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Clinical Analysis of 61 Systemic Lupus Erythematosus Patients With Intestinal Pseudo-Obstruction and/or Ureterohydronephrosis

A Retrospective Observational Study

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Abstract: The objective of this article is to investigate the clinical features of intestinal pseudo-obstruction (IPO) and/or ureterohydronephrosis in systemic lupus erythematosus (SLE).

Sixty-one SLE patients with IPO and/or ureterohydronephrosis were analyzed retrospectively. A total of 183 cases were randomly selected as controls from 3840 SLE inpatients without IPO and ureterohydronephrosis during the same period. Patients were assigned to 1 of the 3 groups (SLE with IPO and ureterohydronephrosis, SLE with IPO, and SLE with ureterohydronephrosis). The clinical characteristics, treatments, and prognosis were compared between the 3 groups.

There were 57 females and 4 males, with a mean age of 32.0 years. IPO was the initial manifestation of SLE in 49.1% of the cases, whereas ureterohydronephrosis in 32.5%. All patients were initially treated with a high-dose steroid. Thirty-one of these patients (50.8%) also received intravenous methylprednisolone pulse therapy. Two patients died of bowel perforation and lupus encephalopathy, and the other 59 patients (96.7%) achieved remission after treatment. The incidences of fever, glomerulonephritis, nervous system involvement, serositis, erythrocyte sedimentation rate elevation, hypoalbuminemia, hypocomplementemia, and anti-SSA antibody positivity were significantly higher in patients with IPO and/or ureterohydronephrosis than in the control group (without IPO and ureterohydronephrosis). Also, patients with IPO and/or ureterohydronephrosis had higher SLE Disease Activity Index scores than control patients. Compared with SLE patients with IPO, the patients with IPO and ureterohydronephrosis had a significantly higher incidence of gallbladder wall thickening, biliary tract dilatation, and serositis, whereas the patients with ureterohydronephrosis had less mucocutaneous involvement and serositis. Eight of the 47 IPO patients who initially responded well to immunotherapy relapsed; however, all responded well to retreatment with adequate immunotherapy. Of these 8 patients, 4 relapsed following poor compliance and self-discontinuation of steroid or immunosuppressant therapy. The rate of poor compliance with immunotherapy and the number of organ systems involved in patients in the recurrent IPO group were significantly higher than those in the nonrecurrent IPO group.

IPO and ureterohydronephrosis are severe complications of SLE. As patients usually respond readily to early optimal steroid treatment, early diagnosis and timely initiation of glucocorticoid are important to relieve symptoms, prevent complications, and improve prognosis.

(*Medicine* 94(4):e419)

Abbreviations: AIPO = acute intestinal pseudo-obstruction, CIPO = chronic intestinal pseudo-obstruction, CT = computed tomography, ESR = erythrocyte sedimentation rate, IPO = intestinal pseudo-obstruction, SLE = systemic lupus erythematosus, SLEDAI = Systemic Lupus Erythematosus Disease Activity Index.

INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease involving multiple organs and systems. Intestinal pseudo-obstruction (IPO), a rare and poorly understood complication of SLE, which usually coexists with ureterohydronephrosis, could be life-threatening if not treated promptly. Early recognition of SLE-related IPO and ureterohydronephrosis is critical in preventing misdiagnosis and treatment delay. Although previous studies have described the clinical features of IPO and ureterohydronephrosis in SLE, most of them are case reports or small sample size studies. Until now, <40 cases of IPO secondary to SLE are reported in the English literature. In addition, the clinical characteristics of SLE patients with IPO and ureterohydronephrosis, IPO, or ureterohydronephrosis have not been compared before. In the present study, we retrospectively reviewed 61 SLE patients with IPO and/or ureterohydronephrosis, who were admitted to the Peking Union Medical College Hospital in the past 10 years. The primary aim of this study was to analyze the clinical features of IPO and/or ureterohydronephrosis in SLE. In addition, the differences between SLE patients with IPO and ureterohydronephrosis, and those with IPO, or ureterohydronephrosis were also investigated.

Editor: Gabrio Bassotti.
Received: October 1, 2014; revised: December 3, 2014; accepted: December 5, 2014.
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This project was funded by the Chinese National High Technology Research and Development Program, Ministry of Science and Technology (2012AA02A513), and the National Natural Science Foundation of China (81172858 and 81373190).
The authors have no conflicts of interest to disclose.

