Improvement of Anemia in Beta-Thalassemia/Hemoglobin E Patient after Oxymetholone Therapy: A Case Report

Insiripong S
Yingsitsiri W
Boondumrongsgul J
Hematology Unit, Department of Medicine, Maharat Nakhon Ratchasima Hospital, Nakhon Ratchasima

บทคัดย่อ: ภาวะโลหิตจางในผู้ป่วย เบต้า ฮีโมโกลบินอี ดีขึ้นด้วยยา oxymetholone: รายงานผู้ป่วย 1 ราย

สมชาย อินทรศิริพงษ์ พ.บ.
วัชรินทร์ ยิ่งสิทธิ์สิริ พ.บ.
จุรี บุญดารงสกุล พ.บ.
หน่วยโลหิตวิทยา กลุ่มงานอายุรกรรม โรงพยาบาลสมเด็จพระเจ้าอยู่หัวนครราชสีมา รพ.วิทยาศาสตร์

เมื่อผู้ป่วยโรคเบต้า ฮีโมโกลบินอี เกี่ยวกับการรุนแรง สะสมเหล็กไปตามต่อมไร้ท่อ ทำให้ผู้ป่วยมีภาวะโลหิตจางในรูปแบบอี ภาวะร่องใหม่พบในผู้ป่วยที่มีอายุมากกว่า 39 ปี โดยผู้ป่วยในกรณีนี้เป็นผู้ชายไทย อายุ 39 ปี ได้รับการรักษาด้วย oxymetholone คงค่า Hb กลับไปเป็นระดับปกติ ค่า Hb ปกติในการยืนยันการรักษา ค่า Hb ปกติ ค่า ferritin 1,845.6+807.4 ng/mL และค่า testosteron 0.10+0.01 ng/mL ผู้ป่วยไม่ต้องรับเลือดอีก หลังจากได้รับ oxymetholone อาการที่ดีขึ้นเรื่อยๆ ภาวะโลหิตจางของผู้ป่วยในกรณีนี้จะเป็นภาวะโลหิตจางที่เกิดจากปัจจัยที่รากฐานหลัก ได้แก่ ภาวะโลหิตจางที่เกิดจากภาวะฮอร์โมนเพศต่ำ ภาวะโลหิตจางที่เกิดจากภาวะเหล็กเกิน.
Abstract:

When the patients with severe beta-thalassemia/Hb E disease have excessive iron accumulation in various endocrine glands, one of common endocrinopathies is hypogonadism. Our case report is a 39-year old Thai man who was diagnosed as beta thalassemia/Hb E disease and later splenectomized due to hypersplenism since childhood. His Hb level at the steady state is 5.3+0.5 g% and he needs regular blood transfusions for keeping his Hb level about 7.0 g%. During the long term follow-up, the hyperferritinemia (serum ferritin 1,845.6+807.4 ng/mL) and hypogonadism (serum testosterone 0.10+0.01 ng/mL) are additionally documented. He has been treated with deferiprone (GPO-L1®) and oxymetholone (Androlic®) that is the standard drug in the national drug list, 150 mg a day. Within 3 months, his Hb level is found to be 7.7+0.3 g% and ferritin of 674.7 ng/mL and he does not need the blood transfusion any more. However, his secondary sex characteristics are still underdeveloped. The improvement of the Hb level after the treatment of oxymetholone is supposed to be the stimulation of erythropoiesis by androgen via various mechanisms including the stimulation of erythropoietin release, the increasing bone marrow activity and the iron incorporation into the red blood cells. An increase of Hb concentration of our case after oxymetholone therapy may hopefully become the treatment for anemia of beta thalassemia/Hb E that is very common in Thailand while there is no effective treatment, except blood transfusion that may be followed by serious complications.

Keywords : Beta thalassemia/ E, Hypogonadism, Oxymetholone

Introduction

Beta thalassemia / hemoglobin E disease is the genetic disease resulted from the co-inheritance of beta thalassemia allele from one parent and Hb E (α2β26Glu→Lys2) allele from the other. The main clinical manifestation is anemia of which the severity can vary from mild to severe form until the blood transfusion becomes necessary1 The patients who have the severe form of beta thalassemia/Hb E may have the iron overload as the common complication because of the frequent blood transfusion and/or the increased intestinal iron absorption. The organs which can be commonly affected by the iron overload are the heart, the liver, and the endocrine glands. Hypogonadism is one of the common endocrinological complications of the iron overload2.

Oxymetholone is an oral anabolic androgen in the national drug list which can effectively be used not only as a hormone replacement therapy in hypogonadism3 but also the improvement of anemia in sickle cell disease and hypoplastic anemia that is recommended by US FDA since 1997.

Herein we report a case of severe beta thalassemia/Hb E who has to receive the regular blood transfusion every month. After the iron overload and hypogonadism has been treated with the chelating agent and oxymetholone, his hemoglobin concentration is increased.
Case Report

A 38-year old Thai man was diagnosed as severe beta thalassemia/hemoglobin E since childhood. At the steady state, his averaged Hb and other parameters were shown in the table and he needed monthly transfusion with packed red blood cells to keep his Hb level close to 7 g% since then. He was splenectomized at the age of 7 years due to too frequent transfusion.

