

CONCISE REPORT

Acute abdominal pain in systemic lupus erythematosus: focus on lupus enteritis (gastrointestinal vasculitis)

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Objective: To determine the causes of acute abdominal pain in systemic lupus erythematosus (SLE) and to compare the clinical and laboratory data, especially antiphospholipid antibodies and the SLE Disease Activity Index (SLEDAI), between lupus enteritis (gastrointestinal vasculitis) and acute abdominal pain without lupus enteritis in patients with SLE.

Methods: A retrospective study was carried out for all patients admitted with SLE from 1993 to March 2001. The SLEDAI and laboratory data were collected at the time of diagnosis of SLE and at the time of acute abdominal pain. Lupus enteritis (gastrointestinal vasculitis) was diagnosed by clinical investigation and abdominal computed tomographic findings.

Results: Chart review identified 175 patients (20 male, 155 female) who had been admitted with SLE. Of these patients, 38 (22%) presented with acute abdominal pain. Lupus enteritis was the most common cause of acute abdominal pain. Patients were divided into three groups: group 1: lupus enteritis (n=17), group 2: acute abdominal pain without lupus enteritis (n=21), and group 3: SLE without acute abdominal pain (n=137). There was no difference in age and sex among the three groups. Antiphospholipid, anti-RNP, anti-Sm, anti-Ro, and anti-La antibodies did not differ among the three groups. There was no difference in the SLEDAI at the time of diagnosis and at the time of acute abdominal pain between groups 1 and 2. Complement, erythrocyte sedimentation rate, C reactive protein, and anti-dsDNA measured at the time of acute abdominal pain did not differ between groups 1 and 2. A drop in the white blood cell count at the time of abdominal pain was more prominent in group 1 than group 2. In lupus enteritis, the jejunum and ileum were the sites most commonly affected. Rectal involvement was rare. Even though four patients relapsed, all the patients with lupus enteritis, including those who relapsed, responded well to corticosteroid.

Conclusion: Lupus enteritis is the most common cause of acute abdominal pain in SLE. All patients with lupus enteritis responded well to a high dose of a corticosteroid without surgical intervention. The SLEDAI and laboratory data, except leucopenia, do not correlate with the occurrence of lupus enteritis.

Systemic lupus erythematosus (SLE) is a multifactorial autoimmune disease that mostly affects young women, resulting in significant morbidity and mortality. Lupus enteritis, with or without infarction, is one of the most serious complications of SLE. Lupus enteritis may contribute to greater morbidity and mortality, and early recognition and treatment are important if long term survival is to be improved. The occurrence of acute abdominal pain in SLE is a

challenging diagnostic and therapeutic problem. Evaluation of abdominal pain in patients with SLE is complicated by the disease itself and by concomitant disease. The side effects of drugs are also often a problem in evaluation.

The presence of the antiphospholipid antibody (aPL) is more likely to be associated with thrombosis or chronic fetal miscarriages.¹ To the best of our knowledge, the relation between reversible ischaemic bowel disease in SLE and aPL has not been adequately investigated.

In the hope of detecting variables for predicting the occurrence of lupus enteritis, we performed a retrospective case-control study to examine clinical and laboratory variables, particularly aPL and the systemic lupus Disease Activity Index (SLEDAI).²

PATIENTS AND METHODS

Patients

We reviewed the records of patients with SLE who had been admitted to our hospital from 1993 to March 2001 and we identified patients who had presented with acute abdominal pain. All the patients fulfilled the 1982 revised American Rheumatism Association criteria for the classification of SLE.³ During this eight year period, 175 patients (20 male, 155 female) were studied. Of these patients, 38 (22%) presented with acute abdominal pain. Patients were divided into three groups. Lupus enteritis (n=17) (group 1) was diagnosed if at least three of the following signs were seen on a computed tomographic (CT) scan: bowel wall thickening, target sign, dilatation of intestinal segments, engorgement of mesenteric vessels, and increased attenuation of mesenteric fat.⁴ Two control groups were selected. The first control group (n=21) (group 2) comprised patients with acute abdominal pain without lupus enteritis. The second control group (n=137) (group 3) consisted of patients with SLE without acute abdominal pain.

