Intestinal Angina Due to Atherosclerosis in a 45-year-old Systemic Lupus Erythematosus Patient

Masayuki Matsuda¹, Daigo Miyazaki¹, Kana Tojo¹, Ko-ichi Tazawa¹, Yasuhiro Shimojima¹, Masahiro Kurozumi², Daisuke Fukui³, Kenji Sano⁴ and Shu-ichi Ikeda¹

Abstract

We report a patient with systemic lupus erythematosus (SLE) who developed progressive emaciation and postprandial abdominal pain with a 27-year history of corticosteroid treatment. The patient was diagnosed as having intestinal angina based on computed tomography that showed severe stenosis of the superior mesenteric artery (SMA) in addition to complete occlusion of the celiac and inferior mesenteric arteries. Histopathology of the SMA and abdominal aorta showed atherosclerosis with no vasculitis or thrombus formation. Intestinal angina should actively be considered as a possible cause of recurrent abdominal pain in SLE patients, particularly in those with a long history of disease.

Key words: intestinal angina, systemic lupus erythematosus, corticosteroid, atherosclerosis

(DOI: 10.2169/internalmedicine.49.3769)

Introduction

Intestinal angina is an uncommon symptom characterized clinically by recurrent postprandial abdominal pain, and is usually associated with chronic progressive emaciation ascribable to malabsorption and a decrease in food intake (1-4). This symptom appears when severe hypoperfusion develops in at least 2 vessels among the celiac and the superior and inferior mesenteric arteries, which mainly provide blood supply to the gastrointestinal tract (2, 3). Systemic lupus erythematosus (SLE) sometimes shows vascular involvement, but associated intestinal angina is very rare. In this report we describe a patient in his 40s with SLE who developed intestinal angina due to atherosclerosis while being treated with oral prednisolone. We suggest that this complication might be important in the differential diagnosis of recurrent abdominal pain in SLE patients, particularly in those with a long history of disease.

Case Report

An 18-year-old Japanese man with no smoking habit or significant family history was diagnosed as having SLE in a neighboring hospital based on a skin rash on the face, photosensitivity and a positive result for the anti-DNA antibody in serum. His symptoms quickly improved after starting oral prednisolone, which was maintained at a dose of 10 to 15 mg/day for approximately 26 years because of fluctuating systemic arthralgia and skin rash sometimes with hypocomplementemia. As he showed asymptomatic small cerebral infarction with positive results for the anti-phospholipid antibody, blood coagulation was adequately controlled by warfarin. Regular examination at the outpatient clinic revealed normal blood pressure when taking amlodipine at a dose of 5 mg/day. Laboratory tests showed no hyperglycemia but sometimes a slight increase in total cholesterol and triglyceride. When he was referred to our hospital at age 44, the dose of prednisolone was 12.5 mg/day. At age 45 he developed postprandial epigastralgia, appetite loss and watery diarrhea with no obvious precipitating cause. The pain ap-
Figure 1. Enhanced computed tomography demonstrates severe narrowing at the proximal portion of the superior mesenteric artery (arrow in A). This stenotic change was further advanced 4 months later (arrows in B and C). Both the celiac and inferior mesenteric arteries were undetectable possibly because of complete occlusion.

peared in the upper abdomen 10 to 15 minutes after eating, steadily increased, plateaued, and then usually resolved during the next 1 hour. These symptoms gradually worsened with a 10-kg decrease in body weight over a period of approximately 4 months, but no abnormal findings were detected in endoscopic examinations. Abdominal computed tomography (CT) with contrast enhancement demonstrated complete occlusion of the celiac and inferior mesenteric arteries and narrowing at the proximal portion of the superior mesenteric artery (SMA) (Fig. 1A). At age 46 he was admitted to our hospital by ambulance because of sudden-onset peritonitis due to gastric perforation. After surgical closure of the perforation hole with the major omentum he was transferred to our department.

Physical examination showed no abnormal findings except for marked emaciation and an operative scar in the epigastric region. Body height and weight were 177 cm and 52 kg, respectively. Routine laboratory data demonstrated slight anemia (hemoglobin 10.4 g/dL, normal 12.9-17.4 g/dL), hypoalbuminemia (albumin 3.2 g/dL, normal 4.2-5.1 g/dL) and positive inflammatory reactions (CRP 2.12 mg/dL, normal < 0.10 mg/dL) with no hyperlipidemia (total cholesterol 201 mg/dL, normal 120-240 mg/dL; triglyceride 87 mg/dL, normal 30-150 mg/dL). Activated partial thromboplastin time was slightly increased (55.7 s, normal 23.0-38.0 s) probably because of the warfarin therapy. D-dimer was within the normal range (0.7 μg/mL, normal <1.0 μg/mL). Serum complement was normal, and the anti-nuclear and anti-DNA antibodies were ×320 (normal <×80) and 16.5 IU/mL (normal <12 IU/mL), respectively. The anti-cardiolipin IgG antibody was slightly increased (14.2 U/mL, normal <10 U/mL), but the anti-β2 glycoprotein I antibody was negative. Immune complexes in serum were undetectable, and urinalysis showed no proteinuria. Ankle brachial index (ABI, normal 0.9-1.3)/pulse wave velocity (PWV, normal <13.5 m/s) was 1.39/18.74 m/s on the right side and 1.31/19.30 m/s on the left, suggesting systemic atherosclerosis. Brain magnetic resonance imaging demonstrated small abnormal intensities in the white matter of the bilateral frontal lobes and cerebellum with no apparent stenosis in the intracerebral arteries.

