Case Report

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HbH Disease

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Abstract

Background: HbH disease is a nonfatal form of alpha thalassemia syndrome. The alpha thalassemia syndromes are a group of hereditary anemias of varying clinical severity and characterized by reduced or absent production of one or more of the globin chains of hemoglobin molecule. HbH disease is common in Indian Subcontinent but not all the cases detected are reported in literature. Here we report a case of HbH disease in a three year of female patient who presented with history of mild fever and mild distension of abdomen for 15 days.Complete blood count showed HB- 4.4 gm%, TLC – 10.6 X 10^3/uL, platelet count was 358 X 10^3/uL. 8 nucleated RBCs were seen per 100 WBCs. She was given iron therapy for one month but showed mild response only. So a hemoglobin electrophoresis was done.A peripheral blood film was prepared which showed presence of microcytes, few macrocytes, teat drop cells, fragmented cells and polychromatophils and NRBCs. Reticulocyte preparation showed 7% reticulocytes with occasional HbH like inclusions. Hb electrophoresis was done on capillary electrophoresis (Mini cap, Sebia) which revealed a HbH band at zone 15. *Conclusion:* HbH disease is a gentic disease with 25% chance of acquiring the disease with each pregnancy when the partner carries a mutated alpha globin gene. Hence prenatal genetic counselling of family members is necessary. A high index of suspicion is required for a prompt diagnosis and management.

Keywords: HbH Disease; Alpha Thalessemia; Hb Electrophoresis.

Introduction

HbH disease is an inherited disorder of haemoglobin synthesisand is also known as alpha thalessemia [1]. It is a nonfatal form of alpha thalassemia syndrome.The alpha thalassemia syndromes are a group of hereditary anaemias of varying clinical severity and characterized by reduced or absent production of one or more of the globin chains of hemoglobin molecule. The deletional and non deletional mutations affecting the alpha globin genes on chromosome 16p13.3 causes absent or reduced globin chain synthesis resulting in alpha thalessemia syndromes. In HbH disease excess beta chains accumulate as tetramers known as HbH(Beta 4) [2]. HbH disease is the commonest form of alpha thalessemia syndromes and can be detected by Hb electrophoresis by various methods like HPLC, Isoelectric focussing and Capillary electrophoresis. There is a 25% chance of acquiring the disease in each progeny if the affected parent carries the mutated gene [3]. HbH disease is common in Indian Subcontinent but not all the cases detected are reported in literature.

Here we report a case of HbH disease in a three year of female patient.

Case Report

A three year old female patient presented with history of mild fever and mild distension of abdomen for 15 days. The patient was from tribal background. A history of consanguinous marriage was not provided by the parents of the affected child. There was no history of any investigations done in the past either of siblings or of parents. On general examination, the child had gross pallor. Spleen was just palpable.

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There was no hepatomegaly.

Complete blood count showed HB- 4.4 gm%, TLC – 10.6 X 10^3/uL, platelet count was 358 X 10^3/uL. 8 nucleated RBCs were seen per 100 WBCs (Table 1). Due to poor socio economic status other biochemical investigations were not performed so a hemolytic jaundice could not be established biochemically. However she had a mild hemolytic facies . She was given iron therapy for one month but showed mild response only. So a hemoglobin electrophoresis was done.

A peripheral blood film was prepared which showed presence of microcytes, few macrocytes, tear drop cells, fragmented cells and polychromatophils and NRBCs. Reticulocyte preparation showed 7% reticulocytes with occasional HbH like inclusions (Figure 1)

1. Hb electrophoresis was done on capillary electrophoresis (Mini cap,Sebia) which revealed a HbH band of 0.7% (Figure 2)

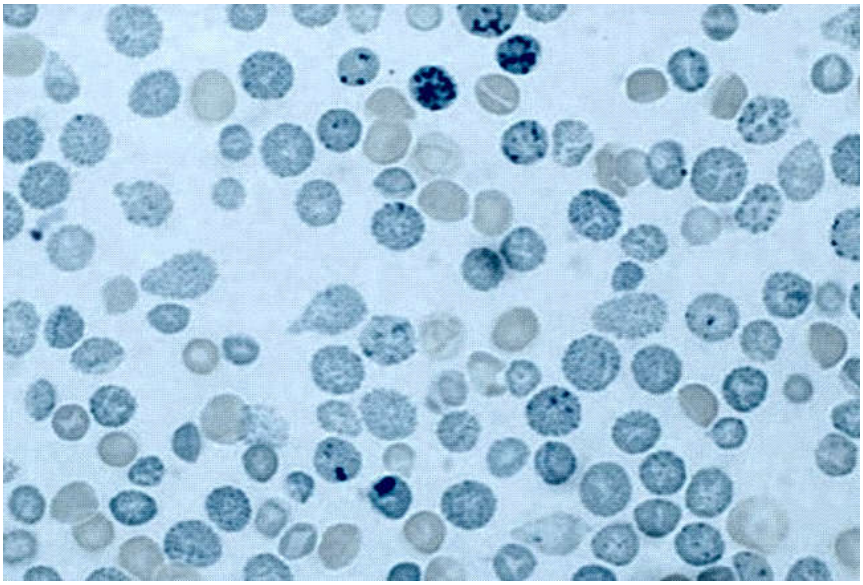

Fig. 1: Golf ball like HbH inclusions in the RBCs along with reti culocytes. (New methylene blue at 1-hour incubation, × 100)

