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Hyperhomocysteinemia Presenting As Acute Ischemic Stroke And Central Retinal Artery Occlusion In A Young Male.

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Abstract: *Hyperhomocysteinemia considered "the cholesterol of nineties", is an independent risk factor of cardiovascular disease and premature atherosclerosis. It is defined as a medical condition characterized by abnormally high levels of homocysteine in the blood.*
Rapidly accumulating evidence links elevated homocysteine levels to thrombosis via several mechanisms such as increased tissue factor expression, attenuated anticoagulant processes, enhanced platelet reactivity, increased generation of thrombin, augmented factor V activity, fibrinolytic potential impairment and vascular injury. Atherogenic nature of homocystiene has a vital role in the development of cardiac or cerebral ischemic strokes. Several observational studies also show the association between hyperhomocysteinemia and recurrent venous thrombosis. We present a 45 year old male ,who presented to us with acute ischemic stroke and central retinal artery occlusion due to hyperhomocysteinemia.

Keywords: *Hyperhomocysteinemia; Acute ischemic stroke; Central retinal artery occlusion*

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I. Introduction

Homocystein (Hcy) is a sulphydryl-containing amino acid metabolite of methionine, a compound essential for intracellular metabolism [1].It is generally not obtained from diet[2] and is synthesized from methionine via S-Adenosyl methioninecycle or used to create cysteine and alpha-ketobutyrate[3].It can be recycled into methionine, this process uses N5-methyl tetrahydrofolateas the methyl donor and cobalamin (vitamin B12)- related enzymes[4]. Thus deficiencies of vitamin B-12, folic acid and vitamin B-6 can lead to high levels of homocysteine [5]. There are various other causes that can lead to hyperhomocysteinemia in the blood: TABLE-1 [8].

High level of homocysteine in the blood(hyperhomocysteinemia) makes the person more prone to endothelial cell injury, which leads to inflammation in the blood vessels, which inturn may lead to atherogenesis, thus resulting in ischemic injury[6].

Hyperhomocysteinemia recently has been recognized as a early modifiable risk factor of hypercoagulability states and atherosclerotic cerebro or cardiovascular diseases[7].

SOME OF THE CAUSES OF HYPERHOMOCYSTEINEMIA
GENETIC DEFECTS
• Cystathionine-B-Synthase Deficiency
• 5,10 Methylenetetrahydrofolate Reductase Deficiency
• Methioninesynthase Deficiency
• Genetic Defects In The Vitamin B-12 Metabolism
VITAMIN DEFICIENCIES
• Lack of folic acid
• Lack of vitamin B-12
• Lack of vitamin B-6
OTHER FACTORS
• Sex
• Lifestyle (smoking, coffee, alcohol)
• Chronic renal insufficiency
• Diabetes mellitus
• Hepatic dysfunction

• Pernicious anaemia • Menopause

TABLE-1[8].

II. Case Report

A 45 year old male patient presented to us with sudden onset weakness of right upper limb and lower limb of 4 days duration along with sudden loss of vision in the right eye. Patient did not complain of loss of consciousness, headache, vomiting,seizures and bowel and bladder incontinence. Patient was not a known case of hypertension, diabetes mellitus and ischemic heart disease. There was no significant past history.

On examination patient was moderately built. Pulse was 88 beats per min regular normal volume. Blood pressure was 138/78 mm Hg. Respiratory rate was 16 breathes per min. His oxygen saturation was 99% while breathing ambient air. There was no pallor, icterus, cyanosis. Patient did not have oedema. JVP was not raised. Cardiovascular and respiratory system examination was normal.

Central nervous system examination: Higher mental functions were intact. Ophthalmologic examination: vision was PR PL in the right eye. Left eye vision was 6/6. Fundus examination: In the right eye revealed pale disc with ghost vessels in supra and infra tentorial segments suggesting Central retinal artery occlusion (figure 1).Ophthalmologic examination was completely normal in the left eye. Other cranial nerve examinations normal.Motor examination power was 3/5 in right upper and lower limb. Plantar reflex extensor on the right side.Sensory system examination was normal.

