Hemoglobin J-Korat Disease: A Case Report

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Abstract: Hemoglobin (Hb) J-Korat, or Hb J-Bangkok or Hb Meinung or Hb Manado is the abnormal hemoglobin resulted from the combination of 2 normal alpha and 2 abnormal beta globin chains whose glycine at the 56th position is substituted by aspartic acid. It is transmitted as an autosomal recessive gene. Its heterozygote has no any clinical or hematological manifestation while its homozygote has never been mentioned, so far. Here we report one case of Hb J-Korat homozygote or disease. She was a 48-year old woman who was referred to the hematologist because of progressive fatigue and chest discomfort due to anemia for one month. The physical examination revealed moderate pallor without jaundice, no thalassemic facy, no hepatosplenomegaly. She was extensively investigated for finding the cause of anemia and finally she was definitely diagnosed to have the iron deficiency anemia, depending on the combination of hypochromic microcytic anemia, low serum ferritin and low serum iron, with the underlying Hb J-Korat disease which was approved by the well trained medical technologist. After the oral iron therapy was accomplished within three months and also the metromenorrhagia which was supposed to be the cause of iron deficiency, was corrected by the gynecologist, she was free from any symptom. But the laboratory tests showed she still had very mild degree of anemia (Hb 11.9 g%), normal red blood cell indices and normal RBC morphology which were supposed to be the manifestation of Hb J-Korat disease per se.

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บทคัดย่อ

Hemoglobin (Hb) J-Korat, หรือ Hb J-Bangkok เป็นฮีโมโกลบินผิดปกติ ที่เกิดจากการรวมตัวของสาย alpha globin ปกติ 2 สายกับสาย beta globin ผิดปกติ 2 สาย โดยที่ตำแหน่งที่ 56 ซึ่งปกติเป็น glycine ถูกแทนที่ด้วย aspartic acid สามารถถ่ายทอดได้ทางพันธุกรรมแบบ aotosomal recessive ผู้ที่มี Hb J-Korat แฝง จะไม่มีความผิดปกติทั้งทางคลินิกหรือทางห้องปฏิบัติการ ส่วนผู้ที่เป็นโรคนี้จนกระทั่งปัจจุบันนี้ก็ยังไม่มีรายงานว่ามีอาการ อาการแสดงหรือไม่อย่างไร ผู้ป่วยเป็นหญิงอายุ 48 ปี ถูกส่งตัวมาพบโลหิตแพทย์ด้วยอาการอ่อนเพลีย หายใจไม่อิ่ม เนื่องจากโลหิตจางเป็นเวลา 1 เดือน ตรวจร่างกายพบเพียงซีดปานกลาง ไม่พบว่ามีดีซ่าน ไม่มีการเปลี่ยนแปลงโครงหน้าและศีรษะแบบธาลัสซีเมีย ตับและม้ามไม่โต ส่งตรวจทางห้องปฏิบัติการหลายอย่างเพื่อหาสาเหตุของอาการโลหิตจาง แล้วในที่สุดได้ให้การวินิจฉัยว่าเป็นโรคโลหิตจางจากการขาดธาตุเหล็ก เพราะผู้ป่วยมีทั้ง hypochromic microcytic anemia, ระดับ serum ferritin ต่ำ และ ระดับ serum iron ก็ต่ำด้วย, พบด้วยว่าผู้ป่วยเป็นโรค Hb J-Korat จากการตรวจพิเศษด้วยนักเทคนิคการแพทย์ที่เชี่ยวชาญ หลังจากให้การรักษาด้วยการรับประทานยาเข้าธาตุเหล็กเป็นเวลา 3 เดือนร่วมกับการรักษาภาวะประจำเดือนออกมากและเรื้อรัง ซึ่งคิดว่าเป็นสาเหตุของการขาดธาตุเหล็กด้วย สูตินรีแพทย์ พบว่าอาการต่าง ๆ ของผู้ป่วยหายเป็นปกติ แต่เมื่อตรวจทางห้องปฏิบัติการก็พบว่ายังคงซีดเล็กน้อย (Hb 11.9 g%) แต่ดัชนีของเม็ดเลือดแดงกลับเป็นปกติและรูปร่างของเม็ดเลือดแดงก็ปกติเช่นกัน ทั้งหมดนี้คิดว่าเป็นอาการแสดงของตัวโรค Hb J-Korat เอง

Introduction

Hb J-Korat, also known as Hb J-Bangkok, J-Meinung, or J-Manado, was firstly reported by Thorup in black American family in 1956[1]. It is an abnormal hemoglobin resulted from the combination of 2 normal alpha and 2 abnormal beta globin chains whose glycine at the 56th position is substituted by aspartic acid. Since then it has been sporadically reported from Indonesian, Indian, French Canadian, Chinese, Hawian, Thais and white American of Swedish origin[2]. Up to now, it is still rare disorder.

Most heterozygotes of this hemoglobinopathy are clinically and hematologically normal[3], their Hb concentration ranges from 15.4 to 15.8 g% with the MCV of 81-89 fL, MCH of 26-29 pg, MCHC of 31-34, normal osmotic fragility, and normal red blood cell (RBC) morphology, just a fast moving abnormal band on Hb electrophoresis which accounts for 51.8-65.8%, the so called Hb J-Korat or J-Bangkok[4].