Clinical features and laboratory data

The demographic data of the patients (sex, age, duration of disease, and duration of abdominal pain) were recorded. SLEDAI was calculated at the time of diagnosis of SLE and at the time of acute abdominal pain. The laboratory data, including the white blood cell (WBC) count, haemoglobin, platelets, complement, erythrocyte sedimentation rate (ESR), C reactive protein (CRP), anti-dsDNA, aPL, anti-Sm antibody, anti-ribonucleoprotein (anti-RNP) antibody, anti-Ro antibody, and anti-La antibody, were measured at the time of diagnosis of SLE. The WBC count, haemoglobin, platelets, complement, ESR, CRP and anti-dsDNA were measured at the time of acute

Abbreviations: aPL, antiphospholipid antibody; β_2 GPI, β_2 glycoprotein I; CRP, C reactive protein; CT, computed tomographic (scan); ELISA, enzyme linked immunosorbent assay; ESR, erythrocyte sedimentation rate; GI, gastrointestinal; SLE, systemic lupus erythematosus; SLEDAI, SLE Disease Activity Index; WBC, white blood cell

Table 1 Autoantibody profile

	Group 1 (n=17)	Group 2 (n=21)	Group 3 (n=137)	p Value
aPL	7/16	10/18	45/83	0.72
LAC	1/15	4/17	20/76	0.26
aCL (IgG/IgM)	6/15	9/17	32/65	0.75
β_2 GPI (IgG/IgM)	2/13	2/11	4/28	0.41
Anti-RNP	4/14	4/19	29/94	0.69
Anti-Sm	2/15	4/19	15/95	0.81
Anti-Ro	7/14	5/17	43/93	0.39
Anti-La	1/14	1/17	12/92	0.60

Group 1, lupus enteritis; group 2, acute abdominal pain without lupus enteritis; group 3, SLE without acute abdominal pain; aPL, antiphospholipid antibody; LAC, lupus anticoagulant; aCL, anticardiolipin antibody; β_2 GPI, β_2 glycoprotein I.

abdominal pain and were compared with levels calculated at the time of diagnosis of SLE. CRP was measured quantitatively by immunonephelometry (N Latex CRP mono, Behring Diagnostics, San Jose, California, USA) (normal 0–6 mg/l). Complements 3 and 4 were calculated by nephelometry (Beckman Array System, Beckman Instruments, Brea, California, USA) (normal 880–2010 mg/l and 160–407 mg/l, respectively). Anti-dsDNA antibody was detected by radioimmunoassay (anti-dsDNA kit, Ortho-Clinical Diagnostics, Rochester, NY, USA) (normal 0–7 IU/ml). A lupus anticoagulant test was performed using dilute Russell viper venom time reagent (STAGO compact, Diagnostica STAGO, France). Anticardiolipin antibody (IgG/IgM) was detected by the enzyme linked immunosorbent assay (ELISA) (Varelisa cardiolipin antibody kit, Pharmacia and Upjohn Diagnostics, Freiburg, Germany). Anti- β_2 -glycoprotein I (anti- β_2 GPI) antibody (IgG/IgM) was detected by ELISA (anti- β_2 GPI-QUANTA Lite Kit, INOVA Diagnostics, San Diego, USA).

Four patients with lupus enteritis (n=17) relapsed. For the 21 episodes of lupus enteritis, CT scanning recorded the sites affected and the characteristic findings.

Statistical methods

Laboratory indices and the SLEDAI were tested by the Mann-Whitney test, Kruskal-Wallis test, and the χ^2 test. A p value of <0.05 was considered significant.

RESULTS

There were no differences in sex (male/female: 2/15, 3/18, 15/122, p=0.90) and age (mean (SD): 34 (12.5), 36 (11.6), 38 (12.2), p=0.29) among the three groups. The average duration (months) between SLE diagnosis and acute abdominal pain was no different between groups 1 and 2 (36 (44.0), 28.8 (33.4), p=0.26). The duration (days) of acute abdominal pain symptoms before admission to hospital was no different between groups 1 and 2 (6.3 (7.4), 8.9 (8.9), p=0.26). Lupus enteritis was the initial manifestation of SLE in 6/17 cases. Lupus enteritis was the most common cause of acute abdominal pain in our data, occurring in 17/38 (45%) patients. Urinary tract infection occurred in 6 (16%), acute gastroenteritis in 5 (13%), pancreatitis in 2 (5%), infectious diarrhoea in 2 (5%), haemorrhagic gastritis in 2 (5%), serositis in 1 (3%), cholecystitis in 1 (3%), IVC thrombosis in 1 (3%), and gastric ulcer in 1 (3%). The frequencies of autoantibodies were compared among the three groups (table 1). The presence of aPL was determined if one of the following three tests was positive on two occasions, at least six weeks apart: lupus anticoagulant test, anticardiolipin antibody, and anti- β_2 GPI antibody.⁵ There was no difference in the positivity of aPL among the three groups. The frequencies of anti-RNP, anti-Sm, anti-Ro, and anti-La were no different among the three groups.

