Case Report **Biochemistry**

International Journal of Pharma and Bio Sciences **ISSN 0975-6299**

EFFECT OF SEVERE HYPERHOMOCYSTEINEMIA SECONDARY TO PERNICIOUS ANEMIA IN YOUNG ACUTE CORONARY SYNDROME

SUMATHI.K.[1*], VIDHYA LOGINI.T.[1] AND PRAKASH.M[2].

[1]Department of Biochemistry, [2]Department of E.N.T. Sree Balaji Medical College and Hospital, Chennai, TamilNadu. (Bharath University)

ABSTRACT

Vitamin B12 deficiency which results in pernicious anemia[1, 2], hyperhomocysteinemia, a known risk factor for venous and arterial thrombosis. We report on a 33-year-old man presented to the emergency room with complaints of vague chest discomfort and pain radiating from the shoulder on both sides to both the fore arms along the ulnar borders. and ECG showed transient J point ST elevation in V1- V4. He has been admitted in cardiac ICU for further management. Found to have Single vessel disease [Distal LAD].Laboratory evaluation revealed pernicious anemia and high serum homocysteine[>50 µmol/L] . Treatment with subcutaneous vitamin B12 results in rapid sustained decline in homocysteine levels with no subsequent thrombotic events through 1 year of follow-up. This case demonstrates that pernicious anemia may cause significant cardiovascular complications due to hyperhomocysteinemia[3,4,5], and should be considered in the diagnosis of a patient with a thrombotic event .

KEYWORD: Pernicious anemia, Hyperhomocysteinemia, Thrombosis.

SUMATHI. K.
Department of Biochemistry, Sree Balaji Medical College and Hospital, Chennai, TamilNadu. (Bharath University)

***Corresponding author**

INTRODUCTION

VitaminB12 deficiency commonly results in Pernicious anemia, due to a lack of intrinsic factor, a protein produced by gastric parietal cells and necessary for absorption of vitamin B12 in the terminal ileum. B12 deficiency and thrombosis resides in the elevation of plasma homocysteine. Studies have shown an association between vitamin B12 deficiency, homocysteine levels and acute coronary syndrome. [5,6]

CASEREPORT

A 33-year-old male glycemic and normotensive presented to the emergency room with complaints of vague chest discomfort and pain radiating from the shoulder on both sides to both the fore arms along the ulnar borders. and ECG showed transient J point ST elevation in V1- V4. The patient received 150 mg of aspirin,75mg of plasix,T.Rosuvas 40mg T.Seloken XL 25 mg ,T. Homochek and a bolus of unfractionated heparin, and was taken for urgent coronary angiography done. Which revealed single vessel disease [Distal LAD] , non occlusive thrombus in LAD.Patient also complained of paresthesias in his hands and feet for a few months prior to the admission. Laboratory assessment was notable for macrocytic anemia with a mean corpuscular volume of 105 fL and hemoglobin of 11.2 g/dL. Cardiac troponin I was11.66 ng/ml , CPKMB 208U/Land CK total 1538U/L.The patient's young age, neuropathy, anemia, and significant thrombus burden prompted an extensive laboratory investigation for hyperocagulability risk factors . The patient was found to have a severely elevated homocysteine level of 50 µmol/L and marked vitamin B12 deficiency. A positive anti-parietal cell antibody test revealed of pernicious anemia as the underlying etiology. Daily parenteral vitamin B12 was initiated, in addition to routine pharmacotherapy for acute coronary syndrome. During his recovery, the patient had several episodes of mild chest pain, without corresponding EKG changes, which resolved with sublingual nitroglycerin. Repeat coronary angiography showed no evidence of residual thrombus. After 6 days of vitamin B12 repletion, the patient's homocysteine level decreased to 12 µmol/L. They discharged the patient to home with the medical advice like subcutaneous vitamin B12 supplementation, aspirin, clopidogrel, Rosuvas, Seloken XL and Alprax. We followed the patient up to 1 year after his acute coronary syndrome. During that time, his neuropathy resolved and he did not demonstrate signs or symptoms of heart failure.

