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CASE REPORT

범발성 장염 소견으로 진단된 전신 홍반 루푸스

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Panenteritis as an Initial Presentation of Systemic Lupus Erythematosus

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Lupus enteritis is a rare, severe complication of systemic lupus erythematosus (SLE), needing prompt diagnosis and proper management. However, SLE rarely presents as lupus enteritis at the time of initial diagnosis. Thus, delayed diagnosis and misdiagnosis are common. We report a case of a 25-year-old woman with lupus panenteritis. The patient had multiple hospitalizations for abdominal pain, nausea, and diarrhea, initially without any other symptoms suggestive of SLE, but was later observed to have malar rash and oral ulcers. Laboratory investigations were compatible with SLE, including positive antinuclear antibody (1:320) with speckled pattern. CT revealed diffuse hypodense submucosal thickening of the stomach, the entire small bowel, colon, appendix, and rectum. Treatment with high-dose corticosteroids followed by maintenance therapy with mycophenolate mofetil, hydroxychloroquine, and azathioprine resulted in clinical improvement. Diagnosis of lupus enteritis requires a high index of suspicion given the low incidence and nonspecific clinical findings. **(Korean J Gastroenterol 2016;67:107-111)**

Key Words: Systemic lupus erythematosus; Enteritis

INTRODUCTION

Systemic lupus erythematosus (SLE) is a systemic autoimmune inflammatory disease with a variety of clinical manifestations. Gastrointestinal (GI) complaints are common in patients with SLE,[1-5] although they are more commonly due to medication side effects or infection than active SLE.[4] Furthermore, because lupus enteritis is rarely the initial presentation of SLE, diagnosticians often do not suspect SLE when GI manifestations appear alone.

Most SLE-related GI complications are caused by vasculitis and immune complex deposition.[5] Symptoms range from mild anorexia to life-threatening bowel perforation.[3] Lupus mesenteric vasculitis is most common, followed by protein-losing enteropathy, intestinal pseudo-obstruction, and acute pancreatitis.[1] SLE-related GI complications are important because they can be life-threatening if not treated promptly.

Lupus enteritis is a rare, serious complication of SLE that can cause significant morbidity and mortality.[2,3] Typical symptoms include abdominal pain, diarrhea, and vomiting. Lupus enteritis usually affects the mesenteric arteries, causing ischemic changes of the small and large bowels. Rectal involvement is rare, likely due to collateral circulation.[6] Here, we describe a 25-year-old woman who presented with panenteritis as the first manifestation of SLE.

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CASE REPORT

A 25-year-old woman who had multiple hospitalizations at an outside hospital for prolonged abdominal pain, nausea, and diarrhea was referred to our hospital. She had no other significant medical history. She had no recorded fever. On exam, there was diffuse tenderness to direct palpation but no rebound tenderness.

Laboratory investigations showed white blood cell count 30,700 cells/mm^3, hemoglobin 16.3 g/dL, and platelet cells 539,000 cells/mm^3. Erythrocyte sedimentation rate was 3 mm/hr and CRP was 7.09 mg/L. Blood chemistry showed AST 50 IU/L, ALT 56 IU/L. BUN, creatinine, total protein, albumin, PT, and aPTT were unremarkable. Urinalysis and urine microscopy showed proteinuria 1+, and the 24-hour urine protein and creatinine were 1.43 g/day, and 833.9 mg/day, respectively.

Because of her symptoms of abdominal pain, diarrhea and leukocytosis, she was treated with antibiotics for presumed enterocolitis. However, her symptoms worsened. Malar rash and oral ulcers were observed upon further examination. We performed additional laboratory tests and a CT scan.

Antinuclear antibody was positive (1:320, speckled pattern). Serum C3 level was 59 mg/dL (normal 90 to 180 mg/dL), C4 level 5 mg/dL (normal 10 to 40 mg/dL), and anti-double strand DNA antibody 2.5 IU/mL (normal $\leq$7 IU/mL). Otherwise, anti-Ro, anti-La, anti-RNP, anti-Scl-70, anti-Jo-1, and anti-Smith antibody were negative. Antineutrophil cytoplasmic antibody immunofluorescence, anti-proteinase 3 antibody and anti-myeloperoxydase antibody were negative. Anti-β2 glycoprotein immunoglobulin (Ig) M and anti-cardiolipin antibody IgM were positive. Lupus anti-coagulant, anti-cardiolipin antibody IgG, and anti-β2 glycoprotein IgG were negative. Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score was 22.

