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Ulcerative Colitis and Limb Loss: A Case Report

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Introduction: Protein C is a precursor of a vitamin K-dependent serine protease, which is activated by thrombin in the presence of endothelial cofactor, thrombomodulin and endothelial cell protein C receptor.
Case Presentation: A 33-year old woman with acute exacerbation of ulcerative colitis was found to have protein C deficiency (serum protein C activity estimated as 35% of the normal activity). Protein C deficiency was diagnosed after the onset of several arterial thromboemboli complications (brachiocephalic and popliteal artery thrombosis) during her hospital admission for exacerbation of ulcerative colitis (UC). Therefore, upper limb below elbow and lower limb below knee amputation were performed for her.
Conclusions: After total proctocolectomy, serum protein C activity remained as 35% of the normal activity, so the patient used warfarin as lifelong anticoagulant. Investigation of other family members revealed normal thrombophilia screening tests.

Keywords:Thrombophilia; *Thromboembolism, Protein C Deficiency*; *Colitis, Ulcerative*

1. Introduction

Protein C is a precursor of a vitamin K-dependent serine protease, which is activated by thrombin in the presence of endothelial cofactor, thrombomodulin and endothelial cell protein C receptor (1-5). To our knowledge, peripheral limb amputation due to protein C deficiency in acute ulcerative colitis (UC) has not been reported in the literature before. The only established treatment for patients with thrombotic complication is heparin therapy followed by life-long warfarin. However, where it is caused by acute ulcerative colitis, management would be removal of the inflamed mucosa by surgery to remove its predisposing factors. It is well known that proteins C and/or S deficiencies cause recurrent venous thrombotic events (6-11). However, the role of protein C and/or S deficiency in patients with peripheral arterial insufficiency and acute UC has not yet been reported to the best of our knowledge.

2. Case Presentation

A 33-year old woman, known case of ulcerative colitis since 1997, teacher and non-smoker, was presented in April 2007 with a history of severe right lower extremity claudication, and inability to bear weight for three days. The patient underwent fogarty embolectomy because of acute arterial insufficiency in lower extremity in a primary public hospital without any improvement, then she was transferred to our center. On admission, the patient had severe pain, coldness, paresthesia, cyanosis in right lower extremity and inability to move her toes. She had no past medical or family history of blood dyscrasia. In physical examination, the patient was uncomfortable and pale. She was tachycardic (pulse rate = 105 beats/min) and febrile (37.9 °C), right leg was cyanotic and cold and peripheral pulses were not palpable below the right knee. All muscles below the knee were paralyzed. Intravenous heparin and antibiotic were administered. Hematological investigation showed leukocytosis (24000), anemia (Hb = 7/5 g/dL) and normal platelet count. Serum urea and electrolytes had normal findings. Echocardiogram and EKG had normal findings. Color Doppler ultrasound of lower extremities showed complete occlusion of the right popliteal artery without flow in the distal part. To manage her leg gangrene, right below knee amputation was performed. During her heparin therapy, she developed symptoms and signs of left forearm ischemia. After brachial angiography demonstrated complete brachial artery occlusion with no response to embolectomy and intravascular dosage of heparin subsequently, left below elbow amputation was performed. Thrombophilia screening was performed and revealed protein C/S deficiency (35% and 48% of the normal levels). Other tests had normal results. Finally, the patient was discharged with warfarin as a life-long anticoagulation therapy. Protein C level remained 35% of the normal level, but protein S

Implication for health policy/practice/research/medical education:
Protein C and S deficiencies can be a consequence of UC leading to peripheral arterial thrombosis. Proper management of UC may reduce the risk of such complications. This article could be helpful for vascular surgeons, colorectal surgeons, gastroenterologists, and hematologists.

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normalized 5 months after total proctocolectomy as the management of colitis. After the operation, histological examination of the resected colon confirmed active ulcerative colitis. The patient recovered well and was discharged on warfarin. The last visit of the patient was one year after proctocolectomy.