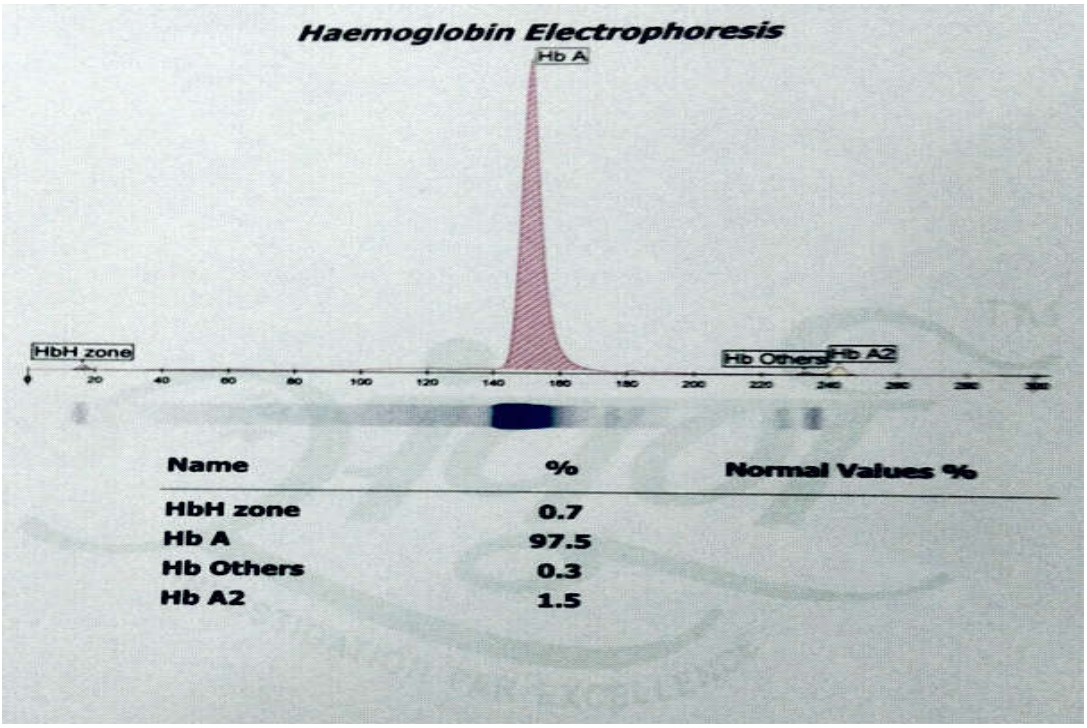

Fig. 2: HbH Band in capillary electrophoresis

Table 1:

Complete Blood Count			
Investigation	**Result**	**Unit**	**Reference Range**
Haemoglobin	**4.4**	g/dL	11 - 16
RBC (Red Blood Cells)	3.25	10^6/uL	4.0 – 5.2
Packed Cells Volume	17.9	%	36-47
Total Leucocyte(WBC)Count	10.6	10^3/uL	5.0-15.0
Differential Count			
Neutrophils	30	%	40-70
Lymphocytes	65	%	20-50
Monocytes	03	%	0-10
Eosinophils	02	%	0-6
Basophils	00	%	0-1
MCV (Mean Corpuscular Volume)	55.1	fL	81-99
MCH (Mean Cell Hb)	13.5	pg	27-32
MCHC (Mean Corpuscular Hb C)	24.6	g/dl	32-36
Platelet Count	358	10^3/uL	150-450

Discussion

HbH disease is common among people of South East Asia, Mediterranean and parts of Middle East [4]. Due to high affinity for oxygen, HbH molecule is not suitable for oxygen exchange. This results in tissue hypoxia which is out of proportion to the level of Hb [5]. HbH on oxidation forms intracellular inclusions which can be detected in peripheral smear by supravital staining [6]. Hemolysis is caused by splenic sequestration of old RBCs and these inclusions can be seen most often in older RBCs.

