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ISCHAEMIC STROKE IN A CHILD: DUE TO A RARE INBORN ERROR OF METABOLISM

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ABSTRACT
Homocysteinemia (Homocysteinuria) is a rare inborn error of amino acid metabolism that has severe but preventable neurovascular complications. We present a case of a 10 year old child who had bilateral anterior lens dislocation, mental retardation, hemiparesis, refractory seizures, stroke and Marfanoid features. He was diagnosed with Homocysteinemia on the basis of raised serum Homocysteine levels and response to Pyridoxine. Homocysteinemia must be considered in pediatric stroke syndromes.

KEYWORDS: Homocysteinemia, Homocysteine, Marfanoid.

INTRODUCTION
Raised homocysteine levels have been implicated in various cardiovascular diseases.[10] The toxic effects of raised homocysteine as seen in inherited homocysteinemia can be severe, and on delayed diagnosis, irreversible. Here we present a patient that came to us with stroke and refractory seizures and was subsequently diagnosed with hereditary homocysteinemia.

CASE REPORT
A 10 year old male was admitted in our hospital with chief complaints of inability to stand since morning, sudden onset weakness of left side of body, altered sensorium and generalised convulsions since evening.

On admission, GCS was E4V3M5. RBS was 119mg/dl. BP was 160/100mmHg. The rest of the vitals were normal.

The child had been discharged from the Ophthalmic ward 3days back after undergoing lens removal and vitrectomy of the left eye for subluxation of lens. He also had subluxation in the right eye for which lens removal was planned at a later date. On examination, child had numerous white hair. He was tall and lean with arm span equal to height.

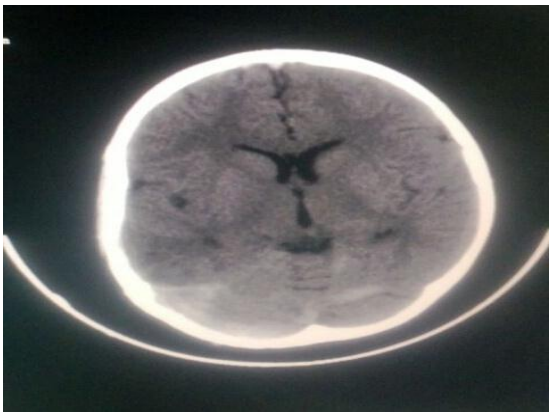

Fig.1. CT scan showing a minimal subdural haematoma of 7mm in the Right occipital region.

He had a high arched palate with crowding of teeth.

Mild deviation of angle of mouth on left side was present.

He had pectus carinatum that was present since his early years. No organomegaly was appreciable.

Cardiovascular and respiratory system examination were normal.

Left sided hemiparesis was noted. Tone was decreased on left side. Tone and power were normal on right side. Deep tendon reflexes were brisk bilaterally. Superfical

reflexes were absent and plantar response was bilaterally extensor.

Both eyes revealed conjunctival haemorrhages. Left eye was dilated with post-op medications and corneal scar was present.Right eye pupil was normally reacting to light.

The child developed seizures that were generalized, tonic clonic in nature after one hour of admission. They were unresponsive to Phenytoin and Sodium Valproate. He was then electively ventilated and a Midazolam 24-hour continuous infusion was started. Midazolam was titrated upto 8mcg/kg/min when a relatively seizure-free interval was achieved. Blood pressure normalised as the seizures were controlled.

We started the patient on vitamin B6 (pyridoxine) with gradual tapering of anti-epileptics. He was started on 200mg/day which was increased to 400mg/day as seizures responded.

He was gradually weaned off the ventilator and gentle physiotherapy was started for the hemiparesis.

CT scan revealed a minimal subdural haematoma of 7mm in the Right occipital region.

Renal color Doppler was normal.

History of the child revealed that he was an issue of consanguineous marriage with his father being mentally subnormal.

The child had developmental delay with gross mental retardation. He had difficulty in seeing and managing routine tasks since he was 4-5years old but no medical aid was sought.

He developed headache 1 month back for which he was taken to the ophthalmology OPD where bilateral anterior subluxation of lens with myopia was discovered. He was operated for the same in the left eye, and discharged with minimal discomfort.

We suspected Homocysteinemia on the basis of bilateral anterior subluxation of lens which is almost pathognomonic for Homocysteinemia.[1] His serum Homocysteine levels were almost 5 times more than the upper limit of the range.

He also had Marfanoid physique and mental subnormality. This along with refractory seizures that immediately responded to Pyridoxine were strong points in favour of a diagnosis of Homocysteinemia.

The child on recovery took discharge on request, but was lost to follow up.

