Fetal hemoglobin in adulthood

Hemoglobina fetal na idade adulta

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Dear Editor,

The clinical expression of fetal hemoglobin (HbF) in adults, including the peri and postpartum periods, is genetically regulated by mechanisms not entirely cleared yet; although the identification of loci and regulators of fetal-to-adult hemoglobin switching as BCL11A, HBS1L-MYB and BACH2 have resulted in new management options.[1-5] The gamma-globin genes of HbF derived from duplications of beta-globin gene clusters, and this Hb is produced by the liver on weeks 6 through 30, followed by the spleen (9 through 28), and the bone marrow (28 through birth); and less than 1% of HbF is not replaced by HbA by 6 to 12 months of age, except for people with hemoglobinopathy.[1] The switch of gamma to beta chain is in bone marrow by a transcriptional mechanism.

Severino *et al*.[2] reported a 24-year-old male with an elevated level of fetal hemoglobin (HbF) in absence of clinical manifestations or another hemoglobinopathy. The electrophoresis revealed HbF (27.3%), decreased HbA (70%), and normal HbA2; as there were no indicative findings of either hereditary spherocytosis, sickle cell anemia, or leukemia, the diagnosis of this rare benign condition was confirmed in the adulthood.[2] The authors stressed the hereditary persistence of HbF synthesis in adults, as an important issue for the research about the most varied genotypes and phenotypes of these cases.[2]

Blain *et al*.[3] searching relationships, reviewed clinical and laboratory data of pregnant women 169 with HbF expression over 1% of total Hb and 176 without the expression. The authors found the maternal origin of HbF and its significant positive correlation with βeta-human chorionic gonadotropin (β-HCG), and glycosylated hemoglobin (HbA1c); besides a significant negative association of the HbF expression with total hemoglobin.[3] HbF had the highest peak in the first trimester, possibly by a β-HCG and HbA1C increase and a decrease of total hemoglobin, with reactivation of the fetal erythropoietic system.[3]

Cato *et al*.[4] performed a multi-ancestry genome-wide association study about HbF gene regulation among 28,279 people and detected 178 conditionally independent genome-wide significant or suggestive variants across 14 genomic windows.

Worthy of note, they defined the mechanisms of HbF switching in vivo, and their findings contribute to the development of more effective therapies for sickle cell disease and β-thalassemia. The authors emphasized the new insights, as the example of BACH2 in regulating HbF.[4]

Gabbianelli *et al*.[5] studied the role of kit/ kit ligand (KL) in the perinatal HbF to HbA switching through the evaluation of both kit and KL on CD34 (+) cells expression levels in plasma of cord blood samples; reactivation of HbF synthesis in KL-treated unilineage erythroid cell cultures; and the functional role of miR-221/222 in the HbF production. The authors concluded that human perinatal Hb switching is controlled by the kit receptor/miR 221-222 complex, besides glucocorticoids and the HbF inhibitor BCL11A; kit expression has a gradual decline related to HbF decreased to < 30% in perinatal life.[5]

The objective of the additional comments is enhancing the awareness and suspicion index of primary health care workers about the occurrence of HbF in adults.

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