Case Report

Hyperhomocysteinemia presenting as exclusive small vessel coronary artery disease (CAD) in a young

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Abstract

We present an extremely rare case of a 26-year-old young male, an engineering student and a staunch vegetarian from early childhood without conventional cardiac risk factors, with hyperhomocysteinemia presenting as acute lateral wall ST elevation myocardial infarction with angiographic evidence of focal critical occlusion of the first diagonal branch. Although homocysteinemia and its association with coronary artery disease is well known, hyperhomocysteinemia with very high level of plasma homocysteine (>100 μmol/l) presenting as an exclusive small vessel coronary artery disease like involving only diagonal branch sparing major coronary vessels has not yet been described in the literature. Our case is unique and the first description of an exclusive small vessel coronary artery disease sparing major coronary vessels in the presence of paradoxically very high-level serum homocysteine (in a young male without conventional cardiac risk factors). Vegetarians should be encouraged to take Vitamin B6 rich food like potatoes, bananas, and garbanzo beans to decrease the likelihood of having severe coronary artery disease secondary to hyperhomocysteinemia.

Keywords: Artery, coronary, disease, hyperhomocysteinemia, young

Case

A 26-year-old male nonsmoker, nondiabetic, non-hypertensive, and normolipidemic presented to the emergency department with history of retrosternal chest discomfort squeezing in nature and radiating to both arms like a flower base with shortness of breath and diaphoresis since last 4 h without any history of palpitation, presyncope, or syncope. During presentation, he had blood pressure of 110/70 mm Hg in right arm supine position with heart rate of 80 beats per minute. Cardiovascular system examination revealed the presence of left ventricular fourth heart sound (LVS_4). Base line electrocardiogram (ECG) revealed lateral wall ST elevation myocardial infarction [Figure 1] with reciprocal changes in the inferior leads, high sensitive Troponin (hs-Troponin) level was moderately raised (146 ng/ml), and all other serum chemistries were within normal limit. The gentleman was completely vegetarian from early childhood, even he had never consumed curd since early childhood due to personal dislike. Echocardiography revealed the presence of mild hypokinesia of the lateral wall with borderline left ventricular systolic dysfunction (EF-54%). He was taken for immediate right transradial coronary angiogram and primary percutaneous intervention (primary PCI). He was administered loading dose of aspirin 325 mg with Ticagrelor 180 mg and atorvastatin 80 mg immediately. Prior to transradial coronary angiogram unfractionated heparin 100 IU/kg was administered intravenously and right transradial coronary angiogram was done which revealed focal critical occlusion of the first diagonal branch [Figures 2 and 3] having occlusive luminal thrombus. The lesion was directly stented with a small drug eluting stent of 2.25 × 15 mm size and we achieved distal TIMI III flow [Figures 4 and 5] and patient was discharged in a stable condition the very next day. The patient's lipid profile was absolutely normal with low density lipoprotein (LDL) of 63 mg/dl. We sent

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Received: 01-08-2021 **Revised:** 02-10-2021
Accepted: 20-12-2021 **Published:** 30-06-2022

Access this article online

Quick Response Code:

Website: www.jfmpc.com

DOI: 10.4103/jfmpc.jfmpc_1539_21

How to cite this article: Das D, Das T, Pramanik S. Hyperhomocysteinemia presenting as exclusive small vessel coronary artery disease (CAD) in a young. J Family Med Prim Care 2022;11:3298-301.

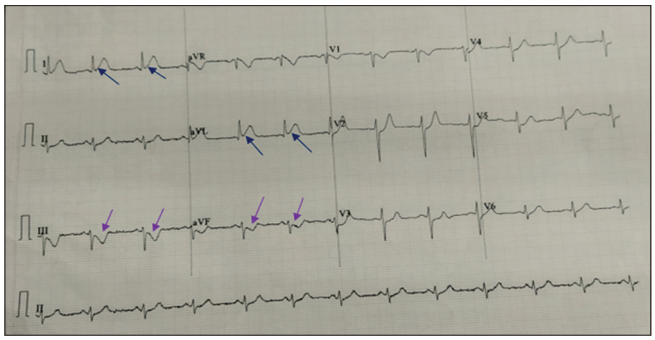

Figure 1: ECG showing ST elevation in I and aVL (Blue arrows) with reciprocal ST depression (Purple arrows) with T wave inversion in III and aVF suggestive of high lateral wall MI

