A Sabahan Family With A Dominantly Inherited β-Thalassemia Due To Haemoglobin Durham-N.C./Brescia [B114(G16) Leu→Pro]: First Case Described In The Malaysian Population


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Abstract

We describe a dominant thalassemia-like phenotype as a result of Hb Durham-N.C. which is caused by a single nucleotide substitution (CTG→CCG) at codon 114 resulting in leucine to proline substitution. Destabilization of heme pocket by amino acid substitutions might lead to formation of unstable β-globin chain which is rapidly catabolized resulting in thalassemia intermedia phenotype. Interestingly, the proband presented with a mild phenotype in contrast to cases which have been reported earlier and this is the first case described in the Malaysian population. The propositus was a seventeen-year-old Bugis female, diagnosed with beta thalassemia carrier during thalassemia screening. She was asymptomatic and her other siblings were healthy. Full blood count revealed mild anaemia with haemoglobin of 10.6 g/dL, raised red cell count (6.27 x 10^6/ul), with low mean corpuscular volume (54.7 fL) and low mean corpuscular haemoglobin (16.9 pg). Peripheral blood film showed hypochromic microcytic red cells with anisocytosis. No basophilic stippling was seen. High Performance Liquid Chromatography revealed increased Hb A_2 (4.9%) and Hb F (2.0%) with presence of abnormal peak (2.8%) at retention time 4.80 min. Capillary electrophoresis identified similar findings with raised Hb A_2 (5.2%) and Hb F (1.8%) level with the presence of an abnormal peak (3%) at Z(S). Beta-globin gene sequencing found a heterozygous state of codon 114[CTG>CCG] Hb Durham-N.C mutation. Subsequent Alpha-globin Multiplex Gap and ARMS-polymerase chain reaction (PCR) were performed and no mutation was found. To conclude, other genetic modifier might have contributed to her milder β-thalassemia phenotype, not detectable by routine molecular methods. More extensive tests are required to identify the genetic modifier, which would help in planning the treatment and genetic counseling.

Keywords: Durham; β-Thalassemia; Dominant

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