ISSN: 0025-7974
DOI: 10.1097/MD.0000000000000419

MATERIALS AND METHODS

Patients

Sixty-one SLE patients with IPO and/or ureterohydronephrosis admitted to the Peking Union Medical College Hospital (PUMCH) between May 2003 and May 2013 were enrolled and analyzed retrospectively. A total of 183 cases were randomly selected as controls from 3840 SLE inpatients without IPO and ureterohydronephrosis in PUMCH during the same period. All patients fulfilled the American College of Rheumatology revised classification criteria for SLE. Ureterohydronephrosis was identified by ultrasound and computed tomography (CT) imaging. A definitive diagnosis of IPO was based on symptoms and signs of intestinal obstruction, evidence of bowel obstruction on plain abdominal x-ray and CT images, and no evidence of anatomical or structural abnormalities. IPO was categorized as acute or chronic on the basis of the clinical presentation.[1,2] Chronic IPO (CIPO) was defined as the onset of 1 or more symptoms of IPO at least 6 months prior to diagnosis, and acute IPO (AIPO) was defined as the onset of 1 or more symptoms of IPO <6 months prior to diagnosis. Patients were not considered to have SLE-related IPO if their symptoms were caused by infections, tumors, side effects of medications such as opioids, or surgical conditions. Patients with IPO and/or ureterohydronephrosis were assigned to 1 of the 3 groups (SLE with IPO and ureterohydronephrosis, SLE with IPO, and SLE with ureterohydronephrosis). There were 32 SLE patients with IPO and ureterohydronephrosis, 21 SLE patients with IPO, and 8 SLE patients with ureterohydronephrosis. The clinical presentations, laboratory findings, treatments, and prognosis were analyzed and compared between the 3 groups. The institutional review board of Peking Union Medical College Hospital approved the study. The study was retrospective and only involved the review of records; therefore, the requirement for written informed consent was waived.

Statistical Analysis

The software package SPSS 21.0 (IBM, Armonk, NY, USA) was used to perform the statistical analysis. Means ± standard deviations (SDs) were used for descriptive analysis. Chi-square tests and Fisher exact test were used to compare categorical data, and independent sample *t* test was used to compare quantitative data between the groups. Statistical significance was set at a value of $P < 0.05$.

RESULTS

Demographic Data

A total of 61 SLE patients with IPO and/or ureterohydronephrosis were included. The mean age at diagnosis was 32.0 ± 10.8 years with a range of 14 to 63 years. There were 57 females and 4 males with a ratio of 14.3 to 1. In addition to IPO and ureterohydronephrosis, 12 patients (19.7%) had gallbladder wall thickening, 6 (9.8%) had biliary tract dilatation, and 3 (4.9%) had esophageal motility disorder.

Clinical and Laboratory Features

Of the 61 patients, 13 (21.3%) had concurrent Sjogren syndrome. Thirty-one patients (50.8%) had fever, and 29 patients (47.5%) had weight loss. Serositis was found in 40 patients (65.6%). Hematological involvement (45 cases, 73.8%), glomerulonephritis (42 cases, 68.9%), and mucocutaneous involvement (42 cases, 68.9%) were the most common features during the entire course of illness. Coexisting lupus involvement of other organ systems included musculoskeletal involvement (27 cases, 44.3%), neuropsychiatric involvement (9 cases, 14.8%), pancreatitis (8 cases, 13.1%), interstitial lung disease (5 cases, 8.2%), and cardiac involvement (4 cases, 6.6%).

Leukocytopenia was found in 31 cases (50.8%), thrombocytopenia in 20 cases (32.8%), and autoimmune hemolytic anemia in 12 cases (19.7%). Hypocomplementemia was found in 52 cases (85.2%), and serum Immunoglobin G (IgG) level was elevated in 26 cases (42.6%). Antinuclear antibody was positive in all patients, and elevated anti-double stranded DNA (dsDNA) antibody was present in 35 cases (57.4%). Anti-Sjögren's syndrome antigen A (SSA) antibody was found in 48 cases (78.7%), anti-Sjögren's syndrome antigen B (SSB) antibody in 9 (14.8%), anti-Ribonucleoprotein (RNP) antibody in 20 (32.8%), anti-Smith (Sm) antibody in 17 (27.9%), and anti-Ribosomal RNP (rRNP) antibody in 15 cases (24.6%). Anticardiolipin antibody was positive in 5 cases (8.2%), anti-β2-glycoprotein 1 antibody in 3 cases (4.9%), and Lupus anticoagulant in 6 cases (9.8%). The average SLE Disease Activity Index (SLEDAI) score was 12.4 ± 5.3 with a range of 2 to 29 (>14 in 29.5% of the cases, 10–14 in 41.0%, 5–10 in 22.9%, and <5 in 6.6% of cases).