Table 2 describes the laboratory indices and the SLEDAI calculated at the time of diagnosis of SLE and at the time of acute abdominal pain. Differences of laboratory indices and the

SLEDAI between two episodes were also measured. A drop in the WBC count at the time of abdominal pain was much more prominent in group 1. Other laboratory indices (haemoglobin, ESR, anti-dsDNA, CRP, C3, and C4) were no different between groups 1 and 2. Thus, only the fall in the WBC count, correlated with the occurrence of lupus enteritis. The SLEDAI calculated at the time of diagnosis of SLE (mean 13.7 (range 6–28) v 17.0 (range 2–42)) and at the time of acute abdominal pain (mean 10.3 (range 2–28) v 12.5 (range 2–26)) did not differ between groups 1 and 2. At the time of diagnosis, the clinical involvement defined in the SLEDAI did not differ among the three groups: the kidney (12/17, 15/21, 85/137, p=0.59), central nervous system (0/17, 4/21, 19/137, p=0.19), skin/mucosa (10/17, 16/21, 92/137, p=0.52), blood (4/17, 12/21, 53/137, p=0.10), and musculoskeletal system involvement (3/17, 10/21, 57/137, p=0.12). Also, the clinical involvement did not differ between groups 1 and 2 at the time of acute abdominal pain. As for most of the laboratory indices, the SLEDAI did not correlate with the occurrence of lupus enteritis.

Of 21 episodes of lupus enteritis, including relapsed cases (n=4), all had bowel wall thickening. Target sign (fig 1) was seen in 14 cases (67%). The jejunum and the ileum were the sites most commonly affected, being involved in 17 (80%) and 18 (85%) cases, respectively. Rectal involvement was rare, occurring in only three (14%) cases. Nineteen of 21 cases had bowel involvement in multiple vascular territories not confined in one vascular territory. Of 21 cases, none had mesenteric vascular thrombosis on abdominal CT scans.

Patients were treated with intravenous high dose methylprednisolone (1 mg/kg/day) and all responded well. Subsequently, intravenous methylprednisolone was switched to oral prednisolone (median 5 days, range 1–34 days) and tapered. Four patients relapsed when the steroid treatment was tapered. However, the patients who relapsed responded well to intravenous methylprednisolone without the addition of other immunosuppressive agents. Surgical intervention was not needed during the follow up of lupus enteritis (median 29 months, range 2–87 months).

DISCUSSION

Gastrointestinal vasculitis, with or without infarction, is one of the most serious complications of SLE. The prevalence of intestinal vasculitis in patients with SLE has been reported to range from 0.2 to 53%.^{6,7} Although the underlying lesion in most cases of gastrointestinal (GI) vasculitis in SLE is a small vessel arteritis or venulitis, vasculitis is not found in all cases. Therefore, we applied the term “lupus enteritis” rather than GI vasculitis to GI tract lesions in our patients with SLE. Medina *et al* looked at the aetiology of abdominal pain in 51 patients with active and inactive SLE using the SLEDAI.⁶ Patients with gastrointestinal vasculitis (19 cases) or thrombosis (three cases) had higher SLEDAI scores than 14 active patients with SLE with non-SLE related acute abdomen. In

Table 2 Laboratory data and SLEDAI. Results shown as mean (SD)

