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The absence of hemoglobin Hb H band in the proven hemoglobin H disease patient due to the iron deficiency anemia

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Abstract

Introduction: Iron deficiency anemia has not only been rarely seen among hemoglobin H disease patients but can mask the diagnosis of hemoglobin H disease also.

Case Presentation: A 50-year-old Thai woman had marked and progressive anemia with just splenomegaly on the physical examination. Her blood tests showed: Hb 3.8 g%, MCV 50.4 fl, MCH 15.4 pg, ferritin 5.0 ng/ml, serum iron 33 ug/dl, TIBC 123 ug/dl, the Hb analysis using the high-performance liquid chromatography method found only A_2A, Hb A_2 2.1 %. Iron deficiency anemia was diagnosed and continuously treated with the oral iron tablets. After two months of treatment, her blood showed: Hb 7.7 g%, MCV 69.3 fl, MCH 20.5 pg, reticulocyte 6.0 %, ferritin 6.2 ng/ml, Hb analysis showed: A_2AH Bart, Hb A_2 1.7 %. The diagnosis of Hb H disease was added. Later Hb H was confirmed by the positive PCR for alpha thalassemia-1, Southeast Asian deletion and alpha thalassemia-2, 3.7 kb deletion, genes. After five months of the iron treatment, Hb 8.8 g%, MCV 59.3 fl, MCH 16.7 pg, ferritin 110.7 ng/ml, Hb analysis: $A_2ABartH$, Hb A_2 1.4 %. The band of Hb H was found after Hb concentration was raised even though the ferritin level was still low.

Conclusion: The absence or presence of Hb H band of the Hb H disease patient on Hb electrophoresis seemingly depended on the hemoglobin concentration more than the sufficiency of the iron storage.

Introduction

Hemoglobin H (Hb H) disease is a genetic disease resulted from the co-inheritance of alpha-thalassemia-1 and alpha-thalassemia-2 heterozygosity. Its main clinical manifestation is mild to moderate hemolytic microcytic anemia, Hb 10.0 ± 1.2 g%, MCV 67 ± 7 fl, MCH 19 ± 2 pg [1] or thalassemia intermedia. As other chronic hemolytic diseases [2], the iron storage, represented by the serum ferritin, is usually normal or increased in this disease [3,4], as compared with the normal control [5]. Moreover 73.9 % of Hb H disease patients have an iron overload [6] although most cases do not need regular blood transfusion [7].

On the contrary, iron deficiency anemia has been rarely reported among Hb H disease patients. Besides the rarity, iron deficiency anemia can mask the diagnosis of Hb H disease by causing the disappearance of Hb H band on the Hb analysis [8]. Now we report a new case of the iron deficiency anemia in the patient with Hb H disease that was confirmed by the genetic approval.

Case presentation

A 50-year-old Thai menopausal woman presented gradually progressive fatigue, frequent fainting and pallor for three months, no obvious blood loss. The physical examination showed moderate to marked pallor without jaundice and just palpable splenomegaly.

The blood tested: Hb 3.8 g%, Hct 12.4 %, MCV 50.4 fl, MCH 15.4 pg, MCHC 30.5 g%, RDW 32.3 %, WBC 8,400/mm^3, platelet 526,000/mm^3, ferritin 5.0 ng/ml, serum iron 33 mcg/dl (normal 35-165), TIBC 123 mcg/dl (normal 200-360), cholesterol 113 mg%, albumin 3.5 g%, globulin 3.0 g%, total bilirubin 0.3 mg%, direct bilirubin 0.1 mg%, alkaline phosphatase 72 U/L, SGOT 14 U/L, SGPT 11 U/L, creatinine 0.97 mg%, serum erythropoietin > 200 mIU/ml (normal 2.60-34.0). The gastroscopy revealed minimal Mallory-Weiss tear 2 points while the colonoscopy revealed unremarkable study.

The hemoglobin analysis using the high-performance liquid chromatography (HPLC) method (BioRad®): A_2A, Hb A_2 2.1 %, Hb F 0 %.

