Case Report:

A case of Hemocystinuria with long term follow up

SK. Rafikul Rahaman*, Kripasindhu Chatterjee*. Prodyut Kumar Mondal*. Nabaendu Chaudhuri **

Department of Pediatric Medicine,* IIMSAR & **BCRH, Purba Medinipur. Address of communication :
Dr SK Rafikul Rahaman Vill Salgechia. Post Tamluk. Distt Purba Midnapur Pin 721636 E-mail ID rrahaman@rediffmail.com

ABSTRACT:

Hemocystinuria (HCU) is a very rare disease and usually missed early in life.The diagnosis is made when the patient developes physical and mental disabilities. Unrecognized patient can die suddenly due to thromboembolic phenomenon. The present case of hemocystinuria was diagnosed when he presented with marfanoid feature and visual disturbance because of ectopia lentis. The child is under follow up for 14 years with adequate treatment with vit-B6, Folic acid methylcobalamin adequately. The child is maintaining almost normal life with normal level of Homocystine. The non verbal I.Q and verbal I.Q. are 92 and 90 respectively .He is now 19 years old and persuing his graduation.

Key Word - Hemocystinuria , Homocysteinemia.

INTRODUCTION :

An Inborn error of metabolism, Homocystinuria is due to cystothionine B-synthase (CBS) deficiency, it results in markedly elevated levels of circulating homocystine. Homocystinuria was first recognized in 1962 [1, 2] and enzyme defect identified two years later [3]. Premature vascular events are the main life threatening complication [1]. The disease gradually affects the different system like physical disabilities in the form of marfanoid habitus, ectopia lentis glaucoma, cataract, osteoporosis with bone deformity, high arched palate, muscle weakness with shuffling gaits. The developmental disabilities are in the form of mental retardation, developmental delay in 65-80% in untreated cases. The mortality is due to thomboembolism in cerebral, pulmonary, renal, and myocardial circulation. Death usually occurs within the 1st yr. of life, if not treated properly. The ectopia lentis is a distinctive feature for early recognition of the disease which must be confirmed.

There are several forms of homocystiuria and are characterized by normal or low blood levels of methionine and the absence of ocular abnormalities. These variants are additional disorders of methionine metabolism, including decreased N-5 methyl tetrahydrofolate homocysteine methyltransferase activity due to vitamine B12 deficiency and decreased N5, 10 methyltetrahydrofolate reductase activity [4]. The diagnosis of the homocystiuria in newborn period needs estimation of blood methionine by spectrophotometry. The Normal range has long range. (0-61µmol /L). In suspected cases, second test is required for confirmation. If the result is positive they should be referred to metabolic disease centre where the clinical evaluation is done followed by confirmatory test and subsequent management. Once the disease is diagnosed, the child needs lifelong medical management, dietary therapy co-ordinated by Nutrition and metabolic specialist.

The treatment comprise of Folic acid, B6, methlobalamine .Treatment should be started early and continued throughout the life. The growth and development of child should be monitored regularly and periodic estimation of homocystine in the plasma and urine should be done.

The vascular events in the form of stroke is one of the commonest cause of sudden death. There is a good association with high circulating

homocystine and coronary heart disease. [5] The carotid artery stenosis is related with high level of homocystine and low level of vit.-B-12.

CASE :

A 5 year old boy born to non-consanguineous parent full term with normal vaginal delivery with normal developmental milestone till the age of 5yrs, presented with defective vision. Ophthalmology consultation was taken and it revealed visual activity was 6/36, N8 in the right eye and 6/18 ; N6, in left eyes. The cover test with glasses for distance and near showed alternate extropia. Pupils were round and reactive to light. There is no relative apparent pupillary defect. Slit lamp examination of both eyes showed infero-temporal subluxation of lens in both eyes. Fundus examination of both eyes were within normal limit.