The hypogonadism was additionally diagnosed at the age of 32 years because of the obvious scarcity of the secondary sex characteristics and short stature meanwhile the serum testosterone was demonstrated to be between 0.10+0.01 ng/mL (normal 3.0-10.6).

Other blood tests included: averaged serum ferritin 1,845.6+807.4 ng/mL (Normal 12-300), serum iron 61.0 mcg% (Normal 35-165), transferrin 213 mcg% (Normal 259-388), erythropoietin 82.7 mU/mL (Normal 2.6-34.0), FBS 116+13.9 mg%, cholesterol 100.5+17.7 mg%, triglyceride 129.5+10.6 mg%, normal kidney and liver function tests. HBsAg, anti-HCV and anti-HIV were all negative, Hb typing: EF, Hb E 70.6%, Hb F 10.6%, PCR for beta thalassemia genotype-positive (IVS 1#5) but negative for alpha-thalassemia-1 genes (SEA and Thai types), Ca 10.1 mg%, P 4.7 mg%.

After the diagnosis of hypogonadism and hyperferritinemia were established, he was regularly treated with oxymetholone (Androlic®) 150 mg a day and concurrently an oral chelating agent, deferiprone. CBC was followed every 3 months. Within two years, the hematological parameters were averaged and compared with those before oxymetholone therapy. And all parameters were analyzed using paired student-T tests, the p-value less than 0.05 was considered statistically significant. All were shown in the table.

| The hematological parameters before and after oxymetholone therapy |
|-----------------|-----------------|-----------------|
|                 | Before          | After           | p-value |
| Hb (g%)         | 5.5+0.6         | 7.4+0.6         | 0.0001  |
| RBC (m/mm³)     | 2.83+0.17       | 3.66+0.28       | 0.0416  |
| WBC (/mm³)      | 12,462+2,366    | 21,155+7,119    | 0.0027  |
| Corrected WBC   | 12,060+2,686    | 11,946+2,571    | 0.9164  |
| MCV (fl)        | 65.7+3.9        | 72.3+4.7        | 0.0018  |
| MCH (pg)        | 19.2+1.9        | 20.1+0.8        | 0.0938  |
| MCHC (g%)       | 28.0+0.9        | 27.4+0.8        | 0.7270  |
| RDW (%)         | 29.8+1.9        | 31.4+2.0        | 0.8300  |
| platelet (/mm³) | 528,727+101,253 | 736,277+35,398  | 0.0001  |
| NRBC            | 7.0+8.8         | 76.8+69.1       | 0.0321  |
| BW (Kg)         | 36.6+1.3        | 40.0+1.0        | 0.0001  |
His Hb concentration as well as RBC count, MCV, platelet count, the nucleated red blood cells (NRBC/100 WBC) and the body weight was increased with statistical significance. He did not need blood transfusion any more but his secondary sex characteristics were still underdeveloped and his libido was not changed. The averaged serum ferritin was decreased from 1,845.6+807.4 to be 951.0+213.0 ng/mL. He could tolerate drug well, neither transmmitis nor other drug side effect was detected.

## Discussion

The Hb concentration is improved with statistic significance after hypogonadism has been treated with oxymetholone for a few months. In case of testosterone deficiency, it causes 10–20% decrease in Hb concentration This phenomenon can be seen even in the young or middle-aged males the elderly men and women the patients with chronic kidney disease or patients after orchidectomy because androgens actually stimulate hematopoietic system by various mechanisms, including the stimulation of erythropoietin release, increasing bone marrow activity and iron incorporation into the RBC And testosterone therapy should be initiated to induce and maintain the secondary sex characteristics, sexual function, the sense of well-being and to directly increase the Hb concentration of 1.6 g%.

Hypogonadism is found to be one of common endocrinopathies (52.7%) among the puberties with beta thalassemia major and is shown associated with hyperferritinemia especially if serum ferritin is >2,500 ng/mL. Berdoukas et al show that if iron levels can be brought to normal with the serum ferritin < 100 ng/mL, there is a significant possibility that there may be a reversal of endocrinopathies without increased adverse events.

Oxymetholone, an anabolic androgen, is administered hopefully to cover his hypogonadism. While the secondary sex characteristics and libido are not obviously improved in our case, his Hb level is strikingly increased from 5.3+0.5 to 7.7+0.3 g% (45.3 %), instead. In fact, oxymetholone is approved by US FDA for the treatment of anemias caused by deficient RBC production, eg., acquired or congenital aplastic anemia, myelofibrosis And it is proved to increase RBC mass in sickle cell anemia and to show hematologic improvement in aplastic anemia.

## Conclusion

A 38-year old man was diagnosed as beta thalassemia / Hb E since childhood and he needs regular transfusion for coping with his severe anemia. He is complicated by hypogonadism and iron excess and treated with oxymetholone 150 mg a day for a few months, his Hb level is increased enough to free him from blood transfusion. The further systemic study should be performed to show whether oxymetholone can improve anemia in most cases of beta-thalassemia / Hb E in order to avoid blood transfusion which has numerous serious complications.
References