	Group 1 (n=17)	Group 2 (n=21)	Group 3 (n=137)	p Value
WBC ($\times 10^9/l$)				
Dx	7.56 (3.79)	4.80 (4.19)	5.44 (3.69)	0.00*
AA	6.79 (3.95)	6.84 (4.54)		0.70
$\Delta(AA-Dx)$	-0.78 (3.58)	2.04 (3.88)		0.01*
Hb (g/l)				
Dx	109 (21)	104 (25)	99 (27)	0.39
AA	115 (17)	109 (19)		0.22
$\Delta(AA-Dx)$	6 (16)	4 (14)		0.98
PLT ($\times 10^9/l$)				
Dx	270.9 (112.0)	139.7 (92.8)	181.4 (101.3)	0.00*
AA	273.4 (97.6)	151.7 (91.6)		0.00*
$\Delta(AA-Dx)$	2.4 (78.4)	11.9 (61.1)		0.91
C3 (mg/l)				
Dx	528 (183)	415 (201)	528 (183)	0.21
AA	562 (201)	551 (352)		0.38
$\Delta(AA-Dx)$	51 (209)	137 (299)		0.35
C4 (mg/l)				
Dx	153 (73)	139 (89)	155 (104)	0.62
AA	135 (65)	174 (109)		0.63
$\Delta(AA-Dx)$	-7.7 (63)	35 (75)		0.25
ESR (mm/1st h)				
Dx	45.6 (32.1)	59.3 (43.7)	59.8 (37.6)	0.39
AA	47.6 (23.7)	59.0 (45.2)		0.65
$\Delta(AA-Dx)$	1.6 (24.5)	-0.28 (20.3)		0.85
Anti-ds DNA (IU/ml)				
Dx	98.9 (140.0)	889.4 (1840.2)	292.1 (675.9)	0.57
AA	243.5 (379.8)	107.9 (208.5)		0.48
$\Delta(AA-Dx)$	115.8 (312.3)	-778.4 (1835.1)		0.10
CRP (mg/l)				
Dx	20 (26)	22 (44)	18 (29)	0.43
AA	23 (28)	32 (48)		0.81
$\Delta(AA-Dx)$	1 (24)	8 (29)		0.60
SLEDAI				
Dx	13.7 (5.9)	17.0 (8.6)	14.2 (6.8)	0.36
AA	10.3 (5.98)	12.5 (8.1)		0.36
$\Delta(AA-Dx)$	-3.4 (4.6)	-4.5 (9.7)		0.67

*Statistically significant using Kruskal-Wallis test or Mann-Whitney test.

Group 1, lupus enteritis; group 2, acute abdominal pain without lupus enteritis; group 3, SLE without acute abdominal pain; WBC, white blood cells; Hb, haemoglobin; PLT, platelets; Dx, at diagnosis of SLE; AA, acute abdominal pain; $\Delta(AA-Dx)$, difference between acute abdominal pain and at diagnosis of SLE.



Figure 1 Abdominal CT scan showing circumferential wall thickening and target sign in small and large bowels. Mesenteric change is also noted with engorged mesenteric vessels and haziness.

our data, lupus enteritis (45%) was the most common cause of acute abdominal pain and the incidence was comparable with the previous report.⁶ Contrary to the previous report of Medina *et al*,⁶ the SLEDAI was similar at the time of diagnosis of SLE among the three groups and at the time of acute abdominal pain between groups 1 and 2. In addition, the SLEDAI calculated at the time of acute abdominal pain was lower than that at the time of diagnosis of SLE in both groups 1 and 2. Thus, it implies that acute abdominal pain, including lupus enteritis, might occur in patients whose disease activities had been under control. Only a drop in the WBC count at the time of acute abdominal pain was much more

prominent in group 1 than in group 2. Therefore, the SLEDAI and laboratory indices, except leucopenia, did not correlate with the occurrence of lupus enteritis.

In SLE and SLE-like conditions, a prevalence of aPL of between 18% and 61% has been reported.¹⁴ Several reports have described an association between intestinal infarction and aPL.⁶⁻⁹ Although mesenteric vascular thrombosis was not found on abdominal CT scans in our series, we compared the incidence of aPL among the three groups, but no differences were found. Therefore, autoantibodies, including aPL, did not correlate with the occurrence of lupus enteritis.

The diagnosis of bowel ischaemia is often difficult to make on the basis of plain radiography and barium studies. The common CT findings in mesenteric ischaemia include dilated bowel, focal or diffuse bowel wall thickening, abnormal bowel wall enhancement (double halo or target sign), mesenteric oedema, engorged mesenteric vessel, and ascites.¹⁰ However, the lack of specificity of these signs is a limitation of CT because they can also be seen in patients with pancreatitis, mechanical bowel obstruction, peritonitis, or inflammatory bowel disease, all of which may mimic intestinal ischaemia.¹⁰ In the present series, the jejunum and ileum were the sites most commonly affected. The segments of bowel thickening were multifocal and not confined to a single vascular territory in 19/21 cases with bowel wall thickening because mesenteric vasculitis may affect several vessels simultaneously.¹¹ It seemed that rectal involvement was rare owing to the rich and multiple blood supply of the rectum. Therefore, in the clinical

investigation of abdominal pain in SLE, involvement of multiple vascular territories on CT scans, in addition to improvement after intravenous prednisolone treatment, may favour a diagnosis of reversible ischaemic bowel disease.

