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Research Article

HOMOCYSTINURIA: A RARE CONDITION PRESENTING AS STROKE IN A CHILD HAVING SICKLE CELL DISEASE (HETEROZYGOUS)

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A B S T R A C T

Homocystinuria is an inborn error of amino acid metabolism in which homocystine accumulates in the blood and produces a slowly evolving clinical syndrome. We are presenting a case of a 14-year-old male child who presented to us with stroke. He was diagnosed as having homocystinuria and was found to have sickle cell trait, and he responded to treatment.

INTRODUCTION

Homocystinuria is a general term for a group of disorders that cause elevated levels of aminoacid homocystine in urine. These disorders primarily occur because of deficiency of any of several enzymes required for the proper degradation or reformation of an essential amino acid called methionine. Elevated levels of methonine can cause a variety of health problems. This methionine-sparing reaction is catalyzed by the enzyme methione synthase, which requires a metabolite of folic acid (5-methyltetrahydrofolate) as a methyl donor and a metabolite of vitamin B12 (methylcobalamin) as a cofactor. Further conversion of homocysteine to cystathionine requires a pyridoxal phosphate-dependent enzyme, cystathionine ß synthase, deficiency of which results in accumulation of homocysteine and reconversion of homocysteine to methionine. [1].

It is characterized by developmental delay, ectopia lentis, progressive mental retardation, skeleton abnormalities resembling Marfan syndrome and thromboembolic episodes. Diagnosis is usually made after 3 years of age, when most of the patients present with subluxation of the lens. Homocystinuria can also occur due to defect in methylcobalamin formation, i.e. homocystinuria type-II, characterized by the triad of megaloblastic anemia, homocystinuria and hypomethionemia. Deficiency of the enzyme methyltetrahydrofolate reductase results in homocystinuria type-III, characterized by homocystinemia, homocystinuria and low-low normal levels of methionine. [2]

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Case Report

A 14 year male boy was admitted to the department of paediatrics of MKCG medical college with complains of right sided headache for 3 days and vomiting for 3 days. There was no history of fever, burning micturation or loose stool. The child was a known case of sickle cell disease (heterozygous). Hence a provisional diagnosis of vascular stroke due to sickle cell disease was made. But on examination it was found that the child was of thin built having marfanoid features, pes pectus with right sided conjuctival congestion and there was corneal opacity present. There was history of convulsions and psychiatric problems like aggressiveness. On opthalmological examination, he was found to have myopia, anterior dislocation of lens with secondary glaucoma and subluxated lens of the right eye. These features pointed towards a diagnosis of homocystinuria. The serum homocysteine level was foung to be 298 micromol/l (normal is 5-16). Thus confirming the diagnosis. The child was treated with folic acid, vitamin b12 and pyridoxine.He was adviced to take low methionine diet.

DISSCUSSION

Homocystinuria is an autosomal recessively inherited defect in the transsulfuration pathway (type-I) or methylation pathway (types II and III). The internationally reported incidence of homocystinuria varies between 1 in 50,000 and 1 in 200,000. [3] Normally, homocysteine is an intracellular intermediate and is not detectable in plasma or urine.

