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Ischemic Stroke in Patient Diagnosed with Ulcerative Colitis in the Active Phase: A Case Report

Aktif Dönemde ve Yeni Tanı Konmuş Ülseratif Kolitli Hastada Gelişen İnme: Olgu Sunumu

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ABSTRACT

Ulcerative colitis (UC) and Crohn's disease are the two major types of inflammatory bowel disease (IBD). The close relationship between inflammation and thrombosis also affects the clinical course and severity of IBD. While venous thrombus is common in IBD, as in many other inflammatory diseases, arterial thrombus, and stroke are rare. Herein, we present a case of a newly diagnosed UC in the active phase of stroke despite being followed up with prophylactic anticoagulant therapy.

Keywords: Ulcerative colitis, inflammation, arterial thrombus, stroke

ÖZ

Ülseratif kolit (ÜK) ve Crohn hastalığı inflamatuvar barsak hastalığının (İBH) iki ana türüdür. Enflamasyon ve trombüs arasındaki yakın ilişki aynı zamanda İBH'nin klinik seyrini ve ciddiyetini de etkiler. Diğer birçok inflamatuvar hastalıkta olduğu gibi İBH'ninde venöz trombüs yaygın iken, arteriyel trombüs ve inme çok nadir görülür. Sunulmuş olan olgu, profilaktik antikoagülan tedavi altında izlenmesine rağmen inme geçiren aktif dönemde ve yeni tanı almış bir ÜK hastasıdır.

Anahtar Kelimeler: Ülseratif kolit, enflamasyon, arteriyel tromboz, inme

Introduction

Ulcerative colitis (UC) is an inflammatory bowel disease (IBD) of the large bowel and is characterized by symptoms, including bloody diarrhea, fecal urgency, and abdominal cramps. Crohn's disease and UC are the two major types of IBD (1,2). Since it has been reported for the first time by Bargen and Barker (3) in 1936, it is known that the risk for arterial and venous thrombosis is increased in IBD. The close relationship between inflammation and thrombosis also affects the clinical course and severity of IBD as seen in many other inflammatory diseases (2-4). Acquired (smoking, use of steroid therapy, immobilization, inflammation, endothelial dysfunction, dehydration, and surgery) and inherited risk factors (factor V leiden mutation and prothrombin gene mutation) were defined for thrombosis (5). In IBD, thrombosis can commonly develop in deep leg veins and the pulmonary system and less frequently in the cerebrovascular system, portal, mesenteric, hepatic, and retinal veins (6-8). While it is less common in the arterial system compared to the venous system, thrombosis can occur in the aorta, retinal, renal, coronary, carotid, and iliac arteries (9,10). Arterial thrombus, particularly stroke, is rare in IBD (11). Until now, observational studies have provided conflicting findings on whether IBD is associated with an increased risk of stroke (11-13).

Case Report

A 46-year-old female patient with known diagnoses of hypertension (HT) and diabetes mellitus (DM), using amlodipine and intensive insulin treatments, neither consuming alcohol nor smoking, without a known allergy, and with family histories of ischemic heart disease in her father and cerebrovascular disease in her brother presented to our gastroenterology outpatient clinic due to complaints of gradually increasing bloody diarrhea, severe fatigue, and high fever for approximately one month. She complained that her bloody diarrhea gradually increased in the last two weeks, occurring more than 30 times in a day, and that almost all of them were bloody and mucousy stool. She also complained of high fever and abdominal pain occurring in the last few days. On physical examination, blood pressure was 130/80 mmHg, temperature was 38.6 °C, and pulse was 98/min. On abdominal examination, there was no rebound tenderness or defense to palpation. With a prediagnosis of UC, rectosigmoidoscopy was performed in