On investigation:

Haemoglobin was 12.4gm/dl, MCV was 105 fl. Total leucocyte count and platelets were normal. Kidney function and liver function tests were normal.C-ANCA, ANA, RA factor, ESR, Protein C, protein S, antithrombin III levels , factor V leiden mutation were normal. Serum vitamin B-12 levels estimated which was 98 ng/ml (normal:200- 900 ng/ml). Serum homocysteine levels estimated which was 60.1micromol/l(normal-4.9-15micromol/l).ECG suggested normal sinus rhythm.2D echo revealed normal study, carotid Doppler study showed complete thrombotic occlusion of right internal carotid artery from its origin. There was sub acute to chronic occlusion of right internal carotid artery just from its origin with no reformation. MRI with MR-angiography revealed multiple bilateral parietal sub acute infarcts with hemorrhagic infarct in right parietal occipital region and thrombosis of right ICA in cervical, cavernous and supra clenoid segments with involvement of right ophthalmic artery(figure 2,3),non visualization of cavernous part of internal carotid artery with narrowing proximally. Digital subtraction angiogram confirmed the same. (figure 4).

Patient was started on inj.vitamin B-12 1000μg i.m daily for seven days and advised to continue inject tions once weekly for four weeks and then monthly for life long. Folic acid 5mg was started orally, Tab. Ecosprin 150mg was added tab pyridoxine 40mg per day was added, he was also given physiotherapy. Patients Vision did not improve. Patients power improved to 4/5 in right upper and lower limb. Patients was discharged on day 7 and awaiting follow up.

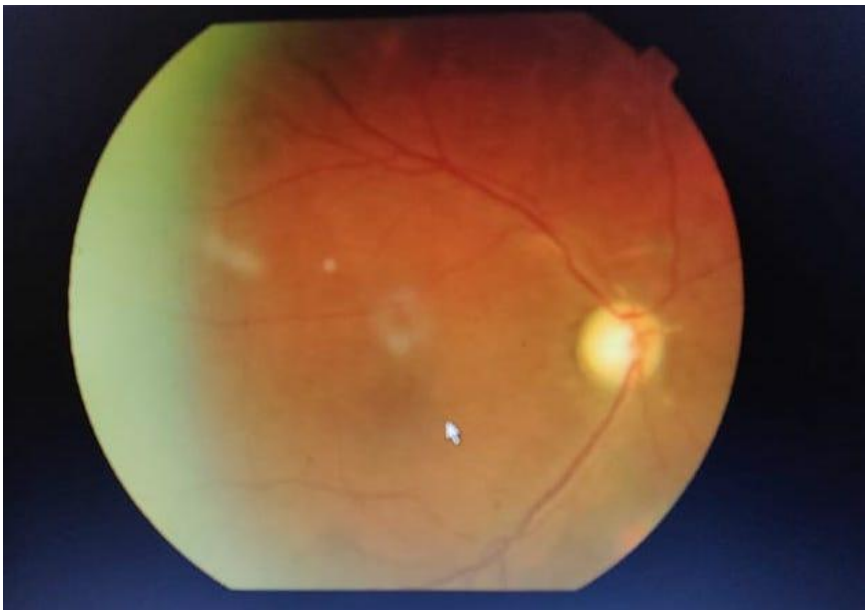

Fig-1: FUNDUS RIGHT EYE; Showing pale disc with ghost vessels in supra and infra temporal segments suggesting CRAO in the right eye.