Because of the paucity of cases of lupus enteritis, no randomised clinical trials have investigated its optimal treatment. Many cases of successful treatment of intestinal vasculitis with high dose prednisolone only have been reported.⁶⁻¹² For corticosteroid resistant GI vasculitis, there have been recent reports of its successful treatment with intravenous methylprednisolone and cyclophosphamide in SLE.¹³ In the current series, all the patients with lupus enteritis responded well to high dose prednisolone (1 mg/kg/day) treatment. Although four patients relapsed, they responded well to high dose prednisolone without the addition of cyclophosphamide. Medina *et al* emphasise the importance of early laparotomy because of the high mortality. In general, the outcome in patients with perforation is poor, with death occurring in more than two thirds of cases.¹⁴ However, as shown in our series, complete resolution of acute abdominal pain took a few weeks and no patients developed GI perforation. Therefore, our data suggest that laparotomy could be delayed unless there was definite evidence that GI perforation had occurred.

In conclusion, our study indicates that lupus enteritis is the most common cause of acute abdominal pain in SLE. The SLEDAI, laboratory indices except leucopenia, antiphospholipid antibody, and autoantibodies do not correlate with the occurrence of lupus enteritis. Intravenous high dose prednisolone is successful for the treatment of lupus enteritis, including patients who have relapsed, without the addition of immunosuppressive agents.

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REFERENCES

- 1 **Alarcon-Segovia D,** Deleze M, Oria CV, Sanchez-Guerrero J, Gomez-Pacheco L, Cabiedes J, *et al*. Antiphospholipid antibodies and antiphospholipid syndrome in systemic lupus erythematosus. A prospective analysis of 500 consecutive patients. *Medicine (Baltimore)* 1989;68:353-65.
- 2 **Bombardier C,** Gladman DD, Urowitz MB, Caron D, Chang CH, and the Committee on Prognosis studies in SLE: Derivation of the SLEDAI. A disease activity index of lupus patients. *Arthritis Rheum* 1992;35:630-40.
- 3 **Tan EM,** Cohen AS, Fries JF, Masi AT, McShane DJ, Rothfield NF, *et al*. The 1982 revised criteria for the classification of SLE. *Arthritis Rheum* 1982;25:1271-7.
- 4 **Byun JY,** Ha HK, Yu SY, Min JK, Park SH, Kim HY, *et al*. CT features of systemic lupus erythematosus in patients with acute abdominal pain: emphasis on ischemic bowel disease. *Radiology* 1999;211:203-9.
- 5 **Harris EN,** Pierangeli SS, Gharavi AE. Diagnosis of the antiphospholipid syndrome: a proposal for use of laboratory tests. *Lupus* 1998;7(suppl 2):S144-8.
- 6 **Medina F,** Ayala A, Jara LJ, Becerra M, Miranda JM, Fraga A, *et al*. Acute abdomen in systemic lupus erythematosus: the importance of early laparotomy. *Am J Med* 1997;103:100-5.
- 7 **Drenkard C,** Villa AR, Reyes E, Abello M, Alarcon-Segovia D. Vasculitis in systemic lupus erythematosus. *Lupus* 1997;6:235-42.
- 8 **Lockshin MD.** Antiphospholipid antibody syndrome. *Rheum Dis Clin North Am* 1994;20:45-59.
- 9 **Sanchez-Guerrero J,** Reyes E, Alarcon-Segovia D. Primary antiphospholipid syndrome as a cause of intestinal infarction. *J Rheumatol* 1992;19:623-5.
- 10 **Taourel PG,** Deneuve M, Pradel JA, Regent D, Bruel JM. Acute mesenteric ischemia: diagnosis with contrast-enhanced CT. *Radiology* 1996;199:632-6.
- 11 **Kirshy DM,** Gordon DH, Atweh NA. Abdominal computed tomography in lupus mesenteric arteritis. *Comput Med Imaging Graph* 1991;15:369-72.
- 12 **Cabrera GE,** Scopelitis E, Cuellar ML, Silveira LH, Mena H, Espinoza LR. Pneumatisis cystoides intestinalis in systemic lupus erythematosus with intestinal vasculitis: treatment with high dose prednisolone. *Clin Rheumatol* 1994;13:312-16.
- 13 **Grimbacher B,** Huber M, Kempis J, Kalden P, Uhl M, Kohler H, *et al*. Successful treatment of gastrointestinal vasculitis due to systemic lupus erythematosus with intravenous pulse cyclophosphamide: a clinical case report and review of the literature. *Br J Rheumatol* 1998;37:1023-8.
- 14 **Hoffman BI,** Katz WA. The gastrointestinal manifestations of systemic lupus erythematosus: a review of the literature. *Semin Arthritis Rheum* 1980;9:237-47.