Systemic Lupus Erythematosus Complicated with Acute Myocardial Infarction and Ischemic Colitis

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Abstract

Acute myocardial infarction (AMI) is one of the most severe manifestations in patients with systemic lupus erythematosus (SLE). Ischemic colitis, mainly caused by intestinal vasculitis, is also one of the most serious, but uncommon, complications in SLE patients. “SLE vasculitis” simultaneously involving cardiac and gastrointestinal vessels has yet to be reported. This is the first report of SLE accompanying AMI, ischemic colitis and perforation of the digestive tract possibly due to SLE vasculitis, which was dramatically improved by treatment with high-dose glucocorticoid.

Key words: systemic lupus erythematosus, vasculitis, acute myocardial infarction, ischemic colitis


Introduction

Overall survival of patients with systemic lupus erythematosus (SLE) has recently been improved (1). However, complications with acute myocardial infarction (AMI) still cause a high mortality risk for SLE patients (2). The median rate of mortality due to coronary artery disease in patients with SLE ranges from 3.5% to 15.7% (3-5). The development of AMI is a critical factor for the prognosis of SLE patients.

Ischemic colitis is also one of the most serious, but uncommon, complications in patients with SLE. Previous studies have shown that severe ischemic colitis in patients with SLE is mainly caused by intestinal vasculitis and that the prevalence of ischemic colitis due to intestinal vasculitis is 0.2% (6). In addition, the mortality rate of vasculitis-induced ischemic colitis is approximately 50% due to perforation of the digestive tract (7).

Inflammation of blood vessels occurs as a complication of SLE (SLE vasculitis), and the prevalence of SLE vasculitis ranges between 11% and 20%, though almost 90% of cases involve small vessels including cutaneous vessels and glomerular capillaries (8). Involvement of the medium-sized vessels, including those in cardiac and gastrointestinal regions, due to SLE vasculitis has been reported to be rare.

Here, we report a previously undocumented case of SLE with simultaneous development of AMI and ischemic colitis, possibly caused by SLE vasculitis, and complicated with perforation of the digestive tract. Of note, the clinical condition was dramatically improved by treatment with high-dose glucocorticoid.

Case Report

A 44-year-old Japanese woman who had been diagnosed as having SLE with high fever, butterfly erythema, interstitial pneumonia, leukocytopenia, decreased serum complement titers and positive anti-double-stranded DNA IgG antibody (ds-DNA) at the age of 18 years had been treated with prednisolone (10 mg/day p.o.) without relapse. She had no previous history of diabetes mellitus, hypertension or hyperlipidemia.

In December 2007, at the age of 43 years, she was admitted to our hospital due to progression of interstitial pneumonia and the occurrence of transverse myelitis as a symptom of central nervous system lupus. Laboratory data showed leukocytopenia (2,480/μL; normal, 3,500-8,500/μL), thrombocytopenia (10.5x10^4/μL; normal, 15-35x10^4/μL), decreased serum complement titers [CH50, 17 U/mL (normal, 30-50 U/mL); C3, 42 mg/dL (normal, 65-135 mg/dL); C4, 6.2 mg/
Figure 1. Clinical course of the patient. mPSL: methylprednisolone, PSL: prednisolone, CPA: cyclophosphamide, MMF: mycophenolate mofetil, AZA: azathioprine, Tac: tacrolimus, ds-DNA: anti-double-stranded DNA IgG antibody.

Figure 2. Colonoscopy findings: Colonoscopy showed the existence of multiple longitudinal ulcers with severe inflammation of the mucosa between the ascending and sigmoid portions of the colon.

dL (normal, 13-35 mg/dL) and elevated ds-DNA titer (34.3 IU/mL; normal, 0-12 IU/mL) (Fig. 1). She was treated with methylprednisolone pulse (1 g × 3 days) (i.v.) therapy and oral high-dose prednisolone (60 mg/day) in combination with cyclophosphamide pulse (500 mg × 1 day) (i.v.) therapy. By July 2008, she had achieved remission again, and the laboratory data had returned to normal. Administrative dose of prednisolone had been reduced to 10 mg/day in combination with oral tacrolimus (1 mg/day). Tacrolimus was administered once daily after the evening meal and whole-blood concentration of tacrolimus, determined approximately 12 hours after administration, was less than 2.5 ng/mL (normal, <10 ng/mL) (9, 10).

