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Case report-Olgu sunumu

The myocardial infarction in a young woman with heterozygous MTHRF and PAI-1 gene mutations.

Heterozigot MTHRF ve PAI-1 gen mutasyonlu genç kadın hastada myokardial infarktüs.

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Abstract
Myocardial infarction in young patient accounts for 6% of all myocardial infarctions. Unlike older patients, the cause of the myocardial infarction in approximately 20% of young patients is not related to atherosclerosis. In this study, we report a case of myocardial infarction at a young woman who do not have classical risk factors for coronary artery disease, however, who was heterozygous for the methylene tetrahydrofolate reductase C677T/G gene mutation and plasminogen activator inhibitor- 1 4G/5G gene variant. Urgent coronary angiography revealed multi-vessel coronary disease, severe stenosis of the proximal left anterior descending artery, total occlusion of the first diagonal artery, and severe stenosis of the proximal circumflex artery. The lesions were thought to be not suitable for percutaneous revascularization and coronary by-pass surgery was performed. The postoperative course was uneventful and she was discharged on 8th day. In conclusion, coronary artery disease in young patient especially without classical risk factors, we suggest that prothrombotic factors should be evaluated.

Key words: Myocardial infarction, young patient, gene polymorphism.

Özet:
Genç hastalarda miyokart enfarktüsü tüm miyokart enfarktüslerinin %6'sını oluşturur. Yaşlı hastalardan farklı olarak genç hastalardaki miyokart enfarktüsünün yaklaşık %20'si aterosklerozla ilişkili değildir. Bu çalışmada, koroner arter hastalığı yönünden klasik risk faktörü bulunmayan ancak heterozigot metilen tetrahidrofolat redüktaz C677T/G ve plazminojen aktivatör inhibitör 1 gen varyasyonuna sahip miyokart enfarktüslü genç bir bayan hastayı sunmaktayız. Hastaya yapılan acil koroner anjiografi çok damarda koroner arter hastalığına işaret etti; sol anterior inen arterde ciddi darlık, birinci diagonal arterde total tıkanma ve proksimal sirkümfleks arterde ciddi daralma vardı. Lezyonların perkütan revaskülarizasyona uygun olmadıkları düşünüldü ve koroner baypas cerrahi uygulandı. Postoperatif dönem sorunsuz geçti ve hasta 8. gün taburcu edildi. Sonuç olarak özellikle klasik risk faktörü bulunmayan genç olgulardaki koroner arter hastalıklarında protrombotik genetik faktörlerin araştırılmasını önermekteyiz.

Anahtar sözcükler: Miyokart enfarktüsü, Genç Hasta, Gene polimorfizmi

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Introduction

Myocardial infarction in young patient (persons under the age of 45 years) accounts for 6% of all myocardial infarctions [1]. In this age group, it is mostly a disease of men. Classical important coronary artery risk factors include hyperlipidemia, smoking, family history, and obesity. Atherosclerosis processes are promoted by these risk factors. Unlike older patients, the cause of the myocardial infarction in approximately 20% of young patients is not related to atherosclerosis [1]. In this population anomalies of the coronary arteries and thrombotic genetic variations are more important than atherosclerosis. However, the relationship between hereditary thrombophilia and arterial thrombotic syndromes such as coronary heart disease, myocardial infarction, and stroke has not been completely established in young patient populations [2, 3].

Methylenetetrahydrofolate reductase gene mutation (MTHFR) usually has high serum homocysteine levels and MTHFR gene mutation is associated with increase in the risk for premature cardiovascular disease [4, 5]. Similarly, plasminogen activator inhibitor- 1 (PAI-1) 4G/5G gene polymorphism has been correlated with plasma level of PAI-1 and higher plasma PAI-1 levels increase the risk of intravascular thrombosis and myocardial infarction [6].

We described a case of myocardial infarction at a young woman in a subject heterozygous for the MTHFR C677T/G and PAI-1 4G/5G gene variant.

Case report

A 43-year old woman was admitted with oppressive chest pain. The patient did not have history of smoking, dyslipidemia, and hypertension. Electrocardiogram revealed sinus tachycardia and signs of anterior acute myocardial infarction. Echocardiography revealed reduced left ventricular systolic function (ejection fraction was measured 45%) with akinesis of anterior wall.