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the patient under emergency conditions. The mucosa was in the appearance of erosion and ulceration continuously from the transverse colon to the anal canal. The mucosa was fragile with spontaneous bleeding (Mayo Endoscopic score: 3). Many biopsies were taken and the tissue sample was sent for cytomegalovirus (CMV) polymerase chain reaction (PCR) (Figure 1). The patient was admitted to our clinic with prediagnoses of fulminant colitis, active UC, and infectious colitis. There were no toxic megacolon findings in the upright abdominal X-ray. Abdominal ultrasound showed no specific findings. Blood test results were as follows: white blood cell: 13,560/mm^3 (normal range: 4,000-10,000 mm^3), hemoglobin: 8.2 g/dL (NR: 12-16 g/dL), C-reactive protein (CRP): 423 mg/L (NR: 0-5 mg/L), ESR: 78/h (NR: 0-20 mm/h), fasting glucose: 220 mg/dL (NR: 70-110 mg/dL), albumin: 3.4 g/dL (NR: 3.5-5.5 g/dL), and hepatitis B surface antigen: negative. Abundant leukocytes and erythrocytes were observed on microscopic examination of fecal specimens. The presence of amebic antigen was negative in the fecal specimens. Clostridium Difficile Toxin A and B were negative in the fecal specimens after three tests were performed. Oral intake of the patient was discontinued due to prediagnoses of activation/fulminant UC (severe active colitis according to Truelove-Witts clinical activity index) based on clinical, laboratory, imaging, and endoscopic findings. Based on these findings, the following treatments were started: mesalazine (4,000 mg/day), methylprednisolone (40 mg/day), ciprofloxacin, metronidazole, intensive insulin treatments, and subcutaneous low molecular weight heparin (LMWH) in prophylactic dose as an anticoagulant agent. During the follow-up of the patient, the fever was ceased on the third day, vital signs were stable, the number of daily defecation increased to about 5-6 times per day, and CRP regressed to 32 mg/dL. We achieved colonoscopic biopsy results while the treatments of the patient were continued and findings consistent with the active phase of UC were reported and CMV-PCR was found to be negative. Meanwhile, the treatments of the patient were continued and her general condition began to improve. However, a sudden onset throbbing headache localized in the frontal region and aphasia developed on the seventh day of hospitalization. The patient's vitals and blood glucose level were normal. On neurological examination, pupils were isochoric, pupillary light reflexes were normal, meningeal irritative sign was absent, muscle strength was full, sensory examination was normal, orientation and cooperation were normal, but there was a slurred speech and repetition disorder. A neurological consultation was performed. No pathological finding was determined on cranial computed tomography (CT) scan. A cranial diffusion magnetic resonance imaging (MRI) was performed at the end of the first hour. An infarct area consistent with thromboembolism related to the posterior branch of the left middle cerebral artery (MCA) and showing restricted diffusion in the insular region of the left parietal lobe was observed (Figure 2). Based on these findings, with the diagnosis of left parietal lobe ischemic infarct, acetylsalicylic acid (ASA) (300 mg) was started as anti-aggregant therapy and the prophylactic LMWH dose was increased. Hypodense areas revealing that ischemia was settled in the left parietal lobe were observed in control cranial CT scan performed at the end of the second day and the ischemic area in the insular region of the left parietal lobe in a cranial diffusion MRI performed at the end of the second day became apparent (Figure 3). No significant narrowing was observed in the cranial and cervical MRI angiographic examinations performed for etiological reasons. Echocardiography was within normal limits. Her elder brother has a history of cerebrovascular accident. Therefore, a hematological consultation was done for thrombophilic etiology. Her tests performed for antinuclear antibody, lupus anticoagulant, anticardiolipin immunoglobulin M (IgM)/IgG, anti-beta 2 glycoprotein IgM/IgG, factor V leiden mutation, and prothrombin gene mutation yielded negative results and her homocysteine level was within normal limits. Levels of her protein C, protein S, and anti-thrombin III activity was planned to be determined after discontinuation of the antiaggregant therapy. With these findings, no thrombophilic condition was determined. During the long-term follow-up of the patient, aphasia gradually decreased with the LMWH and ASA therapies. The patient experienced a new UC attack accompanied with widespread peripheral bilateral arthritis five months after the first diagnosis. She was hospitalized, steroid therapy was restarted, and azathioprine therapy was added. Since she experienced

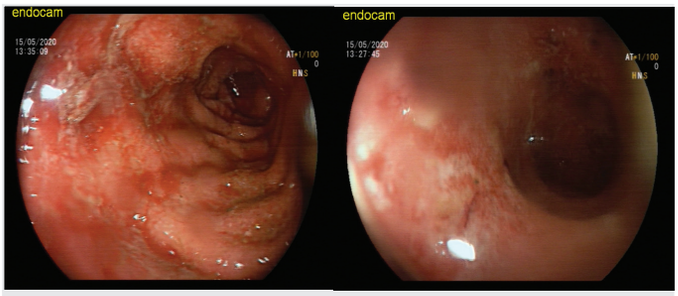

Figure 1. Active ulcerative colitis condition in sigmoid colon and ascending colon (Mayo Endoscopic score: 3)

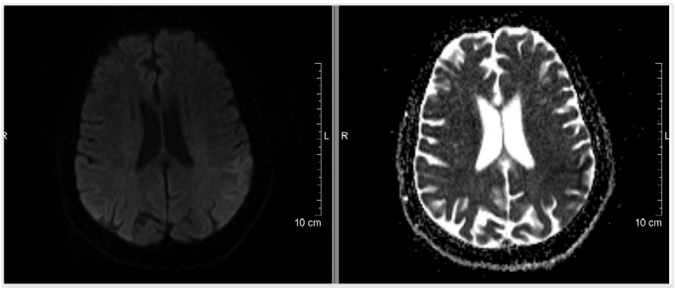

Figure 2. Left MCA infarct in cranial diffusion MRI (performed in the first hour)

MCA: Middle cerebral artery, MRI: magnetic resonance imaging

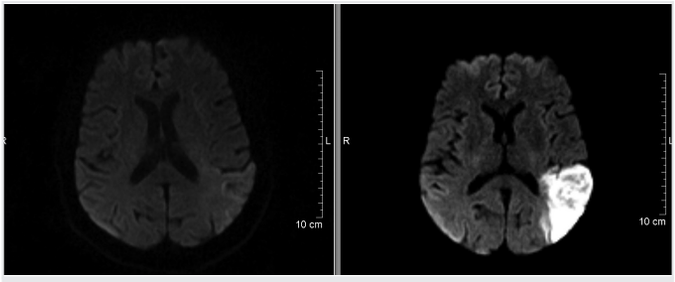

Figure 3. Left MCA infarct in cranial diffusion MRI (performed at the end of the second day)

MCA: Middle cerebral artery, MRI: magnetic resonance imaging

pancreatitis with azathioprine therapy, anti-tumour necrosis factor (TNF) therapy (infliximab) was started. Informed consent was obtained.

