

## Case Report

# Asymptomatic Lupus Cystitis with Bilateral Hydronephrosis

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## Keywords

Cystitis lupus · Systemic lupus erythematosus · Hydronephrosis

## Abstract

Lupus cystitis is a rare complication of systemic lupus erythematosus (SLE). It is characterized by an increase in bladder wall thickness and may be associated with hydroureteronephrosis. Reports, mostly from East Asian countries, indicate that lupus cystitis usually presents with gastrointestinal tract symptoms such as diarrhea, nausea, or abdominal pain. Lower urinary tract symptoms such as dysuria, nocturia, polyuria, and suprapubic pain are also common presenting symptoms. We report a 22-year-old female patient who presented at Cipto Mangunkusumo Teaching Hospital in Indonesia, with profuse and prolonged vaginal bleeding without any other accompanying symptoms. She had a history of polyarthralgias, fever, bleeding gums, anemia, and thrombocytopenia 3 months earlier. Abdominal ultrasound examination revealed bilateral hydronephrosis and a thickened bladder wall; the other organs were normal. Laboratory examination confirmed the diagnosis of SLE complicated by lupus nephritis and lupus cystitis. The patient responded well to the treatment with methylprednisolone. The vaginal bleeding stopped within 2 days, and the laboratory parameters improved. She was discharged on oral methylprednisolone and is scheduled for detailed workup after 1 month.

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## Introduction

Lupus cystitis is a rare complication of systemic lupus erythematosus (SLE), with most cases reported from East Asian countries. Patients with lupus cystitis generally present with gastrointestinal symptoms such as vomiting, nausea, and abdominal pain, sometimes mimicking obstructive ileus [1–3], or with lower urinary tract symptoms such as dysuria, suprapubic pain, polyuria, urgency, and incontinence. Many authors have reported the presence of an increased bladder wall thickness, a decreased bladder volume, and hydronephrosis in these patients [4]. We report an unusual case of a 22-year-old Indonesian female with lupus cystitis without any common symptoms.

## Case Presentation

A 22-year-old female was admitted to our hospital with the chief complaint of heavy menstrual bleeding for 10 days. Blood loss was severe, requiring around 4–5 tampon changes per day, and she complained of feeling dizzy and weak. She was unmarried and had no history of similar menorrhagia.

About 10 months earlier she had prolonged menstrual bleeding at that time, but as the menstrual cycle was normal and the bleeding was not very severe, she had not sought gynecological advice. About 3 weeks earlier she had experienced generalized muscle aches and joint pains (especially involving the upper and lower extremities), along with low-grade fever and bleeding from the gums. She had visited a primary healthcare center, where laboratory examination showed thrombocytopenia (50,000/dL) and anemia (6.5 g/dL). Dengue fever was suspected, and she was given a blood transfusion.

At our hospital she was initially admitted to the obstetrics and gynecology emergency department because of the severe menstrual bleeding. However, after ultrasound examination ruled out gynecological abnormalities, she was referred to the internal medicine department. On examination, her vital signs were within normal limits, but the conjunctiva was pale, and her hair showed a tendency to fall out easily. Multiple erythematous macules were present on the skin; however, there was no “butterfly rash” on the face. Systemic examination was otherwise normal.

Hemogram showed the following: hemoglobin 11.3 g/dL; hematocrit 36%; MCV 76.4 fL; MCHC 31.4 g/dL; serum iron 45 µg/dL; TIBC 279 µg/dL; transferrin saturation 16%; thrombocyte count 55,200/dL; and leucocyte count 7,310/dL (with normal differential count). Kidney function tests showed normal serum urea and creatinine levels, with eGFR of 129.8 mL/min/1.73 m<sup>2</sup> (calculated using the Chronic Kidney Disease Epidemiology Collaboration equation). The random blood glucose level was 105 mg/dL. The lipid profile showed total cholesterol, 218 mg/dL; low-density lipoprotein 161 mg/dL; high-density lipoprotein 27 mg/dL; and triglyceride 150 mg/dL. Liver function tests and serum electrolyte levels were within normal limits. Coagulation function tests showed partial thromboplastin time 9.7 s (11.3); activated partial thromboplastin time 31.8 s (34.7); fibrinogen level 429.9 mg/dL; and D-dimer 0.2 mg/dL. Antinuclear antibody was positive at a titer of 1/1,000, with C3 86.4 mg/dL, C4 15.4 mg/dL, CRP 2.4 mg/dL, and anti-dsDNA 614.5 IU/mL. Lactic acid dehydrogenase was 464 U/L, reticulocyte count 1.42%, immature platelet fraction 6.7%, and serum albumin 3.87 g/dL. Urinalysis showed a large number of erythrocytes, epithelial cells, and amorphous crystals. Proteinuria was present (2+). Total 24-h protein excretion was 1,148 mg. Kidney ultrasound examination was done as a part of routine examination, which revealed bilateral dilatation of

