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 homocysteine level is one of the important risk factors associated with coronary artery disease. We present a 23-year-old male with no other risk factors of coronary artery disease presented to us with acute anterior wall myocardial infarction and was treated with primary percutaneous coronary intervention. During the routine work up post percutaneous coronary intervention significant elevation of serum homocysteine level was seen with markedly low serum 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
The intracellular metabolism of dietary methionine to cysteine releases homocysteine as an intermediate product. This metabolism requires folic acid, vitamin B12 and vitamin B6 [1]. Homocysteine is a sulfur containing amino acid which was first described by Vigneaud in 1931. The serum Homocysteine level is dependent on genetic enzyme defects, especially cystathione beta synthesis and MTHFR (Methyl tetra hydro folate reductase) gene polymorphism, drugs and the deficiency of one or more of Vitamin B12, B6 and follic acid [2].
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) [3]. Mild to moderate elevation of homocysteine is more common in the general population than the severe elevation [4]. Such patients 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 [4].

Hyperhomocysteinemia is one of the rare and independent causes of acute coronary syndrome. It leads to accelerated atherosclerosis by multiple mechanisms and has to be considered when we encounter coronary artery disease especially in young individuals without conventional risk factors. The metabolism of Homocysteine requires vitamin B12, B6 and folic acid. It makes the assessment of Serum Vitamin B12, B6 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 23-years-old male presented to our emergency department with complains of retrosternal chest pain associated with sweating and nausea of 5 hours duration. He was a non smoker and did not have a family history of coronary artery disease or premature deaths. His 12 lead electrocardiogram showed a significant ST elevation in V1, V2, V3 and V4 (Figure 1).

Screening Echocardiography showed hypokinetic left anterior descending artery territory, mild mitral regurgitation and left ventricular ejection fraction of 40%. Emergency coronary angiography was done which revealed significant occlusion with thrombus in mid Left anterior descending artery while the Right coronary artery was normal (Figure 2 and Figure 3). As there was a large thrombus burden in the infract related artery, glycoprotein IIb/IIIa inhibitor (eptifibatide) along with thrombus aspiration with manual device (Thrombosuction) was done initially followed by reduction in thrombus burden.

Successful Primary percutaneous coronary intervention with stent implantation was performed thereafter without any complications like slow flow or no-reflow and the TIMI-3 flow was restored (Figure 4). Patient was admitted in 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 where he was admitted for another 3 days and was discharged.

During hospitalization he was evaluated for the risk factors for the coronary artery disease which revealed a normal fasting lipid profile, blood sugar, renal
function test and complete blood count. He denied any illicit drug use, other medications and tobacco. He was on a complete vegetarian diet for the past 10 years.

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 the serum vitamin B12 level was markedly low (83.2 pg/ml) which was correlated with his strict vegan diet. Serum folic acid, Anti phospholipid antibody, autoimmune profile, inflammatory markers like ESR and CRP, Extended
Figure 3. Coronary angiography LAO cranial view showing normal right coronary artery (RCA).

Figure 4. Coronary angiography LAO cranial view showing good flow in LAD after percutaneous coronary angioplasty with stenting.

lipid profile and thyroid function test all were within normal limits.

With the working diagnosis of intermediary Hyperhomocysteinemia secondary to dietary deficiency of B12 and the former being thought to be one of the risk factor for his coronary artery disease, he was treated with parenteral B12 (30 mcg intramuscular once daily for initial 5 days followed by 200 mcg intramus-
cular 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 his serum vitamin B12 level returned to be normal and plasma homocysteine level done after another 3 months was within normal limits (<3.7 mmol/l).

Six months follow up after discharge revealed good exercise tolerance, no chest pain and normal vital parameters. EKG revealed no new changes and Echocardiography showed did not showed any wall motion abnormalities with left ventricular ejection fraction of 60%.

3. Discussion

Hyperhomocysteinemia is an independent modifiable risk factor for ischemic heart disease and thrombosis [5] [6]. 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 [7] 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 [4]. The mean value of 46.35 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 [8]. Thus the risk is significant in our patient and it explains why he developed acute myocardial infarction at the young age of 23.

As it was unusual for a 23 year old man 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 positive correlation between plasma homocysteine level and ischemic heart disease was shown in a meta-analysis conducted in turkey by Sipahi et al. [8]. The result was compatible with those reported in med lite where the homocysteine level of patient admitted with CAD was found to be higher as compared to control group. Burkit et al. concluded hyperhomocysteinemia as an independent risk factor for coronary artery disease similar to conventional risk factors and increased risk to 3.69 fold [9].

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 [8]. 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 factors like raised serum homocysteine has to 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 of the authors have no conflicts of interest to disclose.

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