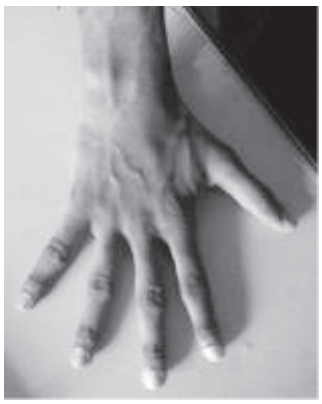

Fig No -1 Arachnodactyly

Fig-2 Steinberg Sign

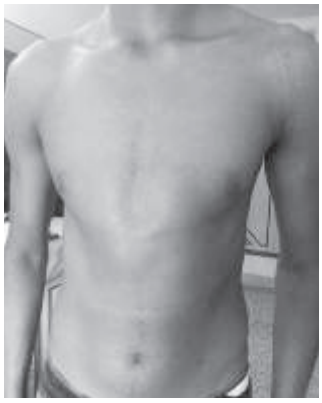

Fig-3 Pectus Excavatum

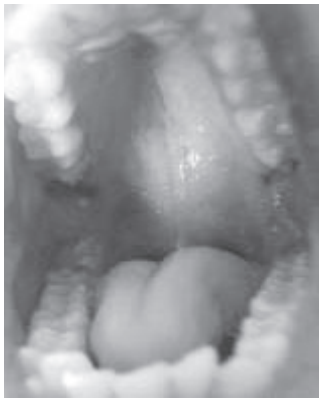

Fig-4 High Arched Palate

On systemic examination,it was revealed that he had arachnodactyly Fig (1), steinberg sign Fig (2), high arched palate Fig (3), pectus excavaturn Fig (4) . IQ test was done which showed non-verbal I.Q.92 and verbal 90.

Investigation showed, normal hemogram with normal renal and hepatic profile. Blood sugar, urine-analysis, Mantoux test were normal. Considering the marfanoid features and ectopia lentis, the metabolic screening for homocystinurea was done and which showed presence of homocystine in urine . Homocystine level in urine were 39µM (Normal : 0-19µM.).

So, Homocystinuria was diagnosed and treatment started with vit B6, Folic acid and methylcobamine .

He was with regular follow up and was compliant with adequate treatment of Pyridoxine (100mg) initially and gradually increased to 200mg. Folic acid 5mg daily & Methyl cobalamine (1000mg) were also given daily along with avoidance of methionine containing food like meat, fish, chicken, egg, garlic, lentils, onion, yogurt, oilseeds, cheese, & with psychological supports. This child has good scholastic performance and he is doing graduation course with adequate maintenance of physical fitness. His present weight is 54.5 Kg, height 172 cm, which is normal as per NCHS Scale & lower segment 85cm.

The only complication he developed was left sided spontaneous pneumothrax with partial collapse of left lungs at the age of 15yrs and which was cured by symptomatic treatment, otherwise he is maintaining almost normal life.

DISCUSSION:

Homocystinuria is a wide spectrum of disease varied from homocystinemia where the patient is asymptomatic to Homocystinuria where the patient is symptomatic. It is a genetically determined disease recessive in character and the locus of the gene is situated in that region. The main defect in the enzyme cystithionine B synthase

(CBS) which is responsible for synthesis of methionine metabolism[1,4,6,] Due to the defect of the enzyme there is a excessive production of Cystine. Excess of Cystine affects the different organs like and usually diagnosed when the systemic involvements occurs.

The world wide incidence is 1 in 3,44000. The higher incidence is seen when the screening is mandatory in newborn period where the incidence is 1 in 65000 [7,8]. CBS deficiency is characterized biochemically by severe hyper homocystinemia, Cystinemia, hypermethionemia. The pathological sequale include ectopia lentis downwards & outwards, osteoporosis, mental retardation in 65-80% in untreated patients. In the present case IQ is non-verbal 92 and verbal 90, such a high IQ is because of early detection and appropriate therapeutic approach.

The serial systemic study by Mudd and Colleagues [9] has documented a comprehensive natural history in 629 patients without treatment that by the age 10 yrs - 10% dislocated knees, by the age of 15 yrs - 50% has Osteoporosis and defect of the spine and by the age of 30 yrs mortality rate is-23%. But those patient who has received the treatment and responsive to Vit. B6, the morality rate is only 4%.

The vascular changes are found in 30% before the age of 20 yrs and 50% by the age of 30 yrs. The present case is aged 19 yrs and has been diagnosed by the age of 5 yrs. During his long term 14 yrs follow-up with adequate treatment of Pyridoxine (100mg) initially and gradually to increase 200mg, Folic acid 5mg daily & Methyl cobalamine (1000mg) daily along with avoidance of methionine containing food , he did not have vascular problems.

The only complication he developed was left sided spontaneous pneumothrax with partial collapsed left lungs at the age of 15yrs and which was cured by symptomatic treatment, otherwise he is maintaining almost normal life.

CONCLUSION:

The Homocystinuria is a very rare disease usually remains undetected because of lack of routine screening in amino acid metabolic defect in new born period. The subsequent presentation of the disease is so varied usually investigated as per the symptomatic presentation and usually it late and the quality of life is miserable and leads death due thromboembolic phenomenon. In present case the early diagnosis and adequate treatment has lead to the quality of life is almost normal. This is possible even in the resource limited semiurban area.

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