Evidence of gene conversion in patient with heterozygous α^0 thalassaemia Southeast Asian (~SEA) deletion

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Abstract

Alpha-thalassemia is caused by deletion of single or double α-globin genes, and/or point mutations in the α-globin genes. The alpha 1-globin (HBA1) and alpha 2-globin (HBA2) are homologous except of few nucleotide differences. Alpha gene conversion may occur through a nonreciprocal transfer of information from HBA1 to HBA2 sequence or vice versa resulting in the production of two homologous recombination sequences. Here, we discovered a case of compound heterozygous α^0-thalassaemia (~SEA) deletion and gene conversion of HBA2 to HBA1. A 14-year-old Malay girl with a positive family history of thalassemia and blood transfusion was investigated. Clinically she was not jaundice and had no hepatosplenomegaly. Full blood count revealed normal haemoglobin (12 g/dL), raised red blood cell (6.33 x 10^6/ul), low mean corpuscular volume (63.5 fl) and low mean corpuscular haemoglobin (19 pg). Peripheral blood film showed hypochromic microcytic red cells with target cells. High performance liquid chromatography identified lowish Hb A (88.5 %), with normal Hb A2 (2.4 %) and Hb F (0.2 %) level. H Inclusion test was negative. Routine molecular analysis with gap-polymerase chain reaction (PCR) method showed homozygous α^0-thalassemia (~SEA/~SEA), a genotype which was asynchrony with the observed clinical presentation. Subsequent DNA analysis using Multiplex Ligation-dependant Probe Amplification (MLPA) and DNA sequencing of both alpha globin genes confirmed the diagnosis of compound heterozygous α^0-thalassaemia (~SEA) deletion and gene conversion of HBA2 to HBA1. The discrepancy of initial phenotype-genotype findings were explained by the limitation of certain routine molecular method. In addition to the nucleotide homology which gives the possibility of an unequal crossing over and/or gene conversion, further studies are necessary to evaluate the possible effect of these changes on α-globin gene expression.

Keywords: SEA deletion; α-thalassemia; gene conversion

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