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Systemic lupus erythematosus (SLE) is frequently accompanied by gastrointestinal symptoms. Although all parts of the gastrointestinal tract may be affected, colonic involvement is quite rare. Colonic ulceration, particularly in the rectum, is associated with a high mortality rate in patients with SLE, despite immunosuppressive therapy. While a standard regimen for treating rectal ulcers complicated with SLE has not been established, combination therapy with steroids and immunosuppressive agents is necessary because of the associated high mortality rate. In this report, we describe a patient with SLE whose condition was complicated with ulcerative lesions in the rectum and sigmoid colon; the lesions were successfully treated with a combination of corticosteroids and tacrolimus therapy. Tacrolimus could be a useful additional or alternative modality for treating rectal involvement in SLE.

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**Abstract** Systemic lupus erythematosus (SLE) is frequently accompanied by gastrointestinal symptoms. Although all parts of the gastrointestinal tract may be affected, colonic involvement is quite rare. Colonic ulceration, in particular in the rectum, is associated with a high mortality rate in patients with SLE, despite immunosuppressive therapy. While a standard regimen for treating rectal ulcers complicated with SLE has not been established, combination therapy with steroids and tacrolimus agents is necessary because of the associated high mortality rate. In this report, we describe a patient with SLE whose condition was complicated with ulcerative lesions in the rectum and sigmoid colon; the lesions were successfully treated with a combination of corticosteroids and tacrolimus therapy. Tacrolimus could be a useful additional or alternative modality for treating rectal involvement in SLE.

**Keywords** Rectal ulcer · Systemic lupus erythematosus · Tacrolimus

**Introduction**

Systemic lupus erythematosus (SLE), a complex autoimmune disease that affects various organs, is frequently accompanied by gastrointestinal symptoms, and lupus enteritis has been reported to be the most common cause of acute abdominal pain in SLE, accounting for up to 45 % of cases [1, 2]. Gastrointestinal vasculitis is one of the most serious complications of SLE, even though the occurrence of colonic lesions is quite rare (0.2 %) [1, 3]. Vasculitis of the bowel may lead to ulceration, hemorrhage, perforation, or infarction, and colonic ulceration, particularly in rectal lesions, has been associated with high mortality rates [4, 5]. Despite immunosuppressive treatment, severe complications, such as perforations of the intestinal tract, may occur, thus leading to an unfavorable prognosis.

Tacrolimus, a T-cell-specific calcineurin inhibitor with cyclosporine A-like immunosuppressive effects, suppresses T cell activation, thereby inhibiting inflammatory cytokine production [6]. In vivo and in vitro studies have shown that tacrolimus is 10 to 100 times more potent than cyclosporine A in inhibiting these processes [7]. Tacrolimus has been approved for use worldwide in organ transplantation and for treating autoimmune diseases, including inflammatory bowel disease (IBD), lupus nephritis, and rheumatoid arthritis [8–14]. Furthermore, several reports have demonstrated the efficacy of tacrolimus in the treatment of various conditions not associated with nephritis, including arthritis, skin eruption, alopecia, cystitis, and hemophagocytic syndrome, in patients with SLE [15–18]; however, its efficacy for the treatment of colonic lesions complicated with SLE has not been reported.

To date, no standard therapeutic strategies for colonic ulcers in SLE have been established. While corticosteroids are routinely used as a first-line therapy, many cases have
been reported to be steroid resistant, and perforations of the intestinal tract may occur after the induction of steroid therapy [3–5]. These findings suggest that combination therapy with steroids and an immunosuppressant is necessary. However, guidelines for the use of potent immunosuppressive agents have not yet been established, and low-dose oral tacrolimus may represent an alternative therapy for the treatment of colonic ulcers in SLE. In the current report, we describe a case of SLE complicated with ulcerative lesions of the rectum and sigmoid colon in which combination therapy with steroids and tacrolimus contributed to the remission of rectal ulcers and had steroid-sparing effects for 12-month follow-up.

