CASE REPORT

Thrombophilia-related lower limb venous ulceration: A case report

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Ekim M, Kim H. Thrombophilia-related lower limb venous ulceration: A case report. Pulsus J Surg Res. 2018;2(2):76-77.

Venous ulceration is an important disorder affecting about 1% of the adult population and is associated with a significant reduction in quality of life. Post-thrombotic syndrome is a well-known risk factor for leg ulcerations. Approximately 40%-60% of patients with Deep Venous Thrombosis (DVT) suffer from post-thrombotic syndrome; about 10% of them develop venous leg ulceration. Factor V Leiden (FVL) mutation is considered a well-established risk factor for venous thrombosis. Patients with DVT and thrombophilic risk factors have an increased risk of post-thrombotic syndrome because DVT occurs earlier in life and is often recurrent and extensive. More than 40% of patients with chronic venous ulceration have at least one thrombophilic risk factor. FVL mutation was reported to be more frequent in patients with venous leg ulceration than control subjects. We report a 46-year-old male patient with thrombosed varicose veins and venous skin ulceration around the left internal malleolus. His medical history included DVT about 3 years ago. The heterozygous FVL mutation was detected. His venous leg ulceration improved with a combination of venoactive drug therapy and four-layer compression dressings.

Keywords: Venous ulceration; Thrombophilia; FVL

INTRODUCTION

Venous ulceration is an important disorder affecting about 1% of the adult population and is associated with a significant reduction in quality of life [1]. Deep Venous Thrombosis (DVT) is the most common cause of venous leg ulcerations that constitute about 60% of cases [2]. Thrombophilia can be described as an abnormality of the coagulation or fibrinolytic system, which leads to hypercoagulability [3]. It has been reported that hypercoagulable states are associated with the development of lower extremity venous ulceration [4]. Thrombophilia may provide a basis for the development of superficial and deep lower extremity venous reflux as a consequence of macrovascular thromboembolic diseases [5]. Thus, thrombophilia may contribute to the pathogenesis of chronic venous ulceration [5]. Factor V Leiden (FVL) mutation in patients with chronic or recurrent chronic venous ulceration has been suggested to be the most common inherited thrombophilic risk factor [6]. It has been reported that if a patient has venous ulceration in the lower limb and a thromboembolic event occurs before the age of 50 years, the FVL mutation should be investigated [7].

CASE REPORT

We report a 46-year-old male patient with thrombosed varicose veins and venous skin ulceration around the left internal malleolus. His complaints were swelling, pain and skin ulceration in the left lower extremity. The edges of the ulceration were irregular (Figure 1). The skin surrounding the ulcer was dark colored due to hemosiderin staining. Physical examination findings were normal except venous insufficiency and ulceration findings. The results of liver and kidney function tests were normal. Homocysteine, vitamin B12, and folic acid levels were found to be normal. Venous Doppler examination of the left lower limb revealed venous reflux and thrombosed varicose veins. His medical history included DVT about 3 years ago. The heterozygous FVL mutation was detected. His venous leg ulceration improved with a combination of venoactive drug therapy and four-layer compression dressings.

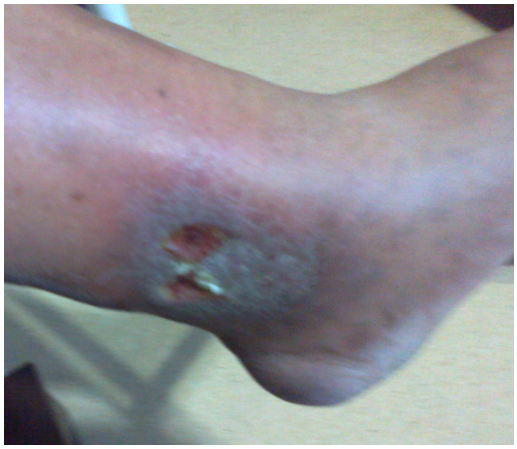

Figure 1 Venous skin ulceration around the internal malleolus.

DISCUSSION

Venous ulceration is one of the most serious complications of Post-Thrombotic Syndrome (PTS) [3]. PTS, a chronic complication of DVT, manifests itself with various symptoms and signs of chronic venous insufficiency. In 5% to 10% of cases, a severe PTS pattern may occur which decreases the quality of life and manifests itself as a venous ulceration [8]. Post-thrombotic syndrome is a well-known risk factor for leg ulcerations. Forty to sixty percent of patients with DVT suffer from post-thrombotic syndrome; about 10% of them develop venous leg ulceration [9]. Patients with DVT and thrombophilic risk factors have an increased risk of post-thrombotic syndrome because DVT occurs earlier in life and is often recurrent and extensive [10].

Venous ulceration is the last stage of the complex of symptoms of chronic venous insufficiency [3]. However, many patients with venous insufficiency will not develop skin ulcers, suggesting that additional factors may play a role in the pathogenesis of venous skin ulcers [4]. It has been suggested that chronic venous ulceration occurs earlier, is more

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Received: October 31, 2018, Accepted: December 03, 2018, Published: December 21, 2018

difficult to heal, and relapses more often in patients with hereditary thrombophilic risk factor compared with those without these risk factors [6].

Dahlback et al [11] identified a previously unrecognized mechanism for thromboembolism that is characterized by poor anticoagulant response to Activated Protein C (APC) due to a polymorphism of factor V (FV), in which glutamine replaces arginine, so cleavage of factor V by APC is inhibited [12]. Bertina et al. [13] showed that the phenotype of the APCR is associated with a heterozygous or homozygous single point mutation in the factor V gene (at nucleotide position 1,691, G→A substitution) which predicts the synthesis of a factor V molecule (FV Q506, or FV Leiden) that is not properly inactivated by APC. This mutant FV molecule, called factor V Leiden (FVL), also known as factor V Q506 or Arg506Gln, is named after the city in the Holland where it was first identified [14]. FVL mutation was found to be higher in patients with DVT in Turkish population (41.47%) [15].

More than 40% of patients with chronic venous ulceration have at least one thrombophilic risk factor [16]. FVL mutation was reported to be more frequent in patients with venous leg ulceration than control subjects [3,9]. This mutation is considered a well-established risk factor for venous thrombosis and ulceration [2].

CONCLUSION

FVL mutation should be investigated in patients with venous ulceration resulting from venous insufficiency associated with DVT. These patients should be monitored closely to prevent DVT recurrences leading to venous ulceration.

ACKNOWLEDGMENT

This study was supported by a grant from Bozok University, The Directorate of Scientific Research Projects (6602c-TF/16-24).

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