

CASE REPORT

A CASE OF HOMOCYSTINURIA PRESENTING WITH SIXTH NERVE PALSY

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ABSTRACT

A 12-year-old boy presented to Medical Department with aphasia since birth and left lateral rectus palsy for five years. His MRI brain revealed bilateral frontal and lacunar infarcts. A coagulation screen was carried out which showed raised homocysteine levels in the blood. Subsequent urinary homocysteine levels were also raised. He was diagnosed as a case of homocystinuria. He was started on folic acid and vitamin B6 therapy and called for follow up after 4 weeks.

Key Words: Aphasia; Palsy; Infarcts; Homocysteine; Homocystinuria.

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INTRODUCTION

Homocystinuria is a biochemically and clinically distinct disorder characterized by increased concentration of the sulfur-containing amino acid homocysteine in blood and urine¹. It is an autosomal recessive inherited disorder of methionine metabolism. It has a prevalence of 1 in 200,000, and is more prevalent in New South Wales, Australia (1 in 60,000 live births), and Ireland¹. There are four major types of homocystinuria, based on the enzyme, co-enzyme or co-factor involved in the methionine pathway.

Ophthalmologic system, skeletal system, central nervous system and vascular system are the commonly involved systems. Patients commonly present with lens dislocation, chest wall deformities, high-arched palate, mental retardation and strokes². We hereby present a case of homocystinuria presenting with isolated sixth nerve palsy.

CASE REPORT

A 12-year-old male was brought to medical out-patients by his mother who gave a history of him being unable to talk since birth. He had also developed some visual defect evident for the last 5 years. The patient had a normal birth, but half hour after delivery, he had experienced fits. He had attained his

developmental milestones slower than normal, and he had mild cognitive impairment too. There was no past history of rheumatic heart disease. He was born to a non-consanguineous marriage. The mother had a history of previous two still births.

On examination, BP = 110/70mmHg. He was conscious, co-operative and well-oriented but aphasic. There were no neuro-cutaneous stigmata. He had left lateral rectus palsy. Rest of the cranial nerve examination was unremarkable. Plantars were bilaterally down-going. Upper and lower limb neurological examinations were unremarkable. Gait was ataxic and slightly tilted towards the left side. Mini-mental state examination could not be performed due to patient's inability to speak. No other cerebellar signs were noticed. Chest, Cardiovascular system, and abdominal examinations were unremarkable.

Peripheral smear showed a hemoglobin = 10.5g/dl, White cell count = 7,500/cmm, platelets = 250,000/cmm, Mean corpuscular volume = 88fl, and normochromic, normocytic blood picture. ESR = 25mm/1st hour. Renal, hepatic and sugar profiles were normal. Serum electrolytes, electrocardiogram and chest x-ray were also unremarkable. An ophthalmology consultation was taken. Visual examination was difficult due to patient continuously moving his eyes, but visual acuity was

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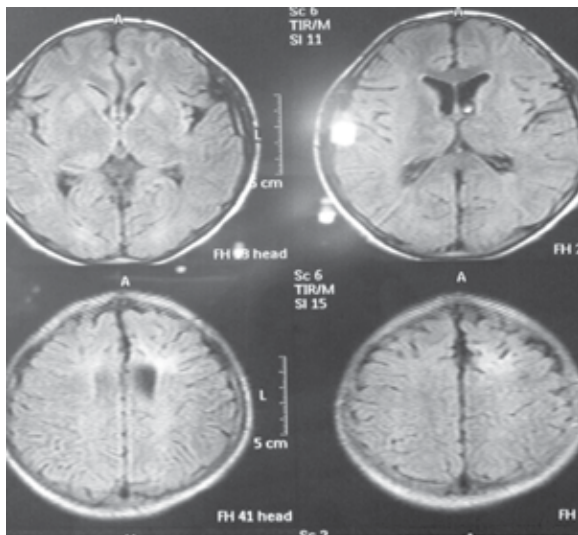
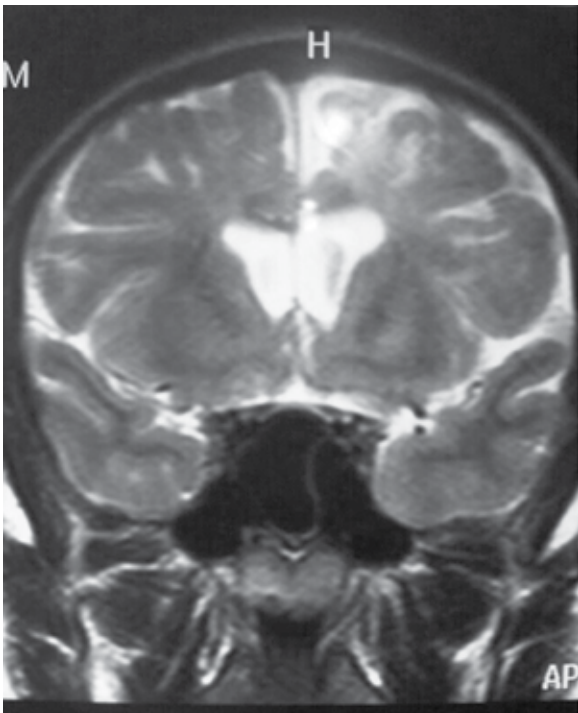
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A case of homocystinuria presenting with sixth nerve palsy



