

## Lupus cystitis presenting with hidronephrosis and gastrointestinal involvement

Cistite lúpica apresentando hidronefrose e envolvimento gastrointestinal

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### ABSTRACT

**Introduction:** Lupus cystitis is a rare manifestation of systemic lupus erythematosus, characterized by thickening of the bladder wall, associated with ureterohidronephrosis. In several cases gastrointestinal symptoms are the main manifestation. The optimal immunosuppressive regimen is still unknown. **Methods:** 16-year-old girl with systemic lupus erythematosus was admitted with dysuria, renal impairment, diarrhea, abdominal pain, nausea and vomiting. An abdominal CT scan demonstrated moderate bilateral dilation from the pelvis to the ureterovesical junction, and the bladder exhibited reduced capacity and diffusely thickened walls. A diagnosis of chronic interstitial cystitis was performed and treatment with high dose methylprednisolone resulted in a significant relief of gastrointestinal and urinary symptoms and a reduction of the bladder thickness with improvement of their capacity. **Conclusion:** Lupus cystitis is a rare and underdiagnosed urinary manifestation of LES and the presence of mild urinary symptoms and abdominal pain may alert about this possibility.

**Keywords:** cystitis, interstitial; lower urinary tract symptoms; lupus erythematosus, systemic.

### RESUMO

**Introdução:** A Cistite Lúpica é uma manifestação rara do Lúpus Eritematoso Sistêmico, caracterizada pelo espessamento da parede da bexiga, podendo estar associada com ureterohidronefrose. Em vários casos, os sintomas gastrointestinais são a principal manifestação e ainda não se sabe qual o regime imunossupressor mais adequado nesta situação. **Método:** Uma jovem de 16 anos de idade com lúpus eritematoso sistêmico foi admitida com disúria, insuficiência renal, diarreia, dor abdominal, náuseas e vômitos. A tomografia computadorizada de abdome demonstrou dilatação moderada de ureter e pelve renal bilateralmente e bexiga exibindo capacidade reduzida e paredes difusamente espessadas. Foi feito o diagnóstico de cistite intersticial crônica e o tratamento com dose elevada de metilprednisolona resultou em um alívio significativo dos sintomas urinários e gastrointestinais e uma redução da espessura da bexiga, com melhora da sua capacidade. **Conclusão:** A Cistite Lúpica é uma manifestação urinária rara e subdiagnosticada do LES e a presença de sintomas urinários leves e dor abdominal devem alertar para essa possibilidade diagnóstica.

**Palavras-chave:** cistite intersticial; lúpus eritematoso sistêmico; sintomas do trato urinário inferior.

### INTRODUCTION

Lupus cystitis (LC) is an uncommon manifestation of systemic lupus erythematosus (SLE) with an incidence that ranges from 0.6 to 2%.<sup>1-3</sup> Current evidence of LC is based almost exclusively in case reports, mainly from East Asian countries.<sup>1,4,5</sup> Therefore, the proper immunosuppressive therapy remains in doubt. For unknown

reasons, simultaneous involvement of the gastrointestinal system is quite common and may even be the main manifestation of the disease.<sup>6,7</sup>

It is estimated that LC is present in up to 22.7% of patients with mesenteric vasculitis, even without urinary symptoms.<sup>8</sup> Given these evidences, in the last few years the concept that all patients with SLE and

gastrointestinal symptoms should have urologic evaluation has gain strength. In this report we described a patient with severe LC and mesenteric vasculitis that was successfully treated with corticosteroids.

## CASE REPORT

A 16-year-old girl presented to the internal medicine unit of a general hospital with a 15-day history of suprapubic pain, urinary urgency and dysuria. On physical examination she presented with tachycardia, tachypnea, dehydration and pallor. Breath sounds showed reduced vesicular murmur in both lung bases. The abdomen was distended and painful on palpation of the epigastric and suprapubic regions, but without signs of peritoneal irritation.