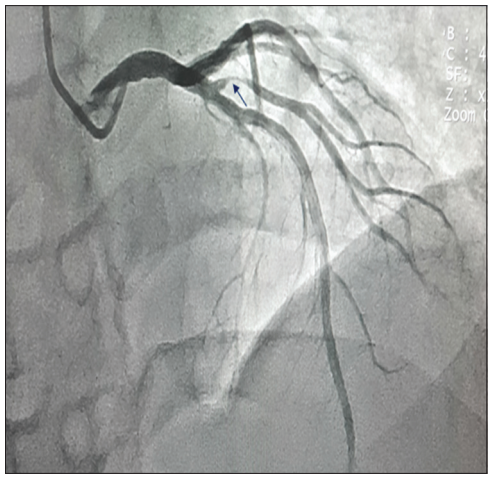

Figure 2: AP cranial view showing critical focal lesion in first diagonal branch

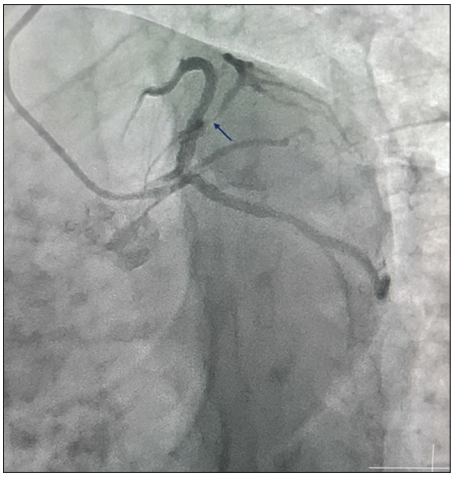

Figure 3: LAO caudal or spider view showing critical occlusion in first diagonal branch

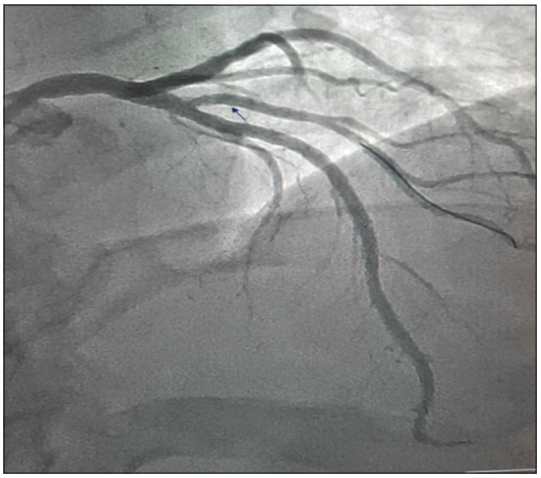

Figure 4: Recanalized first diagonal post stenting with drug eluting stent (DES) in AP cranial view

for serum homocysteine, Lipoprotein little a (Lp a), and Factor V Leiden. Serum homocysteine was quite high with value of 108 μmol/L suggestive of hyperhomocysteinemia and serum Lp a and Factor V Leiden were within normal limit. His serum Vit B_{12} level was quite low with a value of 43 pg/ml (normal 180–1000 pg/ml) and his serum folate was normal with a value of 6.2 ng/ml (3–20 ng/ml). Vit B_{12} deficiency is diagnosed when the serum Vit B_{12} level is below 150 pg/ml and serum Vit B_{12} level <100 pg/ml is known to be defined as severe form of Vit B_{12} deficiency. His serum Vit B_{12} was quite low due to his strict vegetarian nature from early childhood. Our case is the first literature description of exclusive small vessel coronary artery disease in a case of hyperhomocystinemia in a young. We supplemented the patient with oral Vit B_{12} 1000 mcg daily along with Folic acid 1 mg daily with advice to continue the antiplatelets and statins along with regular intake of curd which is a good source of Vit B_{12} along with adequate intake of fresh fruits and vegetables to maintain the serum folate level. He was advised to repeat serum B_{12} during routine regular follow-up in the outpatient department after 1 month.

