Probable Haemoglobin Lepore Trait: A Rare Haemoglobinopathy Case Report from Bangladesh

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Abstract:

Hemoglobin Lepore is one of the rare structural variations of hemoglobin (Hb) that arises from unequal crossing over between the ä and â globin genes. Hb Lepore heterozygous is clinically similar to people with mild thalassemia. Here we reported a 32-years-old male febrile patient diagnosed incidentally as a rare haemoglobin Lepore trait.

Key words: Rare hemoglobinopathy, Haemoglobin Lepore Trait, Bangladesh

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Introduction

Haemoglobin (Hb) Lepore is a structurally abnormal Hb in which the abnormal globin chain results from an unequal crossover between the ä and â genes, because of a misalignment of homologous chromosomes during meiosis [1]. It was first identified in the Lepore family, an Italian-American family, in 1958 [2]. Three variants of Hb Lepore have been identified, each characterized by different gene deletion breakpoints manifesting as various clinical outcomes [3]. In the homozygous state, HbA and HbA2 are absent and hemoglobin is made up of HbF and Lepore only, the level of Hb Lepore ranging from 8% to 30% with a mean value of 15%, the remainder of Hb being HbF. In heterozygous state, the haemoglobin contains HbA, Lepore, HbA2 and a variable amount of HbF, the level of Hb Lepore ranging between 5% and 15%, with a mean level around 10% [2]. The haemoglobin F fraction is usually slightly elevated in Lepore trait as compared to beta thalassemia trait cases [2]. Haemoglobin Lepore homozygous does not have any normal haemoglobin A and usually results in a phenotype ranging from thalassaemia intermedia to major. In all Hb Lepore variants, the synthesis of the 5ØÿÞ5ØýÞ hybrid chain is significantly lower than that of the 5ØýÞ-chain, resulting in an overall reduction in non-5ØüÞ-globin chains [4]. The Clinicohematological profile of hemoglobin Lepore varies depending on the type of hemoglobin Lepore mutation and the number of abnormal hemoglobin genes present. In general, people with hemoglobin Lepore trait are asymptomatic or have mild symptoms, such as mild anemia and fatigue [2]. People with homozygous hemoglobin Lepore have more severe symptoms, such as moderate to severe anemia, splenomegaly, and jaundice [2]. In compound heterozygotes for Hbs S, C, and E with Hb Lepore, the clinical phenotypes are extremely variable but, overall; resemble those of Hbs S, C, or E/5ØýÞ-thalassemia compound state [5-6]. There is few case reports regarding this rare haemoglobinapathy in child published in Bangladesh and worldwide [7-8]. To our knowledge this was the first case report in adult patient having this condition in Bangladesh.

Case presentation:

Our patient is a 32-year-old male who admitted to our hospital with the complaints of high-grade fever and multiple joints pain with joint swelling for 11 days. He also gave history of burning micturition with increased frequency and urgency of urine and severe generalized weakness. There were no personal and/or family history of arthritis; any acute, repeat, or discontinued medications; any allergies. A thorough review of past medical and surgical histories revealed no history of diseases, surgical procedures, any prior hospitalization, and blood transfusion. On query he gave history of one

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of his sisters has been suffering from -Thalassaemia trait. On physical examination we found him moderately anaemic, mild hepatomegaly; both knees and ankles were tender and swollen. On laboratory evaluation, CBC showed Hb 7.9 g/dl, total RBC count 4.33m//ul, HCT 25.2%, MCV 58.1fl, MCH 18.1pg and MCHC 31.2 g/dl (Table 1).

PBF showed microcytic hypochromic cell with anisopoikilocytosis like pencil cells, elliptical cells, pear cells and a few target cells. S. ferritin 1198.85 ng/ml and abdominal ultrasound showed mild hepatomegaly. Hb electrophoresis showed an abnormal pattern with mild elevation in HbS, normal Hb F, mild reduction in HbA, and high HbA2, suggesting a heterozygosity for the beta chain variant of Hb Lepore (Fig 1). Normally electrophoresis report revels HbA 0%-30% (typically near 0%), HbF Up to 95%, HbA2>5% in thalassaemia major, HbA 10%-50%, HbF10%-50%, HbA2>4% in thalassaemia intermedia, HbA >88%, HbF<5%; HbA2>4% in thalassaemia minor, HbS >90%, HbA absent, HbF <10%, HbA2 <3.5% in Hb S disease and Hb D >90%, Hb F and A2 values are unaffected in HbD Punjab [9-11].

