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HYPERHOMOCYSTEINEMIA – A NEGLECTED ENTITY IN THEPREVENTION OF LIFE-THREATENING EVENTS

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INTRODUCTION

Industrialization of the world comes with the bane ofincreasing incidence and burden of life-threatening events like stroke, myocardial infarction and dissections. Lindsay et al., in the year 2020 have estimated an increase in the incidence of stroke cases to be around 13 million annually and have predicted that 1 in 4 people over the age of 25 will have stroke in their lifetime. Myocardial infarction and aortic dissections are no lesser a menace whencompared to stroke.

All through these years, comorbidities like diabetes mellitus, hypertension, deranged lipids were under the main schema when evaluating the above said cases. The magnitude of importance a simple derangement of the amino-acid likehomocysteine carried, was not valued to a desired level and this article aims at highlighting the core relationship between the increased homocysteine levels andits impact in the causation of life-threatening events. This article also highlights how an early diagnosis can aid in the prevention of future events in young individuals.

CASE REPORT 1 – A 36-year-old male Mr. XX was brought to our ER with complaints of pain in bilateral lower limbs, with a feeling of heaviness and numbness, for about 2 hours. The pain was reported to begin below the level of the umbilicus, extending down to involve bilateral lower limbs, which was acute in onset. Patient also reports to have difficulty in moving his limbs.

There was no history of fever, trauma, headache, seizures, backpain, cough with expectoration, alteration in bowel and bladder habits, chest pain or palpitations, profuse sweating, loss of consciousness, blurring of vision.

Patient also denied any recent surgeries or vascular procedures.

Past history revealed that the patient was a known case of coronary artery disease and had sustained a myocardial infarction 8 years back in the age of 28. Further evaluation of the cause for a young MI was not done and the patient was found to be a hypertensive and antihypertensives were prescribed. Patient was on regular medications since then. Patient is also an occasional alcoholic for the past10 years.

Examination of the patient- Patient conscious, oriented, afebrile, with good hydration. JVP was normal and no carotid bruit. Examination of the CNS was normal except for a mild limitation of power (3/5) of the lower limbs. The reflexesin the lower limbs were absent and the sensations were diminished but perceived.

Vitals: Blood pressure: Right upper limb: 120/70 mmHg.

Pulse rate: 98/min equal in bilateral upper limbs with no radio-radio delay.

Absent peripheral pulses in **bilateral** femoral, popliteal, tibial, dorsalis pedis arteries, with cold peripheries.

Urgent CT Angiogram: Filling defect noted in distal abdominal aorta near its bifurcation extending into bilateral common iliac artery causing complete occlusion of left common iliac, near complete occlusion of right common iliac artery which further extends into bilateral internal and external iliac arteries. However, distal right internal and external iliac artery is reformed through collaterals.

Evaluation of the patient showed:

Lipid profile with serum cholesterol- 259mg/dl.

Serum triglycerides: 429mg/dl.

Lp (a) was within normal limits <10.20 mg/dlpT, aPTT, INR within normal limits.

HOMOCYSTEINE LEVELS: >75 micromoles/L (Ref. Value -5.46 – 16.20)
Patient was treated with surgical intervention and succumbed to surgical stress induced myocardial infarction and cardiogenic shock.

CASE REPORT 2 – A 41-year-old male was brought with complaints of weakness of right upper and lower limbs for 8 hours. Patient is a known case of ischemic dilated cardiomyopathy which was diagnosed about 1 month back. No history of diabetes, hypertension, CKD, TB. Known alcoholic.

On examination, patient was conscious, with disturbed higher functions. Follows actions but doesnot respond verbally. Orientation could not be assessed. Patient was afebrile with good hydration.

Examination of CNS showed a power of 2/5 in the Right upper limb and 4/5 in the lower limb, with hypotonia and diminished reflexes with plantar non responsive. Left sided limbs had normal power, tone and elicitable reflexes.

Cortical functions: Memory, orientation couldnot be assessed. Speech – Broca'saphasia.

Sensations: Decreased responsiveness noted in the right side. Cerebellar signs could not be assessed and cranial nerve 7 was affected (UMN palsy).

MRI BRAIN: Cortical infarct involving the fronto parietal region of the Leftside.

