



A case of ulcerative colitis with digital arterial thrombosis

Çağatay Arslan¹, Mehmet İşler², Güçhan Alanoğlu³

¹Department of Medical Oncology, İzmir Tepecik Research and Training Hospital, İzmir, Turkey

²Department of Gastroenterology, Şifa Hospital, Isparta, Turkey

³Department of Hematology, Süleyman Demirel University Faculty of Medicine, Isparta, Turkey

ABSTRACT

Thromboembolic events are rare in the course of ulcerative colitis and related with the activity of the disease. These complications are especially seen in young patients and cause high mortality and morbidity. Arterial thrombotic complications are less frequent and are usually seen after a surgical procedure. Here, we present a 36-year-old man with active ulcerative colitis presenting via digital arterial thrombosis and digital necrosis that was not associated with a surgical procedure.

Keywords: Ulcerative colitis, finger necrosis, digital arterial thrombosis

INTRODUCTION

Thrombotic events related with ulcerative colitis are not frequent but might cause severe complications. The first report of thromboembolic phenomena as a complication of inflammatory bowel disease (IBD) was made by Bargen and Barker in 1936 (1). Their report included 1500 chronic IBD patients, and 18 of them had extensive arterial and venous thrombosis. Since then, several reports were made that confirmed the association. Talbot et al. (2) reported 92 patients had thromboembolic events out of 7199 chronic IBD patients (1.3%) during a 10-year period. The largest study about this phenomenon showed that approximately one-third of patients with thrombosis had active IBD at the time of the thromboembolic event (2). In the same report, 60% of the patients had thrombocytosis not related with sulfasalazine or corticosteroid therapy, and erythrocyte sedimentation rate was increased in 73% of the patients (2). It was suggested that thromboembolic events are more common in young patients with active and extensive disease. It occurs often in unusual sites and is associated with high morbidity and mortality (3).

Here, we report a case of finger necrosis due to digital arterial thrombosis in a young man with active ulcerative colitis (UC). His fingers' distal parts were amputated due to necrosis, but low-molecular-weight heparin was used for the prevention of thrombosis recurrence.

CASE PRESENTATION

A 36-year-old man was admitted with severe hemorrhagic, mucous diarrhea and abdominal pain. He was suffering from diarrhea 10 to 40 times daily for 4 months and lost 22 kgs (25% of original weight). Since that time, he was hospitalized 3 times at different hospitals due to severely active UC. He had pallor, pain, swelling, erythema, and insensitivity at the distal parts of the thumb and index fingers of the right hand 3 weeks ago. By the time it had progressed, movement failure and necrosis had developed (Figure 1, 2).

On the physical examination, pallor and tachycardia were present. Bowel sounds were hyperactive, and the distal parts of the thumb and index fingers of the right hand were gangrenous. His past medical history revealed smoking for 25 years.

Address for Correspondence: Çağatay Arslan, Department of Medical Oncology, İzmir Tepecik Research and Training Hospital, İzmir, Turkey E-mail: arslancagatay@yahoo.com

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Figure 1. Necrotic distal parts of the right hand's thumb and index fingers; volar view. Demarcation borders of necrotic margins draw attention

Laboratory findings showed mild anemia (8.7 mg/dL), thrombocytosis ($760,000/\text{mm}^3$), increased erythrocyte sedimentation rate (63 mm/h), and high serum C-reactive protein (17 mg/dL) levels. He had mild proteinuria (726 mg/24 hours), and creatinine clearance was within normal limits (96 mL/min.). All coagulation parameters, such as prothrombin time (pt), activated partial thromboplastin time (aptt), fibrinogen, protein C, protein S, factor VIII, factor IX, and anti-thrombin III levels, were normal. Serum homocysteine level was 40 (0-10) mg/dL. Serum folate, vitamin B12, serum immunoglobulins, and complement factors C3 and C4 were within normal limits. He was negative for the most frequent prothrombotic mutations, such as factor V G1691A (Leiden), H1299R (R2), prothrombin G20210A, Factor XIII (V34L), B- Fibrinogen (-455 G>A), plasminogen activator inhibitor-1 (PAI-1), genetic polymorphism of platelets (HPA1) (a/b), methylenetetrahydrofolate reductase (MTHFR) (C677T, A1298C), and hemochromatosis gene mutation (HFE) (C282Y). Venereal disease research laboratory, rapid plasma reagin, and treponema pallidum hemagglutination assay tests were negative. Microscopic examination of the stool and cultures was negative. Active ulcerative colitis and polyps were seen on rectosigmoidoscopy, and rectum biopsy revealed acute-phase severe UC.

He was treated with methyl-prednisolone per oral (p.o.) (Prednol, Mustafa Nevzat İlaç Sanayii, Istanbul, Turkey) and mesalazine p.o. and enema (Salofalk, Ali Raif İlaç Sanayii, Istanbul, Turkey). Low-molecular-weight heparin was given for prophylaxis of thrombosis recurrence. The flow was normal at the radial and ulnar arteries with Doppler ultrasonography. The thumb and index fingers' distal parts were gangrenous due to digital arterial thrombosis, and the distal phalanges were amputated. His bloody diarrhea and stool frequency came to normal limits in 30 days, and he was sent home with mesalazine p.o. and enema (Salofalk, Ali Raif İlaç Sanayii, Istanbul, Turkey), nadroparin calcium subcutaneously (Fraxiparine, Glaxo Smith Kline, Brentford, United Kingdom), and methyl-prednisolone p.o. (Prednol, Mustafa Nevzat İlaç Sanayii, Istanbul, Turkey). Ten days



