Effective Thrombolysis with Tirofiban in young Myocardial Infarction case with FV Leiden Mutation

Islamaglu Y[1], Sezen Y[2], Aksakal E[1], Gur M[2]
[1]Department of Cardiology, Turkey, Faculty of Medicine, Ataturk University, Erzurum, Turkey. Department of [2]Cardiology, Turkey, Faculty of Medicine, Harran University, Sanliurfa, Turkey.

Abstract
A 19 year-old man presented with severe chest discomfort. The patient had electrocardiographic evidence of acute anterior-lateral wall myocardial infarction. The patient was taken to the catheterization laboratory for primary percutaneous coronary intervention. Coronary angiography revealed intraluminal filling defects due to a massive thrombus in the proximal segment of the left anterior descending coronary artery. Due to the inappropriate coronary structure and length of the thrombus, percutaneous coronary intervention was not performed. Heterozygous factor V Leiden mutation of patient was positive. Glycoprotein IIb/IIIa inhibitor tirofiban infusion was administered for 48 hours. Control coronary angiography performed at 48 hours showed complete disappearance of the intracoronary thrombus. We present a case of effective thrombolysis with tirofiban in young myocardial infarction case with factor V Leiden mutation.
Key words: Factor V Leiden, Myocardial infarction, Tirofiban
Faktör V Leiden Mutasyonu Bulunan Genç Myokard Enfarktüsünde Trombüsün Tirofiban İle Trombolizisi
Özet
19 yaşında erkek hasta şiddetli göğüs ağrısı ile başvurdu. Hastanın EKG'sinde akut anterolateral myokard enfarktüsü bulundu. Hasta primer perkutan girişim için kateterizasyon laboratuvarına alındı. Koroner anjiyografisinde LAD'nin proksimal segmentinde massif trombüs nedeniyle lümen içerisinde dolum defekti tespit edildi. Trombüsün uzunluğu ve koroner yapının uygun olmamasından dolayı perkutan koroner girişim uygulanmadı. Hastada heterozigot faktör V mutasyon vardı. Glikoprotein Iıb/IIIa inhibitörü tirofiban infüzyonu 48 saat uygulandı. 48 saat sonra kontrol koroner anjiyografi yapıldı, intrakoroner trombüsün tamamen kaybolduğu görüldü. Biz Faktör V Leiden mutasyonu bulunan genç myokard enfarktüsünde trombüsün tirofiban ile başarılı bir şekilde eridiğini gösterdik.
Anahtar Kelimeler: Faktör V Leiden, Myokard İnfarktüsü, Tirofiban

Background

Factor V (FV) Leiden is defined as a mutant factor V, which is resistant to activated protein C. Association of FV Leiden with venous thromboembolism is well established in the literature (1). Several reports have implicated FV Leiden in the development of arterial thrombosis by identifying a role for the mutation in atherosclerosis and myocardial infarction (MI) (2-3). Several cases have also reported that efficient tirofiban infusion resulted in resolution of intracoronary thrombus (4, 5). In this case report, we present a case of effective thrombolysis with tirofiban in young MI case with factor V Leiden mutation.

Case Presentation

A 19 year-old man presented with severe chest discomfort. The patient had only family history as risk factor for coronary artery disease (CAD). His blood pressure was 120/80 mmHg, and heart rate was 63 beat/min and regular. Physical examination was normal. The patient had electrocardiographic evidence of acute anterior-lateral wall MI. Laboratory analysis revealed elevated cardiac enzymes (CK, CKMB) and normal lipid parameters, blood count and chest X-ray. Medical treatment was instituted with 300 mg aspirin, 600 mg clopidogrel, intravenous nitrate, 25 mg meperidine, and low molecular weight heparin. The patient was taken to the catheterization laboratory for primary percutaneous coronary intervention. Left coronary angiography revealed intraluminal filling defects due to a massive thrombus in the proximal segment of the left anterior descending coronary artery (LAD) (Figure-1) with a Thrombolysis in Myocardial Infarction (TIMI) flow grade 2. Circumflex and right coronary arteries were normal. Due to the inappropriate coronary structure and length of the thrombus, percutaneous coronary intervention was not performed. The platelet glycoprotein IIb/IIIa (GP IIb/IIIa) inhibitor tirofiban 0.4 mg . kg^{-1} . min^{-1} bolus over 30 minutes followed by 0.1 mg . kg^{-1} . min^{-1} for 48 hours. Control coronary angiography performed at 48 hours showed complete disappearance of the intracoronary thrombus with a TIMI flow grade 3 (Figure-2). Samples were drawn before angiography for clotting time, bleeding time, protrombine time, INR, activated partial thromboplastin time, D-dimer, fibrinogen, protein C, protein S, von Willebrant factor, plasminogen activator inhibitor 1, microzomal antibody, IgG anticardiolipin antibody, IgM

anticardiolipin antibody, anti ds-DNA antibody, coagulation
factors II, V, VII, and X, and leptin levels due to the unusual age of presentation and all were normal. However, heterozygous factor V leiden mutation was positive. He was hospitalized for 6 days and he was discharged with aspirin, clopidogrel and atorvastatin and he was well on 12 month follow-up. The patient was symptom free during one year of medical therapy with aspirin, clopidogrel, and atorvastatin.