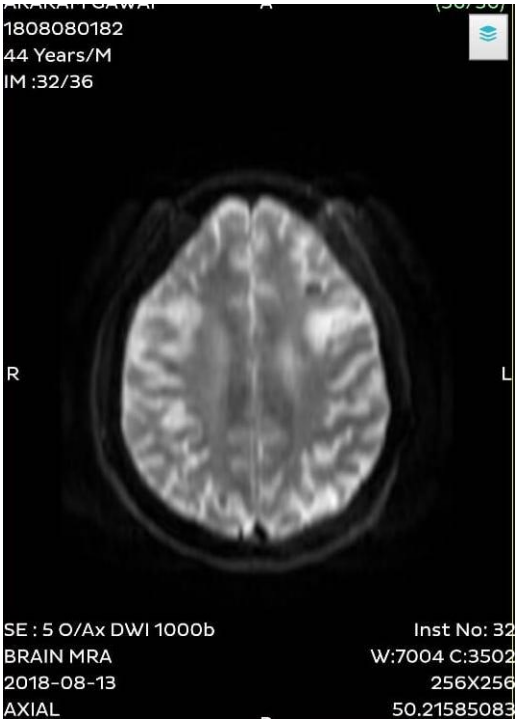

Fig-2: MRI scanBrain

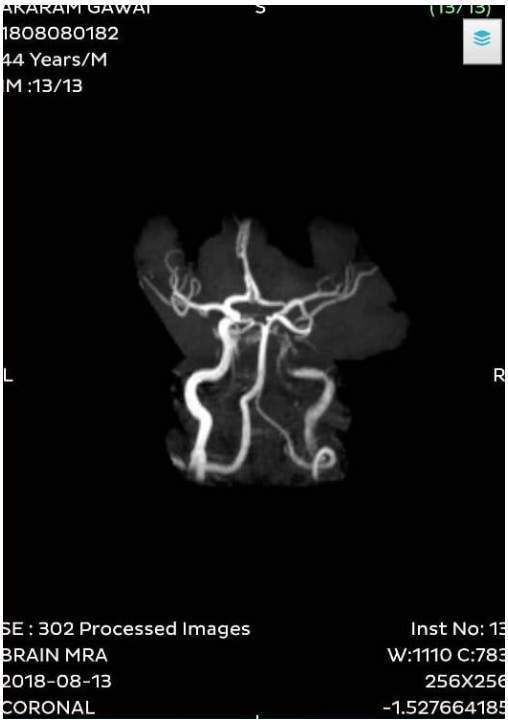

Fig-3: MR Angiography

Suggesting of multiple bilateral parietal sub acute infarcts with hemorrhagic infarct in right parietal occipital region and thrombosis of right ICA in cervical, cavernous and supra clenoid segments with involvement of right ophthalmic artery

