Case Report

HBE homozygous haemoglobinpathy – Fortuitous finding

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Abstract

A 24-year-old male patient presented with the principal complaint of deposits on his teeth and gingival pigmentation. After examination, he was diagnosed with chronic generalized gingivitis. He was further referred for pre-procedural routine blood investigations. Bleeding time, clotting time, and his random blood sugar values were normal. CBC report revealed the presence of erythrocytosis with microcytic hypochromic red blood cells. Following this peripheral smear was taken which reveals the presence of polychromatophils, target cells and a few spherocytes. Haemoglobin electrophoresis by high-performance liquid chromatography (HPLC) was performed which disclosed 90.8% of HbE, suggestive of homozygous haemoglobinopathy. He had no other associated systemic findings, and there was no relevant family history. The patient was informed about his condition and stated to have pre-marital and pre-natal genetic counselling in the future. The patient being a carrier of the thalassaemic trait happened to know his condition incidentally, which could prevent future complications.

Keywords: Codocytes, hemoglobinopathy, thalassemic trait

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INTRODUCTION

Extensive knowledge about systemic disease and their investigations is obligatory for the dentist to promote general health, educate the patient as well as prevent future complications. This case report describes the incidental finding of haemoglobinopathy in an asymptomatic patient, with no family history be useful in precluding the complications to the next generation by taking pre-natal genetic counselling. Haemoglobinopathies encompass inherited disorders of the protein component of haemoglobin (Hb, i.e., the globin chain). Specific populations are particularly at high threat of having a haemoglobinopathy, for example, in Southeast Asia, sub-Saharan Africa and the West Pacific region.[1]

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CASE REPORT

A 24-year-old healthy constructional worker with no anomalous family history was referred to the oral pathology department for his routine blood examinations. He had presented with the complaint of deposits on his tooth and also had the complaint of gingival pigmentation which bothered him aesthetically. He did not have any other relevant medical history or deleterious habits. On intra-oral examination, stains and calculus were seen along with the presence of a few carious teeth.

Routine blood investigations were performed which revealed the bleeding time of about 1 minute 14 seconds, clotting time of 3 minutes 24 seconds and random

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blood sugar of 92 mg/dl. Complete blood count examinations [Figure 1] were done which reported the drop in level of mean corpuscular volume of about 69.5FL (ref range -80–100 FL), mean corpuscular haemoglobin of 22 g (ref range-27–32 PG), mean corpuscular haemoglobin concentration of 31.6G/DL (ref range-33–38 G/DL) and red blood cell distribution width of 18.1% (ref range -11.6–14%).

A peripheral smear [Figure 2] was taken for this patient to look into the structure of RBCs which revealed the presence of polychromatophils, numerous target cells, crowding of red blood cells, and few spherocytes. He was then advised for haemoglobin electrophoresis by the HPLC method. HbE report [Figures 3 and 4] showed the foetal haemoglobin (HbF) value of 3.3% (ref range – 0–2), haemoglobin A2(HbA2) of 5.1% (ref range -2.2–3.5), haemoglobin D (HbD) of 0.8% (ref range – 0–0) and haemoglobin E (HbE) of 90.8% (ref range – 0–0). Skull posteroanterior view was taken which revealed no abnormality.

The patient being asymptomatic with no incidence of disease in his family lineage was advised to have pre-marital and pre-natal genetic counselling for screening of genetic disorders which can be transmitted through him to his offspring in the future.