Clinical Characteristics of IPO and Ureterohydronephrosis

Fifty-three patients had IPO, and of these, 26 (49.1%) had IPO as the onset feature of SLE, whereas in 27 patients IPO was a complication, which occurred 1 month to 12 years (median time of 3.3 years) after SLE diagnosis. There were 21 patients with CIPO and 32 patients with AIPO. The duration from CIPO onset to diagnosis varied from 6 months to 6 years, with a median duration of 22.1 months. The duration from AIPO onset to diagnosis varied from 12 days to 4 months, with a median duration of 52.5 days. The gastrointestinal symptoms included abdominal pain in 47 patients, nausea and vomiting in 45, constipation in 42, abdominal distension in 33, and diarrhea in 26 patients. Plain abdominal radiography showed bowel distension with air–fluid levels in all patients. Dilated bowel loops and bowel wall thickening without mechanical obstruction were the major abdominal CT findings in our study. Eight CIPO patients and 5 AIPO patients underwent colonoscopy with mucosal biopsy, and all patients only showed mucosal inflammation in pathological analysis. Prior to admission, 6 CIPO patients and 2 AIPO patients were misdiagnosed with tuberculosis, 4 CIPO patients and 9 AIPO patients were misdiagnosed with infective enteritis, and 1 AIPO patient was misdiagnosed with acute appendicitis.

Forty patients had ureterohydronephrosis, which was the first manifestation of SLE in 13 patients (32.5%), whereas in 27 patients, ureterohydronephrosis was a complication, which occurred 1 month to 10 years (median time of 2.6 years) after SLE diagnosis. Twenty-six out of 40 patients (65%) had symptoms associated with ureterohydronephrosis, including irritative bladder symptoms (17 cases), dysuria (7 cases), decreased urine output (6 cases), backache (5 cases), and increased nocturia (5 cases). The remaining 14 patients (35%) had no ureterohydronephrosis-related clinical manifestations. Postrenal acute renal failure occurred in 2 cases. Ultrasound was performed in all patients, and showed bilateral ureterohydronephrosis in 36 patients and unilateral ureterohydronephrosis in 4 patients. All patients had hydronephrosis, and 33 patients had ureterectasia, with mean (SD) diameter of renal

pelvis and ureter of 24 (11) mm and 12 (0.5) mm, respectively. Bladder wall thickening was detected in 13 patients. Four patients underwent cystoscopy, which showed a reduction in bladder capacity.

Treatment and Prognosis

All patients were initially treated with a high-dose steroid (prednisone-equivalent dose of 1–2 mg/kg/d). Thirty-one of these patients (50.8%) also received intravenous methylprednisolone pulse therapy (1 g/d for 3 days), followed by prednisone (1 mg/kg/d) or equivalent dosages of another corticosteroid. Additional immunosuppressants were administered in 59 patients (96.7%). The immunosuppressive agents used in this group of patients were intravenous cyclophosphamide (56 cases), cyclosporin A (2 cases), and mycophenolate-mofetil (1 case). Intravenous immunoglobulin therapy was given in 5 cases. Two patients with CIPO died of bowel perforation and lupus encephalopathy, and the other 59 patients (96.7%) achieved remission after treatment.

In total, 51 of 53 (96.2%) IPO patients initially responded well to immunosuppressive treatment and achieved remission. Of these 51 patients, 47 were followed up for 13 to 106 months (median duration, 37 months). Eight patients (17.0%) had recurrent episodes of pseudo-obstruction and the other 39 patients (83.0%) remained in remission. IPO relapse was detected in 4 of 17 (23.5%) CIPO patients and their first relapse occurred at 8, 26, 27, and 27 months after treatment, respectively. Four of 30 (13.3%) AIPO patients relapsed at 5, 6, 13, and 27 months after treatment, respectively. Retreatment with a high-dose steroid or intravenous methylprednisolone pulse therapy reestablished disease control.