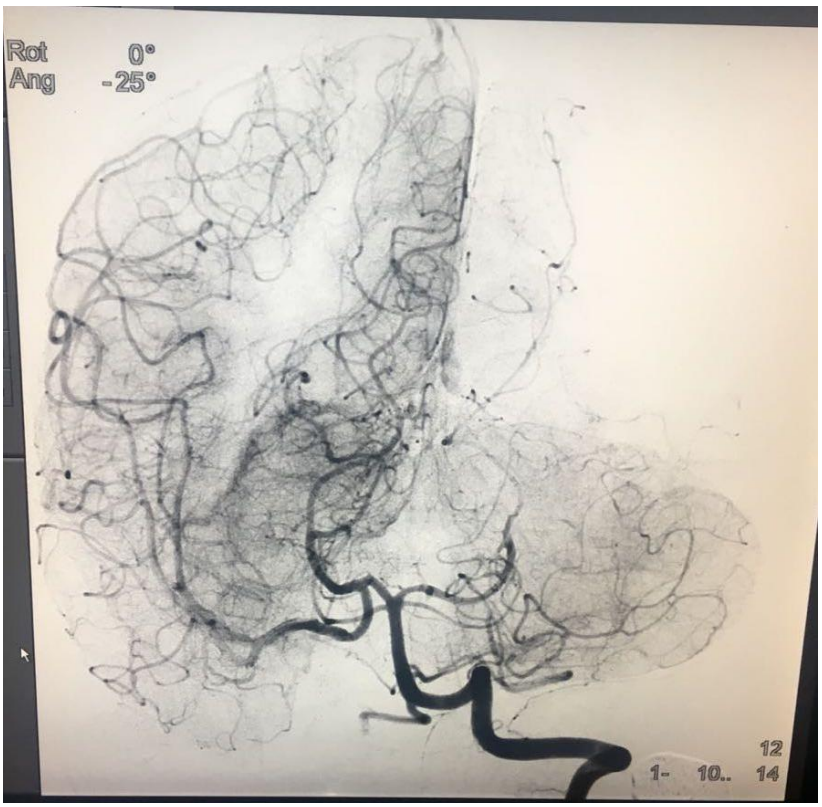

Fig-4: Digital subtraction angiogram showing internal carotid artery obstruction

III. Discussion

It is well established that Hcy increases the risk of developing large and small vessel strokes,

Hyperhomocysteinemia has a multifactorial origin. The factors attributed for the development of hyperhomocysenemia may be genetic, nutritional, pharmacological, and pathological. Epigenetic contributions in form of ethnicity and diet are also known. An increased homocysteine level is associated with a higher risk of strokes. Carotid stenosis is affected in a graded fashion with increased levels of homocysteine[10]. Increased carotid plaque thickness is linearly associated with high homocysteine and low B-12 levels[11,12].

The deleterious effect of hyperhomocysteinemia is mediated primarily via a proatherogenic effect and less likely due to prothrombotic effect, which might be contributory in the large vessel disease[13]. A study revealed that elevated homocysteine levels were associated with cerebral microangiopathy and not with cardioembolic or macroangiopathy-associated ischemic stroke, again emphasizing the proatherogenic effect[14].

All the evidences suggest that hyperhomocysteinemia is both atherogenic and prothrombotic. The various mechanisms through which these proatherogenic state is achieved are, direct endothelial injury, mitogenic effect on smooth muscle cells leading to smooth muscle cell proliferation, impaired endogenous fibrinolysis, endothelial nitrous oxide response, and alteration in arachnoidic acid metabolites like thrombaxane induced vasoconstriction and platelet aggregations[15].

Central retinal artery occlusion (CRAO) is uncommon in the young population[16,17]. Various isolated case reports have reported a diverse and multifactorial etiology which includes cardiac valvular disorders and various vascular inflammatory disorders [18].

In an Indian study which was conducted to determine the etiological factors for central retinal artery occlusion concluded that the commonest factor was hyperhomocysteinemia (21.9%) cases[19]. Elevated homocysteine and low methionine are known factors for retinal vascular occlusions and our patient was having low vitamin B-12 levels and hyperhomocystienemia[20].

Treatment of hyperhomocyetenemia is replacement of pyridoxine, vitamin B 12 and folic acid. These three in combination reduces the homocysteine levels and also provide some clinical benefits. Aniplatelet agents like aspirin, clopidogrel and dipyridamol have been suggested for secondary stroke prophylaxis, secondary stroke prevention basically rest on risk factor reduction[21].

IV. Conclusion:

Our patient was simultaneously having CRAO with stroke. He had diffuse disease involving the internal carotid artery and its branches. Other investigations ruled out etiological factors of stroke in young. Increased homocysteine level, MCV and reduced vitamin B-12 levels makes this case unique suggesting hyperhomocysteinemia and B-12 deficiency causing diffused intracranial vascular disease. Physicians, neurologist dealing with young stroke should keep a possibility of hyperhomocysteinemia in such cases which is the commonest preventable cause in Indian population.

References

[1]. Mudd SH, Finkelstein JD, Refsum H, Ueland PM, Malinow MR, Lentz SR, Jacobsen DW, Brattstrom L, Wilcken B, Wilcken DE, Blom HJ, Stabler SP, Allen RH, Selhub J, Rosenberg IH: Homocysteine and its disulfide-derivative: Asuggested consensus terminology. Arterioscler Thromb Vasc Biol. 2000;20: 1704-1706.

