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Hyperhomocysteinemia – An Independent Risk Factor in a Young Male with Cryptogenic Stroke

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Case Report

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Abstract: Hyperhomocysteinemia has been shown to have increase role in stoke but it has not been proven to be an independent risk factor in cryptogenic stroke. The main purpose of this study was to evaluate whether hyperhomocysteinemia can be an independent risk factor for development of stoke in young adults. We are proposing to establish plasma homocysteine and Vitamin B12 assay as routine tests for the evaluation of cryptogenic stroke in young adults as they can be independent biomarkers for their diagnosis.
Keywords: Hyperhomocysteinemia, stoke, cryptogenic stroke, Vitamin B12

INTRODUCTION

Homocysteine is a thiol-containing non-protein derived alpha amino acid. It is synthesized from methionine involving demethylation reaction in a multi step process. It is further trans-methylated into methionine or trans-sulfurated to cysteine [1]. These multi step reactions utilize tetrahydrofolate and Vitamin B12 for trans-methylation reaction and pyridoxal phosphate for trans-sulfuration reaction [2]. Hyperhomocysteinemia though has been associated with endothelial injury, atherosclerotic plaque formation and is an independent risk factor for coronary artery disease. Hyperhomocysteinemia has been shown to have increase role in stoke but it has not been proven to be an independent risk factor in cryptogenic stroke. Cryptogenic stroke is defined as cerebral ischemia of unknown cause.10-40% [3,4] of stroke is cryptogenic. In this case report we have analyzed the case record and found the patient to have only Hyperhomocysteinemia to be a sole risk factor for cryptogenic stroke with no other known risk factors present.

CASE REPORT

A 21 year old male patient had come to our casualty with complaints of sudden onset of severe headache and right-sided weakness and numbness in both upper and lower limbs with no other associated features. He was a non smoker non alcoholic with no significant medication and past medical illness history. History of coronary artery disease with positive history type 2 diabetes mellitus and hypertension was present in his father. No history of neurological disease in his family.

On arrival the patient was hemodynamically stable conscious oriented with slight slurring of speech. The patient was moderately built with normal BMI and on examination his blood pressure was elevated 140/90 mmHg but otherwise his cardiovascular, respiratory and abdominal findings were normal. On neurological examination right side hemi paresis with mild motor dysphasia was seen. Mental faculties were intact.

On computed tomography examination the patient had a hypo density in his left hemisphere and on magnetic resonance imaging signs of infarct was seen in left middle cerebral artery territory and basal ganglia in left hemisphere. On magnetic resonance angiography left middle cerebral artery occlusion was noted. Carotid and vertebral Doppler was found to be normal. Echocardiography showed small plaques in left anterior descending artery with ejection fraction of 65%.

Laboratory tests performed were routine complete blood count, ESR, renal function tests, fasting lipid profile, thyroid function tests, Vitamin B12 , folate and total plasma homocysteine. Vitamin B12 was done using ELISA and serum total homocysteine using high performance liquid chromatography. His lipid profile was as follows: total cholesterol: 195 mg/dL(<200 mg/dL) HDL: 25 mg/dL (40–80 mg/dL), trigycerides 164mg/dl <150mg/dl) LDL: 137.2 mg/dL (60–130 mg/dL) VLDL 32.8mg/dL (20-45mg/dL), total CHO/HDL RATIO 7.80 (Less than 4.5) Homocystein: 35.22µmol/L (4.44–13.56 µmol/L) and Vitamin B12 level: 50 pg/mL (138–885 pg/mL) and folate 3.5µG/L. Other laboratory tests were within reference limits.

The patient was started on oral therapy of aspirin and clopidogreland vitamin B12 and folate intravenous supplementation and pyridoxal phosphate oral supplementation was started and total plasma homocysteine was serially measured and found to be lowered with regular supplementation. And after 2 weeks the patient was discharged with advice of physiotherapy and regular OPD review. Post a follow up period of 1 year the patient has no recurrence of ischemic events with total plasma homocysteine levels lowered from before and Vitamin B12, folate and pyridoxal phosphate regular supplementation and within normal limits.

