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CASE REPORT

궤양성 대장염을 동반한 면역성 혈소판 감소성 자반증 1예

김현태, 김태오, 김형준, 이순일, 전기정, 이은지, 박승현, 노태훈
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A Case of Immune Thrombocytopenic Purpura Accompanying Ulcerative Colitis

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Ulcerative colitis (UC) is a chronic idiopathic inflammatory disorder of the colon with a variable clinical course of exacerbation and remission. Extraintestinal manifestations of UC, including hematological disorders, such as the rare immune thrombocytopenic purpura (ITP), may be the presenting symptoms. We encountered the case of a 23-year-old man with UC who showed typical symptoms and endoscopic findings. Despite receiving steroid treatment, the patient developed severe thrombocytopenia. He was diagnosed with ITP, characterized by autoimmunity, a demonstrated low platelet count, normal bone marrow, positivity for autoantibody to platelet membrane antigen, and no splenomegaly. We initiated high dose intravenous immunoglobulin immediately for treatment of his steroid-refractory thrombocytopenia. The patient's hematochezia and platelet count improved following immunoglobulin treatment. After discharge, the patient's platelet count was maintained at a stable level and his condition was good. This case suggests that immunoglobulin therapy may be useful for treatment of ITP in UC. **(Korean J Gastroenterol 2014;64:234-238)**

Key Words: Ulcerative colitis; Immune thrombocytopenic purpura; Immunoglobulin

INTRODUCTION

Ulcerative colitis (UC) is a type of chronic inflammatory bowel disease of unknown etiology that affects the entire colon and is characterized by a lack of inflammation in the deeper layers of the colonic wall.[1] Immune thrombocytopenic purpura (ITP) is characterized by low platelet counts resulting from both immune-mediated platelet destruction and suppression of platelet production, which are caused by autoantibodies against platelet membrane antigens.[2] Several reports have described cases of UC associated with extraintestinal symptoms in Korea; however, coexistence of UC and ITP is rare. Previous reports have described the occurrence of ITP in patients with UC and hypothesized that it represents an immunologically mediated extraintestinal manifestation similar to mucocutaneous lesions, hepatobiliary disease, arthropathy, and hematological disorders.[1,3-6] Enhanced exposure to luminal antigens has been suggested as a cause of immune-mediated thrombocytopenia due to the increased mucosal permeability observed in UC patients.[6,7] Few cases of ITP in patients with UC have been reported; as a result, treatment has not yet been clearly established. In the current report, we describe a case of ITP in a patient with UC and discuss causal relationship between the two diseases.

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CASE REPORT

In August 2013, a 23-year-old man presented with a two-week history of bloody diarrhea. He had visited a local hospital and was diagnosed with UC of the pancolitis type, based on the clinical features and colonoscopy findings. Treatment with oral prednisolone (40 mg/day) and 5-aminosalicylic acid (5-ASA) was initiated, but was unsuccessful. After treatment for two weeks, the patient was transferred to our hospital for further treatment. He had no medical or family history of inflammatory bowel disease. On admission, physical examination indicated a body temperature of 36.3°C, heart rate of 88 beats/min, and blood pressure of 120/80 mmHg. Other physical examination findings were not remarkable.

Laboratory examination indicated a hemoglobin level of 9.2 g/dL, white blood cell count of 7,210/mm^3, and platelet count of 37,000/μL. Regarding inflammatory marker levels, his C-reactive protein level was 6.38 mg/dL and the erythrocyte sedimentation rate was 96 mm/h. The patient's coagulation parameters, including prothrombin time and activated partial thromboplastin time, as well as antithrombin, fibrinogen, and D-dimer levels were all normal. The results of liver and renal function tests were also normal.

Stool cultures, including *Clostridium difficile* toxin testing, for the presence of pathogens yielded negative results. Sigmoidoscopy indicated left-sided colitis with friable, erythematous mucosa showing erosions, ulcerations, exudates, and hemorrhage (Fig. 1). Colonic biopsies showed active inflammation with crypt abscesses and gland atrophy, con-