He was allowed to take food 8 days after the operation, but postprandial epigastralgia and watery diarrhea appeared again. The stenotic change at the proximal portion of the SMA was further advanced on abdominal CT (Fig. 1B and C). Percutaneous transluminal angioplasty failed to dilate the SMA. Bypass surgery from the abdominal aorta to the SMA succeeded in increasing hemoperfusion of the gastrointestinal tract, and reduced his postprandial pain. Histopathology of the SMA and abdominal aorta obtained at the bypass surgery showed atherosclerosis with no vasculitis or thrombus formation (Fig. 2).

Discussion

On the basis of typical postprandial abdominal pain with CT findings of complete occlusion or severe narrowing of splanchnic arteries, the present patient was clinically diagnosed as having intestinal angina (3, 4). The clinical effectiveness of the aortomesenteric bypass surgery supports this diagnosis. Insufficient blood supply may have caused fragility of the gastric wall, resulting in the perforation. There are several case reports of SLE associated with aortitis (5, 6), but the histopathology of the SMA tissue obtained from the stenotic portion in the present patient demonstrated no obvious findings indicating vasculitis. The possibility of lupus enteritis was excluded because the patient complained of abdominal pain only in the postprandial phase with no physical findings or laboratory data suggestive of active SLE.

The most common pathology underlying intestinal angina is atherosclerosis (3). The present patient showed abnormal
values in ABI/PWV suggestive of advanced systemic atherosclerosis, and intestinal angina may have appeared as an initial manifestation of it. As atherosclerosis shows a slowly progressive course accelerated by classic risk factors, such as smoking, hyperglycemia and hypertension, intestinal angina usually develops in the 50s or 60s (1). In the present patient, however, the age of onset was 45, which is considerably earlier than expected because the above-mentioned risk factors for atherosclerosis were either absent or well controlled. Male gender is a known risk factor for atherosclerosis (7). The precise mechanisms promoting atherogenesis in the present patient are unclear, but there are 2 other possible factors worth consideration. One is the long-term use of corticosteroid. The present patient had been treated with prednisolone for approximately 27 years when the intestinal angina developed. The effect of corticosteroid on atherogenesis remains controversial, but according to recent reports 10 mg/day or more of prednisone increases serum levels of lipids, such as LDL-cholesterol and triglyceride, resulting in accelerated atherosclerosis (8, 9). Considering that oral prednisolone was given at a dose of 10 to 15 mg/day in the present patient, this drug may have played a role in the atherogenesis, although total cholesterol and triglyceride in serum had been kept at no more than slightly high levels or within the normal range. In future exacerbations of SLE we should more actively consider immunosuppressive agents, such as tacrolimus and cyclosporine A, as a therapeutic option rather than increasing the dose of prednisolone in order to avoid further progression of atherosclerosis.

The other possible factor is SLE itself. Atherosclerosis has recently been recognized as a chronic inflammatory condition with infiltration of monocyte-derived macrophages and lymphocyte populations, particularly T cells (10, 11). These cells migrate into vascular walls in response to chemoattractants, such as monocyte chemotactic protein-1 and adhesion molecules expressed on endothelial cells, transform into lipid-laden foam cells, and contribute to late instability and rupture of atherosclerotic plaques (10, 12, 13). SLE can accelerate this pathogenetic process of atherosclerosis via formation of immune complexes, activation of complements and production of cytokines (13-16). In the present patient laboratory tests on admission demonstrated no abnormal values in either immune complexes or complements, but these molecules may have acted as a harmful mediator inducing accelerated atherosclerosis in the active phase of SLE during a long clinical course. Anti-phospholipid antibodies often detectable in SLE patients also contribute to the development of atherosclerosis by affecting serum lipid levels and/or facilitating formation of foam cells in vascular walls (17-19). The anti-cardiolipin IgG antibody was slightly increased in the present patient, and may have promoted the atherogenesis.

In summary, the severe atherosclerosis of splanchnic arteries frequently responsible for intestinal angina is ascribable to long-term corticosteroid treatment and SLE itself in addition to classic risk factors, such as hypertension and hyperglycemia. Intestinal angina should be actively considered as
a possible diagnosis in SLE patients with recurrent postprandial abdominal pain, particularly in those with a long history of the disease.

Acknowledgement
This work was supported by a grant from Neuroimmunological Disease Division, the Ministry of Public Health, Labor and Welfare, Japan.

References

© 2010 The Japanese Society of Internal Medicine
http://www.naika.or.jp/imindex.html