

## Chronic Intestinal Pseudo-obstruction in Systemic Lupus Erythematosus

Marc-André Leclair, MD, Martin Plaisance, MD, Shana Balfour, MD, Matthieu Touchette, MD



### About the Authors

Marc-André Leclair is a fifth-year resident and Matthieu Touchette is an associate professor in the Internal Medicine Division at the University of Sherbrooke, Sherbrooke, Quebec. Shana Balfour is a fifth-year resident and Martin Plaisance is an associate professor in the Nephrology Division at the University of Sherbrooke. Correspondence may be addressed to [Matthieu.Touchette@USherbrooke.ca](mailto:Matthieu.Touchette@USherbrooke.ca).

### Abstract

Systemic lupus erythematosus (SLE) is a chronic inflammatory disease that can affect any organ of the body. Chronic intestinal pseudo-obstruction (CIPO) is a rare disease of abdominal visceral motility and has been described in SLE. We report the case of a woman presenting with CIPO, bilateral ureterohydronephrosis, and biliary and pancreatic duct dilatation. The management of her bowel problem was helped by the discovery of a class III lupus nephritis, which was treated with steroids, cyclophosphamide, and MMF.

### Case Report

A 25-year-old woman of Filipino origin presented in November 2006 with a 5-day history of diffuse abdominal pain, nausea, vomiting, urinary frequency, and dysuria. She denied any cardiopulmonary, neurological, or systemic symptoms. She did not have arthritis, Raynaud's phenomenon, or rash. Physical examination on admission was remarkable for a distended abdomen with diffuse tenderness but without peritoneal irritation.

She had a nephrotic syndrome with 9 g/d of proteinuria and mild microscopic hematuria, and her creatinine level increased from 45  $\mu\text{mol/L}$  to 75  $\mu\text{mol/L}$ . There was a positive antinuclear antibody, high level of anti-dsDNA antibodies, low C3 and C4 levels, and positive anti-Ro antibodies. An abdominal computed tomography demonstrated pleural effusions, ascites, and thickening of the bladder and bowel from the stomach to the rectum (Figure 1). There was also a bilateral ureterohydronephrosis (Figure 2).

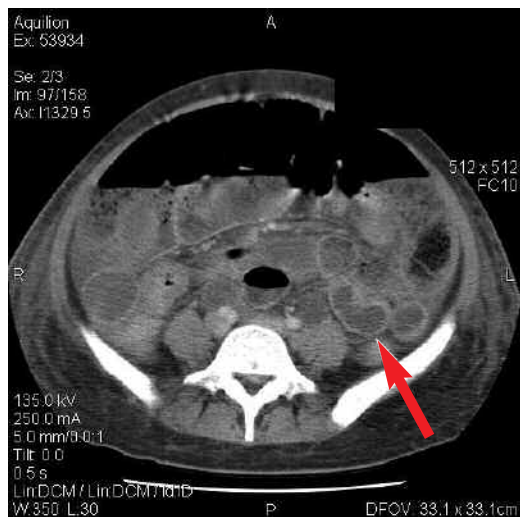


Figure 1. Abdominal computed tomography demonstrating the thickening of the small and large bowel walls.

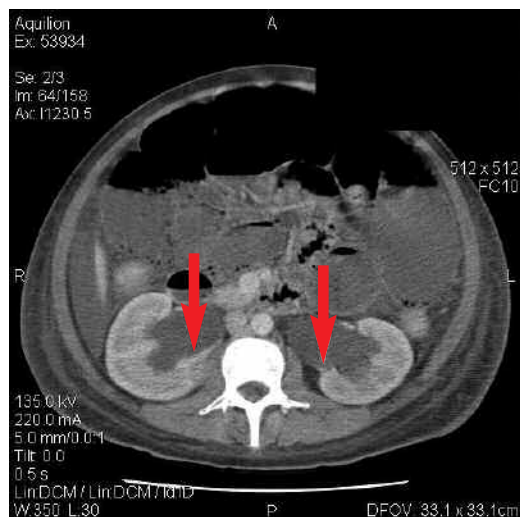


Figure 2. Abdominal computed tomography revealing bilateral ureterohydronephrosis.