CT imaging indicated systemic involvement, including moderate ascites; diffuse hypodense submucosal thickening involving the lower body of the stomach, the entire small bowel, colon, appendix and rectum; wall thickening and enhancement of the urinary bladder and uterus, and bilateral hydronephroureterosis (Fig. 1). Upper endoscopy revealed diffuse edematous mucosal change with hyperemia in the entire stomach (Fig. 2). Sigmoidoscopy showed diffuse edematous and scattered erosions at the sigmoid and rectum (Fig. 3). A biopsy of the sigmoid colon was unremarkable.

During the hospitalization, the patient suffered a seizure episode. The brain MRI showed high signal intensity in tem-

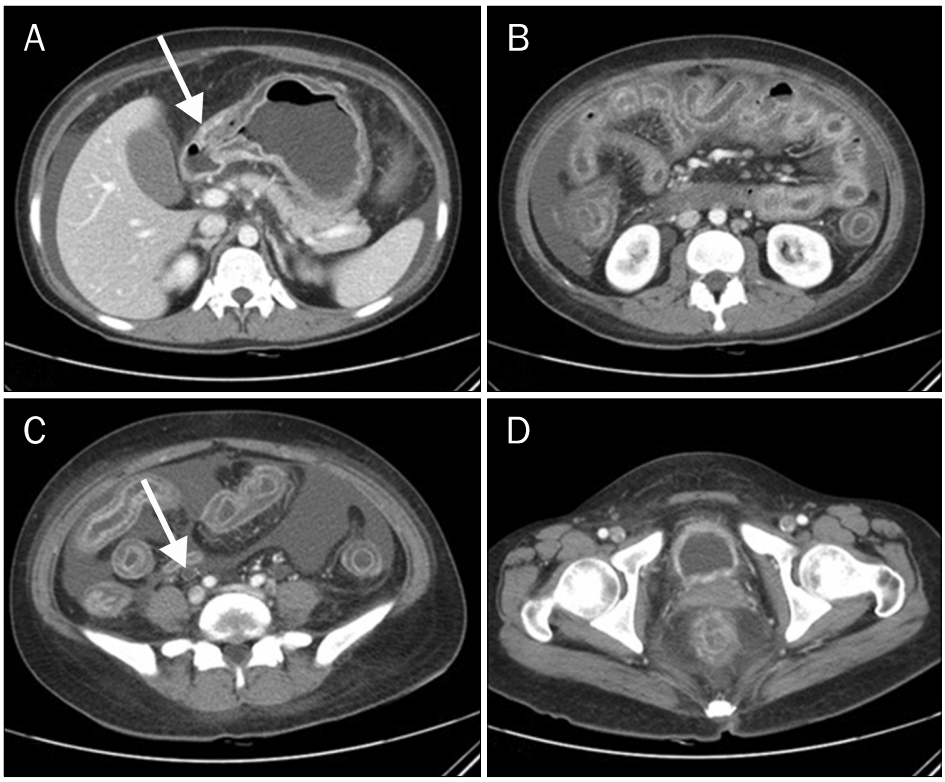

Fig. 1. CT of the patient shows moderate amount of ascites and diffuse hypodense submucosal thickening involving the stomach lower body (A), entire small bowel (B), colon (C), appendix and rectum (D). Submucosal wall thickening of stomach lower body (A, arrow). Focal enhancement of right ureter (C, arrow), suspicious systemic lupus erythematosus involvement.

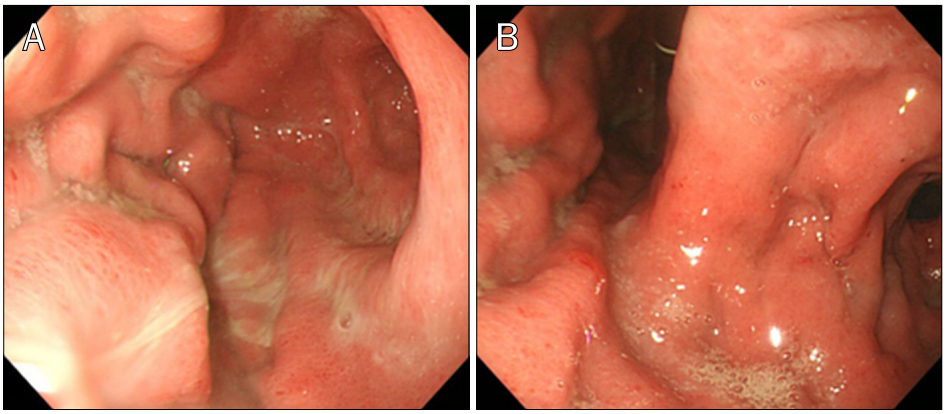

Fig. 2. Upper endoscopy revealed diffuse edematous mucosal change with hyperemia in the entire stomach.