DISCUSSION

Homocysteine is a sulfur-containing amino acid that is converted to methionine via methionine synthase[8, 9,10.] This reaction requires vitamin B12 as a cofactor. The most common cause of severe homocysteinemia is the homozygous deficiency of cystathionine beta-synthetase. In 1969, Kilmer MucCully first described the link between elevated homocysteine levels and atherothrombotic disease in two children with inborn errors of methionine metabolism and diffuse arterial plaques.[9, 12-14] The pathophysiologic mechanism linking hyperhomocysteinemia with vascular events remains unclear, though human and animal studies have demonstrated abnormal endothelial-dependent vasorelaxation in response to elevated serum homocysteine[11]. It appears that increased oxidative stress may lead to decreased bioavailabilty of endothelium-derived nitric oxide[14] In addition, homocysteine contains a reactive thiol group, which can undergo disulfide reactions with cysteine residues in proteins, and potentially alter the function of those required for normal vascular function. The resulting stress in the endoplasmic reticulum may manifest as activation of inflammatory pathways, impaired insulin signaling, dysregulation of lipid metabolism, and apoptotic cell death. Homocysteine has been shown to modulate tissue plasminogen activator binding to vascular endothelial cells, activate clotting factors VIIa and V, and inhibit protein C and heparin sulfate. This complicated interplay of endothelial dysfunction, pro-inflammatory, and pro-thrombotic events has been postulated to lead

to accelerated atherosclerosis, plaque rupture, and thrombosis. [13-14]

CONCLUSION

Thus, there is a significant association between vitamin B12 deficiency, hyperhomocysteinemia and acute coronary syndrome. This shows that vitamin supplementation can result in a rapid reduction in homocysteine levels as well thrombotic events. It also highlights the serious cardiovascular complications due to pernicious anemia.

REFERENCES

1. Toh BH, van Driel IR, Gleeson PA. Pernicious anemia. *New Engl J Med.* 337: 1441-1448. (1997)
2. Limal N, Scheuermaier K, Tazi Z, et al. Hyperhomocysteinaemia, thrombosis and pernicious anaemia. *Thromb Haemostasis.* 96: 233-235.(2006)
3. Melhem A, Desai A, Hofmann MA. Acute myocardial infarction and pulmonary embolism in a young man with pernicious anemia-induced severe hyperhomocysteinemia. *Thrombosis J*; 7: 5.(2009)
4. Carmel R, Green R, Rosenblatt DS,et al. Update on cobalamin, folate, and homocysteine. *Hematology Am Soc Hematol Educ Program.*62-81.(2003)
5. D'Angelo A, Selhub J. Homocysteine and thrombotic disease. *Blood*.90:1-11. (1997)
6. Refsum H, Ueland PM, Nygard O,et al. Homocysteine and cardiovascular disease.*Annu Rev Med.* 49: 31-62.(1998)
7. Cattaneo M. Hyperhomocysteinemia, atherosclerosis and thrombosis. *Thromb Haemostasis.* 81: 165-176.(1999)
8. McCully KS. Vascular pathology of homocysteinemia: Implications for the pathogenesis of arteriosclerosis. *Am J Pathol.*56: 111-128.(1969)
9. Yap S, Boers GH, Wilcken B, Wilcken DE, Brenton DP, Lee PJ, Walter JH, Howard PM, Naughten ER. Vascular outcome in patients with homocystinuria due to cystathionine beta-synthase deficiency treated chronically: A multicenter observational study. *Arterioscl Throm Vas.* 21: 2080-2085.(2001)
10. Lonn E, Yusuf S, Arnold MJ,et al. Homocysteine lowering with folic acid and b vitamins in vascular disease. *New Engl J Med*.354: 1567-1577.(2006)
11. Jamison RL, Hartigan P, Kaufman JS, et al. Effect of homocysteine lowering on mortality and vascular disease in advanced chronic kidney disease and end-stage renal disease: A randomized controlled trial. *JAMA*.; 298: 1163-1170. (2007)
12. Heinz J, Kropf S, Domrose U,et al. vitamins and the risk of total mortality and cardiovascular disease in end-stage renal disease: Results of a randomized controlled trial. *Circulation*.121:1432-1438.(2010)
13. Wald DS, Law M, Morris JK. Homocysteine and cardiovascular disease: Evidence on causality from a meta-analysis. *Brit Med J*.; 325:1202.(2002).