Comparison of Clinical Characteristics Between SLE Patients With IPO and/or Ureterohydronephrosis and SLE Patients Without IPO and Ureterohydronephrosis

As shown in Table 1, the incidences of fever, glomerulonephritis, nervous system involvement, serositis, erythrocyte sedimentation rate (ESR) elevation, hypoalbuminemia, hypocomplementemia, and anti-SSA antibody positivity were significantly higher in patients with IPO and/or ureterohydronephrosis than in the control group (without IPO and ureterohydronephrosis). Also, patients with IPO and/or ureterohydronephrosis had higher SLEDAI scores than control patients.

Comparison of Patient Characteristics and Outcome Between the 3 Groups

The clinical presentations, laboratory findings, treatments, and outcome were compared between 3 groups: SLE patients with IPO and ureterohydronephrosis (32 cases), IPO (21 cases), and ureterohydronephrosis (8 cases); the results are shown in Table 2. Compared with SLE patients with IPO, the patients with IPO and ureterohydronephrosis had a significantly higher incidence of gallbladder wall thickening, biliary tract dilatation, and serositis, whereas the patients with ureterohydronephrosis

TABLE 1. Comparison of Clinical Characteristics Between SLE Patients With IPO and/or Ureterohydronephrosis and SLE Patients Without IPO and Ureterohydronephrosis

Characteristics	SLE Patients With IPO and/or UH (n = 61)	SLE Patients Without IPO and UH (n = 183)	*P* Value
Age, y	32.0 ± 10.8	31.6 ± 10.9	0.805
Female	57 (93.4)	166 (90.7)	0.510
Fever	31 (50.8)	32 (17.5)	<0.001*
Mucocutaneous involvement	42 (68.9)	134 (73.2)	0.510
Glomerulonephritis	42 (68.9)	90 (49.2)	0.008*
Hematological involvement	45 (73.8)	119 (65.0)	0.208
Pulmonary involvement	5 (8.2)	5 (2.7)	0.136
Pulmonary involvement	5		
Nervous system involvement	9 (14.8)	11 (6.0)	0.031*
Musculoskeletal involvement	27 (44.3)	97 (53.0)	0.237
Cardiac involvement	4 (6.6)	4 (2.2)	0.213
Serositis	40 (65.6)	26 (14.2)	<0.001*
Elevated ESR	44 (72.1)	94 (51.4)	0.005*
Hypoalbuminemia	32 (52.5)	62 (33.9)	0.010*
Hypocomplementemia	52 (85.2)	122 (66.7)	0.005*
Elevated IgG	26 (42.6)	82 (44.8)	0.766
Positive anti-dsDNA	35 (57.4)	87 (47.5)	0.183
Positive anti-SSA	48 (78.7)	80 (43.7)	<0.001*
Positive anti-SSB	9 (14.8)	13 (7.1)	0.071
Positive anti-rRNP	15 (24.6)	40 (21.9)	0.658
Positive anti-RNP	20 (32.8)	56 (30.6)	0.750
Positive anti-Sm	17 (27.9)	74 (40.4)	0.079
SLEDAI score	12.4 ± 5.3	10.2 ± 7.3	0.012*

Data are listed as mean ± SD or n (%). dsDNA = double stranded DNA, ESR = erythrocyte sedimentation rate, IgG = Immunoglobin G, IPO = intestinal pseudo-obstruction, RNP = Ribonucleoprotein, rRNP = Ribosomal RNP, SSA = Sjögren's syndrome antigen A, SSB = anti-Sjögren's syndrome antigen B, SLE = systemic lupus erythematosus, SLEDAI = SLE Disease Activity Index, Sm = smith, UH = ureterohydronephrosis.
* $P < 0.05$.

TABLE 2. Comparison of the Clinical Features, Treatments, and Outcome in SLE Patients With IPO and Ureterohydronephrosis, Patients With IPO, and Patients With Ureterohydronephrosis

