Systemic Lupus Erythematosus Associated with Massive Ascites and Pleural Effusion in a Patient Who Presented with Disseminated Intravascular Coagulation

Yo Kageyama, Takashi Yagi* and Mamoru Miyairi

Abstract
A case of systemic lupus erythematosus (SLE) associated with serositis presenting with disseminated intravascular coagulation (DIC) is reported. A 53-year-old woman was admitted because of a fever. Laboratory tests revealed increased plasma levels of fibrinogen degradation products (FDP) and FDP-D-dimer, high titers of anti-nuclear antibody, high serum levels of anti-DNA antibody, immune complexes, decreased serum complements, and persistent proteinuria. A CT scan showed massive ascites and pleural effusion, marked edema and swelling of the mesentery. The patient’s condition and immunological abnormalities improved after steroid therapy. The association of DIC and lupus serositis has never been described in the literature. (Internal Medicine 41: 161-166, 2002)

Key words: vasculitis, immune complex, complement, anti-nuclear antibody

Introduction
Polyserositis is a common manifestation of systemic lupus erythematosus (SLE). Peritoneal, as compared to pleural or pericardial involvement, is relatively rare. Ascites is clinically detected in 4–16% of patients with SLE (1, 2), although evidence of peritoneal inflammation has been found in up to 60% of patients at autopsy (3). Acute lupus peritonitis is characterized by ascites and by significant abdominal pain, in addition to the typical features of a general lupus flare (3). Immune complex-mediated tissue injury has been proposed as a possible mechanism for the pathogenesis of peritoneal inflammation. Disseminated intravascular coagulation (DIC) is caused by a wide variety of serious diseases. In most patients, the underlying process dominates the clinical picture; in some cases, however, DIC may be the initial manifestation of the disorder (4). However, the association of DIC with SLE is extremely rare (5). Here we describe a patient with SLE associated with massive ascites and pleural effusion who presented with DIC.

Case Report
A 53-year-old woman was referred to us on May 21, 2000, from a general practitioner. She had a fever of 38°C and her appetite had been poor for 4 days prior to her visit to the clinic. Antibiotics and some other medications were prescribed. However, she did not respond to the medications and was referred to us for further examination and treatment. On admission, she had a fever of 38.4°C, height was 150 cm and body weight was 53 kg. Her blood pressure was 124/80 mmHg, and pulse rate was 93 beats/min. Her throat, neck, and lungs were normal, and no heart murmur or abnormal heart sounds were audible. No lymph nodes were palpable. Her abdomen was flat and nontender, and costovertebral tenderness was not present. Her appendix had been removed at the age of 18, and she had not visited a doctor since that operation except for the birth of her three children. The laboratory examination on admission revealed thrombocytopenia, an increased serum level of C-reactive protein (CRP), increased plasma levels of fibrin and fibrinogen degradation products (FDP) and FDP-D-dimers (Table 1). In addition, the thrombin-antithrombin complex level was 31.4 ng/ml (normal value is less than 3.0 ng/ml), and she was positive for plasma soluble fibrin monomer complexes. Chest and abdominal X-ray examinations were normal. Based on these results, a diagnosis of DIC associated with a bacterial infection was suspected. A dosage of 1,500 mg/day of gabexate mesilate, 1 g/day of panipenem/betamipron and 2 g/day of cefozoperan was administered after bacterial culture specimens had been obtained from her blood, throat and urine. However, her fever persisted despite these treatments, and her CRP, FDP and D-dimer levels remained high. Her plasma β-D glucan level was 5.3 pg/ml, and endotoxin level was 5.0 pg/ml (normal values are less than 20.0 pg/ml and 10.0 pg/ml, respectively). An acid-fast stain of her gastric juice was negative. A liquor ob-
A bone marrow examination showed normal cellularity, and no abnormal cells were present; however, an increased number of megakaryocytes was observed. On May 30, a CT scan of the abdomen and chest revealed massive pleural effusion and ascites, marked edema and the swelling of the mesenterium (Fig. 1). Immunological examination of the ascitic fluid revealed the presence of anti-nuclear antibodies, anti-DNA antibodies, and immune complexes. These values were higher than those of the serum, if corrected for the amount of protein of the ascites and pleural effusion (Table 2). Examination of the pleural effusion produced similar results. All bacterial cultures upon admission were negative. Treatment with methylprednisolone (1 g/day) and prednisolone (60 mg/day) was initiated. After this treatment, the fever subsided, the CRP serum level decreased, the number of platelets increased, plasma levels of FDP and D-dimer decreased, and the ascites and pleural effusion disappeared within 2 weeks (Fig. 2). Her proteinuria became negative in July. Anti-nuclear antibodies and anti-DNA antibodies decreased to a ratio of 1:640, 79 IU/ml on July 2 and 1:320, 42 IU/ml on August 1. The serum levels of immune complexes decreased, complements increased in accordance with the changes in antibodies. The dosage of prednisolone was tapered by 10 mg every 2 weeks. The patient was discharged on August 10 while continuing to receive prednisolone (30 mg/day).
SLE with Ascites, Pleural Effusion and DIC

