Co-inheritance of compound heterozygous Hb constant spring and a single -α 3.7 gene deletion with heterozygous δβ thalassaemia: A diagnostic challenge


Haemoglobin Constant Spring (Hb CS) mutation and single gene deletions are common underlying genetic abnormalities for alpha thalassaemias. Co-inheritance of deletional and non-deletional alpha (α) thalassaemias may result in various thalassaemia syndromes. Concomitant co-inheritance with beta (β) and delta (δ) gene abnormalities would result in improved clinical phenotype. We report here a 33-year-old male patient who was admitted with dengue haemorrhagic fever, with a background history of Grave’s disease, incidentally noted to have mild hypochromic microcytic red cell indices. Physical examination revealed no thalassaemic features or hepatosplenomegaly. His full blood picture showed hypochromic microcytic red cells with normal haemoglobin (Hb) level. Quantitation of Hb using high performance liquid chromatography (HPLC) and capillary electrophoresis (CE) revealed raised Hb F, normal Hb A2 and Hb A levels. There was also small peak of Hb CS noted in CE. H inclusions was negative. Kleihauer test was positive with heterocellular distribution of Hb F among the red cells. DNA analysis for α globin gene mutations showed a single -α-3.7 deletion and Hb CS mutation. These findings were suggestive of compound heterozygosity of Hb CS and a single -α-3.7 deletion with a concomitant heterozygous δβ thalassaemia. Co-inheritance of Hb CS and a single -α-3.7 deletion is expected to result at the very least in a clinical phenotype similar to that of two alpha genes deletion. However we demonstrate here a phenotypic modification of α thalassemia presumptively as a result of co-inheritance with δβ chain abnormality as suggested by the high Hb F level.