Case Report

Young Man Presenting with Chest Pain

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Abstract

This is a case report of a young man, who had an acute coronary event followed by angioplasty. On further workup he was found out to have hyper-homocysteinemia.

Introduction

Homocystinuria or severe hyper- homocysteinemia is a rare autosomal recessive disorder characterized by elevation in plasma and urine homocysteine concentrations. Clinical manifestations of homocystinuria include developmental delay, osteoporosis, ocular abnormalities, thromboembolic disease, and severe premature atherosclerosis.[1] Moderate hyper-homocysteinemia without the clinical stigmata of homocystinuria is much more common. It is a new independent risk factor for atherosclerotic vascular disease that has been described in the last ten years. It is associated in the third and fourth decades of life with coronary heart disease, stroke, arterial and venous thromboembolism.[2] Hyper-homocysteinemia in the absence of significant homocystinuria is found in individuals who are heterozygous or homozygous for certain genetic defects that impair folate or vitamin B12 metabolism or cause cystathione synthase deficiency. An increased level of homocysteine could be treated with folic acid and other B complex vitamins. The following case report pertains to a young male who developed an anterior wall Myocardial Infarction (MI) and was consequently found out to have a high serum homocysteine level.

Case Report

A 27 years old, unmarried banker, a non-smoker was admitted with a 7 hours history of retrosternal chest pain with profuse sweating and mild shortness of breath (SOB) (NYHA-I). The pain started at 6 am while he was still in bed and the severity of pain actually woke him up. The pain was a constant dull ache, non- radiating and was getting worse on mild to moderate exertion. There was no associated nausea, vomiting, palpitations or dizziness. He reached the hospital 7 hours after the onset of symptoms, where ECG showed ST elevation in leads I, aVL, V1 to V3 with deep inverted T waves.

The patient had been previously healthy with no comorbids. He used to take regular exercise in a gymnasium with no accompanying complaints. Rest of the systemic review was unremarkable. In the past, the patient had heartburn and chronic allergic rhinitis. He was on a balanced diet with normal appetite and sleep pattern. There were no addictions or any illicit sexual relations. The patient's parents were unrelated to each other. His father had died 3 years ago at the age of 56 years with suspected myocardial infarction. The patient's mother and maternal uncle suffered from valvular heart disease and both had prosthetic valve replacement. He had one brother and no other sibling. There was no family history of diabetes, hypertension, tuberculosis or asthma.

On examination, he was medium statured, fully conscious, cooperative, lying comfortably on bed. He was afebrile with a weight of 61 kg. his pulse was 110/minute, regularly regular of normal volume, blood pressure of 110/70 mmHg and respiratory rate of 20/minute. He was not pale, jaundiced or edematous, JVP was not raised. There was no lymphadenopathy and thyroid was not enlarged. The patient had normal heart and breath sounds. Lung basis were clear. Abdomen, neurological and musculo-skeletal examination were unremarkable.

His investigations are as follows:

	1st Set	2nd Set
CPK	791 (270 u/l)	915 (270 u/l)
CKMB	65 (<25 u/l)	67 (<25 u/l)
SGOT	80 (40 u/l)	108 (40 u/l)
LDH	435 (230 - 460 u/l)	585 (230 - 460 u/l)

Echocardiogram

Normal left ventricle size with hypokinesia of interventricular septum, apex and anterior wall. Ejection fraction 45% . Moderate LV dysfunction with regional wall motion abnormality.

Lipids

Total Cholesterol 151 (100-220 mg%), low density lipoprotein 89 (upto 150 mg%), Triglycerides 78 (70-150 mg%).

Random blood sugar 89 mg%, Urea, Creatinine, Electrolytes - normal, Uric acid 4.2 (3.4-7 mg%).

Complete blood count: Hb 16g/dl, MCV 84.3 fl, normochromic, normocytic, TLC 10x109/L(90% N), Platelets 174 x 109/L. ESR 5mm/1st hr, Prothrombin time 14 (11) sec, APTT 23 (23) secs.

Serum B12 198 (193 - 982 pg/ml), RBC - folate 180 (165-760 ng/l), p-ANCA 4.0 (= 6.0 u/ml), c-ANCA 0.5 (= 2.0 u/ml), Total Plasma Homocysteine 14.98 (4.45-12.42 mol/l). (by fluorescent, polarizing immuno-assay method).