Discussion

Herein, we describe a case of ischemic stroke. She was a female newly diagnosed of UC in the active phase. While the activity of the disease was reduced under the treatments with prophylactic LMWH, anti-biotherapy, steroid, and mesalazine, a sudden onset headache and aphasia developed on the seventh day of treatment. A left MCA infarct was determined on the cranial imaging performed. A neurological consultation was done and antiaggregant therapy was started immediately. The dosage was raised to the optimal level. A reduction was determined in the aphasia within few days. During the long-term follow-up of the patient, the aphasia gradually decreased with LMWH and ASA therapies. In our investigations, no inherited thrombophilic risk factor was determined for the stroke etiology. To be in the active phase of UC, use of steroid therapy, HT, and DM can be accepted as risk factors for thrombosis. Our patient experienced a new UC and arthritis attack five months after the first diagnosis during the follow-up. Treatment of our patient was switched to infliximab therapy. This condition was suggestive of an initial thrombotic event that was associated with poor prognosis. In the report presented in 2008 by Joshi et al. (11) a 24-year-old female patient had been diagnosed with UC six months earlier. A severe headache and global aphasia developed while she was taking mesalazine and steroid treatments and an infarct of the left MCA was reported. This patient and our patient were almost identical. The adequate response for steroid treatment was not observed in this case and total colectomy was performed shortly afterward. In our patient, treatment was switched to infliximab therapy (11). Thrombotic events involving the central nervous system are unusual. Cases of cerebral venous sinus thrombosis in IBD are well described (14,15). Arterial thromboembolic complications occur less frequently and majority of these cases seem to occur after surgery (16,17). In the study performed in 2016 by Akpınar et al. (5) in which a total of 3,128 patients with IBD, were retrospectively screened, it was reported that thromboembolic event was observed in 20 patients and thrombosis was seen most commonly in deep leg veins and the pulmonary veins and that cerebral vein thrombosis developed only in 1 patient. Cerebral arterial thrombosis was not reported (5). Pancolonic and active UC have also been suggested as a risk factor for stroke and significant morbidity has been found to be associated with arterial complications (18). Our patient was a case of UC with pancolonic involvement. Her Mayo Endoscopic score was 3, CRP was 423 mg/L, and ESR was 78 mm/hour. She was a serious/severe patient according to Truelove-Witts clinical activity index. Although prophylactic LMWH treatment was started at the beginning from her hospitalization and the disease activity decreased at the end of the third day, a cerebral infarct developed on the seventh day of her hospitalization. Treatment of thrombosis in IBD comprises preventive prophylactic therapy and anti-coagulation therapy. Prophylactic anti-coagulation treatment is recommended in patients with IBD, especially in the active phase of the disease and during hospitalization (19). The agent recommended for prophylactic anti-coagulation treatment is LMWH. In IBD diagnosed with thrombosis, LMWH, warfarin, or rivaroxaban can be used as the treatment options. Durations of the use of the agents in treatment are controversial. While the therapy should be maintained until remission in thrombosis diagnosed during the active phase of the disease, life-long therapy is recommended in thrombosis occurring in the absence of active disease and underlying inherited thrombophilic states (20).

Reports are available on the risk of recurrence and complication of IBD in patients experiencing thrombosis and it will be better to switch the therapy to an upper level (azathioprine and anti-TNF) to establish long-term remission (5). In our patient, a new attack of UC and arthritis developed few months after cerebral infarct. Steroid therapy was administered again and infliximab therapy was initiated as an upper-level therapy. IBD is a prothrombotic condition. Although venous thromboembolic events are more commonly observed, arterial thrombosis can also be seen. Prophylactic anti-coagulation treatment should be necessarily started during hospitalizations, especially in the active phase of the disease. A cerebral infarct developed in our patient despite the prophylactic anti-coagulation treatment during the active phase of the disease. Early diagnosis and treatment are important for the reduction of the morbidity and mortality of patients developing a cerebral infarct. We followed up our patient very closely, performed immediate cranial imaging and neurological consultation, and started the therapy without delay. As a result, aphasia recovered gradually with time.

Unfortunately, we observed that awareness of the high risk for thromboembolic complications in IBD was low. In particular, stroke is not a well-known complication despite being a serious clinical picture with mortality and morbidity. Therefore, we think that it is necessary to potently inhibit the disease activation and inflammation in patients with IBD during the active phase of the disease or during hospitalization. It is also important to start prophylactic anti-coagulation treatment and follow-up the thromboembolic events.

Ethics

Informed Consent: It was obtained.

Peer-review: Externally peer-reviewed.

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