The cardiac enzymes were elevated; CK-MB index 26 U/l (normal range: 0–25 U/l), and troponin I 2.51 ng/ml (normal range: 0–0.04 ng/ml). The serum lipid levels were normal (serum triglycerides 81 mg/dl, HDL-cholesterol 24 mg/dl, and LDL cholesterol 101 mg/dl). Homocysteine level was 16.5 μmol/L (normal range 0.00–12.00 μmol/L). Intravenous fibrinolytic therapy was done. Urgent coronary angiography revealed multi-vessel coronary disease, severe stenosis of the proximal left anterior descending artery, total occlusion of the first diagonal artery, and severe stenosis of the proximal circumflex artery. The lesions were thought to be not suitable for percutaneous revascularization and the patient was referred for coronary by-pass. On the other hand, ultrasound examination of the carotid arteries revealed 50% stenosis of the right internal carotid artery.

To assess the etiopathology of myocardial infarction, we measured a panel of atherosclerotic and prothrombotic risk factors (Table 1). The patient was found to have heterozygous MTHRF C677T/G gene mutation and PAI-1 4G/5G gene variant.

The patient history was positive for deep venous thrombosis. The patient underwent coronary artery bypass surgery. The patient was anticoagulated by intravenous heparin in a dose of 300 U body weight and, activated clotted time was maintained >400 s during cardiopulmonary bypass. Three-vessel coronary bypass surgery was done (left internal mammary artery to left anterior descending artery, aorto-saphenous vein graft to first diagonal branch artery and second marginal branch artery). The intensive care unit course was uneventful and she was discharged on second day from intensive care unit. In the postoperative period, enoxaparin 40mg/day, warfarin, and aspirin were administered. After four days, the patient's INR was between 2.5 and enoxaparin was discontinued. She was educated about her hypercoagulable state and she is being followed up by cardiologists of our institution. The postoperative course was uneventful and she was discharged on 8th day.

Table 1. Genetic profile of the patient.

Detecting Genes	Genotypes
Factor V G1691A	No mutation
Factor V H1299R	No mutation
Prothrombin G20210A	No mutation
Factor XIII V34L	No mutation
β- Fibrinogene -455 G-A	No mutation
PAI-1 4G/5G	5G/4G mutation
Glycoprotein IIIa L33P	No mutation
MTHFR C677T	T/G variant detected
MTHFR A1298C	No mutation
ApoB R3500Q	No mutation

PAI-1; plasminogen activator inhibitor-1 -1, MTHFR; methylenetetrahydrofolate reductase, ApoB; Apolipoprotein B.

Discussion

Currently, the role of the prothrombotic gene variants for coronary artery disease is unclear [2, 3]. However, these genetic variations are important especially in patient who do not have classical risk factors for coronary artery disease.

The patients with MTHFR gene mutation have significantly elevated plasma homocysteine levels [5, 7] and increased homocysteine levels were reported in coronary artery, cerebrovascular, and in peripheral artery diseases. Moreover, recent studies revealed that the C677T polymorphism of MTHFR is a significant independent risk factor associated with the prevalence of myocardial infarction [8].

PAI-1 is the central component of the fibrinolytic system. PAI-1 4G/5G gene polymorphism has been correlated with plasma level of PAI-1 and higher plasma level of PAI-1 might increase the risk for intravascular thrombosis [6]. It has been suggested that there is significant correlation between incidence of myocardial infarction and PAI-1 gene polymorphism [6]. A meta-analysis showed a 20% increased risk of myocardial infarction attributed to the 4G/4G genotype. Another meta-analysis showed that having a 4G allele was associated with 1.06 fold-increased risks for coronary artery disease [6].

Our patient was a low-risk young individual who presented acutely with a classical myocardial infarction due to arterial thrombosis of the coronary artery. The combination of MTHFR C667 T/G and PAI-1 4G/5G gene variant may have increased the risk of coronary artery thrombosis in our case.

Currently, there is no evidence to support or refute for long-term prophylaxis with oral anticoagulation. However, long term anticoagulation is recommended on the findings of small-scale retrospective studies.

In conclusion, coronary artery disease in young patient especially without classical risk factors, we suggest that prothrombotic factors should be evaluated. We believe that detection of these factors may allow to physicians to prevent or delay the development of further coronary artery events.

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