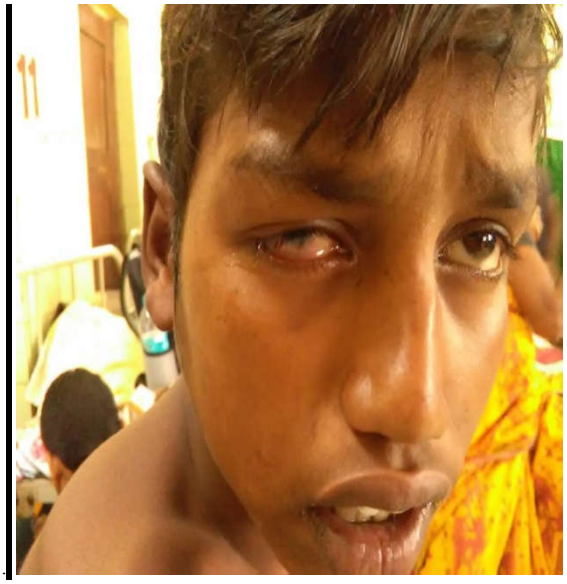

Fig 1 showing conjunctivitis of right eye

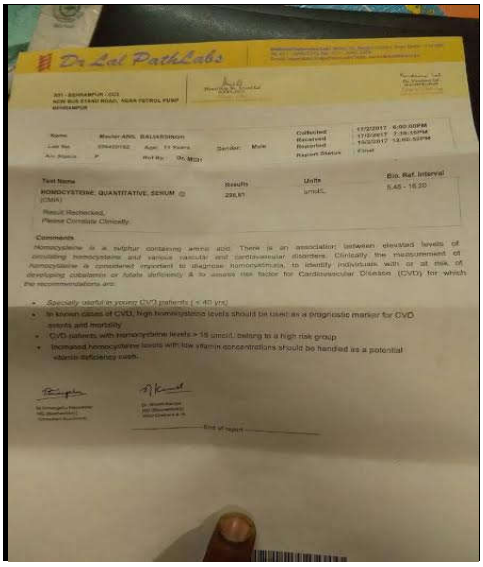

Fig 2 showing high serum homocystine levele

However, when the reconversion of homocysteine to methionine or cysteine is blocked, it accumulates extracellularly and results in homocystinuria.[4] Cruysberg et al. [5] stated that there was a mean delay of 11 years between the first major signs of the disease and final diagnosis of homocystinuria. Lens dislocation is observed in 85% of the patients with homocystinuria. Myopia in excess of 5D is extremely rare in children under 5 years of age. If ocular fundus of a highly myopic patient shows no clear ophthalmoscopic signs of axial myopia and the corneal curvature is not abnormal, then lenticular myopia due to ectopia lentis should be suspected and searched for. So an ophthalmologist may be the first person to diagnose the case of homocystinuria [5,6]. The concentration of folate required to normalize plasma homocysteine levels in patients with sickle cell disease may be higher than that of normal controls and that patients with sickle cell disease have a higher nutritional requirement for folic acid than the general population [7].

Hence in our case the folic acid was given in double the dose. Thromboembolic episodes involving both large and small vessels, especially those of the brain, are common in type-I homocystinuria and can occur at any age. [1] The risk for vascular disease is graded with respect to the level of homocysteine. However, no threshold abnormal value is accepted widely. Several factors have been suggested as the possible cause of accelerated vascular disease. These include - endothelial cell damage, smooth muscle cell proliferation, lipid abnormalities, upregulation of pro-thrombotic factors and downregulation of antithrombotic factors or endothelial-derived nitric oxide [3].

CONCLUSION

Homocystinuria must be kept in mind in the differential diagnosis of pediatric stroke. The treatment of homocystinuria assumes greater significance because institution of specific treatment can prevent progression of this disease and associated complications. Ischemic complications are common in patients with sickle cell disease and hyperhomocysteinemia is a risk factor for arteriosclerosis and venous thrombosis.Thus in rare cases like ours where both coexis, the folic acid requirement is more.

Contributors

Dr. Geetanjali Sethy- revising it critically for important intellectual content.
Dr Nasreen Ali-conception, design and drafting

Conflict of Interest

There was no conflict of interest and no funds received.

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Reference

1. Rezvani I. Behrman RE, Kliegman RM, Jenson HB. Nelson Textbook of Pediatrics. 16th ed. Philadelphia: Saunders; 2000. Defects in metabolism of amino acids. Methionine; pp. 350–2.
2. Bhardwaj P, Sharma R, Sharma M. Homocystinuria: a rare condition presenting as stroke and megaloblastic anemia. *Journal of pediatric neurosciences*. 2010 Jul;5(2):129.
3. E-Medicine-Metabolic diseases and Stroke: Homocystinuria/Homocystinemia. Available from:http://www.emedicine.com/neuro/topic 578.htm [last accessed on 2008]
4. Marrow G, Bamess LA. Combined vitamin responsiveness in homocystinuria. *J Pediatr*. 1972; 81:946–54. [PubMed]
5. Cruysberg JRM, Boers GHJ, Trijbels JMF, D Eutman AF. Delay in diagnosis of homocystinuria: Retrospective study of consecutive patients. 1996; 313:1037- 1040.
6. Johnston SS. Pupil-Block glaucoma in homocystinuria. *Brit. J. Ophthalmol*. 1968; 52:251-256.
7. Lowenthal EA, Mayo MS, Cornwell PE, Thornley-Brown D. Homocysteine elevation in sickle cell disease. *Journal of the American College of Nutrition*. 2000 Oct 1;19(5):608-12.

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