Figure 2. Necrotic distal parts of the right hand's thumb and index fingers; palmar view

after discharge, he was hospitalized for the second time with bloody diarrhea 7 to 8 times daily. The corticosteroid dose was increased. The anticoagulant treatment had been continued for the risk of a new thrombotic event. Microscopic examination of the stool was normal, and cultures were negative, again. Rectosigmoidoscopy showed active ulcerative colitis and pseudopolyps. Biopsy was negative for dysplasia or metaplasia. He was discharged when his stool frequency came to normal limits. Two months after discharge, he was admitted again with bloody diarrhea 8 to 9 times a day. Rectosigmoidoscopy had been performed after a month when his symptoms improved. Colonoscopy revealed hyperemic, edematous colonic mucosa and pseudopolyps, and exudative ulcers were also detected. Barium enema showed whole colonic involvement, with mucosal irregularity and luminal constriction. Total colectomy was performed regarding frequent attacks of the disease and acute and chronic complications that could be seen in the course of the disease, such as thrombotic events or colonic carcinoma. Pathology showed ulcerative colitis and whole colonic involvement. Low-molecular-weight heparin was continued during and 1 month after the operation. Last visit was performed 6 years after the operation. His stool frequency is in normal limits, and he has no symptom of the disease itself or thrombotic event without any treatment.

DISCUSSION

Here, we reported a young man with uncontrolled active ulcerative colitis and finger necrosis due to digital arterial thrombosis. However, it was too late to save the fingers; we think that low-molecular-weight heparin treatment protected the extension and recurrence of the thrombotic event. Arterial thrombotic events are rarely seen and might be related with the activity of the disease. Underlying mechanisms are not clear, and thrombosis might also play role in the pathogenesis of UC.

Inflammatory bowel diseases (IBDs) are disorders with unknown etiology. The etiopathogenesis of thrombotic events related with

IBD is widely debated, and coagulation alterations and fibrinolysis have been suggested to play the major role in this process (4). But, the mechanisms may be more complicated, because no certain factor has been found. These complications are also attributed to the physiopathology of the inflammatory bowel disease itself, and the frequency of thromboembolic complications are thought to be related with the activity of the disease (4). Souto et al. (5) showed that microthrombosis of the intestinal capillaries might be a decisive factor in the pathogenesis of IBD.

The pathogenesis of thrombosis due to UC is not well known, and many factors are implicated, such as elevated fibrinogen, increased platelet counts, decreased antithrombin III, diminished fibrinolysis, increased F VIII, activated protein C resistance, diminished thrombomodulin, elevated homocysteine levels, and increased PA-I (2-4,6). Even thromboembolic events are rare in the course of the disease; arterial thrombotic events are less frequent (6-8). It is a severe, life-threatening condition and the third most frequent cause of death for UC patients. Arterial thrombotic events are usually observed in UC patients after surgical procedures (2). Surgery-unrelated arterial thrombotic conditions are observed less frequently. Thromboses have been reported in the brachial, radial, femoral, popliteal, subclavian, ulnar, carotid, retinal, axillary, renal, iliac and intracerebral, glans penis, and coronary arteries and aorta previously (2,6,7,9-11). Talbot et al. (2) reported a case of Crohn's disease with digital arterial thrombosis after a surgical procedure.

There is no doubt that arterial thrombosis is a severe complication of UC, and it is difficult to treat. There is no consensus for the treatment regimen. There are no reports or studies about the superiority of a treatment protocol. It has been shown that patients who have inherited disorders of coagulation, like von Willebrand's disease or hemophilia, are at lower risk of IBD, and they seemed to be protecting factors from IBD (12). This situation and other procoagulant markers that were shown to play a role during the course of the disease may be a torch for the prevention or treatment of thrombotic complications. These thrombotic events generally recur, and treatment approach may change according to the localization and extension of thrombosis (6). Mikroulis et al. (9) reported the benefit of resection of the colon after arterial thrombosis as prophylaxis for recurrent thrombotic events. Though surgical procedure is suggested, medical anticoagulant treatment is generally necessary. Long-term anticoagulant therapy for the possibility of serious arterial thrombosis in the active period of the IBD is discussed for the risk versus benefit (6). Talbot et al. (2) reported that IBD patients have risk of thrombotic complications confined to severe disease or surgical procedure. Subcutaneous administration of conventional heparin seemed appropriate for these patients; even their patients had recurrent thromboembolic complications despite medical therapy. Oral anticoagulants are associated with the risk of hemorrhage, especially in the long-term treatment. We used nadroparin calcium (Fraxiparine, Glaxo Smith Kline, Brentford, United Kingdom) for the prevention of

new thrombosis, and recurrent thrombotic events were not seen by the following time. During the treatment of IBD with standard agents, like 5-amino-salicylate, sulfapyridine, mesalazine, corticosteroids, and other Immunosuppressive agents, we the clinicians must evaluate the severity of the disease for anticoagulant treatment, as the thrombotic events may already be present or might occur during the course of the disease.

In conclusion, arterial thrombotic events, which are a rare but severe complication of IBD, might be seen in digital arteries and present as gangrenous fingers. We must be aware of this situation, especially in young and severely ill, active IBD patients. However, it was too late for our patient to save the fingers from amputation; by low-molecular-weight heparin treatment, he has been protected from a new attack of thrombosis. During the follow-up of IBD, suspicion of a probable thrombotic event will give the chance of early diagnosis and anticoagulant treatment and save patients from high morbidity and mortality. Though a routine approach for this situation is not clear, consideration should be given to heparin, low-molecular-weight heparin, or other medical choices for the treatment or prevention of thrombotic events. Since postsurgical risk of a new thrombotic process exists, a thrombotic event is still an indication for colectomy. Further studies are needed to reach a consensus for the treatment of this troubling complication.

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