**Discussion**

The present patient presented with a high fever and a loss of appetite. The laboratory data upon admission, such as the increased plasma FDP, D-dimer and thrombin-antithrombin complex levels, thrombocytopenia, the presence of a plasma-soluble fibrin monomer complex, and the elongation of the prothrombin time, were compatible with a diagnosis of DIC. She had a high CRP serum level, however, bacterial cultures were negative, an acid-fast stain was negative, her plasma levels of β-D glucan and endotoxin were normal, chest radiography was normal, and a CT scan of her chest and abdomen were unremarkable except for a small amount of pleural effusion. Thus, the elevation in CRP concentration was thought to be caused by SLE (6), even though the serum CRP concentration is not typically elevated in patients with SLE. DIC is primarily a thrombotic process; the basic pathophysiology, irrespective of etiology, is an entry into circulation of procoagulant substances that trigger the systemic activation of the coagulation system and platelets, leading to the disseminated deposition of fibrin-platelet thrombi. DIC always has an underlying etiology, which must generally be identified and eliminated for the successful treatment of the coagulopathy. Known underlying etiologies include infections, obstetric complications such as amniotic fluid embolism, malignancies, liver failure, acute pancreatitis, respiratory distress syndrome, trauma such as crushing injuries and vascular disorders such as giant hemangioma. However, no abnormal findings were found in the present case except for the high serum titers of anti-nuclear antibody, anti-DNA antibodies and immune complexes and the low serum complement levels. DIC in the present case was considered to arise from

![CT scan of the chest and abdomen showing massive pleural effusion (upper), ascites and marked edema and swelling of the abdomen (lower).](image)

**Table 2. Laboratory Data of Serum, Ascites and Pleural Effusion**

<table>
<thead>
<tr>
<th></th>
<th>Serum</th>
<th>Ascites</th>
<th>Ascites corrected*</th>
<th>Pleural effusion</th>
<th>Pleural effusion corrected*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gravity</td>
<td>1.015</td>
<td>1.024</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protein (g/dl)</td>
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<td>2.4</td>
<td>1.024</td>
<td>2.8</td>
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<tr>
<td>LDH (IU/l)</td>
<td>608</td>
<td>365</td>
<td>379</td>
<td></td>
<td></td>
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<tr>
<td>Glucose (mg/dl)</td>
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<td>78</td>
<td>86</td>
<td></td>
<td></td>
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<tr>
<td>Cytology</td>
<td>Class I</td>
<td>Class I</td>
<td>Class I</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ziel Neelsen stain</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bacterial culture</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td></td>
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<tr>
<td>Adenosine deaminase (IU/l)</td>
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<td>11.6</td>
<td>10.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-nuclear Ab</td>
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<td>1:640</td>
<td>1:1600</td>
<td>1:640</td>
<td>1:1371</td>
</tr>
<tr>
<td>Homogeneous</td>
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<td>1:640</td>
<td>1:1600</td>
<td>1:640</td>
<td>1:1371</td>
</tr>
<tr>
<td>Speckled</td>
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<td>1:640</td>
<td>1:1600</td>
<td>1:640</td>
<td>1:1371</td>
</tr>
<tr>
<td>Anti-DNA Ab (IU/ml)</td>
<td>143</td>
<td>21.5</td>
<td>53.8</td>
<td>23.6</td>
<td>50.5</td>
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<td>IC (Clq) (µg/dl)</td>
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<td>5.0</td>
<td>12.5</td>
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<td>10.3</td>
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<tr>
<td>IC (anti C3D) (µg/dl)</td>
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<td>18.4</td>
<td>46.0</td>
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<td>C3 (mg/dl)</td>
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<td>8.0</td>
<td>20.0</td>
<td>9.4</td>
<td>20.1</td>
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<tr>
<td>C4 (mg/dl)</td>
<td>10</td>
<td>3.5</td>
<td>8.8</td>
<td>3.6</td>
<td>7.5</td>
</tr>
</tbody>
</table>

*Values of ascites and pleural effusion were corrected for the amount of protein of ascites and pleural effusion.
Gabexate mesilate 1,500 mg/day
Panipenem/betamipron 1 g/day, Cefozopran 2 g/day
Prednisolone 60 mg/day
Methyl prednisolone 1,000 mg/day

Figure 2. Clinical course after admission.

