Haemoglobin E trait and probable α -thalassaemia in a black American family: a family study

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SUMMARY This is a report of haemoglobin E trait in a black American family with no known Asian ancestry. The father appears to be heterozygous for both haemoglobin E and α -thalassaemia. The mother is normal both clinically and haematologically. Three children carry Hb E trait alone. The youngest son has a normal haemoglobin pattern and appears to have α -thalassaemia.

Haemoglobin E (Hb E), an anomaly of the β -chain of human haemoglobin, is widely distributed in south-east Asia and adjacent areas,¹ the greatest incidence being in the Burmese,² Siamese,³ Cambodians,⁴ Indonesians,⁶ and Malaysians.⁷

Sporadic cases have been reported in other parts of the world: haemoglobin E has been found in India,⁸ Persia, Qatar,¹⁰ Turkey,¹¹⁻¹³ Egypt,¹⁴ and Greece.¹⁵ Sporadic cases in South Africa and in the Netherlands are probably the result of Indonesian immigration. A single German family with Hb E was reported by Betke.¹⁶ Haemoglobin E has not been encountered in tropical Africa, in American Indians, in Europeans (other than those mentioned), or in Japanese.¹⁷

A review of published reports failed to show reports of Hb E in blacks, other than one American black man mentioned by Bunn *et al.*¹⁸ This report describes a black American family with Hb E trait and probably α -thalassaemia.

Methods

Red cells, haemoglobin, haematocrit, and MCV were measured with the Coulter S-Plus electronic counter. Haemoglobin F was estimated by the one minute alkaline denaturation method of Singer *et al.*¹⁹ The Helena Hb electrophoresis procedure was used for Hb electrophoresis on cellulose acetate at pH 8.6 and citrate agar pH 6.4. Urea acetate electrophoresis was done using the method of separation of globin chains described by Schneider.²⁰ The oxidative instability test was done by the method of Frischer and Bowman.²¹ Serum iron and total

iron binding capacity were done by the methods of Giovanniello and Pecci²² and Ramsay,²³ respectively.

Case reports

The proband is a 43-year-old black man who was seen because of respiratory tract infection. Haematological evaluation showed moderate anaemia. Examination of the peripheral blood smear showed hypochromia, microcytosis, and a moderate number of target cells. A solubility test for haemoglobin S (Sickledex test) was negative. Haemoglobin electrophoresis on cellulose acetate at pH 8.6 showed an abnormal haemoglobin migrating in the A₂ position (fig 1). Haemoglobin electrophoresis on citrate agar at pH 6.4 showed a single band in the

FIG 1 Haemoglobin (Hb) electrophoresis on cellulose acetate at alkaline pH.

1- A/C
2- Patient
3- A/A
4- Patient
5- S/C
6- S/S
7- Patient
8- A/A ↑ F

FIG 2 Haemoglobin (Hb) electrophoresis on citrate agar at acid pH.

A position (fig 2). Heat stability test was negative. Urea acetate electrophoresis showed a slow β -chain. The abnormal Hb constituted approximately 24% of the total Hb, fetal Hb was 0.8%, and the rest was Hb A. Haemoglobin E trait was confirmed by the oxidative instability test.

The patient's father is dead and his mother was not available for testing. He has six children, two girls and four boys, ranging in age from 14 to 24 years (fig 3). All the family were clinically healthy. Haematological studies are shown in the table.

FIG 3 Distribution of haemoglobin E and α -thalassaemia trait in the family.

TABLE Haematological data

Pedigree No	Age	Hb	RBC	MCV	MCH	MCHC	Hb pattern	Hb components E	F	A ₂	Fe*	TIBC	Reticulocytes
1	43	12.2	5.06	75	24.1	31.6	AE	24	0.8	—	67	315	69
2	42	12.1	4.87	93.4	32.4	34.7	AA	0	0.6	2.6	103	243	64.8
3	24	14.4	5.01	83.7	28.8	34.3	AE	33	1.2	—	—	—	—
4	23	11.1	3.89	82.7	28.6	34.6	AA	0	0.5	2.5	125	276	97.9
5	22	15.7	5.6	82.4	28.1	34	AA	0	0.6	2.6	—	—	—
6	20	14.7	5.21	82.4	28.2	34.2	AE	32	1.2	—	—	—	—
7	18	11.4	4.13	81.5	27.5	33.8	AE	36	1	—	104	321	65
8	14	12.3	4.69	77	26.2	34	AA	0	0.8	2.6	87	303	72

*Normal serum Fe (45 to 155 μ g/dl)

In the family members with Hb E, the percentage of Hb E was somewhat higher in the children than in the father. The father (I.1) had mild anaemia, low MCV, target cells on peripheral smear, and normal Fe and TIBC. The daughter (II.7) also had mild anaemia, a low normal MCV, and normal Fe and TIBC, while the two affected sons (II.3, II.6) were not anaemic and had low normal MCV. One son (II.8) who did not have Hb E had mild anaemia and microcytosis with normal haemoglobin A₂ and F, and normal Fe and TIBC. Another daughter (II.4) has mild anaemia with low normal MCV and normal Fe and TIBC. A son (II.5) and the mother (I.2) were haematologically normal.

Discussion

While Hb E is known to have a high gene frequency in south-east Asia and adjacent areas, published reports of Hb E in blacks are very scarce. The possibility of Asian ancestry to explain the occurrence of Hb E trait in this family was considered, but the family is not aware of it, and there is nothing about their appearance to suggest it. It was reported by Chernoff *et al*²⁴ that in the heterozygous state the production of Hb E seems to proceed at a rate somewhat lower than Hb A. As a result, the distribution of the two haemoglobins in the red cells is usually approximately 60% Hb A and 40% Hb E. Such subjects are usually asymptomatic. However, subjects homozygous for Hb E have a mild anaemia characterised by microcytosis and target cells.

It is known that the interaction of α -thalassaemia with abnormalities of Hb E results in suppression of the abnormal Hb.²⁵ The father's Hb E was only 24%, which is at the lower extreme for Hb E trait. This, together with otherwise unexplained microcytosis, hypochromia, and the presence of target cells, suggests that the father may well be a double heterozygote for both Hb E and α -thalassaemia genes. The three children who have Hb E trait but no microcytosis had higher Hb E (32 to 36%) than their father.

The three children with Hb E trait showed no stigmata of thalassaemia, while the youngest son (II.8) has a normal Hb pattern but very likely has α -thalassaemia on the basis of anaemia, microcytosis, normal A₂ and fetal Hb, and normal Fe and TIBC. Because the mother is clinically and haematologically normal, it could be assumed that the father and youngest son do indeed have α -thalassaemia.

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