

Two rare hemoglobin variants in the Çukurova Region of Turkey: Hb E-Saskatoon and Hb G-Coushatta

Türkiye'nin Çukurova bölgesinde görülen iki nadir hemoglobin: Hemoglobin E-Saskatoon ve Hb G-Coushatta

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Abstract

Hb E-Saskatoon and Hb G-Coushatta are rare hemoglobin variants that are not a health problem. Herein we present a Turkish woman that was diagnosed as homozygous Hb E-Saskatoon (only the second such case reported from Turkey) and a Turkish boy diagnosed as heterozygote Hb E-Saskatoon. Additionally, 2 Turkish sisters diagnosed as heterozygote Hb G-Coushatta are presented.

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Özet

Hb E-Saskatoon ve Hb G-Coushatta herhangi bir sağlık sorununa yol açmayan nadir görülen iki hemoglobin varyantıdır. Hb E-Saskatoon vakası Türkiye'de rapor edilmiş ikinci homozigot vakadır. Bu çalışmada, bir homozigot ve bir heterozigot Hb E-Saskatoon tanımlanmıştır. Başka bir olgu da iki kız kardeş heterozigot Hb G-Coushatta olduğu belirlenmiştir. (*Turk J Hematol* 2011; 28: 323-6)

Anahtar kelimeler: Hb E-Saskatoon, Hb G-Coushatta

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Introduction

Hb E-Saskatoon [β 22(B4); AAG→AAA (Glu→Lys)] has been known since 1967 when it was described in a Canadian woman of Scottish origin was found to carry the variant [1-4]. Since then, this variant has been reported in Scotland, Spain, Japan, Greece and Turkey [1-10]. This variant and Hb E (β 26; Glu→Lys) has the same electrophoretic properties on both acidic and basic electrophoretic fields. While Hb E is thalassemic abnormal hemoglobin, carrier and homozygous Hb E-Saskatoon do not cause any clinical symptoms [1-11].

Hb G-Coushatta [β 22(B4); AAG→ACG (Glu→Ala)] was first identified in American Coushatta Indians; it has also been found in Thai, Korea, Algeria, Thailand, China, Japan and Turkey [9,12-14]. there were also previously reported cases of Hb G-Coushatta from different regions of Turkey. This variant was previously reported in Kastamonu from Dincol et al. and also Hb G-Coushatta has also been reported in Denizli and Muğla [9,13,15].

We reported two cases of carrier Hb E-Saskatoon one of the cases was found homozygous and the other case heterozygous for Hb E-Saskatoon. In another case, two sisters were found heterozygous for Hb G-Coushatta.

Materials and Methods

Informed consent was obtained from each patient and blood samples, with EDTA as anticoagulant, were taken for hematological and hemoglobin analysis. Hematological data were determined in an automatic cell counter (Coulter T180). Hemoglobin variants were firstly characterized by cellulose acetate electrophoresis [16]. HPLC (Agilent 1100) was used for quantification and separation of abnormal hemoglobin, Hb A₂ and Hb F. DNA was isolated from peripheral white blood cell by the method of Ponca et al. [17] ARMS was especially used for the identification of common mutations (Hb S, Hb C, Hb E and Hb D) found in Cukurova [18]. Sequence analysis was applied to the cases that could not be determined by the ARMS method [19].

Results

We report one case of Turkish women that were found to homozygous Hb E-Saskatoon (Figure 1A) and one case of heterozygous for this abnormal hemoglobin who are living in Adana (Figure 1B). Hematological parameters of simple Hb E-Saskatoon heterozygous are found within normal limits and the abnormal hemoglobin is found 36.74% of total hemoglobin (Table 1).

