CASE REPORT

Double heterozygous for hemoglobin S and hemoglobin E – a case report from central India

A. A. Dani · A.V. Shrikhande

Abstract Double heterozygosity for HbS and HbE is rare. HbS and HbE are seen in SC, ST and OBC communities from this part of country. Inter caste marriages amongst these communities have resulted into this compound heterozygous condition. Double heterozygous state for HbS and HbE is clinically silent as compared to HbS- β Thalassaemia and HbSS cases. At Regional Hemoglobinopathy Detection and Management Center, we report a case of 15- year-old male, *Teli* (OBC) by caste who came for screening for sickle cell disorder. Sickling, solubility test and Hb electrophoresis on agar gel at alkaline pH was carried out. His sickling and solubility tests were positive and on hemoglobin electrophoresis it showed two bands one at Hb A₂ position and another at HbS position. For further confirmation sample was subjected for quantitation of haemoglobin on high performance liquid chromatography (HPLC), Bio-Rad. On quantitation he was having HbS 59.8%, HbE 33.5% and HbF 3.2% confirming his double heterozygous state for HbS and HbE. On family screening his father turned out to be sickle cell trait and mother as hemoglobin E trait.

Keywords Hemoglobinopathy · HbE · HPLC · HbSE

Abbreviations

Hb - Hemoglobin
 HbA₂ – Hemoglobin A₂
 HbC – Hemoglobin C
 HbD – Hemoglobin D
 HbE – Hemoglobin E
 HbF – Fetal Hemoglobin
 HbS – Sickle Hemoglobin
 HPLC – High Performance Liquid Chromatography
 Glu – Glutamic acid
 I.G.M.C. – Indira Gandhi Medical College
 Lys - Lysine
 MCH - Mean Corpuscular Hemoglobin
 MCHC - Mean Corpuscular Hemoglobin Concentration
 MCV – Mean Corpuscular Volume
 OBC – Other Backward Class
 O/E – On Examination
 RBC – Red Blood Cell
 RDW – Red Cell Distribution Width
 SC – Schedule Caste
 ST – Schedule Tribe

Introduction

Prevalence of abnormal haemoglobins varies considerably with geographic location and racial groups. Four hemoglobin variants, HbS, HbE, HbC, HbD; each affects millions world wide [1]. HbS, HbE and HbD are widely prevalent and occur in several populations in different parts of the country [2, 3, 4, 5].

The sickle cell haemoglobin is widely distributed all over India [3, 4, 6, 7]. In India the prevalence of sickle cell gene varies from 4–44%. The frequency distribution of HbS

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in central zone of India is 22.5–44.4% [8]. Hb E 26^{glu->lys} is second most common hemoglobinopathy found in the world [1]. Hb E has a wide spread distribution being most frequent in the eastern and north eastern part of India [9, 10]. Sporadic reports are also available from other parts of the country including Maharashtra [11, 12]. Average gene frequency has been found to be 10.9% for north eastern states of India [9]. The gene frequency reported in Western Maharashtra is 0.6% [13].

During year 2004 we screened 13600 samples at Regional Hemoglobinopathy Detection and Management Centre, I.G.M.C. Nagpur for sickle cell disorder by doing sickling, solubility test, Hb electrophoresis and HPLC. Sickling was done by using freshly prepared 2% solution of sodium metabisulfite, Solubility test by using high molarity phosphate buffer and Hb electrophoresis on agar gel at alkaline pH by using Tris EDTA Borate Buffer and HPLC on Bio-Rad VariantTM.

We report an interesting case of compound heterozygosity for HbS and HbE.

Case report

During our screening programme a 15-year-old male, *Teli* (OBC) by caste came for screening for sickle cell disorder. He was having history of repeated upper respiratory tract infections, easy fatigability and weakness. O/E Pallor present, icterus absent, spleen was just palpable. Complete hematological profile was done.

His sickling and solubility test were positive. Hb electrophoresis on agar gel at alkaline pH (8.6) showed two bands one at HbA₂ position and another at HbS position. Band at HbA₂ position was prominent so suspected to be of either raised HbA₂ or HbE. For further confirmation sample was subjected for quantitation of haemoglobin on high performance liquid chromatography (HPLC), Bio-Rad. Looking at the results of Hemoglobin electrophoresis and HPLC the case was diagnosed as double heterozygous for hemoglobin S and hemoglobin E [14] and hence family screening was advised.

Results

Table 1 was showing hematological profile of all family members of HbSE case. Patient's Hematological profile was Hb 8gm/dl, RBC count 3.63 millions/cumm, MCV 66.9fl, MCH 22pg, MCHC 32.9% and RDW 15.1. On quantitation Hb E was 33.5%, HbS 63.8%, HbF 3.2% and was diagnosed as double heterozygous for HbS and HbE.

On family screening it was found that his father and brother were having positive sickling and solubility test. Father's hemoglobin was on lower side of normal, brother was having low hemoglobin. Both were having raised RBC count, MCV less than 80 fl, MCH less than 27 pg, MCHC on lower side of normal and normal RDW. On quantitation Hb A was more than 60%, Hb S around 25%, Hb F around 1% and both were diagnosed as sickle cell trait.

Mother was having negative solubility test her hematological profile was Hb 9gm/dl, RBC count 3.28 millions/cumm, MCV 87.2fl, MCH 27.4pg, MCHC 31.5% and RDW 22. On quantitation Hb A was 64.2%, Hb E 25.3%, Hb F 1.1% and was diagnosed as HbE trait.

Discussion

This is first case of double heterozygous condition for HbS and HbE reported from central India. HbS is prevalent in this part of country and most commonly seen in schedule caste community. HbE cases are also reported from this part of country and commonly seen in OBC community. Our case belongs to Teli (OBC) community. He was clinically asymptomatic with microcytic hypochromic anemia. Patients with HbSE may have mild anemia and microcytosis along with approximately 30% HbE and patients are usually asymptomatic [15].

As against the sickle cell trait father and brother of this patient were having Hb S around 25%, MCV less than 80 fl, MCH less than 27pg and raised RBC count these findings are suggestive of sickle cell trait with coexistent α thalassaemia or iron deficiency anemia [16]. Further studies are required for confirmation of coexistent α thalassaemia or iron deficiency anemia.

Table 1 Hematological work up of family of HbS-E case

Sr no	Relation	Hb gm/dl	RBC m/cumm	MCV Fl	MCH Pg	MCHC %	RDW	HbA %	HbE %	HbS %	HbF %
1	Patient	8	3.63	66.9	22	32.9	15.1	-	33.5	59.8	3.2
2	Father	12.2	5.3	77.2	23	29.8	13.9	60.8	-	25.3	0.9
3	Mother	9	3.28	87.2	27.4	31.5	22	64.2	25.3	-	1.1
4	Brother	8.5	4.16	68	20.4	30	14.7	62.4	-	25	1

Conclusion

Double heterozygosity for HbS and HbE is first of its kind reported from this part of India. HbS and HbE are seen in SC, ST and OBC communities from this part of country. Inter caste marriages amongst these communities have resulted into this compound heterozygous condition. Double heterozygous state for HbS and HbE is clinically silent as compared to HbS- β Thalassaemia and HbSS cases. Mass screening for detection and counseling to prevent further spread of these genes in community is required.

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