[2]. Selhub J. "Homocysteine metabolism". Annual Review of nutrition. 1999;19:217-246.

[3]. Champe PC and Harvey RA. "Biochemistry. Lippincott's Illustrated Reivews"4th ed. Lippincott Williams and Wilkins. 2008.

[4]. Sibrian-Vazquez M, Escobendo JO, Lim S, Samoei GK, Strongin RM."Homocystamides promote free –radical and oxidative damage to proteins".Proc. Natl. Acad. Sci. U.S.A. January 2010;107(2): 551-4.

[5]. Miller J.W. Nadeau, M.R. Smith, D Selhub J. "Vitamin B-6 deficiencies vs folate deficiency: Comparison of responses to methionine loading in rats". The American Journal of Clinical Nutrition.1994;59(5): 1033-9.

[6]. Hankey GJ. Is plasma homocysteine modifiable risk factor for stroke? Nat Clim Pract Neurol. 2006;2: 26-33.

[7]. Abraham R, John MJ, Calton R, Dhanoa J. Raised serum homocysteine levels in patients of coronary artery disease and the effect of vitamin B-12 and folate on its concentration. Indian journal of clinical biochemistry 2006;111: e289-e293.

[8]. Welch NG,Loscalzo J. Homocysteine and atherothrombosis. N Engl J Med. 1998;338: 1042-50.

[9]. Mangge H, Becker K, Fuchs D, Gostner JM. Antioxidants, inflammation and cardiovascular disease. World J Cardiol. 2014;6(6): 462-77

[10]. Yoo et al studied both intracranial and extracranial vessels by MR angiography and reported that homocysteine levels were higher in patients with 2- or 3-vessel stenoses than in those with 1-vessel stenosis.

[11]. Malinow MR. Hyperhomocysteinemia: A common and easily reversible risk factor for occlusive atherosclerosis. Circulation 1990;81:2004-06.

[12]. Parnetti L, Caso V, Santucci A, Corea F, Lanari A, Floridi A, et al. Mild hyperhomocysteinemia is a risk-factor in all etiological subtypes of stroke. Neurol Sci.2004;25:13–17. doi: 10.1007/s10072-004-0219-5.

[13]. Eikelboom JW, Hankey GJ, Anand SS, Lofthouse E, Staples N, Baker RI. Association between high homocysteine and ischemic stroke due to large and small artery disease but not other etiologic subtypes of ischemic stroke. Stroke 2000;31:1069-75.

[14]. Evers S, Koch HG, Grotemeyer KH, et al. Features, symptoms and neurophysiological findings in stroke associated with hyperhomocysteinemia. Arch Neurol 1997;54:1276-82.

[15]. Modi M, Prabhakar S, Majumdar S, Khullar M, Lal V, Das C P. Hyperhomocysteinemia as a risk factor for ischemic stroke: An Indian scenario. Neurol India 2005;53:297-301

[16]. Brown GC, Magargal LE, Shields JA, Goldberg RE, Walsh PN. Retinal arterial obstruction in children and young adults. Ophthalmology 1981;88:18-25.
[17]. Greven CM, Slusher MM, Weaver RG. Retinal arterial occlusion in young adults. Am J Ophthalmol 1995;120:776-83
[18]. Gold D. Retinal arterial occlusion. Trans Sect Ophthalmol Am Acad Ophthalmol Otolaryngol 1977;83:392-408
[19]. Ratra D, Dhupper M. Retinal arterial occlusions in the young: Systemic associations in Indian population. Indian J Ophth.almol 2012;60:95-100
[20]. Narayanasamy A, Subramaniam B, Karunakaran C, Ranganathan P, Sivaramakrishnan R, Sharma T, et al. Hyperhomocysteinemia and low methionine stress are risk factors for central retinal venous occlusion in an Indian population. Invest Ophthalmol Vis Sci 2007;48: 1441-6.

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