Characteristics	SLE Patients With IPO and UH (n = 32)	SLE Patients With IPO (n = 21)	SLE Patients With UH (n = 8)
Age, y	29.7 ± 9.9	33.1 ± 9.4	38.3 ± 15.6
Female	28 (87.5)	21 (100.0)	8 (100.0)
Secondary Sjogren syndrome	5 (15.6)	6 (28.6)	2 (25.0)
Clinical and laboratory characteristics			
Fever	16 (50.0)	11 (52.4)	4 (50.0)
Mucocutaneous involvement	21 (65.6)	18 (85.7)‡	3 (37.5)‡
Glomerulonephritis	20 (62.5)	17 (81.0)	5 (62.5)
Hematological involvement	23 (71.9)	17 (81.0)	5 (62.5)
Pulmonary involvement	4 (12.5)	0 (0)	1 (12.5)
Nervous system involvement	3 (9.4)*	3 (14.3)	3 (37.5)*
Musculoskeletal involvement	12 (37.5)	13 (61.9)	2 (25.0)
Cardiac involvement	1 (3.1)	2 (9.5)	1 (12.5)
Serositis	27 (84.4)†,*	12 (57.1)†,‡	1 (12.5)‡,*
Pancreas involvement	6 (18.8)	1 (4.8)	1 (12.5)
Gallbladder wall thickening	12 (37.5)*,†	0 (0)†	0 (0)*
Biliary tract dilatation	6 (18.8)†	0 (0)†	0 (0)
Esophageal motility disorder	2 (6.3)	1 (4.8)	0 (0)
Elevated ESR	22 (68.8)*	16 (76.2)	6 (75.0)*
Hypoalbuminemia	16 (50.0)	12 (57.1)	4 (50.0)
Hypocomplementemia	28 (87.5)	19 (90.5)	5 (62.5)
Elevated IgG	18 (56.3)*	7 (33.3)	1 (12.5)*
Positive anti-dsDNA	17 (53.1)	14 (66.7)	4 (50.0)
Positive anti-SSA	24 (75.0)	19 (90.5)	5 (62.5)
Positive anti-SSB	5 (15.6)	3 (14.3)	1 (12.5)
Positive anti-rRNP	9 (28.1)	5 (23.8)	1 (12.5)
Positive anti-RNP	14 (43.8)	5 (23.8)	1 (12.5)
Positive anti-Sm	11 (34.4)	4 (19.0)	2 (25.0)
SLEDAI score	12.6 ± 5.7	13.0 ± 5.0	9.9 ± 3.8
Treatments			
Corticosteroid (Pulse IVMP/HDS)	20/12*	9/12	2/6*
Immunosuppressant	32 (100.0)*	21 (100.0)	6 (75.0)*
Intravenous immunoglobulin	4 (12.5)	1 (4.8)	0 (0)
Prognosis (improvement/progression)	31/1	20/1	8/0

Data are listed as mean ± SD or n (%). dsDNA = double stranded DNA, ESR = erythrocyte sedimentation rate, HDS = high-dose steroid therapy (1–2 mg/kg/d prednisone equivalent), IgG = Immunoglobin G, IPO = intestinal pseudo-obstruction, Pulse IVMP = pulse intravenous methylprednisolone therapy at 1 g/d for 3 days, RNP = Ribonucleoprotein, rRNP = Ribosomal RNP, SSA = Sjögren's syndrome antigen A, SSB = anti-Sjögren's syndrome antigen B, SLE = systemic lupus erythematosus, SLEDAI = SLE Disease Activity Index, Sm = smith, UH = ureterohydronephrosis.

* $P < 0.05$, patients with IPO and UH versus patients with UH.

† $P < 0.05$, patients with IPO and UH versus patients with IPO.

‡ $P < 0.05$, patients with IPO versus patients with UH.

had less mucocutaneous involvement and serositis. There were significant differences in gallbladder wall thickening, nerve system involvement, serositis, ESR, IgG levels, and treatments between the patients with ureterohydronephrosis and patients with IPO and ureterohydronephrosis.

Comparison of Characteristics and Treatment Regimens of Recurrent and Nonrecurrent IPO in SLE Patients

Of the 8 recurrent IPO patients, 4 patients relapsed following poor compliance and self-discontinuation of steroid or immunosuppressant therapy. The characteristics and treatment regimens of the recurrent patients were compared with those of the nonrecurrent IPO patients. As shown in Table 3, the rate of poor compliance with immunotherapy and the number of organ systems involved in patients in the recurrent IPO group were significantly higher than those in the nonrecurrent IPO group. Further analysis showed that the recurrent AIPO group had a significantly higher rate of poor compliance with immunotherapy than the nonrecurrent AIPO group, whereas the recurrent CIPO group had significantly higher SLEDAI scores and more visceral involvement than the nonrecurrent CIPO group.

