Thalassemia intermedia in HbH-CS disease with compound heterozygosity for β-thalassemia: Challenges in hemoglobin analysis and clinical diagnosis

Abstract

Co-inheritance of α-thalassemia with homozygosity or compound heterozygosity for β-thalassemia may ameliorate β-thalassemia major. A wide range of clinical phenotypes is produced depending on the number of α-thalassemia alleles (-α/αα --/αα, --/-α). The co-inheritance of β-thalassemia with α-thalassemia with a single gene deletion (-α/αα) is usually associated with thalassemia major. In contrast, the co-inheritance of β-thalassemia with two α-genes deleted in cis or trans (--/αα or -α/-α) generally produces β-thalassemia intermedia. In Southeast Asia, the most common defect responsible for α-thalassemia is the Southeast Asian (SEA) deletion of 20.5 kilobases. The presence of the SEA deletion with Hb Constant Spring (HbCS) produces HbH-CS disease. Co-inheritance of HbH-CS with compound heterozygosity for β-thalassemia is very rare. This study presents a Malay patient with HbH-CS disorder and β° /β +-thalassemia. The SEA deletion was confirmed in the patient using a duplex-PCR. A Combine-Amplification Refractory Mutation System (C-ARMS) technique to simultaneously detect HbCS and Hb Quong Sze confirmed HbCS in the patient. Compound heterozygosity for CD41/ 42 and Poly A was confirmed using the ARMS. This is a unique case as the SEA α-gene deletion in cis (-- SEA/αα) is generally not present in the Malays, who more commonly posses the two α-gene deletion in trans (-α/-α). In addition, the β-globin gene mutation at CD41/42 is a common mutation in the Chinese and not in the Malays. The presence of both the SEA deletion and CD41/42 in the mother of the patient suggests the possible introduction of these two defects into the family by marriage with a Chinese.

Keyword: Amplification refractory mutation system; CD41/42; Duplex-PCR; Hb constant spring; Poly A; Thalassemia intermedia