the disease activity of SLE. The patient had serositis (pleuritis and ascites), a renal disorder (persistent proteinuria, 1.5 g/day, with granular and tubular casts), a hematologic disorder (lymphopenia of 928/mm³, thrombocytopenia of 37,000/mm³) and anti-nuclear antibodies. She was diagnosed as having SLE according to the criteria of the American College of Rheumatology (7, 8). The fact that she had autoimmune-mediated thrombocytopenia and her dramatic response to steroid therapy further support a diagnosis of SLE. Shimamoto et al reported that in 120 cases of SLE patients, 8 patients (6.7%) had DIC complications (9). However, in all these patients, an infection preceded the DIC. DIC caused by the disease activity of SLE itself is quite rare. In 1993, Tanaka et al reported that only 11 cases of SLE associated with DIC and without any other complications, such as infection, had been reported in the literature (5). Since then, we have been able to find only 4 case reports of SLE with DIC, with the exception of abstracts (6, 10–12). In most of these cases, the development of DIC occurred several months to 18 years after the onset of SLE. We have found only 3 cases where SLE and DIC presented simultaneously, as in the present case (12–14). Reviewing the reported cases of SLE accompanied by DIC (5, 6, 9–12), we found that infections were associated only in the cases reported by Shimamoto et al (9); however, out of the 16 cases of SLE associated with DIC whose underlying condition was other than infection, 14 cases were complicated by vascular involvement.

The pathogenesis of DIC in SLE patients is not fully understood. Lupus anticoagulant and anti-cardiolipin antibodies, which are often found in cases of SLE, are responsible for local intravascular coagulation. Circulating anticoagulants have been demonstrated in several cases of DIC associated with SLE (5, 15, 16). However, not all lupus patients with DIC have circulating anticoagulants, including the present case (6, 15); therefore, no definite association between the presence of circulating anticoagulants and the development of DIC can be made. Kerr et al (15) suggested that vasculitis is involved in the pathogenesis of DIC in patients with SLE. They hypothesized that circulating immune complexes activate the complement component, which can injure vascular endothelial cells, resulting in the release of tissue thromboplastin-like substances (17). Clinically, most of the reported patients with DIC who were not associated with infection have been reported to be complicated by vascular involvement (5, 6, 9–12). Indeed, vasculitis and/or complement depositions have been histologically shown in cases of SLE accompanied by DIC (11, 16, 18). In the present case, the level of circulating immune complexes was high, and
the level of serum complements was low, indicating the formation of antigen-antibody complexes at the beginning of the disease. Furthermore, although we could not obtain histological evidence of vasculitis, the findings of marked edema and the swelling of the mesenterium visible on the abdominal CT scan strongly suggest the presence of vasculitis in that region.

The presence of ascites and/or pleural effusion in patients with SLE is generally considered to be associated with severe nephrotic syndrome, constrictive pericarditis, congestive heart failure, portal hypertension, malignancy and/or peritoneal infection (19). However, none of these factors were found in the present case. The pathogenesis of serositis in SLE is considered to be a vasculitis of the pleura or peritoneum caused by immune complex deposition and the activation of complements. Deposits of complement and immunoglobulins were demonstrated in the vessels of the peritoneum (20–22), as was the presence of immune complexes and autoantibodies and the decreased complement levels in the ascites and pleural effusion (23–27). In the present case, immunological examination of the ascites and pleural effusion revealed the presence of anti-nuclear antibodies, anti-DNA antibodies, complements and immune complexes. When these values were corrected according to the ratio of protein in the serum and ascites and pleural effusion, the anti-nuclear antibodies and immune complex values in the ascites and pleural effusion were higher than those in the serum, while the complement levels were lower than those in the serum (Table 2). These results indicate that a complement cascade reaction may have been locally activated by immune complexes in the peritoneal space. In addition, the findings of marked edema and the swelling of the mesenterium visible on the CT scan strongly suggest the presence of serositis in the abdominal cavity. Edema and swelling of the bowel wall have been reported as a characteristic sign of lupus peritonitis (27–29). In the present case, however, marked edema and swelling of the mesenterium was noted. Since the mesenterium and bowel wall are both covered by the peritoneum, our findings also indicate severe serositis. Finally, these fluids disappeared completely after steroid therapy. These results suggest that the ascites and pleural effusion in the present case were due to serositis resulting from SLE. It is well known that lupus cystitis is complicated by lupus serositis. Although we did not perform a cystoscopic examination, the possibility of lupus cystitis is low since she did not complain of pollakisuria or hydrenephrosis and thickening of the bladder wall was not observed on the CT scan.

To our knowledge, the association of lupus serositis and DIC has never been described in the literature; this is the first case of SLE associated with serositis and DIC in which vasculitis is considered to be the underlying pathogenesis of both conditions. In addition, the findings of marked edema and the swelling of the mesenterium as a result of massive serositis have never been described in the literature. These findings, combined with the abnormal immunological data for the ascites, indicate the presence of vasculitis in the mesenterium, causing DIC and serositis in the present case.

References

22) Weinstein PJ, Noyer CM. Rapid onset of massive ascites as the initial
26) Houtman PM, Hofstra SS. Lupus peritonitis presented as vague abdomi-
29) Tsutsumino M, Harigai M, Taniguchi A, et al. Lupus cystitis and perito-