20/40 in right eye and 20/60 in left eye. An MRI brain was planned.

T2 and FLAIR (fluid-attenuated inversion recovery) high signal intensity areas were seen in bilateral frontal regions and lacunar areas. An impression of bilateral frontal and lacunar infarcts was made. The patient was further investigated for etiology of infarcts. Prothrombin time, Activated partial thromboplastin time, Echocardiography and Carotid Doppler were unremarkable. Coagulation screening revealed Factor V Leiden = 1.0 (0.86-1.1) Protein C = 81% (70-140). Protein S = 80% (67-140) and Homocysteine level = 24.41 micro mole/liter (5-15). 24 hour Urinary Homocysteine levels =

15 micro mole/gram creatinine (0-9.). The patient was therefore diagnosed as a case of Homocystinuria. He was started on folic acid and vitamin B6 supplementation and called for follow up after a month.

DISCUSSION

Our patient appears to be suffering from Type III Homocystinuria which is caused by a deficiency of methylene tetra-hydrofolate reductase. Though the enzyme levels could not be assayed due to inavailability of the facility, but the clinical features of our patient coincide with features of Type III homocystinuria. This enzyme reduces 5,10-methylene tetrahydrofolate to form 5-tetrahydrofolate, which provides the methyl group needed for remethylation of homocysteine to methionine². Genetic abnormalities are reported on chromosome¹ pertaining to methylene tetrahydrofolate reductase (MTHFR).

Clinical features vary from apnea, seizure, microcephaly, coma and death to developmental delay, ataxia, and motor abnormalities or even psychiatric manifestations³. Premature vascular disease or peripheral neuropathy has been reported as the only manifestation of this enzyme deficiency in some patients⁴. Adults with severe enzyme deficiency may even be completely asymptomatic. The aphasia and left lateral rectus palsy in our patient can be attributed to vasculopathic manifestations of homocystinuria.

The disease is diagnosed by moderate homocystinemia and homocystinuria. The methionine concentration is low or low normal. Diagnosis may be confirmed by the enzyme assay in cultured fibroblasts or leukocytes or by finding causal mutation in the MTHFR gene⁵. Prenatal diagnosis can be offered by measuring MTHFR enzyme activity in cultured chorionic villus cells or amniocytes, by linkage analysis in informative families, or by DNA analysis of the mutation⁴.

Treatment of severe MTHFR deficiency is done with a combination of folic acid, vitamin B6, vitamin B12, methionine supplementation, and betaine³. Betaine seems to be most beneficial. It activates alternate pathways for the metabolism of homocysteine and hence prevents its accumulation. Aspirin, clopidogrel, and aspirin-dipyridamole may be prescribed for secondary stroke prophylaxis⁶.

Our patient was born to a non-consanguineous marriage, and still developed homocystinuria which is an autosomal recessive disorder. This raises an important question whether homocystinuria has other modes of transmission that need to be investigated.

CONCLUSION

Homocystinuria is not an uncommon cause of strokes and coagulopathies in young patients and should be considered in the differentials of atypical presentations of blood dyscrasias.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

Badshah A: Case presentation and discussion writing.

Humayun M: Helped in diagnosis of the case.

Haider I: Reference writing.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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