J Inherit Metab Dis (2007) 30:811
DOI 10.1007/s10545-007-0546-6

SHORT REPORT

Marfanoid features in a child with combined methylmalonic aciduria and homocystinuria (CblC type)

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Received: 27 December 2006 / Submitted in revised form: 28 May 2007 / Accepted: 5 June 2007 / Published online: 4 September 2007

Online citation: JIMD Short Report #079 (2007) Online

Summary Cobalamin is an essential cofactor for two mammalian enzymes: methionine synthase and methylmalonyl-CoA mutase. Patients with the cobalamin C (CblC) defect have combined methylmalonic aciduria and homocystinuria. Recently, the gene responsible for the CblC type, *MMACHC*, was identified, which enables molecular diagnostics. In this study, we describe two siblings, a 16-year-old girl and her 11-year-old brother, of a consanguineous family who presented with a very distinct clinical manifestation. The girl presented at the age of 13 years with macrocytic anaemia, cognitive regression and Marfanoid features such as increased arm-span, arachnodactyly, joint hyperlaxity and scoliosis. Her brother presented at the age of 10 months with developmental delay and behavioural abnormalities. Biochemical analysis showed severely increased homocysteine and methylmalonic acid levels in plasma of both siblings. In addition, plasma cysteine levels were decreased in the girl but not in her brother. The diagnosis of CblC defect was confirmed by genomic sequencing of the coding exons of the *MMACHC* gene. Two heterozygous mutations were identified in both siblings; the common c.271dupA p.Arg91LysfsX14 and a novel mutation, c.1A>G p.Met1?. Therapy consisting of folic acid, vitamin B_6, l-carnitine and intramuscular vitamin B_{12} resulted in a clear improvement of biochemical parameters and, importantly, resulted in amelioration of the Marfanoid features in the girl. These data might suggest that low cysteine levels account for the Marfanoid features observed in the girl and indicate that the CblC type of combined methylmalonic aciduria and homocystinuria should be considered in the differential diagnosis of patients with Marfanoid features.

Communicating editor: Brian Fowler

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Electronic Supplementary Material
The online version of this article (doi:10.1007/s10545-007-0546-6) contains supplementary material, which is available to authorized users.