Lower Extremity Arterial Occlusions in Association with Crohn's Disease: Case Report

Crohn Hastalığı ile Alt Ekstremite Arteryel Oklüzyonlarının Birlikteliği

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ABSTRACT Arterial thrombosis which is rarely described in patients with inflammatory bowel disease (IBD), and its etiology is still unknown. We are reporting two female cases with arterial thrombosis who had Crohn Disease. The first case was presented with signs of embolism into her right foot. A thrombectomy was performed but ischemia extended. Eventually the right leg was amputated just above the knee. The second case was a 35-year-old woman who was presented with iliac mural thrombi as a source of arterial embolization in the left leg resulting in digital amputation in spite of medical treatment. We conclude that antithrombotic prophylaxy is mandatory in patients with IBD whether the patient is in remission or not.

Key Words: Crohn disease; arterial occlusive diseases

ÖZET İnflamatuar barsak hastalığı (İBH) ile ilişkili arteryel tromboz nadir olarak tanımlanmış olup etiyolojisi halen tam bilinmemektedir. Çalışmada Crohn hastalığı tanısı olan iki kadın hastada arteryel tromboz antitesi sunulmuştur. İlk hasta sağ alt ekstremitede olan akut arteryel tromboz ile başvurmuş olup yapılan trombektomiye rağmen iskemi ilerlemiştir ve diz üstü amputasyon yapılmıştır. Otuzbeş yaşındaki ikinci vaka ise iliyak kaynaklı sol alt ekstremite arteryel embolisi nedeniyle hastaneye yatırılmış ve medikal tedaviye rağmen sol ayak parmakları seviyesinden amputasyon yapılmıştır. İBH'lı hastalarda, hastalık remisyonda olsun ya da olmasın tromboembolik komplikasyonlar açısından proflaksi uygulanmasının yararlı olabileceği kanısındayız.

Anahtar Kelimeler: Crohn hastalığı; arteriyel oklüzif hastalıklar

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Thromboses of arterial and venous systems are well-recognized during the course of patients with inflammatory bowel disease (IBD). The mechanism of thrombosis is not clear and these complications are the major cause of mortality and morbidity.[1] Although, arterial complications are less encountered, it is frequently associated with Crohn's disease (CD).[2]

In this report, we are presenting two CD patients with arterial occlusions in their lower extremities and superficial femoral arteries due to extensive thrombosis which were complicated with limb and toe amputations. The aim of this report is to emphasize the importance of anticoagulation

prophylaxis in patients with CD and discuss possible coagulation mechanisms which are responsible for the etiology of thrombosis.

CASE REPORTS

CASE 1

54-year-old female nonsmoker patient applied to the emergency department with the complaints of rest pain, pallor and coldness in the right foot. On her physical examination; drop foot was seen in her right limb. Pulses of the right popliteal artery and to its distal were not palpable. Ankle brachial index was measured to be 0.86 on the left and 0.1 on the right foot. Emergent digital subtraction angiography demonstrated diminished diameters of the right superficial and deep femoral arteries, total occlusion of the right superficial artery just before the Hunter channel and weak filling of the distal vessels (Figure 1 a, b). There was no clinical or angiographic support showing any relation with the etiology of atherosclerosis or arteritis. Her hematological parameters were within normal limits, except for the hemoglobin value which was 9.7 g/dl and hematocrit was 34.3%. Detailed coagulation system analysis was made and shortened activated partial thromboplastin time (15.6 second), increased blood fibrinogen level (584 mg/dl) and diminished protein S activity were found. Normal values of the erythrocyte sedimentation rate, leukocytes and CRP levels were thought to be in conjunction with the remission status of the disease. Four months ago, she had the definite diagnosis of CD and she was under the treatment of mesalazin (3 x 400 mg/day) and prednisolone 20 mg/day however was taking neither anticoagulant nor antiaggregant therapy. Low molecular weight heparin (LMWH) was started and emergent operation was performed. Popliteal artery was explored and thrombus was palpated inside the artery. Approximately 1-2 cm^3 in volume old thrombotic material was evacuated with transverse arteriotomy. Fogarty catheter could not be advanced more than 10 cm to the proximal or to the distal. Forward flow and back flow could not be achieved. Distal back flow was found extremely insufficient. Operation was terminated and intravenous iloprost was started with the dosage set to1 ng/kg/h. Embolic origin could not be documented