When Hb J-Korat combines with Hb E ($alpha_2 beta^{26glutlys}_2$), the individual with this double heterozygosities is still similar to the one with Hb E heterozygisity without Hb J-Korat, viz, free from anemia, Hb concentration of 12.3 g% in female, MCV of 79.7 fL, just only on the Hb typing which shows only Hb E of 30.4% and Hb J Korat of 69.8%[4]. Also Hb J-Korat used to be found in the form of triple heterozygosities with alpha-thalassemia-1 with Hb Constant-Spring trait[5].

From one survey in Korat (Nakhon Ratchasima), there were nine with Hb J-Korat from 1,923 participants (0.468 %)[6]. In the successive survey in Trung, Pattaloong and Krabi in 2007, Hb J-Korat was found in only one from 3,368 blood samples (0.0297 %)[7].

Most reports always mention only the heterozygous state of Hb J-Korat[8] or the combined form with other hemoglobinopathies such as Hb E[9], or sickle cell heterozygote[10], there has never been report mentioning of Hb J-Korat disease or homozygosity, so far. Here we report the case of Hb J-Korat disease from the town where the hemoglobin was originally named after.

Case Report

A Thai female, 48 years of age, was referred to the internist and finally the hematologist because of progressive fatigue and chest discomfort for one month. She had never experienced any paroxysmal nocturnal dyspnea, orthopnea or any constitutional symptom. Her physical examination revealed just only moderate pallor without jaundice, no thalassemic facy, no hepatosplenomegaly. She was one of three siblings and most family members were unremarkable. Laboratory tests included: Hb 7.0 g%, Hct 23.8 vol%, MCV 57.9 fL, MCH 17.1 pg, MCHC 29.6 RDW 21.4, WBC 6,100/mm^3, platelet 336,000/mm^3, hypochromia 1+, microcytosis 2+, reticulocyte 0.5%, BUN 7.0 mg%, creatinine 0.7 mg%, CK-MB mass 1.9 (0-20) ng/ml, Troponin-I 0.01 (Normal 0.1-1.0), FBS 125 mg%, uric acid 3.5 mg%, serum ferritin 1.5 ng/ml, serum iron 35 mg/dL (normal 50-175) and total iron binding capacity (TIBC) 140 mg/dL (normal 250-460).

Chest film and EKG were unremarkable study. Hb typing: F 1.9%, A_2 2.4%, the remainder was an abnormal band which was later proved to be homozygous Hb J-Korat[5].

She was definitely diagnosed as iron deficiency anemia on top of Hb J-Korat disease and treated with ferrous sulfate (60 mg elementary iron) 3 tablets a day as well as folic acid (5 mg) 1 tablet a day. The gynecologist was consulted for the proper treatment of metromenorrhagia which was supposed to be the underlying cause of iron deficiency anemia. CBC was followed one and three months later, and here was her CBC at the 3rd month: Hb 11.9 g%, Hct 37.2 vol%, MCV 96.0 fl, MCH 33.4 pg, MCHC 34.1, RDW 13.1 WBC 7,400/mm^3, plt 497,000/mm^3, and normal RBC morphology.

The pedigree study could not be performed because the relatives realized that Hb J-Korat did not have any detrimental effect even in the form of the homozygosity.

Discussion

Our case was demonstrated to habor Hb J-Korat or Hb J-Bangkok using the method described by Fucharoen et al in 2001[5]. And because the major fraction on Hb typing was Hb J-Korat with Hb F of 1.9% and Hb A_2 of 2.4%, without Hb A, therefore, she was presumed to be the homozygote of Hb J-Korat.

At the steady state, she does not have any symptom or hepatosplenomegaly and her Hb concentration after the iron deficiency anemia has been optimally corrected, is found to range from 11.5 to 11.9 g%, Hct of 35.5%-37.2%, all RBC indices are within normal ranges as well as the RBC morphology. And all these are presumed to be the characteristics of Hb J-Korat disease per se.

Hb J-Korat behaves closely similar to Hb E in nearly all aspects. They are both the abnormal single amino acid substitution of beta globin chain. The former is the substitution of glycine with aspartic acid

at the 56th position whereas the latter is the substitution of glutamic acid with lysine at the 26th position. For heterozygous state, both of them do not express any clinical or laboratory abnormality while for the homozygous state, both have minimal anemia (Hb 11.9 vs. 11.4±1.3 g%) but a bit difference in the RBC indices which are found to be definitely normal for the former but obviously lowered for the latter (MCV 96.0 vs 58.0±5.2 fL, MCH 33.4 vs. 19.3±1.9 pg, MCHC 34.1 vs. 33.2±1.2 and RDW 13.1 vs. 18.0±1.4)[11].

However, the possibly co-incident alphathalassemia-1 and alpha-thalassemia-2[5] which could not be recognized on the Hb typing, should have been studied for making sure that her minimal anemia comes exclusively from Hb J-Korat disease itself.

Conclusion

The female of child-bearing age was firstly diagnosed as iron deficiency anemia on top of Hb J-Korat disease. After the full treatment with iron, she responded well. It should be proposed that no hepatosplenomegaly, mild anemia (Hb 11.5-11.9 g%) with normal RBC indices and normal RBC morphology are the characteristics of Hb J-Korat disease.

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