Recurrent Acute Coronary Syndromes With Normal Homocystein Level: A Mutation of MTHFR Gene

Normal Homosistein Düzeyi ile Beraber Rekürren Akut Koroner Sendromlar: Nadir Bir MTHFR Gen Mutasyonu

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ABSTRACT

A 29-year-old female patient, complaining of squeezing retrosternal chest pain, was admitted to our emergency department. Her angina pectoris had started fifteen days ago and accentuated during the last two days. In her medical history, it was determined that during the last four years she had been admitted to hospitals with the same complaint twice, troponins were found to be elevated, she was hospitalized and coronary angiography (CAG) was totally normal. The young woman with recurrent acute coronary syndrome had a mutation in the MTHFR gene. On the determination of normal coronary arteries, we have demonstrated the localization of myocardial infarction via magnetic resonance imaging. In our case we have found no other risk factors except MTHFR 1298 gene mutation for coronary artery disease. MTHFR 1298 gene mutation may cause this state of hypercoagulopathy.

Key Words: Acute coronary syndrome, cardiac emboli, heterozygous mutation of MTHFR A1298C gene, young patient

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ÖZET

Yirmi dokuz yaşında bayan hasta sıkıştırıcı retrosternal göğüs ağrısı ile acil servisimize başvurdu. Hastanın ağrısı uyku boyunca, 15 gün önce başlamış ve artıp azalan karakterde, son 2 gündür yoğun şekilde idi. Hastanın öyküsünde son 4 yılda, iki kez aynı yakınmalar ile hastaneye başvurduğu, troponin yüksekliği olması üzerine yatırılıp koroner anjiografi yapıldığı ve koroner arterlerin tamamen normal saptandığı öğrenildi. Tekrarlayan akut koroner sendromu olan bayanda MTHFR gen mutasyonu saptandı. Koroner anjiografinin normal saptanması üzerine, myokardiyal infarktüs lokalizasyonunu kardiyak manyetik rezonans görüntüleme ile gösterdik. Olgumuzda MTHFR1298 gen mutasyonu dışında herhangi bir koroner risk faktörü saptamadık. MTHFR gen mutasyonunun tek başına hiperkoagülopatiye neden olabileceğini gösterdik.

Anahtar Sözcükler: Akut koroner sendrom, kardiyak emboli, heterozigot MTHFR A 1298 C mutasyonu, genç hasta

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INTRODUCTION

Acute myocardial infarction (AMI) generally occurs due to stenotic thrombus formation on a ruptured atherosclerotic plaque but it is rare in young patients. Sometimes myocarditis may mimic AMI in this group of patients. In 1-12% of cases of AMI normal coronary arteries (NCA) are found angiographically (1). In the etiology of AMI with NCAs, hypercoagulopathy, cigarette smoking, cocaine abuse may play a role (2). In such cases mostly coronary embolism of a thrombus and/or vasospasm is responsible in pathogenesis. Synergistic effect may be noticed in cases who have several such predisposing factors together. In our case we have found no other risk factors other than heterogeneity of MTHFR A1298C gene allele which may cause a hypercoagulable state.

CASE REPORT

A 29-year-old female patient, complaining of squeezing retrosternal chest pain, was admitted to our emergency department. Her angina pectoris had started during sleep fifteen days ago and with waxing and waning pattern, it intensified during the last two days. In her medical history, we learned that 4 and 2 years ago she had been admitted to hospital with the same complaint twice and as troponins were found to be elevated, she was hospitalized and coronary angiography (CAG) was performed. Coronary anatomy was totally normal and no stenosis was detected. She had no traditional risk factors such as diabetes mellitus, hypertension, hyperlipidemia, cigarette smoking or family history. She was not sedentary and her body mass index was in normal limits. She had no substance or alcohol addiction and had no medical treatment including oral contraceptives.