Protein C- 115 (72 - 106%), Protein S- 82 (70 - 120%)

Anti-cardiolipin: IgG 1.5 (10 - 60 GPL/ml), Anti-cardiolipin IgM 4.6 (>10 - >60 MPL/ml).

Figure 1. ECG Cardiac Enzymes consistent with Acute anterior wall MI.

In the light of above findings of acute myocardial injury, the patient was managed with oxygen, opiod analgesics, I/V nitrates, ß blocker, Aspirin, GP IIb-IIIa antagonists and immediate angiography was planned. The angiogram revealed proximal LAD artery osteal stenosis of about 70-80%. There was also a thrombus at the site of stenosis with compromised antegrade flow. Balloon angioplasty was done and a stent was inserted. As the patient had hyper-homocysteinemia, he was started on oral folic acid (5 mg) and B-complex preparation. Family screening for homocysteinemia revealed his younger brother to have a high homocysteine level (19.58 µmol/l).

Figure 2. Coronary angiogram before angioplasty.

Discussion

In 1969, McCully reported autopsy evidence of extensive arterial thrombosis and atherosclerosis in two children with elevated plasma homocysteine and homocystinuria.[3] However 20 years later, interest in hyper-homocysteinemia has been renewed. Recent epidemiological studies have demonstrated that hyper-homocysteinemia is an independent risk factor for atherosclerosis in the coronary, cerebral and peripheral vasculature.[4,5]

Elevations in the plasma homocysteine concentration can occur due to (i) genetic defects in the enzymes (e.g T mutation of MTHFR enzyme, ß cystathione deficiency etc.) involved in homocysteine metabolism, (ii) nutritional deficiencies (e.g folic acid, B12, B6) (iii) some chronic medical conditions, e.g. hypothyroidism, chronic renal failure, SLE and (iv) drugs, e.g. theophylline, bile acid resins, methotrexate, levodopa and nicotinic acid.[5,6] Cigarette smoking also may elevate homocysteine levels.[7]

Homocysteine has primary atherogenic and prothrombotic properties. Histopathologic hall marks of homocysteine induced vascular injury include intimal thickening, elastic lamina disruption, smooth muscle hypertrophy, marked platelet accumulation and the formation of platelet enriched occlusive thrombi.[3] Prothrombotic effects of homocysteine have been demonstrated in patients with acute coronary syndrome.[1] These include attenuation of endothelial cell, tissue plasminogen activator binding sites, activation of factor VIIa and V, inhibition of protein C and heparin sulphate, raised fibrinopeptide A and prothrombin fragments 1 & 2, raised blood viscosity and raised endothelial antihrombotic activity due to changes in thrombomodulin functions.[1,6]

Hyper-homocysteinemia has been linked to vascular events[1], including:

* myocardial infarction, other coronary syndromes and recurrent coronary events,

* premature coronary heart disease,

* cardiovascular and total mortality, adverse outcomes after angioplasty,

* carotid artery stenosis, stroke, recurrent stroke, and silent brain infarcts,

* heart failure.

A randomized controlled trail on 553 homocysteinemic patients showed that folic acid, vitamins B6 and B12 significantly decreased the incidence of major adverse events after PTCA.[8] Studies done in Pakistan have also shown positive correlation between moderate hyper homocysteinemia and Ischaemic Heart Disease (IHD).[9,10]

According to fluorescent polarizing immuno-assay technique the normal total fasting plasma homocysteine level ranges between 4.45-12.42 µmol/l. A value above this range is considered as hyper-homocysteinemia. Several techniques can be used for determination of homocysteine in plasma: (radioenzymatic assays, ion exchange chromatography, fluorescent polarizing immuno-assay, and high performance liquid chromatography (HPLC). The most suitable method for clinical purpose is HPLC with fluorescence detection.

It is recommended that all patients with premature atherosclerotic disease and a paucity of more conventional risk factors should be screened for hyper-homocysteinemia. Homocysteinemic patients with premature coronary artery disease should be treated with folic acid (1 mg/d), vitamin B6 (10 mg/d) and vitamin B12 (0.4 mg/d). Family screening should always be done on patients with hyper-homocysteinemia.

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