Case series of homozygous and compound heterozygosity of Hb Malay, the diagnostic features and transfusion requirements

ABSTRACT

Hb Malay was first described in 1989 following an investigation of anaemia in a 22-year-old Malay gentleman who was homozygous for this b chain variant. This Hb variant is caused by AAC à AGC mutation at codon 19 of the b globin gene resulting in the substitution of serine for asparagine [1]. The mutation creates cryptic RNA splice site in exon 1 of the b-globin gene leading to an abnormal RNA processing. Thus, this mutation not only produces variant haemoglobin but also a mild b+ thalassemia phenotype [2]. A retrospective analysis was carried out at the Clinical Haematology Laboratory, Hospital Ampang, Selangor, Malaysia from 2012 to 2015. A total of 12 cases of confirmed heterozygous, homozygous or compound heterozygous of Hb Malay were collected. The diagnostic workups in this centre included complete blood count (CBC), blood smear, haemoglobin analysis and molecular study. Table 1 shows the haematological characteristics of Hb Malay and its combination with other thalassaemia/ haemoglobinopathies. Table 2 shows the clinical features and transfusion requirements of various presentation of Hb Malay. The definitive diagnosis of Hb Malay can only be made by molecular analysis. Both reverse phase high performance liquid chromatography (HPLC) for haemoglobin variant and capillary zone electrophoresis (CZE) cannot differentiate between Hb A and Hb Malay as it is co-migrated. Previously, it was reported that there was an increased production of Hb F between 12-32% in cases of homozygous Hb Malay and compound heterozygous Hb E/Malay [3]. In our case, the Hb F levels in homozygous Hb Malay were 47.4% and 30%, respectively (Case 1 and 2). Patients with homozygous Hb Malay were non-transfusion dependent with average haemoglobin of 7 to 8g/dL, whereas in Hb Malay trait the haemoglobin level was normal. The Hb E/ Malay patients were also asymptomatic, although the average haemoglobin was lower (10g/dL) compared to the classical Hb E trait (12.4g/dL) [5]. Hb F level in Hb E/ Malay was reported to be above 12% [3], in one of our cases, the Hb F was only 3.3% (Case 4). Molecular analysis showed this patient was also homozygous for 158 Gγ Xmn polymorphism, as well as -α3.7 deletion. This was rather an interesting finding as this polymorphism was associated with higher level of Hb F [4]. Similarly, the presence of alpha thalassaemia was reported to reduce the Hb E percentage to less than 25%, but in this case the Hb E was 52.6% [5]. Compound heterozygous of Hb Malay/ Beta thalassaemia resulted in thalassaemia intermedia with variable phenotypes depending on the type of mutations. The other 2 combinations of Hb Malay with Hb S and HPFH also presented as thalassaemia intermedia. These findings were in keeping with the phenotype of Hb Malay resembling b+ thalassaemia.

Keyword: Hb Malay; Thalassaemia