pseudo-obstruction.^[16]

IPO can occur at any time during the disease course of SLE, and in two-thirds of cases it can be a presenting symptom of SLE.^[2] SLE-IPO is especially challenging to diagnose when IPO develops before an underlying diagnosis of SLE is established. IPO typically occurs in active SLE, although there are reports of IPO in patients with quiescent disease.^[17] Compared to patients without IPO, SLE patients with IPO tend to have more alopecia, polyserositis, leukocytopenia, elevated C-reactive protein (CRP), hypoalbuminemia, hypocomplementemia, and positive SS-A/Ro autoantibodies.^[2,7,8] Approximately two-thirds of patients with SLE-IPO have SS-A/Ro autoantibodies.^[2] Pyeloureterectasis,

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peritonitis, hypocomplementemia, hypoalbuminemia, and elevated CRP have been identified as risk factors for IPO in patients with SLE.^[2,18] Owing to the variability in SLE features among patients with IPO, IPO should be considered in all SLE patients presenting with GI symptoms.

SLE-IPO is thought to result from smooth muscle dysmotility of the GI tract, and associated hydronephrosis and hepatobiliary dilatation likely also result from smooth muscle dysmotility. Although the exact pathophysiology remains unknown, proposed mechanisms for smooth muscle damage include myopathic, neurogenic, and vasculitic processes. Pathogenic autoantibodies targeting smooth muscle and immune complex deposition on the muscle and/or nerve are possible immunologic mechanisms that have been implicated. To date no specific autoantibodies have been identified among patients with SLE-IPO.

There are several published reports of GI histopathology from patients with SLE-IPO, all of which were obtained from post-mortem examinations or from intestinal resections.^[7,15,19–22] These reports showed damage to the muscularis layer of the GI tract with sparing of the muscularis mucosa.^[19] In particular, the outer longitudinal layer of the muscularis propria was disproportionately affected with fibrosis and loss of smooth muscle, with relative sparing of the inner layer of the muscularis propria.^[20,21] Hill et al^[20] captured the progression of the disease on sequential biopsies, and showed that in the early phases there is extensive myocyte necrosis and inflammation within the muscularis propria, which later develops into atrophy and fibrosis with decreased number of smooth muscle cells. Innervation of the GI tract was intact and there was no evidence of ganglionitis or vasculitis.^[15] Taken together, these studies are suggestive of a primary myopathic process.^[21]

Herein we report on a case of lupus intestinal pseudo-obstruction and associated ureterohydronephrosis. This case demonstrates the difficulty in clinically distinguishing lupus-IPO from lupus mesenteric vasculitis (LMV), 2 disease entities that are commonly mistaken in the literature. It also highlights the importance of recognizing this syndrome as it is usually responsive to immunosuppression and can lead to significant morbidity without prompt treatment.

2. Case report

A 40-year-old African-American female with long-standing SLE presented to the emergency room with recurrent abdominal pain, distension, and emesis. She had a 10-year history of SLE and immunological findings consistent with the 2012 SLICC criteria for SLE. Clinical features included oral ulcers, alopecia, and malar rash that were successfully treated with hydroxychloroquine 400 mg per-oral per day (QD). Immunological findings included anti-nuclear antibodies at a titer of 1:640 (speckled pattern), positive SS-A/Ro antibodies, positive ribonucleoprotein antibodies, and hypocomplementemia.

Her first episode of GI symptoms occurred 8 months before our initial evaluation when she was 8 weeks' pregnant. At that time, magnetic resonance imaging (MRI) of her abdomen showed a small bowel obstruction, ascites, and new right-sided hydronephrosis. She had a diagnostic laparoscopy that did not reveal a mechanical obstruction or adhesions. Therefore, it was thought that these findings may be reflective of SLE disease activity. She was treated empirically with 60 mg of prednisone and her small bowel obstruction resolved within a week of starting prednisone. Around this time she experienced a spontaneous abortion.

Antiphospholipid antibodies were negative. The prednisone was tapered off over the course of several months, and she returned to her usual state of health. Five months before our evaluation she developed recurrent abdominal pain, distension, and emesis. A computed tomography (CT) scan of her abdomen showed small bowel distension and thickened bowel loops with air–fluid levels, as well as ascites and marked bilateral hydronephrosis. Mucosal biopsies of her stomach, small bowel, and colon from esophagogastroduodenoscopy and colonoscopy were normal. She was again treated empirically with 60 mg of prednisone and had rapid resolution of her symptoms within weeks.