DISCUSSION

IPO in SLE is a rare and severe disorder of the gastrointestinal tract characterized by ineffective intestinal propulsion with signs and symptoms of intestinal obstruction but without a mechanical cause. Common symptoms include dysphagia, gastroesophageal reflux, abdominal pain, nausea, vomiting, bloating, abdominal distension, constipation or diarrhea, and

TABLE 3. Comparison of Characteristics and Treatment Regimens of Recurrent and Nonrecurrent IPO in SLE Patients

Characteristics	IPO Patients		AIPO Patients		CIPO Patients	
	Recurrent Patients (n = 8)	Nonrecurrent Patients (n = 39)	Recurrent Patients (n = 4)	Nonrecurrent Patients (n = 26)	Recurrent Patients (n = 4)	Nonrecurrent Patients (n = 13)
Age, y	28.1 ± 12.6	30.9 ± 9.2	27.5 ± 11.0	29.8 ± 9.2	28.1 ± 15.6	33.2 ± 9.3
Female	7 (87.5)	37 (94.9)	3 (75.0)	25 (96.2)	4 (100.0)	12 (92.3)
Ureterohydronephrosis	7 (87.5)	21 (53.8)	4 (100.0)	14 (53.8)	3 (75.0)	7 (53.8)
Fever	5 (62.5)	22 (56.4)	4 (100.0)	15 (57.7)	1 (25.0)	7 (53.8)
Mucocutaneous involvement	5 (62.5)	32 (82.1)	2 (50.0)	22 (84.6)	3 (75.0)	10 (76.9)
Glomerulonephritis	4 (50.0)	29 (74.4)	1 (25.0)	20 (76.9)	3 (75.0)	9 (69.2)
Hematological involvement	6 (75.0)	31 (79.5)	2 (50.0)	22 (84.6)	4 (100.0)	9 (69.2)
Pulmonary involvement	2 (25.0)	2 (5.1)	1 (25.0)	1 (3.8)	1 (25.0)	1 (7.7)
Nervous system involvement	2 (25.0)	4 (10.3)	1 (25.0)	3 (11.5)	1 (25.0)	1 (7.7)
Musculoskeletal involvement	4 (50.0)	18 (46.2)	2 (50.0)	12 (46.2)	2 (50.0)	6 (46.2)
Cardiac involvement	2 (25.0)	1 (2.6)	1 (25.0)	0 (0)	1 (25.0)	1 (7.7)
Serositis	7 (87.5)	27 (69.2)	4 (100.0)	18 (69.2)	3 (75.0)	9 (69.2)
Elevated ESR	7 (87.5)	28 (71.8)	3 (75.0)	19 (73.1)	4 (100.0)	9 (69.2)
Hypoalbuminemia	4 (50.0)	20 (51.3)	3 (75.0)	13 (50.0)	1 (25.0)	7 (53.8)
Hypocomplementemia	8 (100.0)	36 (92.3)	4 (100.0)	24 (92.3)	4 (100.0)	12 (92.3)
Elevated IgG	3 (37.5)	18 (46.2)	2 (50.0)	14 (53.8)	1 (25.0)	4 (30.8)
Positive anti-dsDNA	4 (50.0)	24 (61.5)	3 (75.0)	16 (61.5)	1 (25.0)	8 (61.5)
Positive anti-SSA	6 (75.0)	33 (84.6)	2 (50.0)	21 (80.8)	4 (100.0)	12 (92.3)
Positive anti-SSB	0 (0)	6 (15.4)	0 (0)	4 (15.4)	0 (0)	2 (15.4)
Positive anti-rRNP	2 (25.0)	11 (28.2)	2 (50.0)	10 (38.5)	0 (0)	1 (7.7)
Positive anti-RNP	4 (50.0)	12 (30.8)	2 (50.0)	10 (38.5)	2 (50.0)	2 (15.4)
Positive anti-Sm	2 (25.0)	11 (28.2)	2 (50.0)	9 (34.6)	0 (0)	2 (15.4)
SLEDAI score	10.0 ± 5.7	13.9 ± 5.3	10.0 ± 5.7	14.2 ± 5.2	15.2 ± 9.2‡	10.5 ± 4.0‡
Number of organ systems involved	4.3 ± 1.5*	2.8 ± 0.9*	3.8 ± 1.5	2.9 ± 0.9	4.8 ± 1.5‡	2.6 ± 0.9‡
Corticosteroid (pulse IVMP/HDS)	5/3	22/17	3/1	16/10	2/2	6/7
Immunosuppressant	8 (100.0)	39 (100.0)	4 (100.0)	26 (100.0)	4 (100.0)	13 (100.0)
Intravenous immunoglobulin	0 (0)	5 (12.8)	0 (0)	4 (15.4)	0 (0)	1 (7.7)
Poor compliance with immunotherapy	4 (50.0)*	2 (5.1)*	2 (50.0)†	1 (3.8)†	2 (50.0)	1 (7.7)