His blood sugar was raised, S. Creatinine 3mg/dl, CRP 312 mg/L, anti-CCP negative, X-ray lumbosacral spine negative, urine RME and culture, blood culture and procalcitonin were negative. He was diagnosed as a case of undifferentiated arthritis, Hb Lepore trait, acute kidney injury and DM. Two-unit of red cell concentrate were given him to maintain Hb around 10g/dl. Patient was discharged with folic acid 5mg along with other medications.

Table-I

Complete blood count: the results showed low Hb, low MCV, low MCH, and normal MCHC. MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; RBC, red blood cell count.

Haematology Report

(Estimations were carried out by HORIBA Automated Haematology & Verified manually)

Test Name	Result	Unit	Reference Range
Hemoglobin (Hb)	7.9	gm/dl	Male:12.5-17.0, Female:11.0-15.0 Infant/child:13.0-19.0
ESR (Westergreen)	106	mm/1st hr	Male:0-10, Female:0-20
Total WBC Count (TC)	24,160	/cumm	Adult:4000-11000, Infant:6000-18000 Child:5000-15000, At Birth:10000-25000
Differential WBC Count (DC)			
Neutrophils	86	%	Adult: 40-70, child: 20-50
Lymphocytes	08	%	Adult: 20-40, child: 40-75
Monocytes	04	%	Adult: 02-08
Eosinophils	02	%	Adult: 01-06
Basophils	00	%	Adult: 00-01
Total Cir, Eosinophils	483	/cumm	Adult: 50-450
Total RBC Count	4.33	m/ul	Male: 4.5-6.5, Female: 3.8-5.8
HCT/PCV	25.2	%	Male: 40-54, Female: 37-47
MCV	58.1	fL	Adult: 76-94
MCH	18.1	pg	Adult: 27-32
MCHC	31.2	g/dL	Adult: 29-34
RDW-CV	14.7	%	Adult: 11.0-16.0
RDW-SD	34.4	fl	Adult: 35-56
PDW	20.4	fL	Adult:35-56
Total Platelet Count (PC)	3,69,000	/cumm	Adult: 150,000-4,50,000
MPV	9.8	fL	Adult: 7.0-11.0
PCT	0.36	%	Adult: 0.1-0.2
P-LCR	39.0	%	Adult: 13.0-43.0
P-LCC	144	10^3/uL	Adult: 44.0-140.0

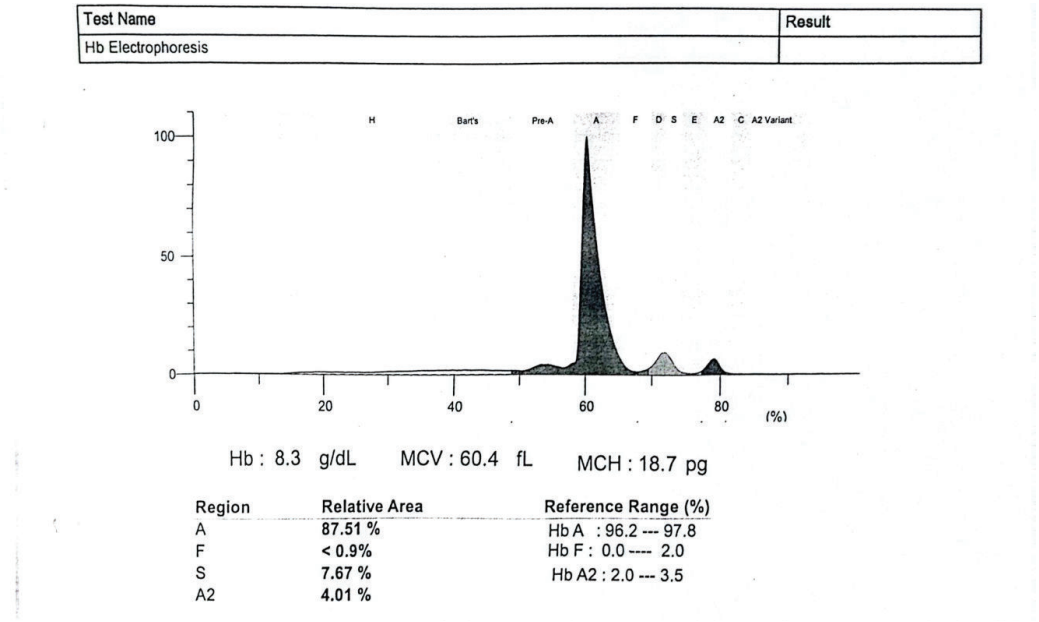

Figure 1: *The capillary electrophoresis technique showed the abnormal band as HbD.*

