Abstract: PB3227

Title: COMPOUND HETEROZYGOSITY OF HB O ARAB AND B THALASSEMIA MUTATIONS. HEMATOLOGICAL AND CLINICAL PHENOTYPE IN 8 CASES.

Abstract Type: Publication Only

Topic: Thalassemias

Background:

Hemoglobin (Hb) O-Arab is an abnormal hemoglobin characterized by the substitution of lysine for glutamic acid at position 121 of the β-globin chain. Heterozygotes for Hb O-Arab trait are clinically asymptomatic and they may have elevated MCHC and a slight decrease in MCV. Patients homozygous for Hb O-Arab may present a mild hemolysis with borderline splenomegaly. Its combination with beta thalassemia mutations results in benign to transfusion-dependent anemia.

Aims:

We report the laboratory profile and clinical phenotype of patients with coinheritance of Hb O-Arab and thalassemic mutations, diagnosed in Thalassemia Prevention Unit of Northern Greece during the last 20 years.

Methods:

Eight patients: 6 were compound heterozygous Hb O-Arab/β-thalassemia, 1 compound heterozygous Hb O-Arab/β- thalassemia and ααα (anti3,7/αα), and 1 homozygous Hb O-Arab.

Results:

Four of them were Pomaks of Thrace in Greece and the homozygous O Arab was a Bulgarian woman diagnosed during pregnancy (on the 12th week). Diagnosis was carried out at a relatively old age (28.8 years old. The homozygous form was not symptomatic. The most severe forms were a) a compound heterozygous girl heterozygous [Hb O-Arab/β- thalassemia and ααα (anti3,7/αα)] who required blood transfusions from the age of 4 years old and b) a compound heterozygous woman (53 years old) with Hb = 8.3 g/dL, who underwent a splenectomy and received blood transfusions occasionally. The beta-thalassemia mutations found in our cases were the IVSII-745 (C>G) and the CD39(C>T) mutation.

Summary/Conclusion:

Evolution of this disease is generally good with a long lifespan of patients. In male population it seems that the situation is more benign as no one from our cases had any transfusion so far. Nevertheless, the clinical phenotype of the combinations can lead to more severe disease with transfusion dependence and depends on the underlying β thalassemia mutation, simultaneous presence of α globin triplication (heterozygosity or homozygosity), as well as the sex. Identification of such combinations is important for the genetic counselling of couples in countries as Greece where there is a high percentage of carriers.

Table: Characteristics of Hb O-Arab cases

	Heterozygotes for Hb O-Arab + betaThalassemia	**Homozygous for Hb O-Arab**
Sex	Male	Male
Age at diagnosis (years)	25	54
Hb (g/dL)	11.3	11.7
Hct (%)	33.3	37.8
RBC M/uL	5,500	4,530

	Heterozygotes for Hb O-Arab	Homozygous for Hb O-Arab
MCV (fL)	60.5	83.0
MCH (pg)	20.5	28.8
HbA2 (%)	3.8	4.6
HbF (%)	8.3	6.0
Hb O Arab (%)	80.0	86.1
Beta Thalassemia mutation	CD39 (C>T)	CD39 (C>T)
Alpha Thalassemia mutation	-	-

Hb: Haemoglobin; Hct: Hematocrit; RBC: Red blood cells; MCV: Mean corpuscular volume; MCH: mean corpuscular hemoglobin.

Keywords: Hemoglobinopathy, beta thalassemia, Hemoglobin variants