

Two Cases of Homocystinuria From Coastal Andhra Pradesh

K. Santhi Devi¹, P. Veerraju¹ and B.S. Sridhara Rama Rao²

1. Department of Human Genetics, Andhra University, Waltair 530 003, Andhra Pradesh, India

2. Department of Neurochemistry, NIMHANS, Bangalore 560 029, Karnataka, India

KEY WORDS Homocystinuria. Mental Retardation. Screening Programme.

ABSTRACT Three hundred and fifteen mentally retarded children (of both sexes and below 15 years of age) with an IQ varying from mild to severe categories drawn from schools and special institutions for mentally retarded children from different areas of Visakhapatnam, Vizianagaram, East Godavari, Krishna and Guntur districts of Andhra Pradesh, South India were screened for inborn errors of metabolism. Out of 315 children 2 cases of homocystinuria were detected.

INTRODUCTION

Homocystinuria, as due to cystathionine β -synthetase deficiency, was first reported (Field et al., 1962; Carson and Neil, 1962) and the enzyme defect was identified (Mudd et al., 1964). It is to be the second most common metabolic disease associated with mental retardation, the first being phenylketonuria. In the most frequently seen type called type-1, cystathionine is not synthesized from homocysteine and serine due to the deficiency of the enzyme cystathionine β -synthetase in the liver. Cystathionine β -synthetase deficiency is inherited as an autosomal recessive trait, shown both by pedigree studies (McKusick, 1972) and studies of enzymes in parents of affected children (Mudd and Levy, 1983). A number of derivatives of homocysteine and methionine are also present in abnormally elevated amounts in plasma and urine of cystathionine - β synthetase deficient patients (Mudd and Levy, 1983). Homocystine is not found in the urine of normal individuals. Here, we present two cases of mentally retarded children with elevated urinary levels of homocystine and methionine.

MATERIAL AND METHODS

The subjects for the present study were children below 15 years age group drawn from

schools and special institutions for mentally retarded children from different districts of Andhra Pradesh namely: Vizianagaram, Visakhapatnam, East Godavari, Krishna and Guntur. The identification of mentally retarded children was mainly based on IQ tests developed by American Association on Mental Deficiency (Ingalls, 1978).

Sodium cyanide nitroprusside spot test was conducted and 24 hours urine samples were collected with toluene as a preservative. Clear urine obtained after centrifugation and deproteinized plasma samples were subjected to paper chromatography (Rao et al., 1982). Amino acids were quantified using an automatic amino acid analyzer (Beckman Model 119CL).

Case I : KR, a 14 year old boy child from Vizianagaram district had a history of delayed milestones, convulsions, mental retardation, inability to talk, drooling of saliva, inability to attend his needs or carry out any work, marfanoid features (extremities and digits being long) and ectopia lentis. He was born at full term and after a normal delivery (at home). The mother had no illness during pregnancy. The parents were non-consanguineous. Physical examination showed height 157 cm; weight 45 kg; head circumference 72 cm; chest circumference 51 cm.

Case II : DVS, a 13 year old girl child from East Godavary district had convulsions, mental retardation, lack of clear speech, drooling of saliva, inability to attend to her needs, unable to walk properly, marfanoid features (extremities and digits being long) and extopia lentis. She was born at full term and after forceps delivery (at hospital). Mother had one abortion before the birth of this child. The mother had mental stress during pregnancy. The parents were consanguineously related (UN). History of mental illness was present in the family. Physical examination showed height 130 cm;

weight 30 kg; head circumference 58 cm and chest circumference 67 cm.

The aminogram of urine showed the presence of homocystine and methionine in both the patients. Plasma amino acids were normal in both the patients. The values of amino acids are indicated in table 1. The quantity of homocystine excreted in urine of Case-I is 45 mg/gm creatinine and in Case-II is 54 mg/gm creatinine. The quantity of methionine in urine of Case-I is 58 mg/gm creatinine and in Case-II is 34 mg/gm creatinine. (The normal ranges are as follows : homocystine-0 mg/gm creatinine; methionine- Traces - 25 mg/gm creatinine).

Table 1 : Homocystine and methionine levels noted in patients and controls

Subjects	Homocystine (mg/g creatinine)	Methionine (mg/g creatinine)
<i>Patients</i>		
Case-I	45	58
Case-II	54	34
Controls	0	0-25

The most consistent biochemical finding in homocystinuria is abnormal excretion of homocystine in urine. No patient in the untreated state and beyond the period of early infancy has yet been described without this abnormality. The presence of homocystine is easily suspected when the urinary cyanide nitroprusside reaction is positive. The results of selective screening among the mentally retarded, the mentally ill and those with a traumatic dislocation of the optic lens have also been reported (Mudd and Levy, 1983).

The prevalence of homocystinuria in institutionalized patients with mental retardation in USA is about 0.02% which is lower than a previous estimate from Northern Ireland (0.3%). A total of 16 cases of homocystinuria have been reported from India (1, 3, 9-10). The two cases of homocystinuria detected during the present study are the first to be reported from the Coastal districts of Andhra Pradesh, South India.

Most of homocystinuric cases have mental retardation, marfanoid features and ectopia lentis. Once mental retardation and ectopia lentis are well established these cannot possibly be reversed. However, if one detects the disease very early in life by screening all sibs of probands and if therapy is started early, one can considerably reduce the risk of the dislocation of lenses as well as mental retardation.

ACKNOWLEDGEMENTS

The author K. Santhi Devi is grateful to CSIR, New Delhi for their financial support during the study.

REFERENCES

- Ambani, L.M., Patil, Z.M., Narasinga Rao, B.S., Mehta, B.G. and maskati, B.T. : Homocystinuria - Response to pyridoxine therapy. *J. Assoc. Phys. Ind.*, **27** : 713-717 (1979).
- Carson, N.A.J. Neill, D. W. : Metabolic abnormalities detected in a survey of mentally backward individuals in Northern Ireland. *Arch. Dis. Child.*, **37** : 505 (1962).
- Desai, A.D. : Homocystinuria : One case with peripheral neuropathy. *Neurol. (India)*, **22** : 141-146 (1974).
- Field, C.M.B., Carson, N.A.J. Cusworth D.C., Dent, C.E., Neill, D.W., *Abstracts of the X International Congress of pediatricians* (Lisbon), p.274 (1962).
- Ingalls, R.P. : *Mental Retardation - The Changing Outlook*. John Wiley, New York (1978).
- Mudd S.H. Finkelstein Irreverre, F., Laster, L. : Homocystinuria. An enzymatic defect. *Science*, **143** : 1443 (1964).
- Muskick V.A.; *Heritable Disorder of Connective Tissue*. CV Morby, St. Louis 4th Ed. (1972).
- Mudd S.H. Levy H.L. ; Disorders of transulfuration. In J.B. Wyngaarden, J.B. Stanbury, D.S. Fredrickson, J.L. Goldstein, and M.S. Brown, (Eds). *The Metabolic Basis of Inherited Disease*. McGraw-Hill, New York, 5th Ed. (1983).
- Rao, B.S.S., Jayasimha, N. and Subhash, M.N. : Biochemical screening in mental retardation. *Ind. J. Pediatr.*, **49** : 361 - 365 (1982).
- Verma, I.C. Sud, N. and Manerikar, S. : Homocystinuria : Report of two cases in siblings. *Ind. Pediatr.*, **11** : 753 - 557 (1974).
- Rao, B.S.S., Chandrakala, B.K. : *Inborn Errors of Metabolic Basis of Inherited Disease*. Vol. I & II McGrawHill information services Co., Health Professions Div., New York (1989).