Data are listed as mean ± SD or n (%). AIPO = acute IPO, CIPO = chronic IPO, dsDNA = double stranded DNA, ESR = erythrocyte sedimentation rate, HDS = high-dose steroid therapy (1–2 mg/kg/d prednisone equivalent), IgG = Immunoglobin G, IPO = intestinal pseudo-obstruction, Pulse IVMP = pulse intravenous methylprednisolone therapy at 1 g/d for 3 days, RNP = Ribonucleoprotein, rRNP = Ribosomal RNP, SSA = Sjögren's syndrome antigen A, SSB = anti-Sjögren's syndrome antigen B, SLE = systemic lupus erythematosus, SLEDAI = SLE Disease Activity Index, Sm = smith.

* $P < 0.05$, recurrent IPO patients versus nonrecurrent IPO patients.

† $P < 0.05$, recurrent AIPO patients versus nonrecurrent AIPO patients.

‡ $P < 0.05$, recurrent CIPO patients versus nonrecurrent CIPO patients.

involuntary weight loss.[3] Based on the clinical presentation, IPO is classified as acute or chronic. CIPO differs from AIPO by the presence of recurrent obstructive symptoms for at least 6 months.[1,2] In SLE, IPO is often associated with ureterohydronephrosis and interstitial cystitis, and may involve the esophagus and gallbladder. The underlying mechanism of IPO is not fully understood, but it may involve primary myopathy, neuropathy, vasculitis, or antibodies directed against the visceral smooth muscles, causing muscular damage and dysmotility.[4–8]

In the present study, 6 patients had biliary tract dilatation without mechanical obstruction presenting together with IPO and ureterohydronephrosis. Since Pardos-Gea et al[9] first reported an association between IPO with ureterohydronephrosis and biliary tract dilatation in a patient with SLE, there have only been 3 other cases reported in the English literature.[9–12] The pathophysiology of biliary tract dilatation remains unclear, but concurrent dilatation of 3 hollow viscera may suggest a smooth muscle dysmotility. As biliary dilatation can lead to complications such as cholecystitis, cholangitis, and generalized sepsis, clinical physicians should be aware of the possibility of biliary dilatation when evaluating SLE patients with IPO and ureterohydronephrosis, and appropriate imaging of biliary tracts should be obtained early in the investigation.

In our study, SLE patients with IPO and/or ureterohydronephrosis had higher incidences of glomerulonephritis and nervous system involvement and higher SLEDAI scores than SLE patients without IPO and ureterohydronephrosis. This suggests that SLE patients with IPO and/or ureterohydronephrosis are in a serious condition and should be paid great

attention. IPO may manifest as the initial presentation or as a complication of SLE. Narváez et al[13] reviewed 21 cases of IPO in SLE, and showed that IPO was the initial manifestation of SLE in 41% of the cases. Similarly, we found that IPO was the initial manifestation of SLE in 49.1% of the cases. Forty patients had ureterohydronephrosis, which was the first manifestation of SLE in 13 (32.5%) cases. As IPO and ureterohydronephrosis in SLE lack specific clinical manifestations, the diagnosis of the true underlying disease is often delayed,[14] and may result in life-threatening complications such as bowel necrosis, bowel perforation, and renal failure.[10,15] SLE should be highly suspected in patients with unexplained IPO and/or ureterohydronephrosis even in the absence of other typical lupus manifestations, and the relevant laboratory tests, in addition to obtaining a thorough history and performing a physical examination, should be done quickly. Also, before SLE-related IPO is diagnosed, other causes of secondary pseudo-obstruction with a similar presentation, such as paramalignant pseudo-obstruction, autoimmune gastrointestinal dysmotility, and opioid-induced pseudo-obstruction, should be excluded. In addition, we found that in 35% of SLE patients, the ureterohydronephrosis was asymptomatic on initial diagnosis, suggesting that physicians should routinely screen patients with SLE-related IPO for coexisting ureterohydronephrosis or interstitial cystitis.