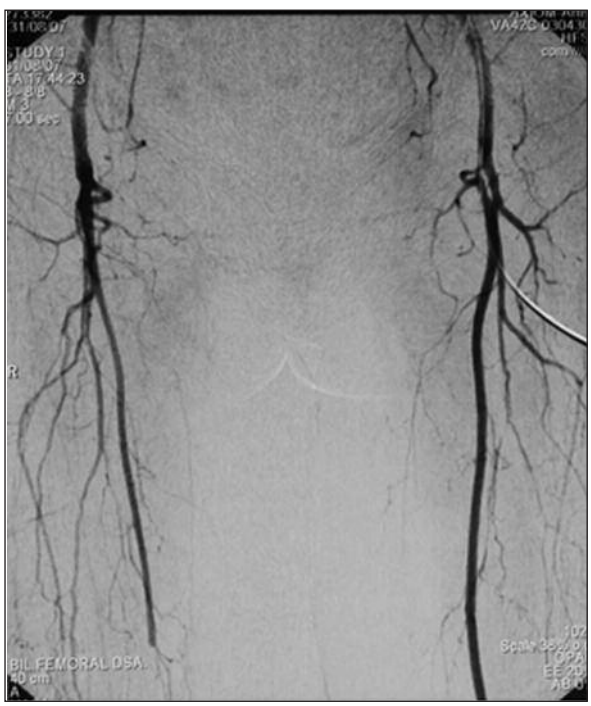

FIGURE 1a: Angiography of diminished diameters of the right superficial and deep femoral artery and total occlusion of the right superficial artery.

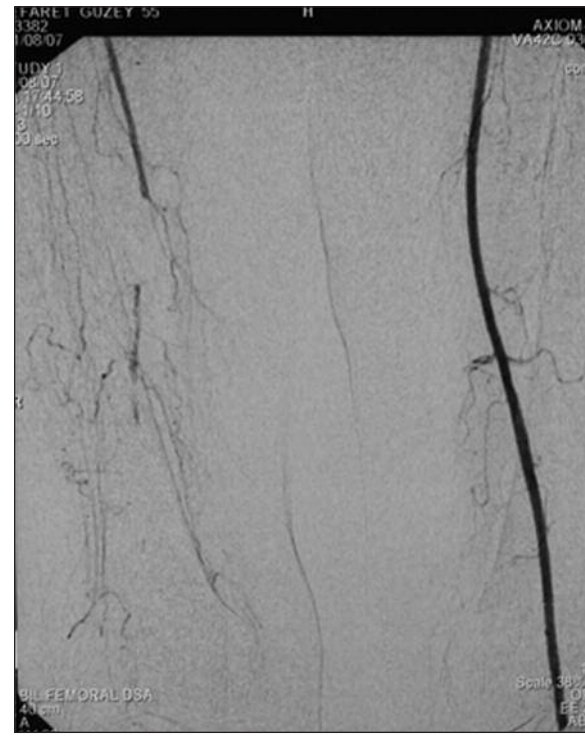

FIGURE 1b: Angiography showing the weak distal run off of the right leg.

in the postoperative detailed examination of the patient. Right leg ischemia extended just above the knee level under the treatment of LMWH and iloprost. Leg amputation over the knee was performed and her postoperative course was uneventful. The patient was discharged after anticoagulation with warfarin 35 mg/week and the level of INR was adjusted to be between 2-3. The patient was readmitted to the hospital with the complaints of extensive petechias. Her INR level was found to be high, so warfarin treatment was stopped and combination of aspirin and clopidogrel was started. The follow up of the patient after two months was uneventful.

CASE 2

Thirty five year old female patient with the smoking habit (1 package/day) admitted to the emergency department with the complaints of rest pain, coldness and discoloration of the left leg and necrosis at the tip of the toe. She was hospitalizied in the cardiovascular surgery ward. On her examination, pulses of the anterior and posterior tibial arteries of the left leg were not palpable. Doppler ultrasonography demonstrated monophasic flow pattern in the anterior tibial artery and occlusion of the posterior tibial artery. Digital substraction angiography showed thrombus formation partially occluding the common iliac artery and occlusion of the one third distal of the anterior tibial artery, total occlusion of the posterior tibial artery and occlusion of the one third of the peroneal artery. Symptoms of the patients relived gradually after ten days with the treatment of heparin and iloprost. Control digital substraction angiography showed disappearance of the thrombus located inside the left common iliac artery. Hematological values were in normal range. There were no any other laboratory values that could be attributed for a tendency to coagulation or activation of the disease. Diagnosis of CD in this patient was made eight months ago and she was on a medical therapy with mesalazin (3 x 400 mg/d) and prednisolone 20 mg/d. Warfarin was added to the present medication of the clinically healed patient and was discharged after the arrangement of INR values to be between 2 and 3. In the follow-up period, left toe necrosis was demarcated and resulted in amputation.

DISCUSSION

Ocular, thromboembolic and hepatobiliary complications are the most common extraintestinal complications of IBD.[3]