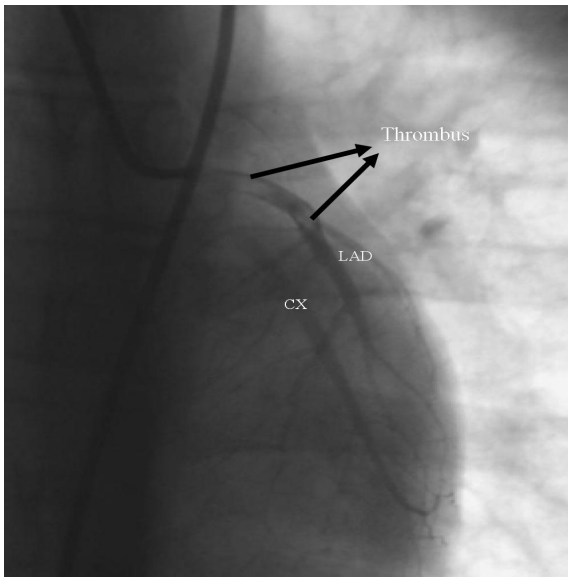

Figure-1. The left coronary angiography in the left anterior oblique view demonstrating intraluminal filling defects due to massive thrombus in the proximal segment of the left anterior descending coronary artery.

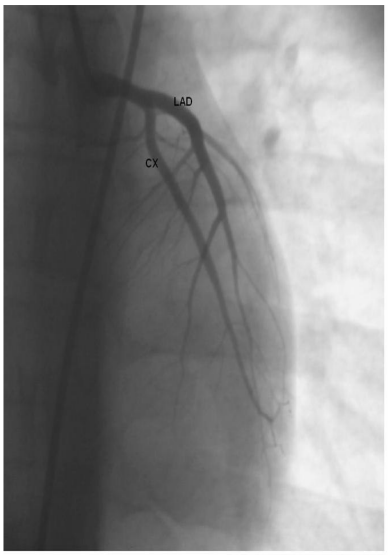

Figure- 2. Control coronary angiography performed after tirofiban infusion showing complete disappearance of the intracoronary thrombus.

Discussion

Thrombotic events may not only be critical in facilitating the occlusive process by intermittent contribution to arterial plaque growth, but also in initiating the acute manifestations of ischemia by impeding blood flow following rupture of atherosclerotic plaques (6). Thrombus formation may be directly responsible for cases of CAD by production of occlusive thrombi in the absence of atherosclerosis. Defects in the coagulation system are known to be associated with increased risk of CAD and MI and that a point mutation in the FV gene accounts for the majority of all genetically induced thrombotic events.

Factor V Leiden is known to be a common risk factor for venous thrombosis (1) but it is still debated whether this mutation is associated with arterial thromboembolism. Several investigators found a significant association between factor V Leiden and CAD (2, 3, 7), whereas other studies reported no association of APC resistance or factor V Leiden with CAD (8, 9). Rosendaal et al. (7) showed a relatively high prevalence of the factor V Leiden mutation in young female smokers who had suffered from MI. Recently, Gurlertop et al. (3) reported factor V Leiden mutation may be one of the important risk factors in developing CAD. Holm et al. (10) described two young females with MI who were homozygous for the FV mutation. Heinrich et al. (11) also described a FV Leiden homozygous male in their study who had an MI at an early age. While FV Leiden heterozygosity alone may not be an independent predictor for CAD or MI, the homozygous state could play a more substantial role in development of disease. However, in our case, although heterozygous factor V leiden mutation was positive other coagulation factor levels were normal. Since the factor V leiden mutation has been associated with thromboembolic disease, it is possible that its presence is related to a thrombotic event, such as

an acute MI. Therefore, in our case, heterozygous factor V leiden mutation to be held liable for anterior-lateral MI associated with thrombosis.

Therapeutic approaches are direct balloon angioplasty / stent deployment, bypass surgery, intra-coronary thrombolytic treatment or medical treatment for the treatment of coronary artery thrombosis (12). However, there is no certain algorithm available for the treatment of coronary artery thrombosis. In our case, due to the inappropriate coronary structure and length of the thrombus, coronary angioplasty and/or stent procedures were not performed. Spontaneous reperfusion has been reported in 11% of patients within 4 hours of the clinical onset, reaching 35% at 12 to 24 hours after onset of MI due to an endogenous fibrinolytic process. It is believed anticoagulant and antiplatelet medications contribute to thrombus dissolution. Glycoprotein IIb/IIIa receptor antagonists are potent antiplatelet agents by inhibiting the final common pathway of platelet aggregation. Jayasundera et al. reported a case in which tirofiban achieved reperfusion in an acutely thrombosed RCA (5). Akdemir et al. have also reported that dissolution of a huge spontaneous coronary artery thrombus with a GP IIb/IIIa inhibitor tirofiban (4). The contribution of GP IIb/IIIa inhibitor therapy to clot dissolution remains unclear. GP IIb/IIIa inhibitors inhibit acute de novo thrombosis under high-shear flow conditions. Endogenous fibrinolytic activity continues afterwards in all patients with ACS. GP IIb/IIIa inhibitors, although not having primary fibrinolytic activity, can be helpful for dissolving coronary thrombus by assisting spontaneous fibrinolysis. In our case, tirofiban had a beneficial effect on coronary thrombus dissolution.

In conclusion, factor V leiden mutation to be related with acute myocardial infarction associated with thrombosis. Intensive antiaggregant therapy with tirofiban and clopidogrel may avoid percutaneous coronary intervention in patients with acute coronary syndrome due to intracoronary thrombus associated with factor V Leiden. Intensive antiaggregant therapy with tirofiban and clopidogrel may be effective in such cases.

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Correspondence to:
Yahya Islamaoglu, MD, P.K: 112,
Department of Cardiology, Faculty of Medicine,
Ataturk University, Erzurum, Turkey
Tel.: + 90 532 7900683
Fax: + 90 414 3129785
Email: rize_yahya@hotmail.com