the pelvicalyceal systems showing hydronephrosis grade 1 on the left kidney (Fig. 1a) and grade 2 on the right kidney (Fig. 1b) without evidence of kidney cyst or stones. Moreover, ultrasound examination on the urinary bladder shows an increased bladder wall thickness (Fig. 1c).

Based on these findings, we diagnosed SLE complicated by lupus nephritis and lupus cystitis. Treatment was started with intravenous methylprednisolone (62.5 mg/day; 1.5 mg/kg/day). The vaginal bleeding stopped within 2 days, and the patient's general condition improved. Laboratory parameters also showed good response to corticosteroid therapy. After 5 days of intravenous therapy, the patient was switched to oral methylprednisolone (1 mg/kg/day). She was discharged from hospital on the 8th day, with the advice to continue methylprednisolone at the same dose and she is scheduled for follow-up after 1 month.

## Discussion

SLE is an autoimmune disease that affects different organs, and patients may present with signs and symptoms related to the involved organ. Only a few cases of lupus cystitis have been reported, and most of these have been from East Asian countries [5]. According to retrospective studies from Korea and China, lupus cystitis may occur in 0.5–2.3% of all SLE patients [1–3]. The highest incidence of 2.3% was reported by Koh et al. [1] in 1,023 Korean SLE patients who were followed for 15 years. Yuan et al. [2] and Zhang et al. [3] reported incidence rates of 0.5 and 0.6%, respectively, in Chinese populations. The high number of cases reported in Asian populations – especially East Asian populations – might be due to the nature of SLE as well as a better awareness of the condition. SLE is generally much more severe in Asians, and the incidence of renal involvement is especially high [6]. Although Indonesia comprise of more than 200,000,000 people, as to date, this is the first report of lupus cystitis from Southeast Asia compared to East Asian countries who generated numerous report of such rare SLE complication. East Asian countries such as South Korea, Japan, and China are far more developed than most Southeast Asian countries, and this factor might contribute to a better reporting of rare SLE complications. The present case report is the first from the Southeast Asia region.

Up to 61.1% of the lupus cystitis patients present with lower urinary tract symptoms such as dysuria, nocturia, urgency, polyuria, and suprapubic pain. Gastrointestinal symptoms present in 94.4% of the lupus cystitis patients such as vomiting, nausea, diarrhea, abdominal pain, and even pseudoobstruction and paralytic ileus, are also common initial symptoms; in fact, gastrointestinal symptoms were more common than urinary tract symptoms in this group [7]. Yuan et al. [2] reported that out of 3,823 lupus patients with mesenteric vasculitis, 868 (22.7%) had lupus cystitis as well. Immunohistochemical studies have revealed the deposition of IgG and C3 in the walls of the arterioles in the bladder and intestine, suggesting that a common autoantigen and chronic inflammation may be responsible for the co-occurrence of gastrointestinal and bladder symptoms in these patients [8, 9].

Our patient was unusual, as she did not have any gastrointestinal symptoms. Lower urinary tract symptoms were also absent, although she did have bilateral hydronephrosis (Fig. 1a, b) and a thickened bladder wall (Fig. 1c). In an autopsy study, histological abnormalities were found in the bladder wall of an SLE patient who did not have lower urinary tract symptoms, showing that a silent progression of the disease is possible [10]. Zhang et al. [3] observed bladder involvement at presentation in some SLE patients, whereas in others it appeared only about 5 years after SLE diagnosis. The main finding in lupus cystitis is an increased thickness of the bladder wall due to chronic interstitial cystitis, with pathological examination showing

deposition of immune-mediated complex in the bladder wall [7, 11]. Ultrasonographic examination and a computed tomography scan may reveal bilateral hydronephrosis or hydroureteronephrosis in addition to bladder wall thickening [12, 13]. Fibrosis of the ureterovesical junction and edema of the bladder wall caused by deposition of immune-mediated complex leads to decreased bladder capacity and detrusor muscle spasm, and the ensuing vesicoureteral obstruction and reflux has been suggested to be the cause of the hydronephrosis in our patient. Ultrasonographic abnormalities were present in our patient, but she presented without any usual symptoms of cystitis lupus.