Thromboembolic complications are associated with IBD in an incidence of 1.2-7.4% but this rate reaches to much higher frequencies of 39% in autopsy study reports.[1] Follow-up problems of the cases and asymptomatic course of the deep venous thromboses are the main reason of this distinction. Arterial thromboembolic complications are encountered much less frequent. These events may involve the aorta, mesenteric arteries, cerebral arteries and the arteries of the upper and lower extremities.[2,4-6] Accepted rule in the ethiology of thrombogenesis is stasis, injury of the vessel wall and changes in the coagulation system. Fluid loss of patients in the acute period of the IBD, obligatory sedentary life style, and usage of corticosteroids and moreover inevitable intraabdominal interventions for some of the patients in spite of the medical therapy are the reasons that may be helpful to explain the thromboembolic complications of the venous system.[1-7] One of the prospective studies from England showed that IBD, surgery and usage of oral corticosteroids are the independent risk factors for deep venous thrombosis and pulmonary embolism.[8] Intimal injury and/or embolic origin are the foreground for such complications in the arterial system. While, Levy and colleagues found a premature atherosclerosis at the aorta and its distal part in patients with CD who were corticosteroid treatment dependent, in contrary to this, literature demonstrated that atherosclerosis was observed only in one of thirteen patients with CD and thrombus could not be excluded in the others.[2,4] It means that limited number of intimal injury was found clinically and these cases also have cardiovascular risk factors. It could not be explained clearly whether these atherosclerotic changes are related to the IBD or cardiovascular risk factors. Occurrence of the atherosclerotic obstruction in young ages in six cases of Levy et al.

makes us think that IBD may provoke development of the atherosclerotic process.[2] Arteritis or atherosclerotic alterations could not be observed in the pathological assessment of the cases with the occlusion of the aorta and/or its branches in the other reported studies.[4-7] Coagulation abnormalities are being questioned in these conditions. Increased production of thromboplastin, increased levels of anticardiolipin antibodies, factor-V, factor-VIII and fibrinogen were found in patients with IBD. It is reported that low concentration of antithrombin III, thrombositosis, shortened life-span of platelets and self platelet aggregation may cause coagulation abnormalities.[1] However, Novacek and colleagues ascertained antithrombin level decrease in one and increase of anticardiolipin levels in two among 12 cases with IBD with aortic mural thrombus.[4] Again, coagulation abnormalities could not have been detected in a female patient who had thrombotic occlusion of the superior mesenteric artery and celiac artery and in another male patient with internal carotid artery occlusion who both had IBD.[5,6] It is conspicuous that most of the patients were in the active period of the disease, under the treatment of oral corticosteroids and ceased smoking. Risk factors could not be observed only in one case with mesenteric artery occlusion.[6] Our two cases were found in remission during the admission to the hospital. Increased fibrinogen level and decreased protein S activation were detected in the first case who was under the treatment of oral steroids. Platelets, factor V and VIII and fibrinogen are the acute phase reactants and their levels might be increased by tissue injury and inflammation. On the other hand, it is known that protein S inhibits coagulation by deactivating factor V and VIII after being activated (Levels of plasminogen activators in the circulation are increasing).[1] Because of this, decreased activation of protein S increases the risk of thrombosis. Protein S activation was dropped down to 20.1%. High levels of fibrinogen and low levels of protein S activation would be helpful for the explanation of the thromboembolic complications in this case; therefore these pathological values might be a cause for such a complication in the basis of CD. Smoking and steroid treatment were the detectable risk factors in our second case. It is shown that smoking causes microthromboembolies by damaging the endothelial cells morphologically, impairing the synthesis of prostaglandins and increases aggregation capacity of the platelets. It is understood that disease often becomes active in smoking CD patients and necessity for surgery is increased. There is a close relation between the smoking induced focal thrombosis and the activation of CD.[6] Obstruction of the iliac artery and its distal branches with thrombosis might be started in such a condition and later on might have become a chronic process. In the light of all these findings, it is possible to say that unknown risk factors trigger coagulation cascade and causes such complications.

We recommend that all patients with IBD whether they are in remission or not should be put on treatments concerning thromboembolic complications.

REFERENCES

1. Koenigs KP, McPhedran P, Spiro HM. Thrombosis in inflammatory bowel disease. J Clin Gastroenterol 1987;9(6):627-31.
2. Levy PJ, Tabares AH, Olin JW. Lower extremity arterial occlusions in young patients with Crohn's colitis and premature atherosclerosis: report of six cases. Am J Gastroenterol 1997;92(3):494-7.
3. Süleymanlar İ. [Complications developing during the course of inflammatory bowel disease: diagnosis and treatment]. Turkiye Klinikleri J Surg Med Sci 2006;2(15):73-80.
4. Novacek G, Haumer M, Schima W, Müller C, Miehsler W, Polterauer P, et al. Aortic mural thrombi in patients with inflammatory bowel disease: report of two cases and review of the literature. Inflamm Bowel Dis 2004;10(4):430-5.
5. Prior A, Strang FA, Whorwell PJ. Internal carotid artery occlusion in association with Crohn's disease. Dig Dis Sci 1987;32(9):1047-50.
6. Sanghavi P, Paramesh A, Dwivedi A, Markova T, Phan T. Mesenteric arterial thrombosis as a complication of Crohn's disease. Dig Dis Sci 2001;46(11):2344-6.
7. Paradis K, Bernstein ML, Adelson JW. Thrombosis as a complication of inflammatory bowel disease in children: a report of four cases. J Pediatr Gastroenterol Nutr 1985;4(4):659-62.
8. Huerta C, Johansson S, Wallander MA, García Rodríguez LA. Risk factors and short-term mortality of venous thromboembolism diagnosed in the primary care setting in the United Kingdom. Arch Intern Med 2007;167(9):935-43.