About her previous clinical history, she was diagnosed with SLE two years ago, after presenting malar rash, photosensitivity, oral ulcers, polyarthritis, anemia and focal proliferative nephritis. One month after SLE diagnosis she showed mental confusion, auditory and visual hallucinations and seizures, resulting in a diagnosis of lupus meningoencephalitis. Pulse therapy with methylprednisolone was initiated, followed by monthly cyclophosphamide, with a good initial response.

She used azathioprine and prednisone irregularly, but she also was ingesting alcohol and other illicit substances. One year later she developed lower urinary symptoms, abdominal pain, vomiting and diarrhea and immunosuppressive treatment was discontinued due to clinical suspicion of infection.

At this time she was submitted to computed tomography (CT) of the abdomen, which showed mild bilateral pyeloureteral ectasia, likely secondary to bladder distention and mild diffuse wall thickening, with enhancement after intravenous administration of iodinated contrast media, suggesting an inflammatory/infectious process.

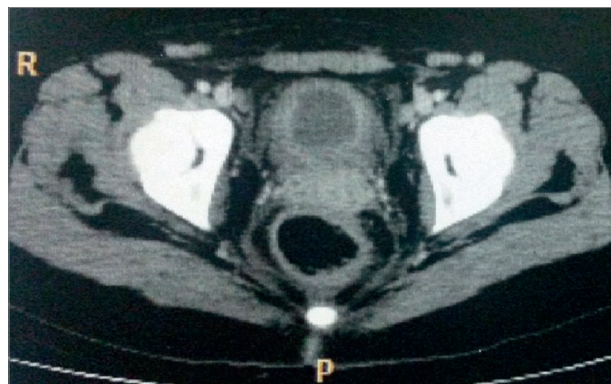
CT also showed multiple, elongated different-sized lymph nodes, distributed at the mesenteric root, especially near the splenic hilum. At this time, laboratory tests revealed: C3: 37.5 mg/dl (NR: 85-160 mg/dl), C4: 10.2 mg/dl (NR: 12-36 mg/dl), a positive direct Coombs test and anti-DNA, Creatinine (Cr) 1.86 mg/dl and the urinalysis showed pyuria (90-100 pus cells/field), hematuria (12-14 red blood cells/field), negative nitrite and amorphous urate crystals, but no bacterial growth in urine and blood cultures. Her symptoms improved after administration of

piperacillin + tazobactam associated with hydration and analgesics.

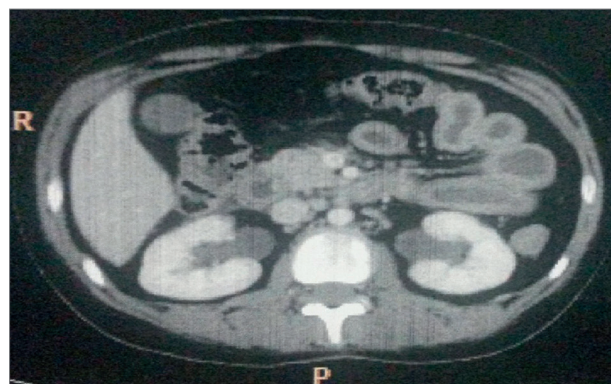
She evolved with a progressive decrease of creatinine levels and after three days of vigorous hydration, renal function recovered (Cr = 0.7 mg/dl). At this point, she underwent an abdominal CT, which showed a small amount of free fluid in the abdominal cavity and small lymph nodes in the splenic hilum and along the superior mesenteric chain, measuring less than 1 cm on its minor axis and a diffuse thickening of small bowel.