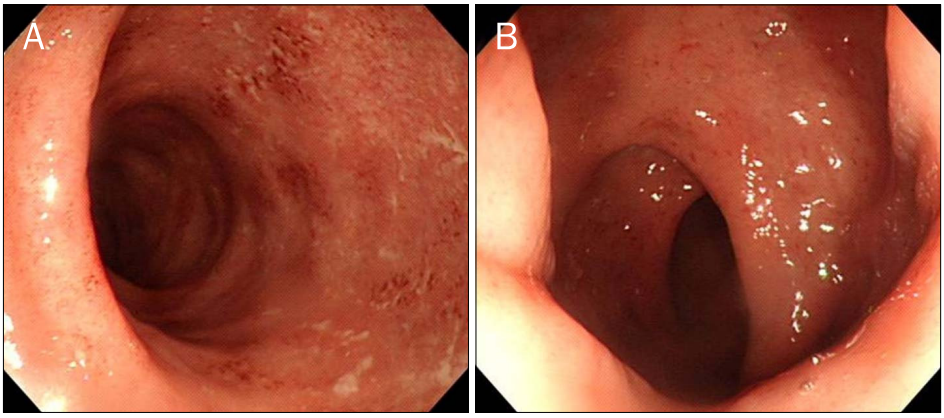

Fig. 1. Sigmoidoscopic findings. (A) Sigmoidoscopic findings in the sigmoid colon, is showing friable mucosa and shallow ulcers with exudate. (B) Sigmoidoscopic findings in the rectum, is showing edematous and erythematous mucosa.

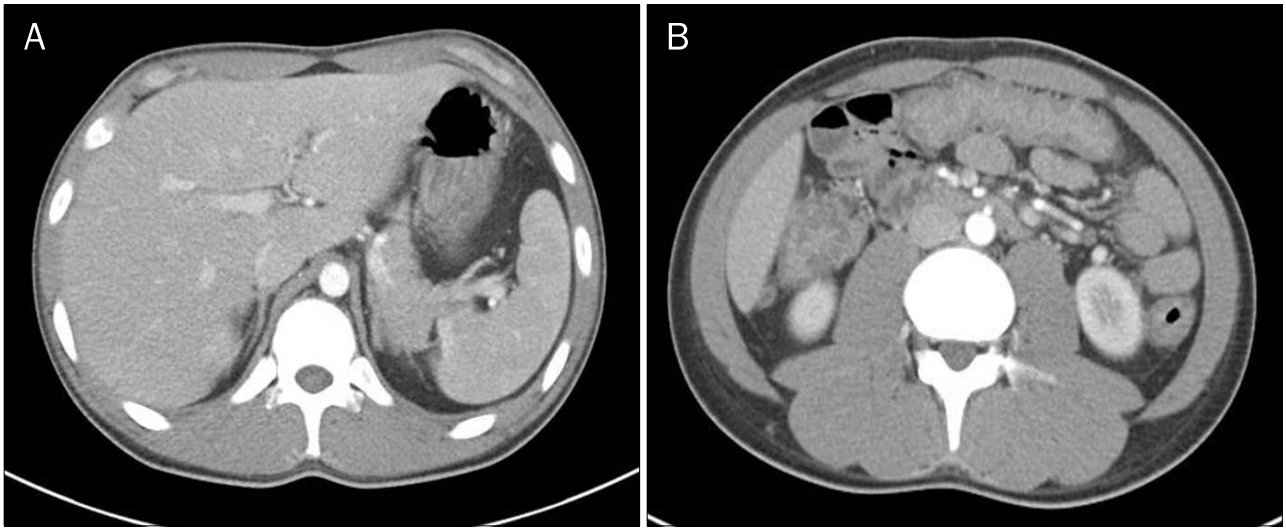

Fig. 2. Abdominal computed tomography is showing diffuse bowel wall thickening, submucosal edema, and pericolic fat infiltration of the entire colorectum, sparing cecum, and no evidence of splenomegaly.

sistent with a diagnosis of UC. No cytomegalovirus inclusions were noted. Abdominal computed tomography scan showed diffuse bowel wall thickening of the entire colon (Fig. 2).

Combination treatment of total parenteral nutrition, oral 5-ASA, and steroid therapy (62.5 mg of methylprednisolone daily; 17 consecutive days) was initiated. However, the patient still experienced intermittent bloody diarrhea, and his serum platelet count continued to decrease during treatment. He received eight units of platelet concentrates on alternate days. Two weeks prior to admission, laboratory examinations performed at another local hospital indicated a platelet count of 107,000/μL. Therefore, we suspected a diagnosis of drug-related thrombocytopenia and discontinued administration of 5-ASA. However, his platelet count did not improve. A peripheral blood smear showed anemia with blood loss and severe thrombocytopenia, but no other morphologic abnormalities were observed. We performed additional laboratory tests, including Coombs test, autoimmune antibody test, and viral serology tests (including those for the human immunodeficiency virus and hepatitis C virus). However, the results were not remarkable, with the exception of a positive result on an anti-platelet antibody test.

After consulting a hematologist, we performed bone marrow aspiration on day 10, which indicated a normocellular marrow with a normal number of megakaryocytes and normal morphology (Fig. 3).