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On physical examination, her blood pressure was 110/70 mmHg, heart rate was 75 per minute and rhythmic. Cardiac auscultation revealed no pathological sounds. On electrocardiography no ischemic change was noticed. She was hospitalized because of elevated troponin-I levels. Optimal medical treatment was started. Troponin-I levels increased from 18.07 ng/ml to >50 ng/ml. Her transthoracic echocardiography revealed no pathological finding. CAG was performed and normal coronary arteries were visualized (Figure 1). In her cardiac magnetic resonance imaging (MRI), subendocardial contrast enhancement in the septal and posterior superior wall at the left ventricular apical level, which may be relevant to embolic events, was detected (Figure 2). After a few days, she had been discharged with acetylsalicylic acid 100 mg/day and enoxaparine 0.6 cc to be administered subcutaneously twice a day because of a probability of coagulopathy. One month later, in order to investigate hypercoagulable state, protein S and C activity, active protein C resistance, antithrombin III, Factor VIII, Von Willebrand Factor, homocysteine, p-ANCA, c-ANCA, lupus anticoagulant, anticardiolipin IgM and IgG, ANA, anti ds-DNA, folic acid and vitamin B12 levels were studied and all were found to be in normal limits. The only pathological finding was heterogeneity of methylenetetrahydrofolate reductase (MTHFR) A1298C gene allele.

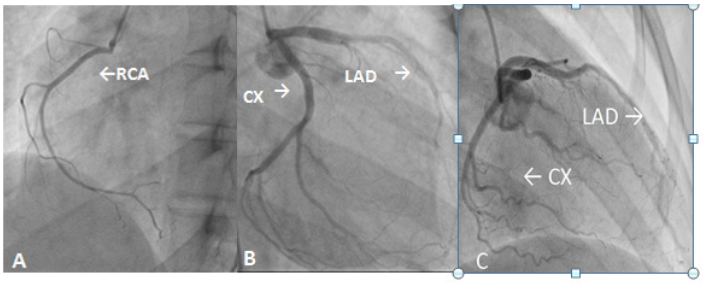

Figure 1.Conventional angiography demonstrating A)normal RCA B)normal LAD and CX arteries (arrows)

RCA-Right coronary artery, LAD-Left anterior descending, CX-Circumflex

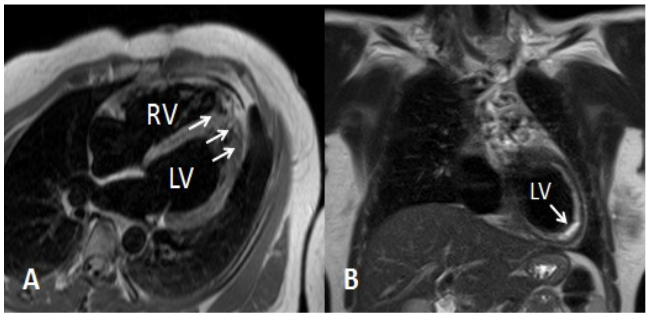

Figure 2. Cardiovascular magnetic resonance demonstrating subendocardial contrast enhancement A) in the septal and B) in the posterior superior wall at the left ventricular apical level (arrows) RV: Right ventricle, LV: Left ventricle

DISCUSSION

MTHFR is one of the three enzymes that play a role in homocysteine metabolism. Mutations in C677T and A1298C alleles are the two common MTHFR polymorphisms and are related to increased premature MI and premature coronary artery disease (3,4). Mutations in C677T allele are characterized by a reduced enzyme activity, a mild elevation of plasma homocysteine, and low plasma folate level whereas mutations in A1298C allele seem to rather affect regulatory properties of the enzyme without causing hyperhomocysteinemia (5).

In a case-control study, Szczeklik et al studied the prevalence of MTHFR polymorphism-the C677T and A1298C alleles-in male patients under the age of 50 years who had angiographically documented CAD. The frequency of both homozygotes and heterozygous carriers of the 1298C allele, was significantly higher in early onset CAD than in controls and homocysteine levels were found to be in normal limits (5). In a recent study carried on diabetic subjects, those with the A1298C polymorphism had lower levels of homocysteine as compared with individuals with C677T polymorphism (6).

Contrast-enhanced Cardiovascular Magnetic Resonance (CMR) is relatively a new imaging technique in assessing cardiovascular diseases. It also identifies areas of necrosis, scarring and ischemia. It is superior to single photon emission computed tomography (SPECT) -a nuclear imaging technique- in detecting subendocardial infarction. It is an invaluable diagnostic tool in the evaluation and management of patients with known or suspected cardiovascular disease especially when the other diagnostic modalities like coronary angiography or echocardiography fail to document etiology (7).

CONCLUSION

Heterozygous mutation of A1298C allele of MTHFR gene may be related to repetitive acute coronary syndromes caused by micro emboli to coronary vasculature and should be kept in mind especially in young patients with no other traditional risk factors. In such cases CMR may aid in documenting the subendocardial infarcts.

Conflict of Interest

No conflict of interest was declared by the authors.

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