The kidneys demonstrated moderate bilateral dilation from the pelvis to the ureterovesical junction, and the bladder exhibited reduced capacity and diffusely thickened walls (Figures 1 and 2). She underwent cystoscopy with bladder biopsy, and histological examination showed nonspecific chronic cystitis, with the presence of lymphocytes in the chorion and epithelial cells, as well as reactive epithelial hyperplasia associated with focal vascular congestion, without any particular finding of lupus. Due to instability and clinical signs of systemic inflammatory response, the patient was treated with broad-spectrum antibiotics.

**Figure 1.** Computed tomography demonstrated thickening of the bladder wall with marked reduction of its filling capacity.



**Figure 2.** Diffuse small bowel wall thickening and bilateral hydronephrosis.



In addition, a nasogastric open tube was inserted and parenteral nutrition was started. Electrolyte replacement and hemodynamic support were also performed. After clinical stabilization, methylprednisolone (1000 mg/day for 3 days) was administered, followed by 1 mg/kg oral prednisone. The patient showed progressive improvement of gastrointestinal and urinary symptoms and was discharged with a prescription of oral prednisone and azathioprine, which was replaced by mycophenolate mofetil (MMF) after six months.

Eleven months after discharge MRI showed mild bilateral hydronephrosis without evidence of obstructive processes, and slight diffuse bladder wall thickening (Figures 3 and 4). The correlation of this study with previous CT demonstrates greater fullness, and less bladder wall thickening. She is currently receiving outpatient treatment with 20 mg/day prednisone and 1 g MMF.

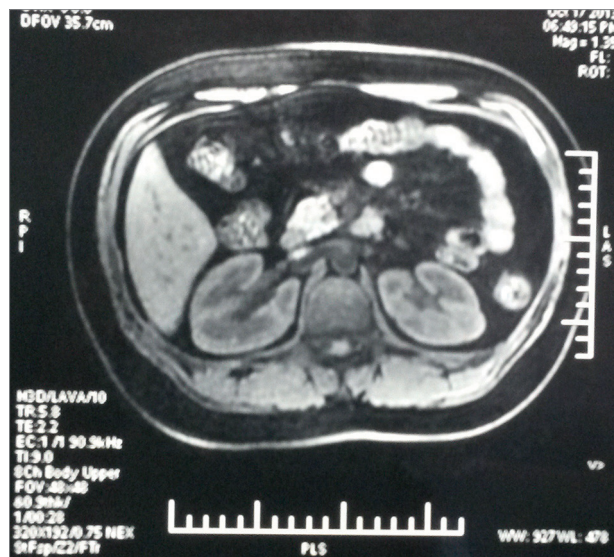
**Figure 3.** Magnetic resonance imaging of the abdomen demonstrating a reduction of bladder wall thickening and an increase in its filling capacity after methylprednisolone.



## DISCUSSION

Fister (1938) reported a case of interstitial cystitis in a patient with SLE, and no other apparent etiology.<sup>9</sup> Forty-five years later, Orth *et al.* used the term LC to describe six cases of cystitis with bladder wall thickening and ureterohydronephrosis without

**Figure 4.** MRI of the abdomen demonstrating significant reduction of hydronephrosis after methylprednisolone.



other identifiable causes, in patients with SLE, and reported a strong association with gastrointestinal and neurological symptoms.<sup>10</sup>

Unfortunately, almost all existing information about LC is based on case reports.<sup>5,7</sup> Its incidence is approximately 1.2% in patients with SLE, but it is believed that asymptomatic LC may be more common than previously thought, since a study that evaluated the autopsies of thirty-five SLE patients without urinary symptoms found interstitial cystitis in 11 of them.<sup>4,11</sup> In a series of 18 cases from China, the average time between diagnosis of SLE and the development of cystitis with hydronephrosis was approximately 15 months.<sup>1</sup> However, cystitis may be the initial manifestation of SLE.<sup>1,7,10</sup>

In this report, the first manifestation was confused with an episode of infectious cystitis, and given that her symptoms improved with hydration and antibiotics. The patient remained asymptomatic for 18 months and her initial urinary symptoms showed significant involvement of the bladder, with signs of chronicity at biopsy. It is noteworthy that the patient did not use the immunosuppression regimen correctly in the maintenance phase, which may have caused disease progression.

