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Hemoglobin E-Saskatoon and pregnancy: Report of two cases

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Abstract

Hemoglobin E-Saskatoon (β22-Glu-Lys) is found worldwide but is extremely rarely. Two cases of pregnant women who carried the abnormal hemoglobin and the various problems that arise from it are reported. A discussion of the combinations with other abnormal hemoglobin is also presented.

Key words: genetic counseling, Hb E-Saskatoon, pregnancy, sickle cell trait, thalassemia.

Introduction

Hemoglobin (Hb) E-Saskatoon (β22-Glu-Lys) was first observed in 1967 by Vella *et al*. in Canada when a woman of mixed Dutch and Scottish origin was found to carry the variant.[1] A little later in 1969, Kaltsoya *et al*. from Greece report the first case of a compound heterozygosity for Hb E-Saskatoon and β-Thalassemia.[2] Since then, the variant has been found in Scotland, Spain, Turkey and Japan.[3] This abnormal hemoglobin, which has the same electrophoretic properties as hemoglobin E (β26-Glu-Lys), is very rare but seems to be innocuous. On the contrary, hemoglobin E is the hallmark of South-East Asia. It is mostly limited to the region and it is estimated that 30 million South-East Asians are heterozygous for Hb E and one million are homozygous for Hb E. The coinheritance of Hb E and β-thalassemia or hemoglobin S or C, causes symptomatic phenotypes with moderate to severe anemia and requires genetic counseling for parents and family members.

The identification of Hb E-Saskatoon is made by hemoglobin electrophoresis and ion exchange high pressure liquid chromatography (HPLC) as well as DNA studies that include gene amplification using polymerase chain reaction (PCR), denaturating gradient gel electrophoresis (DGGE), DNA sequencing and allele-specific oligonucleotide probe (ASO) hybridization.

We report two cases of pregnant Greek women that were found to carry this abnormal hemoglobin.

First Case

A 35-year-old, healthy woman in the 12th week of her second pregnancy asked for consultation in the hemoglobinopathy prevention unit as her husband was heterozygote for sickle cell disease. The hematological data were Hb = 13.3 g/dL, hematocrit = 38.5%, red cell count = $4380 \times 10^3/\mu L$, mean corpuscular volume = 88.1 fL, mean corpuscular hemoglobin = 30.4 pg. The blood films were normal. Electrophoresis revealed a variant with electrophoretic properties of Hb E (Fig. 1). HPLC isolation revealed an unknown variant (40%) eluting as hemoglobin S. DNA studies included gene amplification using PCR, DGGE electrophoresis, direct sequencing and ASO hybridization and showed that the woman was heterozygote for hemoglobin E-Saskatoon. Genetic counseling could be very difficult because of the rarity of the case, but their first child

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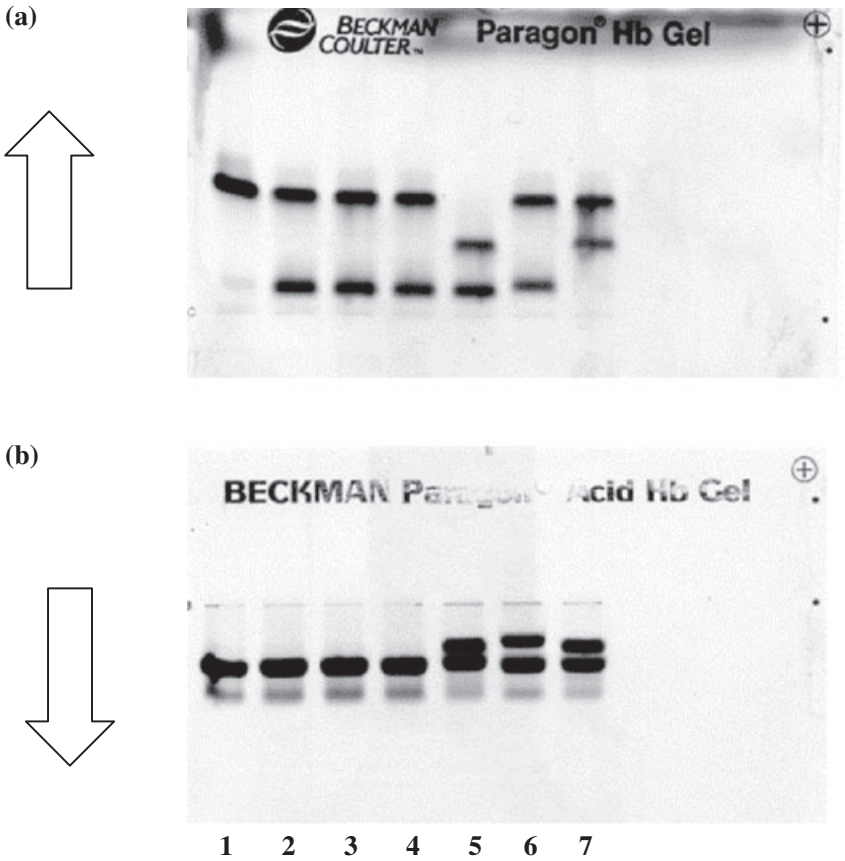