Her medical history revealed similar episodes in the past. She first presented in October 2005 with the same clinical and radiological picture described above. However, several confounding anomalies were found. First, the initial ascites tap showed 35% eosinophils and there was a mild blood eosinophilia of  $0.5 \times 10^9/\text{L}$ , which brought the diagnosis of eosinophilic gastroenteritis into consideration. The second tap showed no eosinophils. Second, cryoglobulins were positive but were later retested negative. An upper gastrointestinal endoscopy, a Gastrografin follow-through, and a cystoscopy were normal. A diagnostic laparoscopy was ultimately performed. It was normal, but a visceral peritoneal biopsy revealed our last distracting result: Congo red positive deposits. At that time, she quickly became asymptomatic with steroid treatment that had been started for a possible eosinophilic gastroenteritis, and colchicine was added considering a possible form of familial amyloidosis.

In July 2006, she presented again with a similar episode of pseudo-

obstruction. She had stopped her colchicine about 1 month previously during an episode of *Clostridium difficile*-related diarrhea. The steroids had also been weaned off rapidly. She quickly responded once again to steroids.

In November 2006, the patient was admitted and bowel rest initiated with parenteral nutrition. She became diffusely edematous with a gain of 16 kg in 2 weeks. A renal biopsy was performed, demonstrating changes consistent with a class IIIa lupus nephritis (Figure 3). Not being able to tolerate oral medication, she was treated with intravenous methylprednisolone for 3 consecutive days and intravenous cyclophosphamide 500 mg every 2 weeks for 3 months, which was then switched to MMF 1 g twice a day and oral prednisone. After 4 months of follow-up, she had remained asymptomatic with complete resolution of the intestinal pseudo-obstruction. Abdominal ultrasonography, however, demonstrated a persistent bilateral hydronephrosis associated with biliary tract and Wirsung's duct dilatation. Pancreatic and liver blood tests were normal. A non-nephrotic range proteinuria persisted with a normal creatinine. In September 2007, she showed signs of recurrence of her lupus nephritis while under MMF 1 g twice a day and prednisone 5 mg OD but no digestive or bladder symptoms.

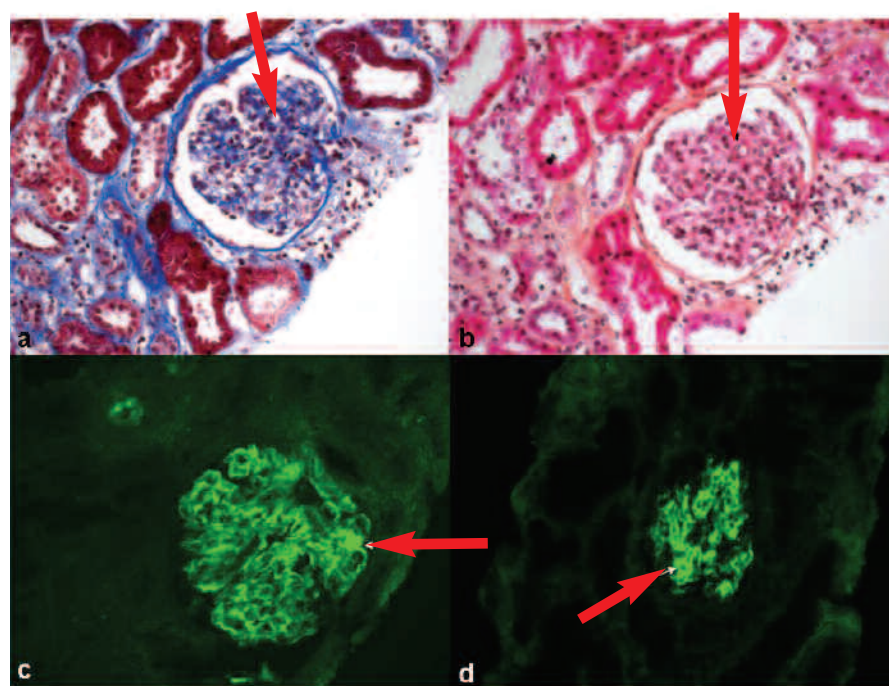


Figure 3. Kidney biopsy. Trichrome staining (*panel a*) and PSA staining (*panel b*) show mild segmental endocapillary proliferation without crescent. There is a strong mesangial and capillary “full house” immunofluorescence positivity (*panel c* C1q and *panel d* IgG). Arrows show endocapillary immune deposits occluding a capillary lumen (*c*) or giving a wire loop shape (*a*, *b*, and *d*).