Thus, the patient was diagnosed with ITP in addition to UC according to the criteria established by the International Working Group for ITP.[8] He had no history of autoimmune or immunodeficiency disorders, liver disease, use of drugs for

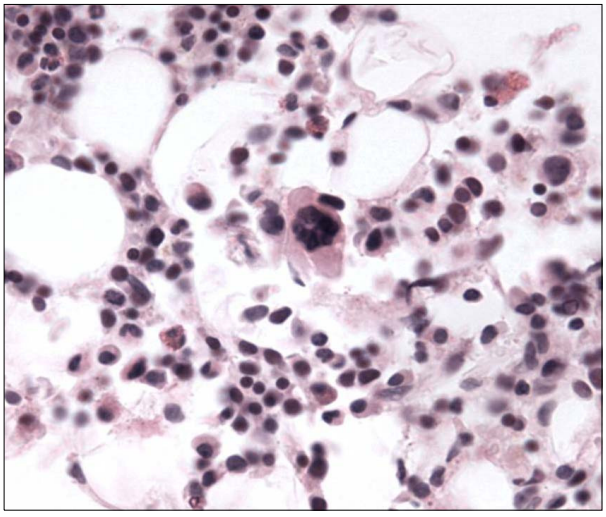

Fig. 3. Bone marrow biopsy finding is showing normocellularity with normal megakaryocytes (H&E, ×40).

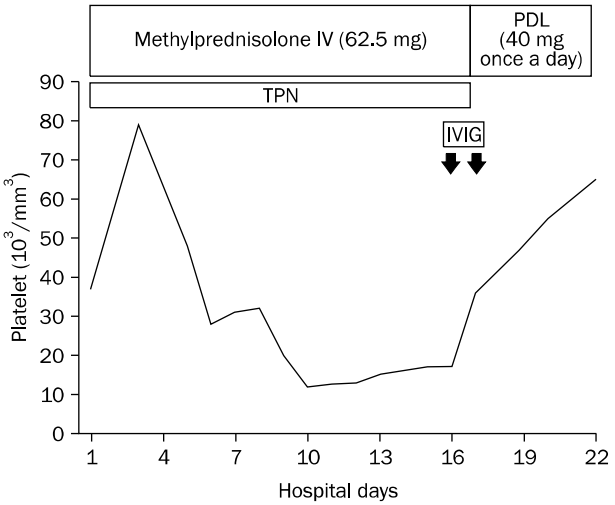

Fig. 4. The course of platelet count and treatment in the ulcerative colitis. IV, intravenous; IVIG, intravenous immunoglobulin; TPN, total parenteral nutrition; PDL, prednisolone.

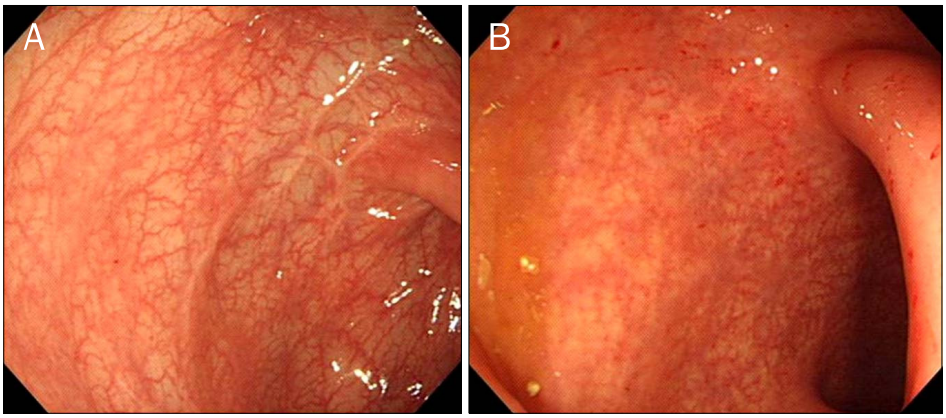

Fig. 5. Colonoscopic findings. (A) Colonoscopic findings in the sigmoid colon, is showing scarry changes of mucosa. (B) Colonoscopic findings in the rectum, is showing healing mucosa.

thrombocytopenia, or inherited thrombocytopenia. Based on the laboratory data, other causes of secondary thrombocytopenia, including viral infections, disseminated intravascular coagulation, hemolytic uremic syndrome, and lymphoproliferative disorders were excluded. In recent years, several studies have proposed a possible association of *Helicobacter pylori* infection with ITP.[9-11] We performed endoscopy and a rapid urease test; *H. pylori* infection was not detected. Therefore, we did not perform *H. pylori* eradication.