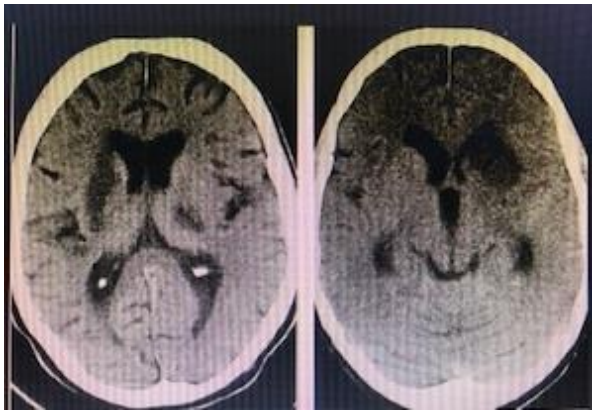

Fig-1: CT scan of patient showing a hypo density in his left hemisphere

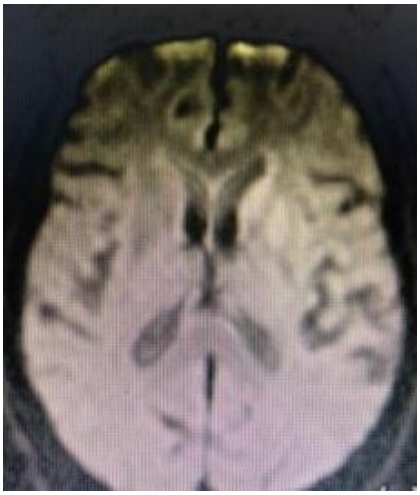

Fig-2: MRI of patient showing signs of infarct was seen in left middle cerebral artery territory and basal ganglia in left hemisphere

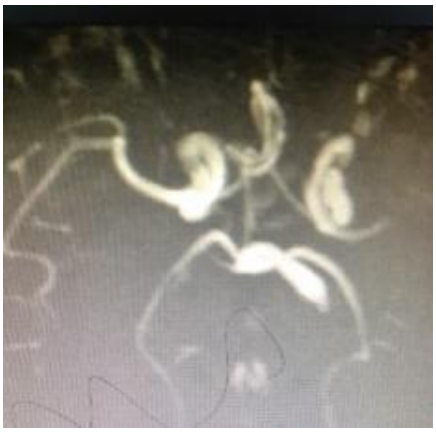

Fig- 3: MRA showing left middle cerebral artery occlusion

DISCUSSION

The main purpose of this study was to evaluate whether hyperhomocysteinemia can be an independent risk factor for development of stoke in young adults. Studies have shown the relevance and association of hyperhomocysteinemia with other co morbid factors [5,6] but no study has shown Vitamin B12 deficiency with increased homocysteine levels as an independent risk factor for the development of cryptogenic stroke[7]. In our case the cryptogenic stroke[3] was defined according to TOAST terminology of stroke with no known cause.

This patient had no previous illness was normotensive normoglycemic with normal BMI not a smoker non alcoholic and no history of any medications taken. This was his first episode of hemiparesis and on regular follow up with Vitamn B12 folate and pyridoxal supplementation his serial homocysteine levels were found to be lowered and he at the end of 1 year follow up had no ischemic events.

Studies have shown strong association of hyperhomocysteinemia with coronary artery disease and emboli and peripheral vascular occlusive diseases. Homocysteine (Hcy) levels of more than 15 µmol/L increases the risk of disease pathogenesis and 100 µmol/L are considered severe and may be caused by genetic enzymatic defects of Hcy metabolism [9] and are a risk for venous thrombosis and premature atherothrombosis [8]. The most frequent form of hyperhomocysteinemia is usually caused by insufficient dietary vitamin co-factors, renal dysfunction or hypothyroidism and is usually follows a mild to moderate course [10]. The high blood homocysteine increased by influence by diet, genes, hormones or metabolic changes was found to result in thromoboembolic processes due to atheroschlerosis[10]: resulting in changes in the connective tissue in the form of atherosclerotic plaques, fibrosis, calcifications, proteoglycan deposition, and tissue injury in the arterial elastic layer[8]. In addition, homocysteine being a potent procoagulant, it affects platelets, coagulation process resulting in endothelial injury and atherothrombotic plaque formation [11].

In our case report we have proven that cases with isolated Vitamin B12 induced Hyperhomocysteinemia can be treated to prevent occurrence of future ischemic episodes by regular supplementation with Vitamin B12 (2 mg/day) Folate (15 mg/day) and Pyridoxal (30mg/day).

CONCLUSION

We are proposing to establish plasma homocysteine and Vitamin B12 assay as routine tests for the evaluation of cryptogenic stroke in young adults as they can be independent biomarkers for their diagnosis. We also propose to treat them with regular supplementation of Vitamin B12 Folate and Pyridoxal thereby preventing future ischemic episodes.

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