No specific autoantibodies have been found in lupus patients with IPO and/or ureterohydronephrosis; however, a few case reports have noted the high prevalence of anti-SSA antibodies. Mok et al[5] reported 6 cases of SLE-related IPO and showed that 83.3% of the patients were positive for anti-SSA antibodies. Chen et al[16] reported that 5 of the 6 (83.3%) SLE patients with ureterohydronephrosis and cystitis had anti-SSA antibodies. In our series, 78.7% patients had anti-SSA antibodies, which is consistent with the previous observations. Positivity for anti-SSA antibodies was significantly higher among SLE patients with IPO and/or ureterohydronephrosis than among SLE patients without IPO and ureterohydronephrosis. This indicates that anti-SSA antibodies may play a pathological role in muscular dysmotility.

The treatment of choice for SLE-related IPO and ureterohydronephrosis is a combination of high-dose intravenous corticosteroids, immunosuppressants, and supportive interventions.[3,10,17,18] Early diagnosis and timely initiation of treatment are crucial for the recovery of visceral peristaltic function. In SLE patients, IPO and ureterohydronephrosis show an excellent response to early optimal steroid therapy.[19] A delay in therapy initiation or an inadequate steroid dose may lead to advanced and irreparable tissue destruction including fibrosis and atrophy of the muscularis propria, resulting in failure to regain functional peristalsis.[10,20,21] In our study, all patients were initially treated with a high-dose steroid. Of these patients, 50.8% also required a 3-day pulse of methylprednisolone therapy, and 96.7% showed a good response to the treatment. These findings indicate that although IPO and ureterohydronephrosis in SLE are particularly severe complications, they can be successfully treated with timely administration of the appropriate steroid therapy. Further analysis showed that the treatments including steroid and immunosuppressant administration were more aggressive in patients with IPO and ureterohydronephrosis than in patients with ureterohydronephrosis. Furthermore, 23.5% of CIPO patients and 13.3% of AIPO patients relapsed in our study. However, these patients responded well to retreatment with a high-dose steroid or intravenous methylprednisolone pulse therapy. Our result also showed that the recurrent AIPO group had a significantly higher rate of poor compliance with immunotherapy than the nonrecurrent AIPO group. This finding suggests that self-discontinued steroid or immunosuppressant therapy may be 1 cause of AIPO relapse, indicating that clinicians should ensure therapy compliance by discussing with patients the need for long-term immunosuppressive therapy to maintain remission.

The SLEDAI score in our series ranged from 5 to 10 in 22.9% of the cases, and was <5 in 6.6%. This result is consistent with previous reports showing that IPO and ureterohydronephrosis can occur with low systemic disease activity even in a stable state of other organ involvement.[22] Moreover, in our study, the SLEDAI scores indicated high disease activity in only 29.5% of the patients, but 50.8% of the patients needed a 3-day pulse of methylprednisolone therapy, suggesting that in SLE patients with IPO and/or ureterohydronephrosis the SLEDAI score is not a reliable reference for evaluating the disease activity and deciding the initial dose of steroids. It has to be emphasized that the SLE patients with IPO and/or ureterohydronephrosis should all be regarded as having active SLE independent of the scoring and given early aggressive treatment.[19]

This study has some limitations. First, our findings are based on the results of a single-center, retrospective study; therefore, the possibility of selection bias cannot be excluded. The study population was restricted to Chinese individuals; therefore, it remains to be determined whether our results can be generalized to other ethnicities and populations of different backgrounds. Second, the number of patients who underwent colonoscopy in our study was relatively small, and none of the patients underwent full-thickness bowel biopsy. Although such biopsy may not be absolutely necessary, it can help to elucidate the pathophysiology of IPO in SLE. Further investigation is required to examine the pathological features of full-thickness biopsy samples. Finally, the follow-up was relatively short, and the clinical characteristics of recurrent and nonrecurrent IPO in SLE were compared using a relatively small number of patients; therefore, a larger study with longer-term follow-up should be initiated in the future to fully assess the long-term effectiveness of immunosuppressive treatment and to determine prognosis.

In conclusion, IPO and ureterohydronephrosis are rare but severe complications of SLE. Patients usually respond readily to early optimal steroid treatment. Awareness of these complications can facilitate rapid diagnosis and therefore prompt timely initiation of appropriate medical treatment to control the disease, prevent complications, and improve prognosis.

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