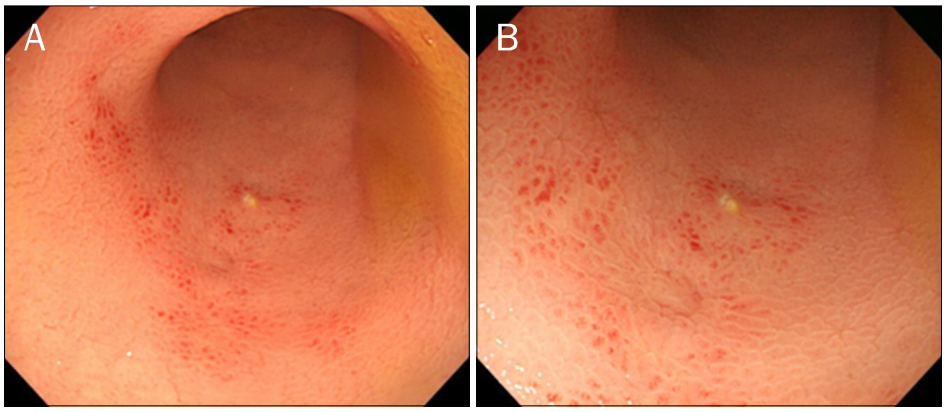

Fig. 3. Sigmoidoscopy showed diffuse edematous and scattered erosions at the sigmoid colon.

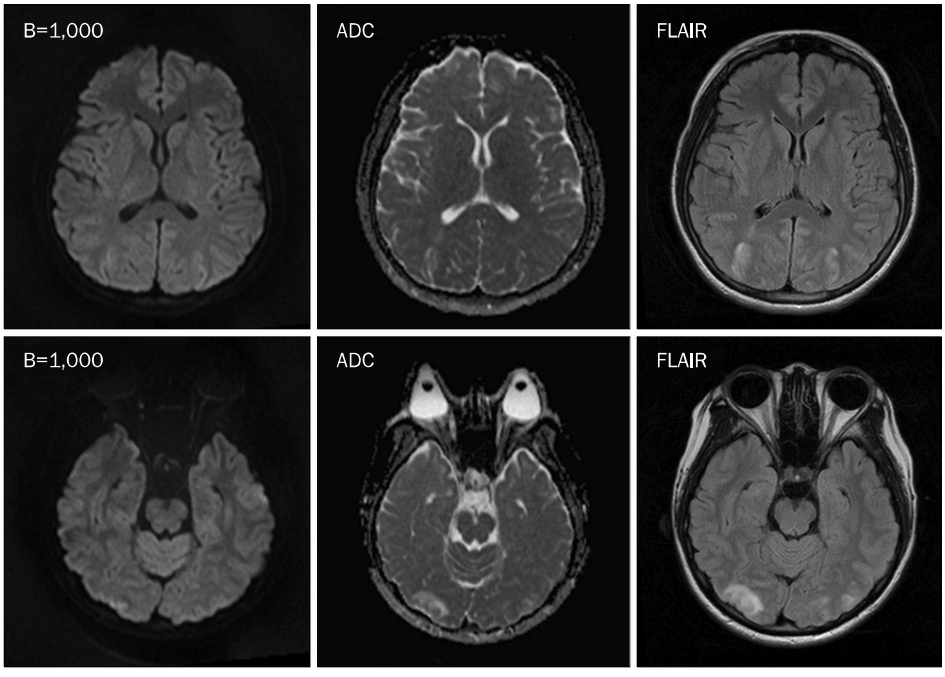

Fig. 4. The brain MRI showed high signal intensity in temporal, parietal, and occipital area.
B value, diffusion gradient strength; ADC, apparent diffusion coefficient; FLAIR, fluid attenuated inversion recovery.

poral, parietal, and occipital areas (Fig. 4), and the electroencephalogram findings were suggestive of a partial seizure disorder in left occipital area. Renal biopsy showed mesangiopathic lupus nephritis.

Treatment with high-dose corticosteroids (methylprednisolone 1 g pulse for five days) improved the GI symptoms.

