THE LEFTWARD DELETION 4.2 KB ALPHA-THALASSEMIA IN TWO SICKLE CELL ANEMIA SIBLINGS

DELEÇÃO 4,2KB DA ALFA-TALASSEMIA EM DOIS IRMÃOS COM ANEMIA FALCIFORME

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The presence of –αthal 3.7Kb deletion is associated with better prognosis of Sickle Cell Anemia (SCA) patients, but here are not reports in the literature regarding association of –α thal 4.2Kb and its importance among SCA clinical outcome. In this report, we describe Hemoglobin profile and laboratory findings of two siblings who have SCA and are silent carriers of –α thal 4.2Kb. Both described patients have severe anemia, lower rates of Mean Corpuscular Volume (MCV) and a high leukocytes count. Further studies are required to establish a possible association between –α thal 4.2Kb and SCA severity.

Keywords: Alpha thalassemia, sickle cell anemia, hemoglobin.

A presença da deleção –α thal 3.7Kb está associada com melhor prognóstico de pacientes que possuem anemia falciforme (AF), contudo não existem estudos na literatura a respeito da associação da –α thal 4.2Kb com a evolução clínica desses pacientes. No presente relato são descritos achados laboratoriais e perfil de hemoglobina de dois irmãos que possuem AF em associação com a –α thal 4.2Kb. Ambos os pacientes apresentam anemia acentuada, baixos índices de Volume Corpuscular Médio (VCM) e contagem de leucócitos elevada. Estudos adicionais são necessários para elucidar uma possível associação entre a –α thal 4.2Kb e a gravidade da AF.

Palavras-chave: doença falciforme, doença SC, talassemia, haplótipos.

Alpha-thalassemia, the most common single-gene disease in the world, is characterized by a reduction or complete absence of α-globin gene expression. Many deletions have been described in the Alpha (α)-globin gene located at the short arm of chromosome 16, but the most prevalent are the –α thalassemia with 3.7 kilobases (Kb) deletion (–α thal 3.7Kb) and the –α thalassemia with 4.2 Kb (–α thal 4.2Kb) which are originated by homologous recombination between misaligned chromosomes[4].

Sickle cell anemia (SCA) patients have heterogeneous clinical manifestations, including hemolysis, chronic inflammation and painful crisis. The presence of –α thal 3.7Kb deletion is associated with better prognosis of SCA patients[5]. There are not reports in the literature regarding association of –α thal 4.2Kb and its importance among SCA clinical outcome.

In this report, we describe two siblings from Bahia State in Brazil, who have SCA and are silent carriers of –α thal 4.2Kb.

Whole-blood samples were collected from the *HBSS* patients attending the out-patients clinic in HEMOBA. Hematological analyses were carried out using an electronic cell counter, Coulter Count T-890 (Coulter Corporation, FL, USA). The hemoglobin (Hb) profile and HbF levels were investigated by high performance liquid chromatography (HPLC / VARIANT I; BIO-RAD, CA, USA). Biochemical markers analyses were measured in serum by immunochemistry assay (A25 system, BIOSYSTEMS SA, Barcelona, Spain).

DNA was isolated from the white blood cells (WBC) by FlexiGene DNA Kit, Qiagen (USA), according to the manufacturer's recommendations. Beta-globin gene haplotypes were investiged by PCR-RFLP[6]. The alpha-thalassemia was confirmed in the two siblings by a single-tube multiplex PCR method to detect the wide type, the –α thal 3.7Kb, and –α thal 4.2Kb alleles, using primers previously described[3].

The study was approved by the Oswaldo Cruz Research Foundation's Human Research Board (number CAAE 0024.0.225.000-06), and the study was based in accordance with Declaration of Helsinki of 1975, as revised in 2000 and all subjects or official responsible filled out a written informed consent form.

The patient number 1 is a 7-years-old afro-descendent boy, which has had recurrent hospitalizations (more than 3) with many painful crisis, meningitis episode and blood transfusion history. The patient number 2 is a 5-years-old afro-descendent girl and her clinical history indicated recurrent hospitalizations (more than 9), pneumonia episode and blood transfusion history. Moreover, this patient has been submitted to splenectomy surgery.

The laboratory findings and hemoglobin profile of both patients are described in the Table 1, which shows severe anemia, lower rates of Mean Corpuscular Volume (MCV) and Mean Corpuscular Hemoglobin (MCHC), a high leukocytes count and an increase of iron and ferritin serum levels that

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Table 1. Hemoglobin profile and laboratory findings of the two -$\alpha^{4.2}$/SCA patients.

	Patient 1	Patient 2
Age (years)	7	5
Gender	Male	Female
Hemoglobins (%)		
S	90.8	86.2
Fetal	5.8	10.6
A2	3.4	3.2
Beta-globin gene Haplotypes	Ben/Car	Ben/Car
Hemolysis		
Erythrocyte, million/mL	2,84	2,27
Hemoglobin, g/dL	6.9	5.5
Hematocrit, %	21.9	18.1
Mean Cell Volume, fL	77.1	79.7
Mean Cell Hemoglobin, pg	24.3	24.2
Reticulocytes Count, %	8.0	5.0
Lactate dehydrogenase,U/L	248	376
Leukocyte		
Leukocyte Count, /mL	16,300	34,300
Platelets		
Platelets cunt, thousand/mm^3	296	268
Iron metabolism		
Iron serum, mcg/dL	715	858
Ferritin, ng/mL	1,391.3	529.50
Lipidic metabolism		
Total Cholesterol, mg/dL	112	129
HDL Cholesterol, mg/dL	29	36
LDL Cholesterol, mg/dL	71	76
VLDL Cholesterol, mg/dL	12	17
Tryglicerides, mg/dL	62	86
Hemolysis plus Hepatic		
Aspartate aminotransferase, U/L	65	66
Total bilirrubin, mg/dL	1.4	0.5
Direct bilirrubin, mg/dL	0.6	0.2
Indirect bilirrubin, mg/dL	0.8	0.3
Hepatic		
Alanine aminotransferase, U/L	73	22
Renal		
Urea nitrogen, mg/dL	12	11
Creatinine, mg/dL	0.4	0.4
Total protein, g/dL	7.1	6.8
Albumin, g/dL	3.8	3.3
Globulin, g/dL	3.3	3.5
Inflammation		
C-reactive protein, mg/mL	39.2	103
Alpha 1 antitrypsin, mg/dL	222	250
ASLO (UI/mL)	132	133

could be associated with an increase of reactive oxygen species (ROS) and consequently with a increase of clinical severity[2]. The coexistence of alpha-talassemia and SCA has been related with a higher survival rates and a decreased hemolysis markers and with a frequent vaso-occlusive episodes and painful crisis[1], but the same approach is not available for the -$\alpha^{4.2Kb}$/SCA association, requiring further study.

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