Due to a lack of response to steroids, 1 g/kg of immunoglobulins was administered intravenously on two consecutive days (days 16 and 17). After this infusion, the patient's symptoms improved and the number of platelets increased from 17,000/μL to 65,000/μL (Fig. 4). Therefore, we switched his medication to 40 mg of oral steroids, and then gradually reduced the steroid dose by 5 mg every week.

The patient was discharged on day 22, and his serum platelet count had recovered to 98,000/μL on day 21 after discharge. Subsequently, at three months after discharge, colonoscopic findings (Fig. 5) and CRP, ESR levels showed mucosal healing and normal levels, respectively.

DISCUSSION

Since Edwards and Truelove[12] originally described three patients with both ITP and UC in 1964, few cases of the coexistence of ITP and UC have been reported. UC may be concomitant with hematological disorders such as iron deficiency anemia due to colon bleeding, megaloblastic anemia caused by malabsorption of vitamin B12 or folic acid, and autoimmune hemolytic anemia.[13,14] However, although the number of reported cases has recently increased, no definitive correlation between UC and ITP has been proposed.

ITP is presumed to be related to the destruction of antibody-coated platelets by macrophages and suppression of megakaryocytopoiesis via production of specific IgG autoantibodies from the patient's B cells.[13] In UC patients with ITP, one proposed hypothesis is that the increased permeability and translocation of antibodies to luminal bacterial antigens by bowel inflammation might lead to platelet antibody formation through cross reactivity.[6] ITP occurs during the active stage of UC, which is characterized by extensive and significant colonic inflammation, leading to degradation of platelet glycoproteins and subsequent antibody formation.[6] Approximately half of affected patients with both diseases respond well to steroid treatment. However, in other cases, surgery such as splenectomy or colectomy is required.[3,4]

In the current case, we administered steroid therapy for management of UC, which could also serve as a treatment for ITP.[15,16] However, the thrombocytopenia did not improve. Therefore, we utilized other treatment options, including immunoglobulin therapy. The increase in platelet count, which can be expected to persist for approximately one week following immunoglobulin infusion,[14] usually occurs on the 2nd-3rd day after initiation of immunoglobulin treatment. Intravenous immunoglobulin is used to manage internal bleeding when the platelet count remains very low even after several days of corticosteroid treatment.[13] The mechanism of action of immunoglobulin is presumed to involve the temporary interference with the function of the mononuclear phagocyte system Fc receptor.[17] This treatment is known to be effective in approximately 80% of patients, although it does not frequently result in sustained remission.[18] In the current case, following management with high-dose intravenous immunoglobulin, the patient's platelet count increased, and bloody diarrhea improved, without the need for surgical treatment. After discharge, he visited the outpatient clinic regularly for management.

Our analysis of cases in Korea and abroad, including the current case, indicates that ITP should be suspected in patients with UC symptoms that do not respond to treatment and those who present with worsening thrombocytopenia. In addition, we suggest that ITP can be diagnosed by use of an anti-platelet antibody test and bone marrow examination. In addition, although several treatment methods are available, steroids should be considered as the first line of treatment. If this treatment does not yield a response, immunoglobulin management is preferred rather than immediate surgical operations such as splenectomy or colectomy. Nevertheless, for drug-refractory ITP in cases of severe UC, surgery can be performed, depending on the severity of the disease, tolerance of steroids, and the patient's preferences regarding surgery.[13] There are no guidelines for the appropriate surgical procedure for such cases, and to the best of our knowledge, no comparative studies have yielded suitable and useful results on the diagnosis and treatment of this condition. In the current case, surgery was not performed because the condition improved following immunoglobulin management.

A few reports in Korea describe cases of the coexistence of UC and ITP that could not be controlled with medical treatment. These patients were treated with splenectomy only or splenectomy and colectomy.[19,20] However, it remains unclear whether ITP can be effectively treated with splenectomy only, colectomy only, or a combined surgery. Therefore, the most suitable surgical procedure should be determined for use as the final treatment in cases resistant to medical treatments such as steroids, immunosuppressive drugs, and immunoglobulin, or in cases where medical treatment is contraindicated.

In the current case, UC with ITP, which was refractory to medical treatment with high-dose prednisolone, responded to rescue therapy with immunoglobulin. Thus, we avoided the need for surgical treatment such as splenectomy or colectomy. In conclusion, although immunoglobulin therapy is known to be effective for only a short duration, we suggest that immunoglobulin therapy may be useful for treatment of UC-related ITP that is refractory to steroids and can therefore be helpful in avoiding the need for surgery.

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