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Original Research Paper

Cardiology

ACUTE CORONARY SYNDROME IN A YOUNG MALE SECONDARY TO HYPERHOMOCYSTEINEMIA

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ABSTRACT Homocysteine is sulfur containing intermediary amino acid formed by the demethylation of dietary methionine to cysteine. The raised serum homo- cysteine level is one of the important risk factors associated with coronary artery disease. We present a 16-year-old female with no other risk factors of coronary artery disease presented to us with acute inferior wall myocardial infarction and was treated with dual antiplatelets and anticoagulation. During the routine work up, significant elevation of serum homocysteine level was seen with markedly low se- rum vitamin B12 level and was treated for it along with standard therapy for acute myocardial infarction. The case illustrates the need to incorporate a plasma homocysteine level during work up of coronary artery disease especially in young patients, more importantly in those without any conventional risk factors.

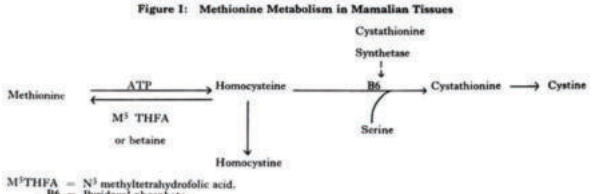
KEYWORDS : Hyperhomocysteinemia, Young, Myocardial Infarction, Risk Factors

1. INTRODUCTION

Homocysteine is a Sulfur containing amino acid which was first described by Vigneaud in 1931. The Homocystinuria is an inborn error of intracellular metabolism of dietary methionine, first described by Carson and Neil in 1962. Homocysteine is either trans methylated to methionine via a reaction requiring folate or vitamin B12 or trans sulfated to cystathionine via a reaction requiring pyridoxal 5' phosphate [12].

Mudd in 1964 pointed out that the defect was in a deficiency of enzyme Cystathionine synthetase which mediated the conversion of homocysteine to cystathionine. The enzyme deficiency results in an accumulation of homocysteine. Homocystinuria is heritable in an autosomal recessive manner. McCully was the first to propose in 1969 that homocysteine is leading to atherosclerotic plaque formation by directly affecting cells in the arterial wall and that high homocysteine levels are a risk factor for cardiovascular disease.

Figure I: Methionine Metabolism in Mamalian Tissues



M^3THFA = N^3 methyltetrahydrofolic acid.
B6 = Pyridoxal phosphate.
ATP = Adenosine triphosphate.

Hyperhomocysteinemia can be classified as mild to moderate (homocysteine level > 15 - 30 mmol/l), Intermediate (homocysteine level > 30 - 100 mmol/l), and severe (homocysteine level > 100 mmol/l) Mild to moderate elevation of homocysteine is more common in the general population than the severe elevation Patients with severe homocysteinemia are at markedly elevated risk for premature atherothrombosis such as venous thromboembolism.

The exact mechanism though is unknown, the endothelial dysfunction, accelerated LDL oxidation, reduced arterial vasodilation, oxidative stress, and platelet activation secondary to increased homocysteine is suggested to be Hyperhomocysteinemia induced atherosclerotic complication like coronary artery disease in young

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The metabolism of Homocysteine requires vitamin B12, B6 and folic acid. It makes the assessment of Serum Vitamin B_{12}, B_6 and Folic acid and their supplementation in cases where we strongly suspect Hyperhomocysteinemia as a potential cause of coronary artery disease.

2. Case Report

A 16-years-old female presented to our emergency department with complains of retrosternal chest pain associated with sweating and nausea of 5 hours duration. She denied any illicit drug use, other medications, and tobacco. She was on a complete vegetarian diet.

She did not have a family history of premature coronary artery disease or sudden cardiac deaths. Her 12-lead electrocardiogram showed a significant ST elevation in II, III and aVF ().

Screening Echocardiography showed hypokinetic right coronary artery territory, mild mitral regurgitation and left ventricular ejection fraction of 40%. Emergency coronary angiography was done which revealed significant 60% occlusion with thrombus in proximal right coronary artery while the left main coronary artery, left anterior descending coronary artery and left circumflex artery were normal (). As there was a large thrombus burden in the infract related artery, glycoprotein IIb/IIIa inhibitor (tirofiban) along with thrombus aspiration with manual device (Thrombosuction) was done initially followed by reduction in thrombus burden.

Post angiography, Patient was shifted to intensive care unit with eptifibatide infusion for initial 12 hours. His chest pain and ECG changes improved within few hours of procedure and was shifted to general ward next day. Patient was started with dual antiplatelets (aspirin and clopidogrel) and anticoagulation with low molecular weight heparin.

During hospitalization she was evaluated for the risk factors for the artery disease. Her fasting lipid profile was as follows- HDL: 45mg/dl (N:40-80mg/dl). LDL: 100 mg/dl (N:60-130 mg/dl), total cholesterol 180mg/dl (N:130-200 mg/dl), total triglycerides: 110mg/dl (N: 50-150mg/dl).

Fasting serum Homocysteine level done 2nd day after the procedure showed an intermediate elevation with level of 46.35 mmol/l (normal range being 3.7 - 13.9 mmol/l) and her vitamin B12 levels were also low: 50pg/ml (N:140-885 pg./ml) which was correlated with her strict vegan diet. Serum folic acid, Anti phospholipid antibodies and Factor V Leiden mutation were negative. Her renal function and thyroid function tests were normal.