Our patient also had lupus nephritis as shown by the high 24-h urinary protein excretion. Patients with lupus nephritis have decreased T-suppressor cells, increased CD4+ cells, hyperactivity of B-cells, and an increased production of proinflammatory cytokines. B-cell hyperactivity results in an increased autoantibody production and the deposition of antibody-antigen complex in target organs. In the kidney, deposition is mostly at the base of the glomeruli, in the mesangial layer, and the interstitial tissue of the proximal tubules. This deposition activates a series of inflammatory cascades that result in glomerular damage and decrease in renal function. Lupus nephritis is more common and more severe in Asians, and Cheng et al. [14] have therefore recommended the use of lower cutoff points (<300 mg) for proteinuria in Asian populations. The authors also suggest that renal biopsy needs to be performed to accurately measure disease progression in patients with lupus nephritis.

SLE may be associated with menstrual cycle irregularities. Shabanova et al. [15] found a significant association between the SLE Disease Activity Index and menstrual abnormalities such as menorrhagia. According to the authors, SLE patients had lower estradiol and progesterone levels than healthy controls. Such hormonal imbalances – as well as the thrombocytopenia that was detected – could explain the prolonged heavy bleeding during menstruation in our patient. Although the chief complaint of the patient was the prolonged and heavy bleeding, we could not determine a direct relationship between the occurrence of lupus cystitis with the menorrhagia in this patient, as no such report had stated such a relationship, and no further immunohistochemistry was planned to see the relationship in our patient.

In conclusion, lupus cystitis is a rare manifestation of SLE and has mainly been reported from East Asian countries. To the best of our knowledge, this is the first report of lupus cystitis from the Southeast Asian region. Furthermore, our patient did not experience the common symptoms of lupus cystitis, as the chief complaints was only menorrhagia. Thus, lupus cystitis should be suspected in SLE patients even in the absence of obvious lower urinary tract or gastrointestinal symptoms. This is worth noting because lupus cystitis is a rare complication of SLE, which could progress silently without any symptoms. Therefore, we encourage all treating physicians to be more aware of possible bladder involvement in SLE. An abnormal urine sample and ultrasound examination should prompt evaluation of the patient for possible bladder involvement so that treatment can be instituted early and further complications can be prevented.

### Statement of Ethics

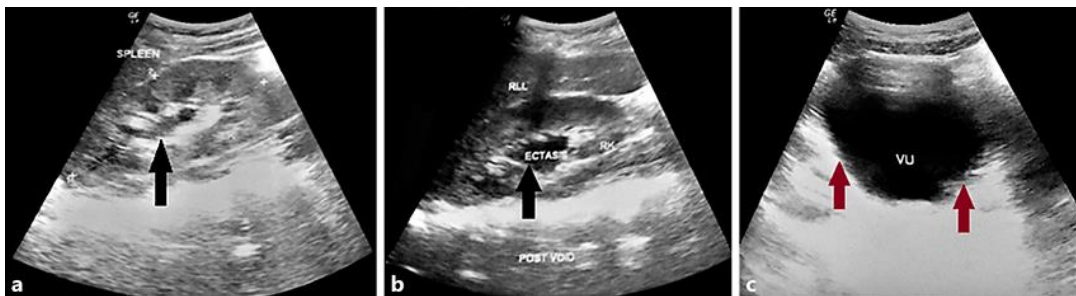
The Ethics Committee of the hospital and the university deemed ethical approval to be unnecessary.

## Disclosure Statement

The author has no conflicts of interest to report in relation to the publication of this article.

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**Fig. 1.** Ultrasound results from the kidney and urinary bladder. **a** Left kidney ultrasound examination showing enlargement of the renal pelvis as a sign of grade 1 hydronephrosis (arrow). **b** Right kidney ultrasound examination enlargement of the pelvicalyx system as a sign of grade 2 hydronephrosis (arrow). **c** Increased thickness of the bladder wall (red arrows) as evidence of the ongoing inflammation caused by lupus cystitis.