HbH disease often has a mild presentation. It has a wide spectrum of clinical presentations ranging from asymptomatic cases to development of severe anemia and rarely Hydrops foetalis in uterus may be observed [7]. HbH disease is the commonest form of alpha thalassemia intermedia and the most severe non fatal form of alpha thalassemia syndromes. The alpha thalassemia syndromes are a group of hereditary anemias characterized by reduced or absent production of one of the alpha globin chains of hemoglobin molecule. The oxygen carrying capacity of RBCs is dependent on Hemoglobin, a tetramer protein comprising of 4 globin chains bound to the haem molecule. There are 4 major globin chains, alpha, beta, gamma and delta. HbA is dominant in adults composed of 2 alpha and 2 beta chains.

A very tightly controlled globin chain production keeps the ratio of alpha and non alpha chains at 1:00. Decreased production of $alpha_2$ globin $alpha_1$ globin gene results in relative excess of beta chains which are less stable, causing a clinical disease called alpha thalassemia [8,9]. From a genetic stand point alpha thalassemia are extremely heterogeneous. They are broadly classified according to whether the loss of alpha globin gene is complete or partial ie. Alpha $^{(0)}$ thalassemia or alpha $^{(+)}$ thalassemia.

Inheritance of one normal alpha globin gene leads to a condition called HbH disease. The loss of 3 alpha globin genes results in abundant formation of HbH. The excess beta chains aggregate into tetramers accounting for 5-30% of Hb level in patients with HbH disease [10] RBCs that contain HbH are sensitive to oxidative stress so a hemolysis may occur if oxidants such as sulphonamides are given to such patients.

The North American TCRN study showed that 85% of patients with alpha thalassemia are Asians, 4% are white and 11% are of other ethnicities including African, black, mixed ethnicity and unknown [11].

For patients with HbH disease the overall survival rate is fairly good with most patients reaching upto adulthood. Some patients may require repeated blood transfusions with complications of iron overload. This may contribute to increased morbidity and mortality in such patients. They are also prone to develop hypersplenism , gall stones, leg ulcers, infections and venous thrombotic episodes due to hemolysis. In patients with HbH disease 20-40% total Hb is Hb Bart's along with HbA, HbA2 and HbF. In silent carriers however the percentage is only 1-2% with low or normal amounts of HbA2 [12].

Conclusion

HbH disease is a gentic disease with 25% chance of acquiring the disease with each pregnancy when the partner carries a mutated alpha globin gene. Hence prenatal genetic counselling of family members is necessary. A high index of suspicion is required for a prompt diagnosis and management.

Conflict of Interest

none

References

1. Chan V, Wong MS, Ooi C, Chen FE, Chim CS, Liang RH, et al. Can defects intransferrin receptor 2 and hereditary haemochromatosis genes account for ironoverload in HbH disease? Blood Cells Molecules & Diseases. 2003; 30: 107–11.
2. Higgs DR, Bowden DK. In: Disorders of Haemoglobin; Genetics, Pathophysiology, and Clinical Management. Steinberg MH, Forget BG, Higgs DR, Nagel RL (eds) Cambridge, United Kingdom: Cambridge University Press; Clinical and Laboratory Features of á-Thalassaemia Syndromes; 2001; pp. 431–69..
3. Cooley's anaemia foundation Web : alpha thalessemia.
4. Borgna-Pignatti C, Galanello R. Thalassemias and related disorders: Quantitative disorders of hemoglobin synthesis. In: Greer JP, Foerster J, Lukens JN, Rodgers GM, Paraskevas F, Glader B,editors. Wintrobe's clinical hematology. 11 th ed. Philadelphia: Lippincott Williams and Wilkins; 2004; p. 1319-65.
5. Benesch RE, Ranney HM, Benesch R, Smith GM. The chemistry of Bohr effect.II. Some properties of hemoglobin H. J Biol Chem. 1961; 236: 2926-9.
6. Kattamis C, Tzotzos S, Kanavakis E, Synodinos J, Metaxotou-mavrommati A. Correlation of clinical phenotype to genotype in haemoglobin H disease. Lancet 1988; 1: 442-4.
7. Chui DHK, Fucharoen S, Chan V. Haemoglobin H disease: not necessarily a benign disorder. Blood. 2003; 101: 791–800.
8. Chui DH. Alpha-thalassemia: Hb H disease and Hb Barts hydrops fetalis. Ann N Y Acad Sci. 2005. 1054: 25-32.
9. Piel FB, Weatherall DJ. The a-thalassemias. N Engl J Med. 2014 Nov 13; 371(20): 1908-16.
10. Liu YT, Old JM, Miles K, et al. Rapid detection of alpha-thalassaemia deletions and alpha-globin gene triplication by multiplex polymerase chain reactions. Br J Haematol. 2000 Feb.; 108(2): 295-9.
11. Alexandra C Cheerva, ,Max J:,Alpha Thalessemia; emedicine.medscape.com, article 955496.
12. Giambona A, Passarello C, Renda D, Maggio A. The significance of the hemoglobin A(2) value in screening for hemoglobinopathies. Clin Biochem. 2009 Dec.; 42(18): 1786-96.