DISCUSSION

Homocysteine, an intermediate compound of Methionine degradation is required in its transsulfuration. Homocysteinemia has 3 major forms, with around 40% having the vitamin B6 responsive Classic Homocysteinemia caused by deficiency of Cystathione β synthase deficiency inherited as an autosomal recessive condition with an estimated incidence of 1/10,000 to 1/40,000.[2]

Clinical manifestations during infancy are nonspecific and may include failure to thrive and developmental delay. In early childhood, after subluxation of the ocular lens (ectopia lentis) occurs medical help may be sought for severe myopia and iridodonesis. Astigmatism, glaucoma, staphyloma, cataracts, retinal detachment, and optic atrophy may develop later in life. Progressive intellectual disability is common with psychiatric and behavioral disorders occurring in more than 50% of affected patients. Convulsions occur in approximately 20% of patients. Marfanoid skeletal abnormalities may be encountered: patients are lean, with elongated limb, arachnodactyly, and various degrees ofscoliosis, pectus excavatum or carinatum, genu valgum, pes cavus, high-arched palate, and crowding of the teeth. Generalized osteoporosis, especially of the spine, is the main roentgenographic finding.[1] Thromboembolic episodes involving both large and small vessels, especially those of the brain, are common and may occur at any age, with around 30% occurring before 20 years of age.[1,3,8] Optic atrophy, paralysis, cor pulmonale, and severe hypertension (from renal infarcts) are among the serious consequences of thromboembolism, which is caused by changes in the vascular walls and increased platelet adhesiveness secondary to elevated homocystine levels. They are the main cause of morbidity and mortality.[10] The risk of thromboembolism increases after surgical procedures.[1]

Atherosclerosis, apoptosis, and neurological disorders result from oxidative stress and lipid metabolism and transport alterations caused by elevated homocysteine levels.[7]

Diagnosis is generally by detection of elevated Methionine or homocystine or homocysteine in bodily fluids (freshly voided urine/ serum). Enzyme assay and DNA analysis are also available forconfirmation.

Treatment includes high doses of vitamin B6 (200-1000mg/24 hours) which may also prevent certain complications like decreased IQ, ocular deformities, and cardiovascular accidents.

Folate repletion, methionine-restricted diet and Betaine supplementation may be considered in cases that are not responding to plain B6.

Homocysteinemia being the second most common treatable aminoacidopathy after Phenylketonuria, should

be actively looked for in unexplained cases of seizures and stroke in children.[10] Newborn screening and familial testing will identify and prevent complications. Heterozygous carriers are generally asyptomatic but have increased incidence of thromboembolic events and coronary heart diseases.Patients with an early diagnosis and treatment have more favorable clinical responses for growth index, controlled refractory seizures, neurodevelopmental status, and neuroimaging findings.[4] Neuroimaging findings include brain atrophy and/or white matter involvement.[5]Prophylactic pyridoxine in these cases may prevent adverse cardiovascular outcomes.[6,3]

REFERENCES

1. Iraj Rezvani and David S. Rosenblatt. Methionine. In: Kliegman, Stanton, St Geme,Schor, editors.Nelson Textbook of Pediatrics. 20th ed. Philadephia. Elsevier; 2016; 643-646.
2. R.V. Patil S.G. Kulthe K.F. John Boby S.C. Karande M.K. Jain. Chronic Pancreatitis in Homocystinuria. Indian Pediatr.1995.
3. Mudd SH, Skovby F, Levy HL, et al. The natural history of homocystinuria due to cystathionine p-synthase deficiency. Am J Hum Genet 1985; 37: 1-31.
4. M. Antònia Vilaseca, Dolores Moyano, Rafael Artuch, Imma Ferrer, Mercè Pineda, Esther Cardo, Jaume Campistol, et al. Selective Screening for Hyperhomocysteinemia in Pediatric Patients. Clinical Chemistry. March 1998 vol. 44 no. 3 662-664.
5. El Bashir H, Dekair L, Mahmoud Y, Ben-Omran T. Neurodevelopmental and Cognitive Outcomes of Classical Homocystinuria: Experience from Qatar.JIMD Reports. 2015; 21: 89-95.
6. Parvaneh K, Narjes J, Mohammad Reza A, Sayena J, and Habibeh N B. Homocystinuria: Diagnosis and Neuroimaging Findings of Iranian Pediatric patients Iran J Child Neurol. 2015 Winter; 9(1): 94–98.
7. R Cerone, G Minniti, M C Schiaffino, R Lorini and P G Mori. Plasma Homocysteine Concentrations in Healthy Pediatric Patients and in Patients with Homocystinuria (HC) and Combined HC and Methylmalonicaciduria: A Useful Biochemical Marker for A Risk Factor of Vascular DiseasePediatric Research 1999; 45: 765–765.
8. Priyanka S, RD Senthilkumar, Vani B, Elayanambi S, Anubha M, Amitabh S, and Shantanu S. Mining literature for a comprehensive pathway analysis: A case study for retrieval of homocysteine related genes for genetic and epigenetic studies. Lipids in Health and Disease 2006; 5: 1.
9. Kwon HM1, Lee YS, Bae HJ, Kang DW. Homocysteine as a predictor of early neurological deterioration in acute ischemic stroke.Stroke. 2014 Mar; 45(3): 871-3.
10. K. Jagadish Kumar, S. Harsha,1 V. G. Manjunath, and S. Mamatha. Transient ischemic attack in a child with homocystinuria. J Pediatr Neurosci. 2012 May-Aug; 7(2): 157–158.