Similar to previous reports, the patient had predominantly gastrointestinal symptoms and abdominal CT also demonstrated a diffuse thickening of small bowel. Zhang *et al.*,<sup>1</sup> in a study with 18 cases of LC, observed that 77.8% of patients were admitted with gastrointestinal symptoms. Other case reports

have demonstrated an association between LC and enteritis up to 94.4% of the patients.<sup>7</sup>

Recently, Yuan *et al.*<sup>8</sup> studied 3823 patients with lupus mesenteric vasculitis and found that LC occurred concurrently in 22.7% of the cases. It is believed that autoantibodies that target the bladder and intestinal mucosa may be responsible for this association.<sup>5,12</sup> In the present study, we also observed an increase in pancreatic enzymes and mesenteric lymphadenopathy, a rare but previously reported occurrence in patients with active LC.<sup>3,6,12</sup>

Chen *et al.*<sup>12</sup> reported six cases of LC, three of whom had pancreatitis or mesenteric lymphadenopathy. Due to acute kidney injury on arrival, which can raise amylase and lipase, and the absence of changes in pancreatic CT, we cannot confirm pancreatitis in this case. In regard to lymphadenopathy, the last abdominal CT revealed that this finding regressed after immunosuppressive treatment.

Another important finding is the association between LC and central nervous system involvement, since our patient had a history of lupus psychosis and seizures, 18 months before the onset of LC symptoms. There are reported cases of this association, generally with worse prognosis.<sup>1,10,12</sup> The fact that organs other than the bladder are usually affected strongly suggests that patients with LC have more aggressive forms of SLE and hence should be treated with a more aggressive immunosuppressive regimen.

The most common urinary symptoms are suprapubic pain, urinary urgency, nocturia and dysuria with sterile urine, which are present in up to 61.1% of the patients.<sup>5,7,8</sup> In this report the patient had no urinary symptoms for 18 months but continued to exhibit progressive cystitis, with significantly reduced bladder capacity (Figure 1). There are other reports of LC in the absence of urinary symptoms, which shows the silent character of the disease and the need for explore the urinary tract of patients with gastrointestinal symptoms, even without urinary complaints, especially in the presence of ultrasonographic signs suggesting bladder or ureter involvement.<sup>6,12</sup>

The most feared alteration of LC is obstructive uropathy, due to bladder wall inflammation and thickening, which reduces bladder capacity and induces a secondary ureterohydronephrosis, the last presented in approximately 92% of the patients.<sup>5,7,8</sup> The prognosis of bladder function is highly dependent

on the time between diagnosis and treatment, since there may be fibrosis, obstructive uropathy and irreversible loss of renal function.<sup>6,7</sup>

With regard to treatment, corticosteroids have been considered the first choice therapy, since it induces a significant improvement of gastrointestinal symptoms, ureterohydronephrosis regression and a reduction of bladder thickening.<sup>10</sup> However, since not all cases respond well to steroids, cyclophosphamide, cyclosporine and tacrolimus are alternatives to resistant cases.<sup>1,7,13</sup>

In this report, the lower urinary tract symptoms only improved after reintroduction of methylprednisolone and we opted for a maintenance therapy with MMF. Three months after the introduction of the immunosuppressive regimen, MRI showed a significant improvement in bladder thickening and capacity (Figure 3).

As with other SLE manifestations, the timing of corticosteroid introduction may be crucial to achieving a better response. However, in the present study, there was marked reduction in bladder thickening with treatment, even after one year without regular immunosuppression. This data suggests that the inflammatory process that induces bladder wall thickening in LC could be completely reversed with high doses of corticosteroids.<sup>14,15</sup> There is little experience with the use of MMF in LC and more studies are needed to determine the best long-term immunosuppressive regimen.

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