Clinical features and molecular analysis in Thai patients with Hb H disease

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Background: The a-thalassemias are the most common inherited disorders of hemoglobin synthesis in Thailand. Normally, one pair of each of the two a-globin genes, a1 and a2, resides on each copy of chromosome 16. In HbH disease, three of these four a-globin genes are affected by a deletion, a mutation, or both. We studied the a-globin gene abnormalities and the clinical features and hematologic findings of Thai patients with HbH disease in southern Thailand.

Methods: We assessed the clinical features, hematologic values, growth assessment, transfusion therapy, and serum ferritin levels of 147 patients with HbH disease. We determined the two pairs of a-globin genes.

Results: HbH disease in 83 of the 147 patients (56 percent) was the deletional type of HbH, in which three of the four a-globin genes are deleted (−/−a). The remaining 64 patients (44 percent) was the nondeletional type of HbH disease, in which two a-globin genes are deleted and a third is mutated (−/αα). All 83 patients with the deletional type of HbH were double heterozygotes of a-α-thalassemia, a deletion of both a-globin genes from one chromosome and a-α-thalassemia, a deletion of the a1 or a2-globin gene from the other chromosome. The SEA type of a-α-thalassemia was detected in the majority of the Thai patients with HbH disease (98%) and the Thai type of a-α-thalassemia was a minority (2%). A 3.7 kb deletion accounted for 91% of a-α-thalassemia, and a 4.2 kb deletion made up the rest (9%) of the deletional HbH disease. A variety of mutated a-globin genes was found in the patients with nondeletional type of HbH disease, the Constant Spring variant was the majority of the disease (89%), followed by the Pakse (α-α) variant (6%) and the Quong Sze (α-α) variant (3%). Newborns with HbH disease had hemolytic anemia; newborns with a nondeletional genotype had higher proportions of HbBart’s than those with a deletional genotype. Twenty-one percent of children with HbH disease had growth deficiency. A genotype-phenotype correlation was found; patients with the nondeletional type of HbH disease had more symptoms at a younger age, more severe hemolytic anemia, more growth deficiency, more dysmorphic facial features (Thalassemia facies), larger spleens, larger livers and higher serum ferritin levels, and required more transfusions than patients with deletional HbH disease.

Conclusions: A genotype-phenotype correlation was found in Thai patients with HbH disease. Patients with the nondeletional type have more severe disease than those with the deletional type of the disease.

Keywords: HbH disease, Alpha thalassemia, Thai, children, Thailand