Test Name	Results	Units	Biological Reference Interval	Test Method	Specimen Type
CBC (COMPLETE BLOOD COUNT)					
TOTAL LEUCOCYTE COUNT	8900	/CMM	4000 - 11000	Electrical Impedance	EDTA / BLOOD
RBC COUNT	6.38	Million/c.mm	MALE - 4.5 - 6	Electrical Impedance	EDTA / BLOOD
HB (HAEMOGLOBIN)	14.0	G/DL	FEMALE- 4.5 - 5 MALE -13 - 17	Cyanmethemoglobin	EDTA / BLOOD
PCV	44.4	%	FEMALE-11.5 - 16 40 - 50	Electrical Impedance	EDTA / BLOOD
MCV	69.5	FL	80 - 100	Calculated	EDTA / BLOOD
MCH	22.0	PG	27 - 32	Calculated	EDTA / BLOOD
MCHC	31.6	G/DL	33 - 38	Calculated	EDTA / BLOOD
RDW	18.1	%	11.6-14	Calculated	EDTA / BLOOD
PLATELET COUNT	3.24	LAC/C.MM	1.5 - 4.0	Electrical Impedance /Light Microscopy	EDTA / BLOOD
NEUTROPHIL	76.1	%	40 - 75	Light Absorbance / Light Microscopy	EDTA / BLOOD
EOSINOPHIL	0.4	%	1 - 6	Light Absorbance / Light Microscopy	EDTA / BLOOD
BASOPHIL	0.3	%	1-2	Light Absorbance / Light Microscopy	EDTA / BLOOD
LYMPHOCYTE	17.5	%	20 - 40	Light Absorbance / Light Microscopy	EDTA / BLOOD
MONOCYTE	5.7	%	2 - 10	Light Absorbance / Light Microscopy	EDTA / BLOOD

RBC- CROWDING (+), MICROCYTIC HYPOCHROMIC WITH MILD ANISOCYTES, POLYCHROMATOPHILS (+), TARGET CELLS (++), FEW SPHEROCYTES

IMPRESSION - ERYHTROCYTOSIS WITH MICROCYTIC HYPCOHROMIC RBCs
ADVICE - HB ELECTROPHORESIS/ HPLC TO RULE OUT HEMOGLOBINOPATHY (HBE/C)

Figure 1: Complete blood count investigations

Investigation	Observed Value	Unit	Biological Reference Interval
Erythrocyte (RBC) Count	6.22	mill/cu.mm	4.7-6.0
Haemoglobin (Hb)	13.5	gm/dL	13.5-18
MCH (Mean Corpuscular Hb)	21.7	pg	27-31
MCHC (Mean Corpuscular Hb Concn.)	31.7	g/dL	32-36
MCV (Mean Corpuscular Volume)	68.5	fL	78-100
PCV (Packed Cell Volume)	42.7	%	42-52
RDW (Red Cell Distribution Width)	17.7	%	11.5-14.0
Foetal Haemoglobin (HbF)	3.3	%	0.0-2.0
Haemoglobin A2 (HbA2)	5.1	%	2.2-3.5
Haemoglobin D (HbD)	0.8	%	0-0
Haemoglobins E (HbE)	90.8	%	0-0
Impression	Suggestive of HbE disease. ? (homozygous HbE). ? (HbE - beta thalassaemia).		
Comment	See remark 1 and 2.		
Nucleated RBC	-	per 100 WBCs	
Other	Erythrocytosis with microcytosis -for clinical correlation.		

Method: Capillary electrophoresis - Whole blood

Figure 3: Haemoglobin electrophoresis estimation by high-performance liquid chromatography

DISCUSSION

Haemoglobin within the erythrocytes is crucial for the existence, transportation of oxygen to the tissues.[1] The inherited disorders of haemoglobin, notably sickle cell disease, thalassaemia and haemoglobin E disorders, are the most common monogenic disorders globally with the autosomal recessive pattern as the mode of inheritance. Approximately 7% of the population are carriers of haemoglobinopathies including thalassaemia, haemoglobin (Hb) E and HbS, and 300,000–500,000 children are born annually with a severe haemoglobin disorder, the majority of them in developing countries.[2] Chernoff and colleagues reported the first case in 1954.

HbE is the most common haemoglobin variant in Southeast Asia as well as in Northeast India.[3] HbE is thalassaemic haemoglobinopathies having structurally abnormal HbE. HbE is variant haemoglobin with a spontaneous mutation in nuclear DNA, which can be a point mutation involving