Several weeks before our evaluation, she returned to medical attention with recurrent abdominal pain and distension as well as new flank pain and dysuria. Urine culture grew *Escherichia coli* and she was diagnosed with pyelonephritis and treated with antibiotics. She was also empirically given 40 mg of prednisone for her GI symptoms. The pyelonephritis resolved, but her abdominal pain and distension progressed even on 40 mg of prednisone and she presented to the hospital. On presentation, her abdomen was markedly distended and tympanic to percussion with hypoactive bowel sounds and mild guarding. CT of her abdomen was similar to previous imaging and showed ascites, significant dilation and thickening of bowel wall loops with associated mucosal enhancement (Fig. 1) and bilateral hydronephrosis (Fig. 2). Her laboratory evaluation was notable for a mild leukocytosis (white blood cell count 11.4K/cumm without bands), hemoglobin 11.7 g/dL, platelets 441K/cumm, creatinine 0.76 mg/dL, normal liver function tests, normal lactate, albumin 3.1 g/dL, c-reactive protein 6.9 mg/dL, and sedimentation rate of 6 mm/h. Stool cultures and infectious work-up were negative. SLE laboratories were notable for a negative anti-dsDNA antibody, low complements (C3 44 mg/dL, C4 6 mg/dL), urine analysis without red blood cells, and 24-hour urine with 341 mg of protein. Renal biopsy showed membranous lupus glomerulopathy (class V) with focal mild mesangial proliferation. The Mayo paraneoplastic panel was negative for autoantibodies associated with GI dysmotility,^[23] including voltage-gated calcium channel antibodies (P/Q-type and N-type), voltage-gated potassium channel antibodies, acetylcholine receptor antibodies

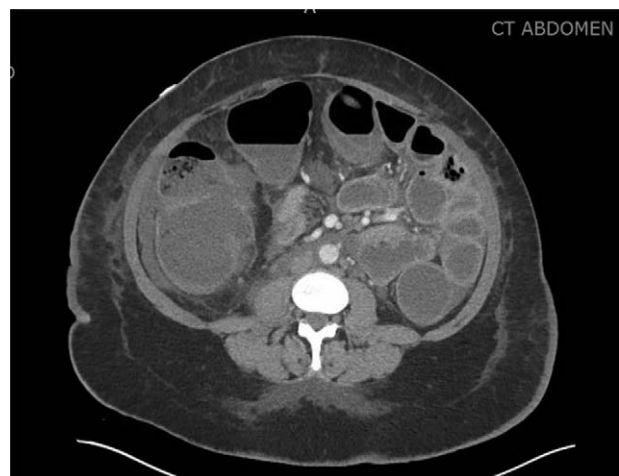


Figure 1. Large dilated bowel loops and bowel wall thickening in lupus intestinal pseudo-obstruction.

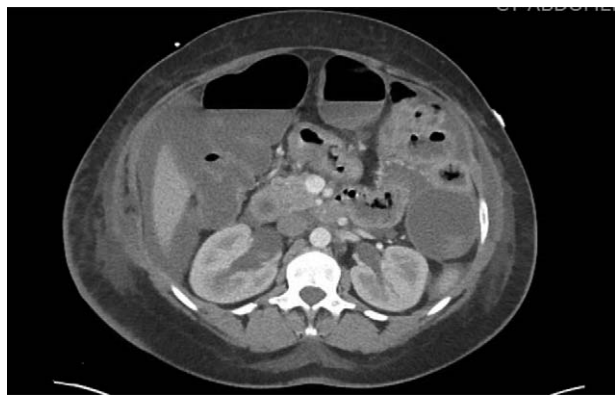


Figure 2. Bilateral hydronephrosis associated with lupus intestinal pseudo-obstruction.

(AChR muscle-type and ganglionic-type), and type 1 anti-neuronal nuclear antibodies.

The patient was diagnosed with intestinal pseudo-obstruction complicated by hydronephrosis. Given that her symptoms worsened even on 40 mg of prednisone, she received 1000 mg solumedrol over 3 days and 1040 mg of intravenous cyclophosphamide, based on a dose of 750 mg/m². She was transitioned to 60 mg of prednisone, and within 2 weeks her abdominal pain and distension resolved and her GI examination returned to normal. One month later, her proteinuria resolved and a follow-up renal ultrasound showed resolution of hydronephrosis. She continued with monthly cyclophosphamide (1040 mg/dose) for 6 months and was transitioned to mycophenolate mofetil (1500 mg twice daily). She stopped mycophenolate mofetil after 1 year and has not had any recurrence of her gastrointestinal or genitourinary symptoms for the past 2 years.