Discussion

Due to the misalignment of homologous chromosomes during meiosis, in-frame fusion between the 5 end of the ä-globin gene and the 3 end of the â-globin gene causes structurally defective haemoglobin (Hb), a type of haemoglobin condition called Hb Lepore. Hb Lepore is a hybrid gene product with a loss of 7.4 kb between the delta and beta-globin genes [1]. Variations in the transitions from the delta to the beta sequences at fusion functions are the cause of the identified three types of Hb Lepore so far [1]. They are Hb Lepore Washington Boston (ä87/â116), Hb Lepore Baltimore (ä50/â86), and Hb Lepore Hollandia (ä22/â50); the first one is the most common and occurs all around the world [1]. Because of inefficient erythropoiesis and reduced red cell survival in all of these variants, the synthesis of excess-chains leads to an imbalance in the globin protein and the clinical signs of thalassaemia[12]. One hospital based study in Bangladesh has reported the prevalence of homozygous hemoglobin lepore 0.02% and Hb lepore trait 0.07%[13], In India, reported prevalence of lepore trait was 0.004%[14].

Only HbF and HB Lepore make up haemoglobin in the homozygous state; the percentage of Hb Lepore ranges from 8% to 30% (with a mean of 15%), while the remaining percentage is HbF. Haemoglobin in a heterozygous state has varying amounts of HbF (1–14%), Hb Lepore (5%–15%), and HbA and HbA2 (~2%)[4]. Lepore heterozygotes, homozygotes, and compound heterozygotes all had much higher HbF levels [4]. Furthermore, compound heterozygotes for Hbs S, C, and E with Hb Lepore also reported. Even though the clinical presentations of these disorders are varied, they usually approximate the compound states of Hbs S, C, or E/thalassemia [8]. Although most Hb Lepore heterozygotes are asymptomatic, a series reported that few heterozygotes had mild to severe anaemia, Jaundice hepato-splenomegaly, only two patients had arthralgia[2]. In addition to being healthy, heterozygotes usually exhibit observable microcytosis and hypochromia, as well as normal Hb levels [6]. In this case there were two-unit of red cell concentrate were given him to maintain Hb around 10g/dl. Clinical signs in homozygotes might vary from Thalassaemia intermedia to a transfusion-dependent course similar to Thalassaemia major [6]. In this case, Hb electrophoresis techniques identified the Hb Lepore variant as HbD. Family history, clinical correlation, CBC result, iron profile, and high-performance liquid chromatography (HPLC) result should be interpreted together to give an appropriate diagnosis. Some HPLC techniques give patterns and pictures reliable enough to make a diagnosis [15]. Being a developing country, we

depend more on biochemical analysis and capillary electrophoresis technique result to detect the different type of haemoglobinopathies along with history, clinical features and lab test. Molecular testing and globin chain analysis are needed to confirm the diagnosis of specific varient of Hb Lepore [8]. Unfortunately, molecular testing of globin chains was not done here due to financial constrain.

Conclusion

A hybrid gene created by fusing the delta and beta genes codes for the structural hemoglobin variant known as Hb Lepore. Clinically, the homozygous state resembles either major or intermedia beta thalassaemia. A variety of techniques, such as the examination of blood counts and red cell indices, hemoglobin electrophoresis, make it simple to make an assumption in the lab. However, DNA characterisation is necessary for confirmation but, that sometimes difficult to do in a developing country. Appropriate clinical management and genetic counseling depend on a precise diagnosis. In pertinent clinical scenarios, it is crucial to remember the uncommon haemoglobinopathy, Hb Lepore. In terms of clinical presentation, it is asymptomatic as similar to people with mild thalassemia sometimes symptomatic and need blood transfusion.