Discussion

Elevated level of plasma homocysteine level is definitely associated with increased risk of coronary artery disease and it is also commonly observed across Asians. Hyperhomocystinemia is associated with major form of coronary artery disease as it involves the major coronary vessels; it involves either the left main coronary artery, left anterior descending coronary artery, left circumflex coronary artery, or right coronary artery. But hyperhomocystinemia exclusively involving small vessel coronaries like diagonals, obtuse marginals, or acute marginal branches has not been described so far in the literature. Our case is a unique and first description of the exclusive involvement of a small coronary vessel that is the first diagonal branch and other coronaries being absolutely normal in a case of hyperhomocystinemia in a young male without conventional cardiac risk factors. Schnyder *et al.*[1] analyzed 549 patients with elevated levels of plasma homocysteine and observed poor outcome in those patients post coronary intervention in the form of major adverse cardiac events (MACE) either in the form of recurrent myocardial infarction, stroke, or death. In their study, homocysteinemia involved the major vessels in the form of either left main coronary artery, left anterior descending coronary artery, left circumflex artery, or right

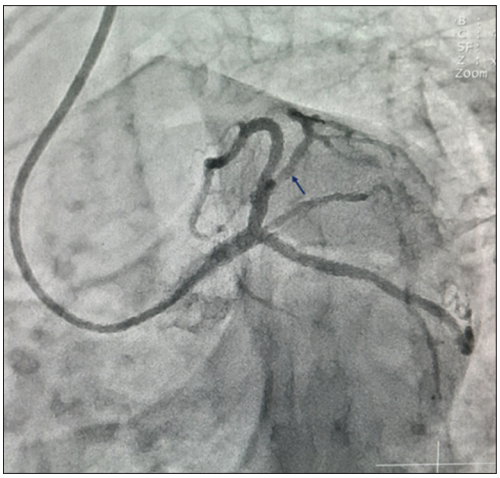

Figure 5: Recanalized first diagonal post stenting with drug eluting stent (DES) in LAO caudal or spider view