3. Discussion

In this report we present a case of a patient with long-standing SLE presenting with recurrent intestinal pseudo-obstruction and associated hydronephrosis. She had a rapid and sustained response to treatment with immunosuppression. This case highlights several important lessons regarding diagnosis and management of this syndrome.

The diagnosis of lupus-IPO is typically made based on clinical presentation and imaging. CT shows dilated bowel loops with air-fluid levels, bowel wall thickening, and ascites.^[24] In this case the patient had a normal laparotomy and 2 colonoscopies with normal histopathology. Patients often undergo laparotomy to rule out a mechanical obstruction, although this is typically unrevealing and can be avoided if there is a high suspicion for SLE-IPO.^[25] Intestinal mucosal biopsies are often normal or show nonspecific edema because the pathology is deeper in the smooth muscle layer,^[26] which underscores the importance of having a high level of suspicion to make a clinical diagnosis. If the diagnosis is still unclear, manometry often demonstrates abnormalities throughout the GI tract, including esophageal aperistalsis, delayed gastric emptying, decreased lower esophageal sphincter pressure, and hypomotility of the stomach and small intestine.^[7,15]

This case also highlights the challenge of distinguishing lupus-IPO from LMV without a full-thickness biopsy. These 2 diseases

are often confused clinically and in the literature.^[16,27] LMV is an ischemic enteritis secondary to vasculitis or vascular thrombosis, whereas SLE-IPO results from dysmotility of intestinal smooth muscle. Both diseases can cause bowel wall edema and thickening, ascites, and bowel dilatation on imaging. Three classic radiologic signs are sometimes seen in LMV and can help narrow the differential, including mesenteric abnormalities such as engorgement of mesenteric vessels or increased number of vessels (“Comb sign”),^[28] bowel wall thickening and enhancement that looks like a target (the “target sign”),^[29] and increased attenuation of mesenteric fat. Although these imaging findings may suggest a diagnosis of LMV, we note that ischemia and bowel wall enhancement can also be seen in SLE-IPO. In the present case, the diagnosis of SLE-IPO was made based on the presence of concurrent urinary tract abnormalities such as ureterohydronephrosis and/or cystitis, which are typically absent in lupus-LMV.

Patients with SLE-IPO and urinary involvement often respond rapidly to immunosuppression, although the necessity of starting a disease-modifying antirheumatic drug and the duration of treatment required remains unknown based on previous reports. SLE-IPO can cause significant morbidity and mortality if not promptly recognized and treated. One study reported an in-hospital mortality rate of 7% among patients with SLE-IPO, which was often from sepsis or bowel perforation.^[2] If IPO is not treated, the smooth muscle layer can become atrophic and fibrotic and will no longer be reversible with immunosuppression.^[30] In severe cases of chronic intestinal pseudo-obstruction, patients may become dependent on total parenteral nutrition.^[31] There are reports of successful treatment with cyclophosphamide, mycophenolate mofetil, azathioprine, cyclosporin A, and intravenous immunoglobulin, although it is unclear whether these patients may have improved with steroids alone.^[32,33] In the present case, treatment with prednisone alone was not sufficient and the patient required initiation of a disease-modifying antirheumatic drug. This patient was able to successfully stop all immunosuppression after 1 year and remain in remission without any GI symptoms, which suggests that patients may not need prolonged treatment to prevent relapses of this disease.

4. Conclusion

Intestinal pseudo-obstruction is a rare complication of SLE that should be considered in any SLE patient presenting with GI symptoms. Early recognition is important to avoid unnecessary surgical intervention and permanent damage to the GI tract. It is often difficult to differentiate SLE-IPO from LMV without a full-thickness biopsy, although the presence of ureterohydronephrosis and interstitial cystitis should strongly raise suspicion for IPO. It is thought to result from smooth muscle dysmotility, although the precise immunologic mechanism remains unknown. Prompt treatment of IPO is most efficacious in the earliest stages, and can induce remission of IPO as well as extraenteric complications.

Author contributions

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