After reducing the corticosteroid dose (methylprednisolone 1 mg/kg), however, massive vomiting and diarrhea recurred immediately. Therefore, the patient is maintained on long-term high-dose corticosteroid (methylprednisolone 500 mg → 250 mg → 125 mg → 62.5 mg → 1 mg/kg). Mycophenolate mofetil, hydroxychloroquine, and azathioprine were added later. She is being seen regularly at our outpatient rheumatology clinic after her long (more than six months) hospitalization.

DISCUSSION

SLE can affect almost any organ system and its course can be highly variable.[6] GI manifestations are common in patients with SLE, more than 50% by some estimates,[7] but they are more often due to causes other than active SLE.[1,4,8] Direct GI involvement by SLE is likely under-diagnosed and under-reported due to non-specific clinical findings.[1] Lupus enteritis is a rare, serious complication of SLE, which can lead to life-threatening ischemia, perforation, and infarction if not treated immediately.[2,3] The prevalence of lupus enteritis is reported to be 0.2-2% in SLE patients overall, and 45-79% in patients with SLE who present with acute abdominal symptoms.[9,10] However, cases of SLE initially presented as lupus enteritis are rare in the literature.

The main pathophysiological features of lupus enteritis are small vessel arteritis and venulitis. Atrophy and degeneration of the media of small arteries, fibrinoid necrosis of the vessel walls, old thrombosis, phlebitis, and monocyte infiltration in the lamina propria can be observed.[11]

The clinical manifestations of lupus enteritis are often non-specific, with mild to severe abdominal pain, diarrhea, and vomiting, sometimes accompanied by impaired intestinal motility or peritonitis. No single finding is diagnostic for lupus enteritis.[3] CRP is typically not highly elevated, and a very high CRP level should prompt investigation into other causes, such as infection. Due to the non-specific clinical manifestations and laboratory findings, diagnosis of lupus enteritis requires a high index of suspicion. With this patient, lupus enteritis was not suspected because she initially had no history or clinical findings suggestive of SLE. After the patient developed malar rash and oral ulcers, lupus enteritis was diagnosed with CT imaging. Smith and Petri[5] described a case of a young woman presenting with lupus enteritis as the initial manifestation of SLE. She had multiple hospitalizations and was diagnosed as lupus enteritis during her fourth admission.

CT scan is the gold standard for diagnosis of lupus enteritis, typically showing bowel wall thickening, bowel dilation, abnormal bowel wall enhancement (target sign), engorgement of mesenteric vessels with increased number of visible vessels (Comb's sign), increased attenuation of mesenteric fat, and ascites.[6] The jejunum and ileum are the most commonly involved sites; the rectum is rarely involved. Reissman et al.[12] first reported a case of gangrenous ischemic colitis isolated to the rectum, and Kim et al.[13] reported the first case of extensive lupus enteritis, from small bowel to rectum. In Kim's case,[13] the CT scan showed diffuse hypodense submucosal thickening involving the stomach lower body, entire small bowel, colon, appendix, and rectum. Although lupus enteritis is considered a form of vasculitis, endoscopic biopsies do not add much benefit, possibly because only superficial tissue is obtained.[10]

Corticosteroids are generally the first line treatment for lupus enteritis based on clinical responsiveness. There has been no randomized clinical trial investigating optimal treatment, likely due to the low incidence of lupus enteritis. Cyclophosphamide or mycophenolate mofetil may be added in case of corticosteroid resistance or involvement of other organs.[2,3] Treatment can be switched to oral corticosteroids once clinical improvement is observed. Hydroxychloroquine, mycophenolate mofetil, azathioprine and low dose corticosteroids could be considered for long-term maintenance treatment, although it is unknown whether they prevent recurrences. Early laparoscopy or laparotomy should be considered if necrosis or perforation is suspected.

If the patient relapses, adding cyclophosphamide to the treatment regimen is recommended. However, an appropriate treatment has not been established in cases where cyclophosphamide fails. Shirai et al.[14] reported a case of recurrent lupus enteritis resistant to conventional therapy that responded to tacroliumus. Oh et al.[15] also reported a case of relapsing lupus enteritis treated successfully with rituximab.

In conclusion, lupus enteritis is a rare, serious complication of SLE. Lupus enteritis should be considered in patients with no history of SLE but with a prolonged course of abdominal pain, diarrhea, vomiting, and CT findings of marked edema of the small and large bowel. Diagnosis of lupus enteritis requires a high index of suspicion but is crucial given the ex-

cellent response to steroid therapy and potentially life-threatening complications such as ischemia, perforation, and infarction.

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