coronary artery. Across their observation in 549 patients, exclusive involvement of a small coronary vessel in the form of diagonal, obtuse marginal, or an acute marginal branch was not observed. Shanshan *et al.*[2] described small coronary artery involvement in about 9.1% of patients with coronary artery disease across 667 patients with hyperhomocystinemia. But exclusive involvement of one small vessel sparing major coronaries was not reported in their series. Shah *et al.*[3] in their study across 118 patients with homocystinemia noted single major vessel coronary artery disease in 108 (92.2%) patients, whereas 10 (7.8%) had more than one major coronary artery involvement; there was no description of exclusive involvement of a small coronary artery sparing the major coronary vessel in patients with hyperhomocystinemia. Across their study, mean plasma homocysteine concentration was 44.5 μmol/L but in our case, it was almost more than two-fold noted across their study. Paradoxically inspite of too high level of homocysteine, patient had coronary artery disease sparing the major coronary vessels and it was limited to a small vessel diagonal only. Contradictory to our observation, Sun *et al.*[4] described the presence of hyperhomocystinemia (>15 μmol/L) in young patients less than 35 years is more commonly associated with multivessel coronary artery disease and left ventricular systolic dysfunction. Karadeniz *et al.*[5] observed a high level of serum homocysteine >18 μmol/L is associated with a high angiographic SYNTAX score but in our patient, although the serum homocysteine level was more than 100 μmol/L, patient had only one diagonal branch coronary artery disease sparing the major ones (SYNTAX score was too low <22). The mechanism of development of coronary artery disease in hyperhomocystinemia includes toxic effect of hyperhomocysteinemia impairing endothelial production of nitric oxide and vessel stiffening by increasing proliferation of smooth muscle cells with adventitial inflammation which lead to development of atherosclerosis.[6] Incorporation of homocysteine into the tissue proteins is the principal mechanism behind toxicity. Yun *et al.*[7] described in the presence of homocystinemia LDL particle size becomes smaller, they become more prone to get oxidative modification and they turn more atherogenic. Bianca *et al.*[8] suggested homocystinemia exerts a prothrombotic effect by enhancing platelet aggregation. Those above three described mechanisms of action make young patients more prone to develop coronary artery disease in the presence of hyperhomocystinemia. Since obesity, alcohol, caffeine consumption, smoking, low level of folate, and Vit B_{12} increase the level of serum homocysteine, young patients are advised to maintain a healthy life style with healthy diet. In our patient, serum Vit B_{12} level was quite low, we orally supplemented it and advised the patient to have one cup of curd daily with lunch and dinner with adequate intake of fresh fruits and green leafy vegetables as persistently high homocysteine level post coronary intervention carries a high risk of MACE in the form of high risk of recurrent myocardial infarction, stroke or death. Chizynski *et al.*[9] described a homocysteine level >17.17 μmol/L is associated with increased risk of double vessel or triple vessel coronary artery disease. But the index patient having very high level of homocysteine (>100 μmol/L) had coronary artery disease confined to the diagonal branch only, also it was also focal in nature not a diffuse one. Mirbolouk *et al.*[10] described a positive association between serum homocysteine level and severity of coronary artery disease quantified by angiographic Gensini score. Our case is a paradoxic presentation of hyperhomocystinemia in a young with a very high level of serum homocysteine being more than 100 μmol/L presenting as a focal small vessel diagonal disease sparing the major coronary vessels which has not yet been described in the literature. Singh *et al.*[11] described a case of triple vessel coronary artery disease in a patient with familial hyperhomocysteinemia with serum homocysteine level of 149 μmol/L (normal 4–15 μmol/L) emphasizing the fact that a very high level of serum homocysteine is associated with major form of coronary artery disease involving the major vessels. But very high level of serum homocysteine presenting as a small vessel coronary artery disease has not yet been described. Kazemi *et al.*[12] described a linear relationship between the level of serum homocysteine and the number of major coronary vessels involved. Normal plasma homocysteine level is 5–15 μmol/L and homocysteine level in the range of 16–30 μmol/l is described as mildly increased, level of 31–100 μmol/l is regarded as moderately increased, and homocysteine level more than 100 μmol/l is regarded as very high level of plasma homocysteine.[13] Therapeutic paradox in treating homocystinemia remains as lowering the serum homocysteine by Vit B_{12} supplementation failed to demonstrate beneficial effect in cardiovascular disease[14] but folate supplementation is associated with improvement in vascular reactivity.[15-18] Our case is first description of exclusive small vessel coronary artery disease sparing major coronary arteries in a young patient with hyperhomocystinemia with very high level of serum homocysteine being more than 100 μmol/l. Vegetarians should be encouraged to take Vitamin B6 rich food like potatoes, bananas, and garbanzo beans to decrease the likelihood of having severe coronary artery disease secondary to hyperhomocysteinemia. Nonuniformity is the rule of nature.

Conclusion

Our case is the first literature description of exclusive small vessel coronary artery disease sparing the major coronary vessels in a case of hyperhomocystinemia with serum homocysteine more than 100 μmol/l in a young male without the presence of conventional coronary risk factors. Although level of serum homocysteine linearly correlates with the severity of coronary artery disease, our case is paradoxic to the same hypothesis and a unique illustration that hyperhomocystinemia can present as an exclusive small vessel coronary artery disease with bless in disguise. Vegetarians should be encouraged to take Vitamin B6 rich food like potatoes, bananas, and garbanzo beans to decrease the likelihood of having severe coronary artery disease secondary to hyperhomocysteinemia. A healthy diet compromising a serve including a cup of curd, a fresh fruit, and a cup of green leafy vegetable can save us from the dangerous consequence of coronary atherosclerosis.

Patient consent

Informed patient consent has been obtained.

Ethical clearance

Institutional Ethical Committee (IEC) clearance has been obtained.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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