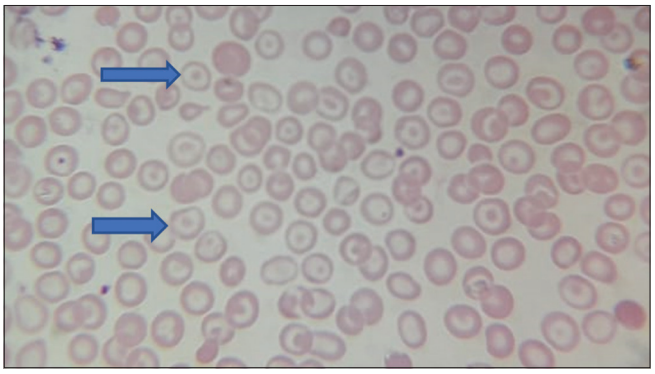

Figure 2: Peripheral smear showing RBC crowding, and the blue arrow indicates the target cells with their characteristic bull's eye appearance

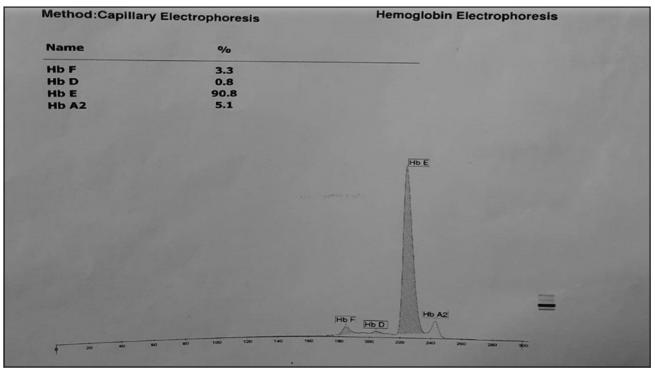

Figure 4: Chromatogram of HbE homozygous

alteration of a single nucleotide or otherwise deletion, insertion or other alteration in more than one nucleotide.[4,5]

The so-called -globinopathies (-thalassemia major, sickle cell syndromes and Hb E-thalassemia) generally present a greater global health burden than the a-thalassemia syndromes. Patients with severe -globinopathies require life-long treatment and clinical management. HbE present in three forms, heterozygous state Hb E trait, homozygous Hb E disease, and most important compound heterozygous Hb E/βthalassemia or Hb E sickle cell anaemia.[6] The biogenesis of structural variants is generally normal except for hemoglobinopathies caused by mutation in -fusion genes (Lepore haemoglobin) or in the -globin chain termination codon (Constant Spring haemoglobins). Thalassemia result from disruption of the standard coordinated synthesis of the globin chains that encompass tetrameric haemoglobin. The thalassemia phenotype includes combinations and varying degrees of hypochromia and microcytosis, anaemia, splenomegaly, reticulocytosis and erythroid bone marrow hyperplasia.[7]

The diagnosis of disorders of haemoglobin chain synthesis usually involves a combination of tests along with detailed clinical history, ethnic background, blood count and peripheral blood film examination. Patients suffering from HbE disease present with chronic anaemia without splenomegaly; blood count often resembles the β-thalassaemia trait which is seen in our case.[8,9] HbE is an extremely common Hb variant with a disease pattern similar to that of β-thalassaemia. Haemolysis can be caused by viral infections and medications due to the presence of unstable Hb. HbE is often associated with thalassaemia, which may result in serious major-form haemoglobinopathies. HbE homozygosity (HbE disease is moderate with microcytic hypochromic anaemia) with possible haemolysis due to exogenous causes which are observed in our case.[8]

The objective of pre-natal haemoglobinopathy screening is to detect and counsel asymptomatic individuals whose offspring are at risk of thalassaemia major/intermedia which was advised to our patient. This comprises universal screening during early pregnancy by complete blood count examination and peripheral smear examination. Any abnormality detected in these tests would further be evaluated and confirmed by HPLC. This is followed by the screening of partners and genetic counselling. Pre-natal diagnosis by chorionic villus sampling (amniocentesis) is to be done.[8,9]

Haemoglobinopathy can be prevented by assessing the carrier status of the couples in the early stages of pregnancy with the help of carrier testing by complete blood count examination and haemoglobin electrophoresis by HPLC. Abnormal Hb variants can interact with thalassaemia trait to give rise to thalassaemia major/intermedia or can be clinically silent. It is essential requisite for dentist to know about these haematological disorders so as to educate patients and to promote their oral health and general health as well.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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