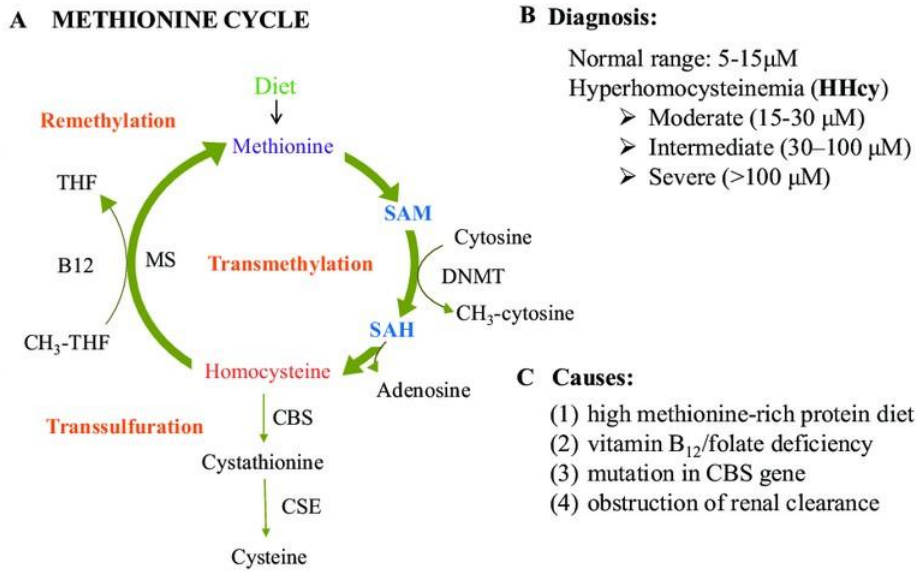
ECHO: Global hypokinesia of all 4 chambers with ejection fraction of 27% Blood investigations: CBC, RFT, LFT were normal.

Lipid profile within normal range. Lp(a) was under normal limits.

Homocysteine: >50 micromoles/L (Ref. Value -5.46 – 16.20).

DISCUSSION

Homocysteine: Homocysteine is a sulfur-containing amino acid and is produced from an essential amino acid methionine. Its concentrations are maintained via trans-sulfuration and remethylation pathways. Methionine synthase remethylates homocysteine back to methionine. Vitamin B12 acts as a cofactor for the above reaction. Folate also contributes to the same. Activities of the enzymes methylenetetrahyrdofolate reductase (MTHFR) and cystathione beta-synthase (CBS) regulate homocysteine levels. Vitamin B6 aids the activity of the cystathione beta synthase enzyme.



D Typical treatment options: vitamin B6/B9/B12 supplementation

Causes for Hyperhomocysteinemia

1. Deficiency of folate, vit.B12, folic acid.
2. Polymorphisms of MTHFR gene may also contribute to elevated homocysteine levels.
3. Certain drugs such as nitrous oxide, methotrexate and antiepileptics have also been proposed to increase the levels of homocysteine.
4. Chronic diseases like decreased renal function, hyperthyroidism, diabetes mellitus, malignancy.
5. Dietary intake of methionine, coffee, alcohol, cigarette smoking and physical inactivity work in consensus to increase the levels of homocysteine by not so clear mechanisms.

Pathogenesis: Hyper-homocysteinemia results in damage to the vessel wall by stimulating the proliferation of smooth muscle cells, increasing the oxidation of low-density lipoprotein (LDL), increasing the synthesis of

pro- coagulants, collagen and also by impairing the endothelial anticoagulant action. It exerts both direct and indirect effects on vascular and endothelial cell arachidonic acid metabolism. It also impairs factor V, protein C activation and decreases thrombomodulin expression.

It has also been shown to decrease the endothelial production of Nitic oxide (NO).

Treatment: The pleasing fact about the treatment of hyperhomocysteinemia is the easy and cheap availability of folic acid, vitamin B12 and vitamin B6. Studies conducted by Homocysteine Lowering Trialists Collaboration have concluded that folic acid (0.5–5 mg daily) reduced the homocysteine concentration by 25%. The addition of vitamin B_{12} (0.5 mg daily) produced an additional reduction of 7% whilst the addition of vitamin B_6 (16.5 mg daily) had no significant effect.

Apart from the above treatment, the treating physician must also bear in mind the other reversible causes of hyperhomocysteinemia like hypothyroidism. Though no conclusive studies have been demonstrated to show the effect of lowering the levels of hyperhomocysteinemia in reducing thrombotic events, simple and early identification of this additional risk factor, in addition to other traditional ways of treatment, might prove beneficial.

CONCLUSION

Hyperhomocysteinemia as a risk factor for life threatening strokes, myocardial infarction and dissections is a topic of recent discussion. Early identification and management of this might prove beneficial in decreasing the incidence or delay the onset of such events in young individuals.

REFERENCES

1. World Stroke Organisation.
2. Journal of Clinical neurology. Hyperhomocysteinemia and neurological disorders: a Review.
3. M. Markis- Hyperhomocysteinemia and thrombosis.
4. The Association between hyperhomocysteinemia and Thoracoabdominal aortic aneurysms in Chinese population – Hindawi Journal.