Figure 1 Hemoglobin (Hb) electrophoresis of the first family members, at alkaline (a) and acid (b) pH reading from left to right. (a): 1: Hb A (normal control), 2–4: Hb E-Saskatoon and Hb A (mother, grand-father, uncle), 5: Hb E-Saskatoon and Hb S (first child), 6: Hb O and A (control), 7: Hb S and A (father). (b): 1:Hb A (normal control), 2–4: Hb A and E-Saskatoon move together in acid pH (mother, grand-father, uncle), 5: Hb S and Hb E-Saskatoon (first child), 6: Hb O and A (control), 7: Hb S and A (father).

Table 1 Hematological data of the first family

Subjects	Hb (g/dL)	Ht (%)	RBC (/μL)	MCV (fL)	MCH (pg)
Case 1	13.3	38.5	4380×10^3	88.1	30.4
Husband	13.2	40.5	4670×10^3	86.8	28.3
First child	12.8	37.8	4980×10^3	75.8	25.7
Neonate	12.6	38	4500×10^3	84.4	27.9

Hb, hemoglobin; Ht, hematocrit; RBC, red cell count; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin.

(four year old girl) was found to be the first case of a compound heterozygocity for Hb-E-Saskatoon and Hb S and was a healthy child.[4] During pregnancy the hemoglobin levels were within the normal limits and the newborn boy carried only the S trait (Table 1).

Second Case

The patient, a 26-year old female, was referred to the hemoglobinopathy prevention unit in the 7th week of pregnancy as her husband carried the β-thalassemic trait (IVS1-110) (Table 2). Her hematological values and the blood films were normal but electrophoresis revealed an E-like variant that in HPLC hemoglobin isolation eluted as S. Hemoglobin screening performed on other members of her family indicated that her father carried the same variant.

Further DNA studies confirmed the diagnosis of heterozygous Hb E-Saskatoon. Preventive measures were not indicated for the couple as there are two reports of compound heterozygosity for Hb-E-Saskatoon and β-Thalassemia that are mild conditions not different from those seen for a classical type of β-thalassemic trait.[5] During pregnancy, hemoglobin levels were within the normal levels and she finally gave birth to a

Table 2 Hematological data of the second family

Subjects	Hb (g/dL)	Ht (%)	RBC (/μL)	MCV (fL)	MCH (pg)
Case 2	11.1	32.9	3460×10^3	95.2	32
Husband	13.3	41.2	5820×10^3	70.8	22.8
Neonate	12	37.6	5000×10^3	70.5	22.3

Hb, hemoglobin; Ht, hematocrit; RBC, red cell count; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin.

healthy boy that carried the thalassemic trait of his father (Table 2).

It was eventually revealed that the two pregnant women were distant relatives from their fathers' sides, coming from the same village in the region of Macedonia in northern Greece.

Discussion

In view of the rarity of such cases of heterozygosity for hemoglobin E-Saskatoon and the worldwide distribution of the variant, it is useful to communicate the data of the two families. Hb E-Saskatoon is thought to be an unstable hemoglobin but its behavior is very mild. Heterozygous carriers are not anemic and pregnancy goes on as if the hemoglobin variant did not exist. As far for the combination and the genetic counseling, until now there is reported data for combinations with β-thalassemic genes, S gene and recently with Hb Lepore-Baltimore.[6]

Hb E-Saskatoon acts differently from hemoglobin E, which when combined with thalassemic genes or the sickle cell trait causes symptomatic and severe phenotypes. The hemoglobin E-Saskatoon trait is rare and innocuous, but identification is important for genetic counseling.

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