**CLINICAL VIGNETTE**

# Thirty-two Year-old Healthy Female with Sudden Onset of Chest Pain While Running: A Rare Case of Myocardial Infarction Associated with Protein-C Deficiency

**Ramtin Anousheh, M.D., MPH; Ramona Mehrinfar-zadeh, M.D.; and Ravi H. Dave, M.D.**

***Abstract***

Inherited thrombophilia has a well-documented role in the pathogenesis of venous thromboembolism (VTE) and pregnancy loss, but its role in development of arterial thrombosis has been subject to controversy due to lack of quality data. We report a case of myocardial infarction in a young healthy individual with confirmed diagnosis of protein-c deficiency.

***Case Presentation***

A 32-year-old healthy active female with unremarkable past medical history on oral contraceptives developed sudden onset of severe chest pain while running. She was taken to the hospital and initial work up revealed abnormal troponin levels confirming diagnosis of non-ST elevation myocardial infarction. Subsequently, she underwent coronary angiography, which was notable for thrombotic occlusion of a small obtuse marginal branch of the circumflex artery; no percutaneous intervention was performed. Transthoracic echocardiography showed preserved LV systolic function without evidence of patent foramen ovale (PFO). She was discharged on antithrombotic therapy and statin and was instructed to stop oral contraceptives. She was then referred to hematology service for thrombophilia work up, which revealed a reduced Protein C plasma levels. She has been treated with antithrombotic therapy and has not had any further events.

***Discussion***

Protein C is a vitamin K-dependent glycoprotein synthesized in an inactive form in the liver. It exerts its anticoagulant function after activation to activated protein C (aPC) by thrombomodulin-bound thrombin. The cardinal role of aPC is inactivation of coagulation factors Va and VIIIa, which will then prohibit production of thrombin and activation of factor X.[1] The inhibitory effect of aPC is enhanced by protein S which is also produced in the liver and is vitamin K-dependent.[1,2]

Hereditary protein C deficiency is subdivided into type I (reduced protein levels) or type II (reduced protein function) without apparent difference in clinical presentation among these sub-groups.[3] It is transmitted as an autosomal dominant disorder; homozygous deficiency can result in purpura Fulminans, which is a rare, life threatening condition with extensive venous thromboembolism and disseminated intravascular coagulation (DIC) in newborns. On the other hand, heterozygous Protein-C deficiency that is confirmed by low plasma level alone is found in 1 in 200 to 1 in 500 persons in the general population–many of whom will remain asymptomatic throughout life. The primary clinical manifestation of this disease is venous thromboembolism of any venous site with the thrombosis in the deep veins of the leg (DVT), mesenteric veins, and pulmonary embolism (PE) being the most common. Approximately 2 to 5 percent of individuals with venous thromboembolism will have inherited protein C deficiency.[3]

Arterial thrombosis including stroke, myocardial infarction, and peripheral arterial thrombosis in young heterozygote adults with protein C deficiency have been previously reported but high quality data to support an association are unavailable.[4-8] Among reported cases of patients with myocardial infarction who underwent coronary angiography almost all had normal coronary anatomy without any evidence of underlying coronary atherosclerosis. Our patient also did not have any major risk factors for coronary artery disease suggesting that protein c deficiency was most likely explanation for thrombotic occlusion in her coronary tree.[4-8]

The diagnosis of protein C deficiency should be suspected in a patient with venous thrombosis of an unusual vascular bed, young otherwise healthy adults with arterial or recurrent venous thrombosis, strong family history of venous thromboembolism (VTE), and warfarin-induced skin necrosis. In these clinical settings, the diagnosis can be established after the patient has recovered from an acute event such as an acute thrombosis or severe inflammatory illness by obtaining laboratory evidence of low protein C levels. The preferred method of diagnosis is a functional assay that can detect both reduced protein levels and decreased function with normal protein levels (type I and type II defects respectively). In case of our patient, the testing was done 4 months after the initial event off of anticoagulation therapy by a functional assay.[9-10]

Acquired risk factors for VTE should also be taken into consideration before subjecting patients to lifelong anticoagulation therapy. These risk factors include pregnancy,

recent surgery, prolonged immobility cancer, trauma, auto-immune disorders such as antiphospholipid syndrome and paroxysmal nocturnal hemoglobinuria (PNH), and drugs such as hormonal contraceptives. Our patient was on OCPs at the time of the event, but the diagnosis was confirmed 4 months after she stopped oral contraception.

Anticoagulation is the cornerstone of therapy for individuals with protein C deficiency who develop a thromboembolic event. Many patients will receive indefinite anticoagulation, but without quality outcome data, the duration of therapy should be individualized according to the age and characteristics of the thromboembolic event such as site and whether the thromboembolism was provoked or unprovoked.[2]

Warfarin therapy has been the traditional drug of choice, but special measures should be followed to reduce the risk of warfarin-induced skin necrosis. Direct oral anticoagulants can be used as alternate therapy although there are no reported trials that have documented their efficacy in patients with inherited thrombophilia.

The use of oral contraceptives should be discouraged in women with protein-c deficiency and other forms of hereditary thrombophilia (antithrombin deficiency, protein S deficiency, factor V Leiden and prothrombin-G20210A mutation). Pregnancy can also increase the risk of venous thromboembolism in these patients as a result of the hormonal changes and subsequent hypercoagulability that are associated with a normal pregnancy. In pregnant patients with protein-c deficiency, management should be individualized based on patient's history, risk profile, and preference. As a general rule, patients with prior history of thromboembolic events should receive antepartum and postpartum anticoagulation.

***Conclusion***

Protein-c deficiency and other inherited thrombophilia can cause arterial thrombosis such as myocardial infarction or stroke in young adults with without any underlying major risk factors for atherosclerosis and should be considered during initial work up of these patients.

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