Case report

A 51-year-old man, who had been diagnosed with SLE and lupus nephritis at 36 years of age, remained in a stable condition while receiving 5 mg prednisolone (PSL) and 150 mg mizoribine daily. Nonsteroidal anti-inflammatory drugs and antibiotics were not prescribed. Before admission to our department, he developed gastrointestinal symptoms and experienced more than 10 episodes of diarrhea associated with abdominal cramps. He presented with an elevated body temperature (37.6 °C); other vital signs were normal. A physical examination revealed mild tenderness of the middle lower abdomen without muscular defense. The palpebral conjunctiva was anemic. No skin rash was evident on either the face or extremities.

Laboratory evaluations revealed mild anemia (Hb 9.8 g/dL) and leukopenia (WBC 2500 × 10^9/L). Routine blood chemistry and coagulofibrinolytic tests were normal. The erythrocyte sedimentation rate was elevated (93.0 mm/h), but C-reactive protein (CRP) was undetectable. Urinalysis findings were positive for urinary protein (1.18 g/day); however, no casts were observed in the urinary sediment. Serum albumin levels were mildly decreased. The results of routine kidney function tests were normal, and creatinine clearance was 94.4 mL/min. An immunological test revealed the patient to be positive for anti-nuclear antibodies, with a titer of 1:160 (a speckled pattern), and anti-dsDNA antibody levels were elevated (81.2 IU/mL). Serum complement levels were normal, and anti-Sm antibodies, anti-U1 RNP antibodies, anti-SS-A antibodies, and rheumatoid factor were positive. Anti-cardiolipin antibodies and lupus anticoagulant were negative. Laboratory data revealed leukocytopenia, proteinuria, and an increase in the anti-dsDNA antibody titers, suggesting elevated disease activity.

An endoscopic examination revealed girdle ulcerative lesions in the rectum (Rs to Ra; Fig. 1a). The fundus of the ulcer and surrounding mucosa were erythrogenic and prone to bleeding. A histopathological examination of biopsy specimens taken from the ulcer showed nonspecific granulation and proctitis, but no evidence of vasculitis. Gastrografin enema radiography detected a stenosis of the sigmoid colon due to an intestinal tract edema (Fig. 1b, arrow). An abdominal enhanced computed tomography (CT) image revealed bowel wall thickening of the rectum (Fig. 1c). The patient’s stool samples were positive for occult blood, and fecal cultures were positive for a small number of Enterobacteriaceae species, but no other pathogens, including Clostridium antigen and acid-fast bacillus. Cytomegalovirus (CMV) infection was excluded because intranuclear inclusions were not observed histologically, and CMV antigen-positive leukocytes were not detected in the patient’s peripheral blood.

The absence of any positive evidence for infective agents and the presence of colonic ulcers were thought to be consistent with a gastrointestinal manifestation of SLE. IBD, such as Crohn’s disease and ulcerative colitis, was considered as a differential diagnosis. Although IBD is rarely associated with SLE, SLE is rarely active at the time of IBD manifestation [19]. Furthermore, neither colonoscopy nor pathological study revealed specific findings that were sufficient to change the diagnosis of IBD.

Treatment with 500 mg intravenous methylprednisolone for 3 days, followed by 50 mg/day oral PSL and 2 mg/day tacrolimus was initiated. As shown in Fig. 2, the gastrointestinal symptoms improved after the start of treatment. Furthermore, treatment with systemic steroids and oral tacrolimus healed the ulcer endoscopically 5 weeks after initiation of therapy (Fig. 2, CF®), and a reduction in PSL dose was possible. The patient was discharged from the hospital in an improved condition and has been monitored on an outpatient basis. Follow-up colonoscopies, which were conducted at 3 and 5 months after the initiation of treatment, demonstrated a reduction in the ulcerated area and regeneration of epithelium covering the surface (Fig. 2, CF® and 3), WBC counts normalized and anti-dsDNA antibody titers and proteinuria were decreased during the subsequent outpatient course (Fig. 2), indicating that the patient’s SLE was under control. Anti-DNA antibodies were examined by radioimmunoassay approximately 12 months after patient discharge and were confirmed to be within normal limits (5.8 IU/mL, normal range <6 IU/mL). Currently, the patient occasionally complains of abdominal pain without diarrhea, and oral tacrolimus has been increased to 3 mg/day. The patient has remained well for 12 months, and PSL has been reduced to 15 mg/day.