She was diagnosed as having severe iron deficiency anemia and continuously treated with the iron tablets and folic acid for 2 months. The blood was tested again: Hb 7.7 g%, Hct 26.1 %, MCV 69.3 fl, MCH 20.5 pg, MCHC 29.6 g%, RDW 20.7 %, WBC 9,100/mm^3, platelet 306,000/mm^3, reticulocyte 6.0 %, ferritin 6.2 ng/ml, serum iron 50 mcg/dl, transferrin 267.9 mg/dL, Hb analysis using the HPLC method: A_2AH Bart, Hb F 0.8 %, Hb A_2 1.7 %

Besides iron deficiency anemia, the diagnosis of Hb H disease was added and the treatment with iron tablets was still going on. After 5 months of treatment: Hb 8.8 g%, Hct 31.2 %, WBC 6,100/mm^3, MCV

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59.3 fl, MCH 16.7 pg, platelet 249,000/mm^3, ferritin 110.7 ng/ml, Hb analysis using the HPLC method: A_2AH Bart, Hb A_2 1.4 %, Hb F 0.2 %. Afterwards, her Hb concentration could be kept between 8.1-9.5 g% while the serum ferritin was between 64.6-254.8 ng/ml.

The PCR for alpha-thalassemia-1 was tested positive for Southeast Asian (SEA) deletion, and for alpha-thalassemia-2 was positive for 3.7 kb deletion genotypes.

The important data before and 2 and 5 months after the iron therapy were summarized in the Table 1.

Discussion

The diagnosis of Hb H disease in our case depended on the document of Hb H bands in the second and the third Hb analyses which were significantly sharp peak on the chromatogram by the HPLC method [9] and later it was confirmed by the genotype study and finally found positive for SEA and 3.7 kb deletions, the common genetic co-inheritance of Hb H disease [10]. Likewise, the iron deficiency anemia was diagnosed because the serum ferritin level was less than 30 ng/ml [11].

When our patient had the Hb level of 3.8 g%, the Hb H band was not apparent on Hb analysis. After 2-month iron therapy, the Hb level was raised to 7.7 g% and the Hb H band was firstly apparent although the serum ferritin was still less than 30 ng/ml. The appearance of Hb H band seemingly depended on the hemoglobin concentration, regardless of the adequacy of serum ferritin. Because in Taiwan, the percentage of Hb H in Hb H disease patients was found ranging from 0.7 to 29.7 % whereas the lowest Hb concentration was 5.5 g% or more [12]. Likewise, Hb H band in Hb H disease patient who was complicated by active rheumatoid arthritis was absent while Hb concentration was 4.4 g%, it became equivocal at Hb of 7.0 g%, and it obviously appeared at Hb of 7.9 g% [13].

While the IDA is diagnosed, other causes of microcytic anemia should also be considered particularly thalassemia [14]. Our case showed that one time of Hb analysis, the common investigation for thalassemia, was not enough. The Hb analysis should be repeated if the Hb which is expected to increase 1-2 g% every two weeks of iron therapy for iron deficiency anemia does not become normal within 3-4 months of treatment [14] particularly in case of adequate iron storage.

The effect of the iron deficiency anemia upon the outcome of Hb analysis has been well recognized, for instance: the percentage of Hb E in Hb E trait with IDA is found to be 20.5 % and becomes 25.5 % after the iron therapy [15]. In beta thalassemia traits with IDA, the percentage of Hb A_2 was found to be 5.4+0.86 %, range 3.8-7.0 % and significantly increased to 5.8+0.78 % after the iron treatment [16]. And IDA could also completely mask Hb H in Hb H disease [8]. With all these documents, Hb analysis should be postponed in cases of suspected thalassemia during having severe IDA until the iron fortification will be completed.

Table 1. The important data before and 2 and 5 months after the iron therapy

Month	before	2 months Rx	5 months Rx
Hb (g%)	3.8	7.7	8.8
Hct (%)	12.4	26.1	31.2
MCV (fl)	50.4	69.3	59.3
MCH (pg)	15.4	20.5	16.7
Ferritin (ng/ml)	5	6.2	110.7
Hb analysis	A_2A	A_2ABartH	A_2ABartH

The only one clue to suspect that our patient should not have pure IDA is the just palpable splenomegaly which can be found around 20.5 % of Hb H disease patients [12]. The MCV and MCH among IDA with Hb concentration 6.2-13.6 g% are 61.2-79.6 fl and 17.0-26.1 pg [17] whereas those of Hb H disease are 43.9-75.1 fl and 15.1-28.0 pg, respectively [12]. Both are mostly overlap between two entities. The MCV and MCH during IDA in our case were 50.4 fl and 15.4 pg which appeared closely similar to those of Hb H disease but less than those of the IDA. However, it could not be simply concluded because the Hb concentration in our patient was 3.8 g%, less than 6.2 g% of the IDA group and there is the correlation between the Hb concentration and the MCV in IDA patients, viz., the lower Hb concentration the lower MCV [18].