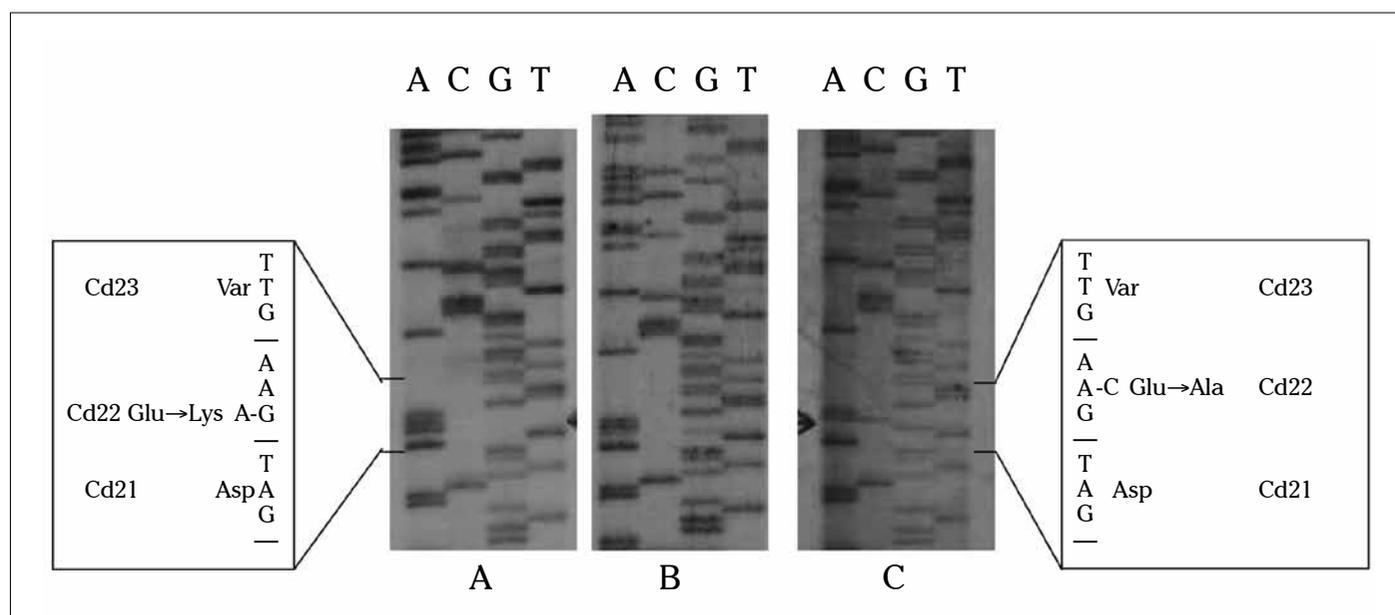


Figure 1. Direct DNA Sequence Analysis of the β Gene Showing the Sense Strand in the Vicinity of Codon 22
 A. Homozygous Hb E-Saskatoon [β 22(B4); AAG→AAA (Glu→Lys)]
 B. Heterozygous Hb E-Saskatoon
 C. Heterozygous HbG-Coushatta [β 22 (B4); AAG→ACG (Glu→Ala)]

Table 1. Hematological Data of Hb E-Saskatoon and Hb G-Coushatta

Name Surname	RBC ($\times 10^{12}/L$)	Hb (g/dL)	Hct (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	Hb† Hb A ₂	HPLC Hb F Hb X*	Genotype
A. S.	5.99	15.1	44.6	74.5	25.3	33.9	AE 2.90	1.20 36.74	AE-Saskatoon
S.A.	4.28	12.4	36.3	84.9	29.0	34.1	EE 2.65	- 81.07	EE-Saskatoon
T. B.	4.46	11.0	34.1	76.5	24.7	32.3	AS 3.32	8.99 37.72	AG-Coushatta
Z. B.	4.64	12.5	38.2	82.4	26.9	32.7	AS 3.72	0.6 40.94	AG-Coushatta

*Percent of abnormal hemoglobin, †Hemoglobin electrophoresis

Discussion

Hb E is more common in Çukurova region, southern of Turkey with a frequency of 0.16-2.4% and this variant is thalassemic, microcytosis and hypochromi [5,11]. A percentage of this hemoglobin is lower than Hb E-Saskatoon. Hb E-Saskatoon was present in 3 unrelated families living Antalya, Aksaray, and Kayseri. One of the subjects was founded with a homozygote Hb E-Saskatoon [5,11]. In Hb E-Saskatoon, the glutamate residue at position 22 (B4) of the β -globin chain, situated on the external surface of the molecule is replaced by lysine [2]. This substitution results in a change of the molecular charge without affecting its stability, solubility and functional properties [2,4]. Hb E-Saskatoon does not cause any major hematological problem in homozygous or in compound heterozygous states with β -thalassemia [5,6]. The only case of homozygosity described so far showed a moderate phenotype expression. The association of Hb E-Saskatoon with β -thalassemia (β^+) does not clinically present any additional risk [1,2,5,6].

The homozygous condition for Hb E-Saskatoon has previously been defined by Birben et al. in Turkey [5]. They reported that homozygous of Hb E-Saskatoon was very mild without any changes in red cell indices. Gürgey et al. indicated that compounds mild [IVSI-6 (T \rightarrow C)] and severe [IVSI-110 (G \rightarrow A)] β -thalassemia mutations with Hb E-Saskatoon result mild hematological pathology [5,6]. Identification of Hb E-Saskatoon is important to differentiate from thalassemic variant (Hb E), because of compound heterozygous Hb E and β -thalassemia show like β -thalassemia major.

Also, there were previously reported cases of heterozygous Hb G-Coushatta from different regions of Turkey [9-11,13,15]. Hb G-Coushatta migrates slightly anodic to Hb S in alkaline pH electrophore-

sis and it has not caused any clinical and hematological abnormalities [9,14]. In this study, we found two cases of heterozygous Hb G-Coushatta from Kayseri, who are sisters (Figure 1C). Heterozygous of this variant was found not anemic and percentage of this hemoglobin was found 37-40% of total hemoglobin when separated with HPLC (Table 1). It is important to differentiate from Hb S.

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Conflict of interest statement

The authors of this paper have no conflicts of interest, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

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