Discussion

Gastrointestinal manifestations are a frequent complication associated with SLE [1, 2]. Although colonic lesions are
quite rare, ulcerative lesions in the large intestine have been demonstrated in several studies [3–5, 20]. Of the 25 cases that have been reported in Japan, complications, such as perforations and fistulas, were observed in 9 patients, 4 of whom died [5]. In another study, perforation was observed in 5 out of 6 cases involving rectal ulceration, and 4 of these patients died, indicating a poor prognosis for such cases [4]. Colonic ulceration, particularly rectal lesions, is associated with a high mortality rate. However, despite this high mortality, ulcerative lesions in the rectum and sigmoid colon were improved by appropriate medical treatment in the present case. We emphasize that early administration of immunosuppressants, such as tacrolimus with high-dose steroid therapy, may contribute to an improvement in its poor prognosis.

Intestinal vasculitis was diagnosed in 45–60 % of SLE patients presenting with acute abdominal pain [1, 21, 22]. In our patient, findings of vasculitis were not obtained from the tissue biopsy specimen. Rectal and sigmoid colon ulcers were presumably caused by vasculitis based on the following facts: (1) a typical vasculitis pattern is difficult to prove on the basis of endoscopic biopsy [4, 5, 20]; (2) the bowel wall thickness detected in abdominal CT (Fig. 1c) was suggestive of bowel ischemia [23]; (3) a drop in the WBC count at the time of acute abdominal pain correlates with the occurrence of intestinal vasculitis, as observed in the present case [1]; and (4) the rectal ulcer responded to immunosuppressive therapy, indicating impressive improvement. Thrombosis of the mesenteric vessels associated with antiphospholipid syndrome (APS) may give rise to mesenteric ischemia [24]; however, APS was excluded because these antibodies were not detected in the present case.

High-dose corticosteroid therapy is considered the treatment of choice for gastrointestinal complications associated with SLE; however, not all patients respond sufficiently, and some may relapse when steroids are tapered. Prior studies demonstrated sustained remission after the use of oral mesalazine and pulse cyclophosphamide when steroid therapy alone was not effective [3, 5]. It should be noted that the outcomes in patients with perforations are extremely poor, and therefore immunosuppressants are clearly necessary for the treatment of colonic ulcers, particularly when rectal lesions are involved.

Tacrolimus, a potent T cell inhibitor, has been successfully administered for the treatment of inflammatory bowel disease, lupus nephritis, and rheumatoid arthritis [9–14]. While various immune response abnormalities have been identified in patients with SLE, aberrant and persistent T cell abnormalities involving signal transduction defects have been recognized as important factors in disease development in the last decade [25]. On the basis of these findings, T cell blockade is thought to be a potential therapeutic target for SLE and its manifestations. Recently,
Tacrolimus has been successfully applied in the treatment of various manifestations without nephritis in SLE [15–18]. Furthermore, tacrolimus, a drug that has been shown to be well absorbed, even in patients with severe colitis, serves as a rational therapeutic option for inflammatory bowel disease that is refractory to conventional therapy [26]. Thus, this immunosuppressive agent was administered to our current patient. Tacrolimus does not act quickly, and its onset of action usually requires 2–4 weeks; thus, we simultaneously initiated high-dose steroid therapy and tacrolimus [27]. Although an improvement in gastrointestinal symptoms may result from high-dose corticosteroid treatment, low-dose oral tacrolimus has also been shown to help maintain the remission of rectal lesions while exerting a steroid-sparing effect. Therefore, tacrolimus could be an additional or alternative modality for treating rectal involvement in SLE.

In conclusion, colonic lesions, particularly those occurring in the rectum, are quite rare in patients with SLE, but are associated with a high mortality rate. The present case demonstrated that combination therapy with steroids and tacrolimus is an effective therapeutic option for treating rectal involvement in patients with SLE.

**Conflict of interest** None.

**References**