3. Discussion

Thromboembolic events are well recognized complications in inflammatory bowel disease which can be arterial or venous type (4-8). While deep vein thrombosis (DVT) and pulmonary embolism (PE) are most common thromboembolic complications in patients with inflammatory bowel disease, arterial thromboembolism in mesenteric vasculature and cerebral arteries can also occur. Thromboembolic complications are not fully understood, and only sporadic cases of arterial thromboemboli have been reported. Arterial thromboembolic complications in patients with ulcerative colitis are usually associated with pancolitis (12, 13) among several conditions leading to a hypercoagulable state in acute UC; proteins C and S deficiencies are the most common causes (1-11). The term hypercoagulable state is generally used for any condition in which the normal balance between coagulation and anticoagulation mechanisms is changed in such a way that patient is predisposed to thrombus formation (13). Protein C and S deficiencies can be congenital or acquired. Congenital form is inherited as an autosomal dominant disease and has two forms: homozygote and heterozygote. Homozygous deficiency of protein C is associated with life threatening thrombotic events in neonatal period, whereas in patients with heterozygous deficiency, protein C levels are less than 60% of the normal value, and they are at a higher risk for venous thrombosis later in their life (late teens and twenties) (3-9). Thrombotic episodes are also aggravated by other factors, such as trauma, childbirth, puerperium, surgical interventions and infections (13). Because both proteins C and S are produced in the liver, acquired deficiencies are usually associated with conditions that interfere with the liver function. The typical clinical manifestations of protein C/S deficiencies include superficial and deep leg veins thrombosis, thrombosis of the mesenterial, cerebral, renal and axillary veins, portal vein thrombosis and pulmonary embolism. To our knowledge, this is the first report of a case with UC leading to upper and lower limbs amputation due to protein C deficiency. However, Oda et al. reported a case of ulcerative colitis with arterial thrombosis which underwent bilateral lower limb amputation due to hypercoagulable state with normal protein C and S (12) levels. Protein C and S deficiencies can be a consequence of UC leading peripheral arterial thrombosis. Therefore, proper management of UC may reduce the risk of such complications.

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Authors' Contribution

Leila Ghahramani: writing the manuscript, and final approval; Abbas Rezaianzadeh: analyzing and interpretation of data, and revising the manuscript for intellectual content; Sam Moslemi and Salar Rahimikazerouni: writing the manuscript, and final approval; Seyed Vahid Hosseini: revising the manuscript for intellectual content, and final approval.

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References

1. Lane DA, Mannucci PM, Bauer KA, Bertina RM, Bochkov NP, Boulyjenkov V, et al. Inherited thrombophilia: Part 1. *Thromb Haemost.* 1996;**76**(5):651–62.
2. Lane DA, Mannucci PM, Bauer KA, Bertina RM, Bochkov NP, Boulyjenkov V, et al. Inherited thrombophilia: Part 2. *Thromb Haemost.* 1996;**76**(6):824–34.
3. Eldrup-Jorgensen J, Flanigan DP, Brace L, Sawchuk AP, Mulder SG, Anderson CP, et al. Hypercoagulable states and lower limb ischemia in young adults. *J Vasc Surg.* 1989;**9**(2):334–41.
4. De Stefano V, Finazzi G, Mannucci PM. Inherited thrombophilia: pathogenesis, clinical syndromes, and management. *Blood.* 1996;**87**(9):3531–44.
5. Allaart CF, Poort SR, Rosendaal FR, Reitsma PH, Bertina RM, Briet E. Increased risk of venous thrombosis in carriers of hereditary protein C deficiency defect. *Lancet.* 1993;**341**(8838):134–8.
6. Sakata T, Kario K, Katayama Y, Matsuyama T, Kato H, Miyata T. Studies on congenital protein C deficiency in Japanese: prevalence, genetic analysis, and relevance to the onset of arterial occlusive diseases. *Semin Thromb Hemost.* 2000;**26**(1):11–6.
7. Sakata T, Kario K, Katayama Y, Matsuyama T, Kato H, Miyata T. Analysis of 45 episodes of arterial occlusive disease in Japanese patients with congenital protein C deficiency. *Thromb Res.* 1999;**94**(2):69–78.
8. De Stefano V, Leone G, Mastrangelo S, Tripodi A, Rodeghiero F, Castaman G, et al. Clinical manifestations and management of inherited thrombophilia: retrospective analysis and follow-up after diagnosis of 238 patients with congenital deficiency of antithrombin III, protein C, protein S. *Thromb Haemost.* 1994;**72**(3):352–8.
9. Clouse LH, Comp PC. The regulation of hemostasis: the protein C system. *N Engl J Med.* 1986;**314**(20):1298–304.
10. Cho YP, Lee DH, Jang HJ, Kim JS, Han MS, Lee SG. Peripheral arterial insufficiency associated with protein C deficiency. *Br J Radiol.* 2002;**75**(898):843–6.
11. Cho YP, Jang HJ, Lee DH, Ahn J, Han MS, Kim JS, et al. Deep venous thrombosis associated with protein C and/or S deficiency: management with catheter-directed thrombolysis. *Br J Radiol.* 2003;**76**(906):380–4.
12. Oda K, Seo M, Okada M, Yamamoto T, Okumura M, Onimura S, et al. [Ulcerative colitis with arterial thrombosis resulting in lower limb amputation, a report of case]. *Nihon Shokakibyo Gakkai Zasshi.* 1994;**91**(7):1234–40.
13. Rabl H, Fruhwirth H. [The clinical importance of protein C and S deficiency for surgical patients]. *Langenbecks Arch Chir.* 1992;**377**(2):75–80.