Conclusion

A 50-year-old Thai woman presented with marked microcytic anemia due to iron deficiency. After the iron treatment, hemoglobin H band could be detected. Therefore, the hemoglobin analysis should be delayed in cases with suspected thalassemia during having severe iron deficiency anemia until the iron fortification could be completed.

References

1. Fucharoen S, Winichagoon P, Pootrakul P, Piankijagum A, Wasi P (1987) Differences between two types of Hb H disease, alpha-thalassemia 1/alpha-thalassemia 2 and alpha-thalassemia 1/Hb Constant Spring. *Birth Defects Orig Artic Ser* 23: 309-315. [Crossref]
2. Brabec V, Cermák J, Sebestík V (1990) Serum ferritin in patients with various haemolytic disorders. *Folia Haematol Int Mag Klin Morphol Blutforsch* 117: 219-227. [Crossref]
3. Galanello R, Melis MA, Paglietti E, Cornacchia G, de Virgiliis S, et al. (1983) Serum ferritin levels in hemoglobin H disease. *Acta Haematol* 69: 56-58. [Crossref]
4. Tso SC, Loh TT, Todd D (1984) Iron overload in patients with haemoglobin H disease. *Scand J Haematol* 32: 391-394. [Crossref]
5. George E, Wong HB, Jamaluddin M, Huisman THJ (1993) Peripheral haemolysis, lipid peroxidation, iron status, and vitamin E in haemoglobin H syndromes in West Malaysia. *Singapore Med J* 34: 241-244. [Crossref]
6. Hsu HC, Lin CK, Tsay SH, Tse E, Ho CH, et al. (1990) Iron overload in Chinese patients with hemoglobin H disease. *Am J Hematol* 34: 287-290. [Crossref]
7. Singer ST, Kim HY, Olivieri NF, Kwiatkowski JL, Coates TD, et al. (2009) Hemoglobin H-constant spring in North America: an alpha thalassemia with frequent complications. *Am J Hematol* 84: 759-761. [Crossref]
8. Insiripong S, Yingsitsiri W, Boondumrongsagul J (2015) Iron deficiency anemia masking hemoglobin H disease: A case report. *Chulalongkorn Med J* 59: 389-393.
9. Wadhwa R, Singh T (2011) Role of HPLC in the detection of HbH disease. *Indian J Pathol Microbiol* 54: 407. [Crossref]
10. Chan AY, So CC, Ma ES, Chan LC (2007) A laboratory strategy for genotyping haemoglobin H disease in the Chinese. *J Clin Pathol* 60: 931-934. [Crossref]
11. Johnson-Wimbley TD, Graham DY (2011) Diagnosis and management of iron deficiency anemia in the 21st century. *Therap Adv Gastroenterol* 4: 177-184. [Crossref]
12. Chao YH, Wu KH, Wu HP, Liu SC, Peng CT, et al. (2014) Clinical features and molecular analysis of Hb H disease in Taiwan. *Biomed Res Int* 2014: 271070. [Crossref]
13. Sripavatakul K, Insiripong S (2017) The appearance of the band of hemoglobin H in a patient of hemoglobin H disease and the activity of rheumatoid arthritis: a case report. *J Med Assoc Thai* 100: 702-705.
14. Zhu A, Kaneshiro M, Kaunitz JD (2010) Evaluation and treatment of iron deficiency anemia: a gastroenterological perspective. *Dig Dis Sci* 55: 548-559. [Crossref]
15. Rahman H, Yunus A, Begum M, Rahman J, Hoque Z, et al. (2004) Coexisting iron deficiency anemia and thalassemia trait. *The ORION Medical Journal* 21:259-261.
16. Verma S, Gupta R, Kudesia M, Mathur A, Krishan G, et al. (2014) Coexisting iron deficiency anemia and beta thalassemia trait: effect of iron therapy on red cell parameters and hemoglobin subtypes. *ISRN Hematol* 293216.

17. Torino AB, Fátima Pererira Gilberti M, Costa E, Lima GAF, Grotto HZW (2014) Evaluation of red cell and reticulocyte parameters as indicative of iron deficiency in patients with anemia of chronic disease. *Rev Bras Hematol Hemoter* 36: 424-429. [Crossref]

18. Tiwari M, Kotwal J, Kotwal A, Mishra P, Dutta V, et al. (2013) Correlation of haemoglobin and red cell indices with serum ferritin in Indian women in second and third trimester of pregnancy. *Med J Armed Forces India* 69: 31-36. [Crossref]