Conflicts of interest disclosure

The authors declare that they have no conflicts of interest.

References:

1. Bhusal A, Bhandari S, Seth T, Sah RP. Homozygous Lepore Syndrome: A case report. Ann Med Surg (Lond). 2022 Jul 14;80:104168. doi: 10.1016/j.amsu.2022.104168. PMID: 36045803; PMCID: PMC9422200.
2. Samira kumar Behera, Shushruta Mohanty, Swetambari Acharya, Swati Das, Lipika Behera. Clinicohematological Profile of Hemoglobin Lepore. International Journal of Pharmaceutical and Clinical Research. 2023Dec30;15(12):1152–7.
3. Bozkurt G, Baysal E, Gu L-H, Huisman THJ. Thalassemia intermedia in two patients with Hb Lepore-b0 -thalassemia (Frameshift codon 8,-AA). 1994; Hemoglobin 18(3):247–250.
4. Saswati Mukhopadhyay. Haemoglobin lepore and beta thalassaemia traits – Prenatal testing by both sequence analysis and MLPA for HBB gene: A case report. 2023; Indian Journal of Obstetrics and Gynecology Research 2024;11(1):112–115.
5. T. H. J. Huisman, Compound heterozygosity for Hb S andthe hybrid Hbs Lepore, P-nilotic, and Kenya; comparison of hematological and hemoglobin composition data, Hemoglobin, 1997; 21(3): 249–257.
6. V. Viprakasit, P. Pung-Amritt, L. Suwanthon, K. Clark, andV. S. Tanphaichitr, Complex interactions of 5ØÿÞ5ØýÞ hybrid haemoglobin (Hb Lepore-Hollandia) Hb E (5ØýÞ26 g'!a) and 5ØüÞ+ thalassaemia in a Thai family, European Journal of Haematology, 2002; 68(2): 107– 111.
7. Aziz MA, Khan WA, Das SA, Banu B. Homozygous Hemoglobin Lepore: A Rare Condition Seen in a Bangladeshi Family. Mymensingh Med J. 2021 Oct;30(4):1172-1176. PMID: 34605493
8. Waye JS, Eng B, Patterson M, Chui DH, Chang LS, Cogionis B, Poon AO, Olivieri NF. Hb E/Hb LeporeHollandia in a family from Bangladesh. Am J Hematol. 1994 Dec;47(4):262-5. doi: 10.1002/ajh.2830470403. PMID: 7977297.
9. Langer AL. Beta-Thalassemia. 2000 Sep 28 [Updated 2024 Feb 8]. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2025. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1426/
10. American Society of Hematology. (2021). Hemoglobin Electrophoresis in Sickle Cell Disease: A Primer for the Clinician. Retrieved from https://www.hematology.org/education/trainees/fellows/hematopoiesis/2021/hemoglobin-electrophoresis-in-sickle-cell-disease.
11. Jawed I, Alam MO, Fatima FB, Johar SA, Shah SAM. Case report—unveiling a case of hemoglobin D-Punjab variant with iron deficiency anemia in Sindh (Pakistan). SAGE Open Medical Case Reports. 2024;12. doi:10.1177/2050313X241272516
12. Pasangna J, George E, Nagaratnam M. Haemoglobin Lepore in a Malay family: a case report. Malays J Pathol 2005;27:33–7.
13. Aziz, A. (2023). Current prevalence of thalassemia and prenatal diagnosis in Bangladesh: A single center hospital based study. *The Global Health Network Collections*. https://doi.org/10.21428/3d48c34a.a0882aa2
14. Mondal SK, Mandal S. Prevalence of thalassemia and hemoglobinopathy in eastern India: A 10-year high-performance liquid chromatography study of 119,336 cases. Asian J Transfus Sci. 2016 Jan-Jun;10(1):105-10. doi: 10.4103/0973-6247.175424. PMID: 27011683; PMCID: PMC4782486
15. Asees MY, Shrateh ON, Jobran AWM, Assi AS. Rare occurrence of hemoglobin Lepore variant in a Palestinian patient: a case report and brief literature review. Ann Med Surg (Lond). 2023 Sep 1;85(10):5219-5222. doi: 10.1097/MS9.0000000000001212. PMID: 37811104; PMCID: PMC10552947.

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