## Discussion

Systemic lupus erythematosus (SLE) is a chronic autoimmune inflammatory disease of unknown cause with a variety of presenting manifestations. It may affect the joint, skin, kidney, nervous system, lungs, serous membrane, or any other organ. It is the most prevalent autoimmune disease, with an annual incidence of 60 per million of

population.<sup>1</sup> The clinical course is characterized by remissions and relapses. Gastrointestinal symptoms are common in SLE and occur in up to 50% of cases. They may be due to primary gastrointestinal disorders, complications from therapy, or SLE itself.<sup>2</sup>

Intestinal pseudo-obstruction can occur abruptly as a complication of several acute illnesses (Ogilvie's syndrome) or chronically (CIPO).<sup>3</sup> CIPO is a rare disease that can be difficult to diagnose. It took a little more than a year to establish this diagnosis in our patient. In an article on 59 adults with CIPO of different etiologies, the median delay between the first symptoms and diagnosis was 8 years. Symptoms can be intermittent or persistent. They are often severe enough to mandate TPN and lead to surgical exploration, such as with our patient.<sup>4</sup> We found another case of lupus-related CIPO complicated by *C. difficile* diarrhea.<sup>5</sup> Bacterial overgrowth is a more frequently described consequence of CIPO, which can explain a diarrhea in these patients with otherwise-absent bowel movement.<sup>4</sup>

CIPO can be idiopathic or secondary to many illnesses and insults. It has been reported as a congenital disorder mainly in children, who also commonly show urinary tract dilatation.<sup>6</sup> In adults, several etiologies have been linked to CIPO, including amyloidosis and eosinophilic gastroenteritis,<sup>7</sup> which contributed to blur our patient's clinical picture. Autoimmune pathologies such as dermatomyositis, systemic sclerosis, and SLE are also secondary causes.<sup>8,9</sup> The largest series of lupus-related CIPO was reported by Mok et al. in 2000 with 18 cases.<sup>10</sup> The mean age of onset was 29 years old (range 15–47 years) with a female-to-male ratio of 8:1. More than half of the patients were Oriental. In 50% of the patients, CIPO heralded the diagnosis of SLE. All had positive ANA and serology suggestive of active disease at the time of presentation. Seventy-five percent of the patients had anti-Ro. It is worth mentioning that ureterohydronephrosis occurred in 70% of patients, a third had documented histological features of chronic interstitial cystitis, and 45% had a concomitant glomerulonephritis. We have found only one other case of CIPO reported with biliary and pancreatic duct dilatation.<sup>11</sup>

The exact physiopathology is still unknown. Manometry studies in these patients demonstrate a wide spectrum of intestinal motility abnormality. The visceral smooth muscle dysmotility can be neurogenic or myogenic. Two cases of lupus-associated CIPO with some small bowel resection showed extensive myocyte necrosis of the lamina propria without significant vascular involvement. This suggests a direct autoimmune involvement of the visceral musculature. Some cases could also be due to an immune-complex mediated vasculitis.<sup>4,5,10,12</sup>

Unlike many forms of CIPO for which little treatment has shown consistent efficacy, most lupus-induced cases demonstrate improve-

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ment with immunosuppression.<sup>10</sup> In our patient, the treatment aimed at her proliferative lupus nephritis seems to control her bowel symptoms.

In conclusion, CIPO is a rare entity that is often hard to diagnose and treat. This case is a good illustration of CIPO as a complication of SLE. CIPO can present as the initial manifestation of SLE or during the course of the disease. The smooth muscle hypomotility is not limited to the bowel. It can involve the bladder, ureters, and biliary and pancreatic ducts, but the main symptoms are related to bowel paralysis. These intestinal manifestations can respond to treatment of SLE with immunosuppressive therapy.

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