However, in early November 2008, she developed upper abdominal pain and bloody diarrhea followed by progression of anemia. Laboratory data showed a decreased hemoglobin level (6.2 g/dL; normal, 11.5-15.0 g/dL) and an elevated serum C-reactive protein (CRP) level (6.0 mg/dL; normal, <0.3 mg/dL), although serum complement titters, ds-DNA titer and anti-neutrophil cytoplasmic antibody (ANCA) titer were shown to be normal (Fig. 1). There was no sign of active SLE in the laboratory data and physical findings. Abdominal computed tomography (CT) showed bowel wall thickening and a target sign between the ascending and transverse portions of the colon, and colonoscopy showed multiple longitudinal ulcers with severe inflammation of mucosa between the ascending and sigmoid portions of the colon (Fig. 2), indicating the existence of colitis. However, biopsy specimens from the ulcers and mucosa showed no specific findings. In addition, CT angiography of the intestine showed no sign of occlusion or vascular injury in medium-size intestinal arteries. Presuming the possibility of infectious colitis, anti-bacterial therapy (penicillin antibiotic) and fasting therapy were performed although no positive finding was shown, including fecal cultures, Clostridium difficile (CD) toxin or serum exams for β-D glucan and cytomegalovirus (CMV) pp65 antigenemia. Her abdominal pain and
bloody diarrhea were slightly improved by the anti-bacterial treatment.

In mid-November 2008, one week after the development of colitis, she suddenly developed severe chest pain; ECG demonstrated marked ST segment elevation in leads V4 to V6. An echocardiogram revealed extensive left ventricular apical wall akinesis. Laboratory data showed elevated serum creatine kinase (CK) level (1,000 IU/L; normal, 41-258 IU/L), elevated serum CK-MB level (97 IU/L; normal, 6-17 IU/L) and positive cardiac troponin T but normal serum complement titers and normal ds-DNA titer (Fig. 1). She was diagnosed as having acute myocardial infarction, and emergency cardiac catheterization was performed. She was found to have multiple complete occlusion of the left anterior descending artery (LAD) and distal left circumflex artery, although there was no clinical sign of typical atherosclerosis or thrombosis by coronary angiography study (Fig. 3). In addition, there was no biochemical data regarding hypercoagulability including normal PT-INR/aPTT, normal protein C/S, normal anti-thrombin III and the absence of anti-phospholipid antibodies (aPL) including anticardiolipin antibodies (aCL), anti-β2 glycoprotein 1 (β2GP1) antibodies and Dilute Russell’s viper venom time (dRVVT). Angioplasty was performed with a 1.5-mm (diameter)/20-mm (length) balloon and distal flow of the LAD was re-established. Considering the possibility of multiple thrombotic occlusion due to an adverse effect of tacrolimus (11, 12), tacrolimus was replaced with mycophenolate mofetile (MMF) at a dose of 1,500 mg/day, and treatment with oral aspirin was started after the development of AMI. Careful observation was performed for cardiac function and accompanying colitis in a coronary care unit. However, upper abdominal pain and bloody diarrhea relapsed, and the colitis has continued under anti-bacterial therapy and fasting therapy.