Anticoagulation was continued for 8 days. Repeat angiography was performed which showed recanalization of right coronary artery. With the working diagnosis of intermediary Hyperhomocysteinemia, she was treated with parenteral B12 (30 mcg intramuscular once daily for initial 5 days followed by 200 mcg intramuscular monthly for 3 months) on outpatient basis and oral folic acid 5 mg daily for 3 months. The above treatment was done in addition to the standard therapy for acute myocardial infarction including dual antiplatelets, high dose statins, beta-blocker and angiotensin converting enzyme inhibitors (ACEI). After 3 months of parenteral supplementation her serum vitamin B12 level returned to be normal and plasma homocysteine level done after another 3 months was within normal limits.

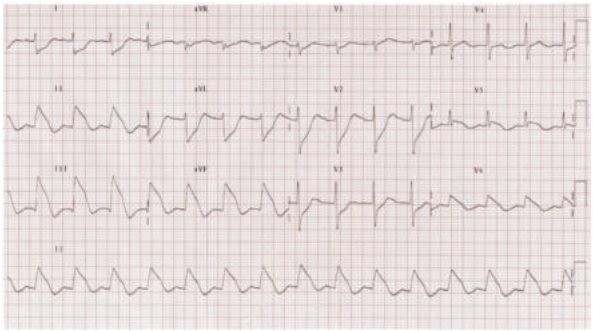

Figure 1. 12 Lead EKG during presentation to emergency.

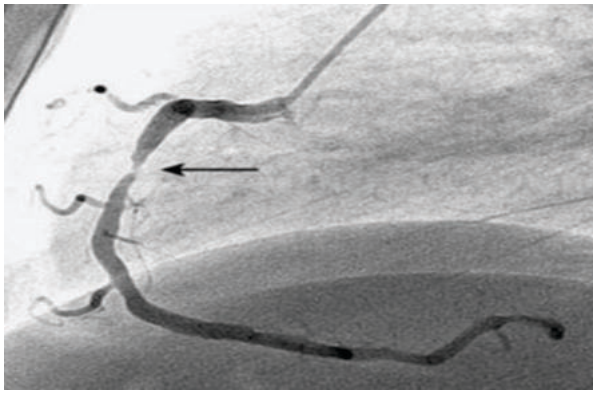

Figure 2. Coronary Angiography LAO view shows significant occlusion of RCA with thrombus.

4. DISCUSSION

Hyperhomocysteinemia is an independent modifiable risk factor for ischemic heart disease and thrombosis It was especially found to be associated with increased coronary artery disease in postmenopausal women []. One meta-analysis showed a positive correlation between plasma homocysteine concentration and ischemic heart disease [10]. The results of a study conducted in a Turkey by Sipahi et al. were compatible with those reported in the world medical literature: the homocysteine plasma levels of patients with coronary artery disease were found to be significantly higher as compared to those of a control group [11]. Bozkurt et al. concluded that Hyperhomocysteinemia is an independent risk factor for coronary artery disease. It increases risk of coronary artery disease by 3.69-fold [9].

Hyperhomocysteinemia is an independent risk factor both in males and females. This association was independent regarding age sex, and appeared as the 4th major risk factor along with family history, DM, and hyperlipidemia. Elevated levels of serum homocysteine may result from geographical variation, racial and ethnic and racial differences, genetic causes, inadequate dietary intake of B12 and folate or in those taking antifolate drugs like methotrexate. Apart from this it is also seen in impaired homocysteine metabolism caused by thyroid and renal insufficiency The mean value of 41 mmol/l in our patient is above 3 times the upper limit of normal range.

It has been found that each 5 mmol/l increase in homocysteine level increases the risk of coronary artery disease by 20% independent of traditional risk factors Thus, the risk is significant in our patient and it explains why she developed acute myocardial infarction at the young age of 16.

As it was unusual for a 16-year-old female with no known traditional risk factors to suffer from acute myocardial infarction, it prompted us to conduct additional lab tests which showed moderate Hyperhomocysteinemia. The latter was thought to be due to markedly low B12 level secondary to his strict vegetarian diet. The normalization of serum homocysteine levels after supplementation of B12 further confirmed our prediction.

The prevention of atherosclerotic cardiovascular disease in a risk group of Hyperhomocysteinemia can be effectively done by dietary supplementation of B12, B6 and folic acid which decreases homocysteine level As the B12 level in our patient was low, it prompted us dietary supplement in addition to patient therapy for the coronary artery disease.

4. CONCLUSIONS

The conventional risk factors of atherosclerosis like diabetes mellitus, hypertension, smoking, and Dyslipidemia may not be present in any of the patients presenting with acute coronary syndrome. Especially in young patients where the conventional risk factors are absent, consideration of presence of novel risk fac- tors like raised serum homocysteine must be considered as an important cause of atherosclerosis in those patients leading to coronary artery disease.

In addition, supplementation of folic acid and vitamin B12 along with the routine treatment of coronary artery disease reduces the serum homocysteine level despite controversial benefits. This will reduce the future events of the recurrence of coronary artery disease in selected patients.

Consent

Informed and written consent is taken from the patient during his discharge for the publication of this case reports and the associated images.

Conflicts of Interest

All the authors have no conflicts of interest to disclose.

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