In early January 2009, she developed sudden and severe abdominal pain with diffuse abdominal tenderness and muscular defense. Emergent abdominal CT showed a perforation of the digestive tract and widely-distributed severe wall thickening of the intestine including the ileum, from the ascending portion through to the descending portion of the colon and rectum. Emergent laparotomy was performed, and perforation in the middle of the transverse colon was detected. The perforation of the colon was surgically sutured and then loop colostomy was formed at the right-upper region of the transverse colon. Biopsy specimens from the dark violet colored stoma mucosa showed evidence of granulation formation, focal destruction and regeneration of the mucosa with inflammatory cell infiltration, indicating the existence of inflammation and injury of the colonic mucosa and ischemic change of the colon (Fig. 4). On the basis of the histological findings obtained from widely-distributed colitis with dark violet colored mucosa, and the clinical data including colonoscopy and abdominal CT, we concluded that ischemic colitis and its complications were due to intestinal vasculitis. Treatment with high-dose glucocorticoid was performed for multi-organ (heart and intestine) and multifocal (widely-distributed ischemic colitis) vascular injury caused by SLE vasculitis. After the commencement of treatment with high-dose prednisolone, the color of the intestinal mucosa improved from dark violet to cherry red; the wall thickening of the intestine on abdominal CT as well as abdominal pain and bloody diarrhea immediately disappeared.

**Discussion**

SLE vasculitis can occur in the absence of a clinical SLE flare, and 25% of patients complicated with vasculitis-induced AMI do not have active SLE (13, 14). Moreover, SLE patients often have many risk factors for coronary artery disease including hypertension, hyperlipidemia, use of glucocorticoids and aPL. In particular, atherosclerosis is one of the most important risk factors for AMI in SLE patients. It has been reported that immune complex deposition and
It has been reported that findings in coronary angiography of a rapid change in coronary luminal diameter, isolated segments with tapered narrowing and the presence of coronary ectasia or aneurysm indicate the existence of coronary vasculitis (17), although coronary angiography has a low sensitivity for detecting active vasculitis. In the present case, the clinical evidence of vasculitis or atherosclerosis was not clearly obtained in coronary angiography. However, multiple vascular occlusion without thrombosis strongly indicated the existence of vasculitis rather than atherosclerosis. Taken together, we considered that the pathogenesis of AMI in the present case was predominantly due to accompanying SLE vasculitis, but partly due to atherosclerosis.

Complications of intestinal vasculitis are also difficult to diagnose. Intestinal vasculitis is rarely confirmed histologically by endoscopic biopsy specimens (18). In addition, mesenteric angiography is not helpful for diagnosing intestinal vasculitis since typical vascular injury preferentially occurs in smaller vessels. Recent studies have shown that bowel wall thickening, a target sign between the ascending and the transverse portions of the colon were only detected by abdominal CT, which did not lead to the diagnosis of intestinal vasculitis.

When SLE patients develop multi-organ and multi-focal vascular injury without the evidence of multiple thrombosis, SLE vasculitis should always be ruled out despite normal physical findings and laboratory data. Successful treatment for SLE vasculitis with high-dose glucocorticoids has been reported to date (21, 22). In addition, recent case reports have stated that high-dose glucocorticoid therapy in combination with cyclophosphamide or azathioprine is effective for glucocorticoid-resistant SLE vasculitis (7, 23, 24). In the present case, the ischemic colitis due to SLE vasculitis was dramatically improved by treatment with high-dose glucocorticoid, and no relapse of myocardial infarction has occurred to date, indicating that vascular injury and occlusion might have been caused by vasculitis due to autoimmune abnormality. The mechanism by which vascular damage due to SLE was improved by glucocorticoid has been unclear; however, the thrombotic process due to lupus or inflammatory activity was also ameliorated by systemic glucocorticoid therapy (25).

This is the first case report of SLE simultaneously complicated with AMI and ischemic colitis, possibly caused by SLE vasculitis, followed by perforation of the digestive tract. In the present case, it was difficult to prove the existence of SLE vasculitis because of undetectable physical findings and laboratory data. However, multi-organ and multi-focal vascular injury may indicate the existence of SLE vasculitis regardless of the lack of typical signs of clinically active SLE. Early diagnosis and treatment with systemic glucocorticoid administration can lead to improvement of the prognosis in patients with SLE.

**The authors state that they have no Conflict of Interest (COI).**

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