# Oxymetholone Improves Aplastic Anemia with an Underlying HIV Infection: A Case Report

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**Abstract:** Oxymetholone is a semi-synthetic androgen and it is found effective in idiopathic aplastic anemia but its therapeutic effect in case of severe aplastic anemia associated with HIV infection has been rarely reported. Herein, we report a 46-year-old Thai man who was newly diagnosed as having aplastic anemia based on the combination of pancytopenia without peripheral blast and the aplasia of the bone marrow from biopsy, concomitantly withan HIV infection. The CD4 count was 437/$mm^3$ whereas the viral titer was 57,720. Oxymetholonetherapy 150 mg. a day was initiated while the HAART was withheld because of CD4 >350/$mm^3$. Other regular treatments included deferiprone 1,500 mg. a day for hyperferritinemia, quinine sulfate 300 mg. before bed time for the night cramp. He regularly attended our clinic every month. The packed red blood cells would be transfused to him if his Hb concentration was less than 7.0 g%. The hematologic parameters were gradually increased every year. Within four years, Hb, WBC and platelet were increased from 6.6 g%, 2,500/$mm^3$, 10,000/$mm^3$ to be 13.2 g%, 4,000/$mm^3$, 30,000/$mm^3$, respectively while the CD4 count was increased from 437 to finally 526/$mm^3$, instead of decrease even lack of HAART. No serious adverse effect of oxymetholone was observed. Pancytopeniaas well as CD4 count in our case was markedly improved after the treatment with oxymetholone possibly due to its stimulating effect upon the proliferation of the hematopoietic stem cells within the bone marrow.

**Key words:** Aplastic Anemia, HIV Infection, Oxymetholone

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**บทคัดย่อ:** **อ็อกซี่เมโธโลนทำให้โรคไขกระดูกฝ่อในผู้ป่วยติดเชื้อเอชไอวีดีขึ้น: รายงานผู้ป่วย**

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Oxymetholone เป็นฮอร์โมนเพศชายกึ่งสังเคราะห์ มีฤทธิ์ในการรักษาผู้ป่วยไขกระดูกฝ่อที่ไม่ทราบสาเหตุ แต่ผลการรักษาไขกระดูกฝ่อที่เกี่ยวข้องกับการติดเชื้อเอชไอวียังมีรายงานน้อย ดังในรายงานนี้ซึ่งเป็นของผู้ป่วยชายไทย อายุ 46 ปี ได้รับการวินิจฉัยใหม่ว่าเป็นโรคไขกระดูกฝ่อชนิดรุนแรง โดยตรวจพบ pancytopenia ไม่พบเซลล์ตัวอ่อนในกระแสเลือด ตัดชิ้นเนื้อไขกระดูกพบว่าเป็นไขกระดูกฝ่อจริง ร่วมกับการติดเชื้อเอชไอวี ตรวจเลือดพบ CD4 count ได้ 437/$mm^3$ ในขณะผล viral titer ได้ 57,720 ให้การรักษาด้วย oxymetholone 150 มิลลิกรัมต่อวัน แต่ยังไม่ได้เริ่ม HAART เพราะ CD4 ยังคงมีมากกว่า 350/$mm^3$ การรักษาอื่นได้แก่ deferiprone 1,500 มิลลิกรัมต่อวัน สำหรับภาวะเหล็กเกินควินีน 300 มิลลิกรัม ก่อนนอนสำหรับภาวะตะคริวที่เกิดบ่อยเวลานอน ผู้ป่วยมารับยาอย่างสม่ำเสมอทุกเดือน และจะได้รับการเพิ่มเลือด ถ้าพบว่าความเข้มข้นฮีโมโกลบิน ต่ำกว่า 7.0 กรัม% ผลเลือดค่อย ๆ ดีขึ้นในแต่ละปี ภายใน 4 ปี พบว่า Hb, WBC และ platelet เพิ่มจาก 6.6 กรัม%, 2,500/$mm^3$ และ 10,000/$mm^3$ ตามลำดับ เป็น 13.2 กรัม%, 4,000/$mm^3$ และ 30,000/$mm^3$ ตามลำดับ ในขณะที่ระดับ CD4 ก็เพิ่มจาก 437 เป็น 526/$mm^3$ ในที่สุดแทนที่จะลดลงเพราะยังไม่ได้รับยากลุ่ม HAART ไม่ปรากฏผลข้างเคียงของ oxymetholone ที่รุนแรง การที่ภาวะ pancytopenia และระดับ CD4 ในผู้ป่วยรายนี้ดีขึ้นมาก หลังจากที่ได้รับการรักษาด้วย oxymetholone เป็นไปได้ว่าเป็นผลจากการกระตุ้นการเจริญเติบโตของเซลล์ต้นกำเนิดของเม็ดเลือดในไขกระดูก

**คำสำคัญ:** ไขกระดูกฝ่อ, การติดเชื้อเอชไอวี, อ็อกซีเมโธโลน

**Introduction**

Oxymetholone is a semi-synthetic anabolic hormonewhich has been accepted to treat the patients with the inadequate production of the red blood cells such as aplastic anemia, congenital or acquired, and sickle cell anemia. Other its indications include the fatigue and wasting in HIV-infected persons[1]. Oxymetholone was found effective in three of four children with aplastic anemia and they remained well even after the termination of treatment[2]. For the adult patients, 11 from 28 patients with idiopathic aplastic anemia showed the clinical and hematological improvement after treatment with oxymetholone with tolerable and reversible side effects[3]. The etiology of aplastic anemia in most cases is not known while the minority of cases can be found associated with benzene, pesticides, animal fertilizer, drugs and chemicals, pregnancy, sero-negativehepatitis[4] and human immunodeficiency virus (HIV) infection[5]

The role of oxymetholone for the treatment of severe aplastic anemia (AA) associated with HIV infection has not been reported. Herein we report a Thai man with aplastic anemia with an underlying

HIV infection of who aplastic anemia and CD4 were much improved after oxymetholone therapy without antiretroviral therapy.

**Case Report**

A 46-year-old Thai man was referred to our hospital because of the severe anemic symptom without obvious blood loss, fever or weight loss. On the physical examination, only marked pallor was noticed, no organomegaly.

CBC Hb 6.6 g%, WBC 2,500/$mm^3$, platelet 10,000/$mm^3$ MCV 97.9 fl, MCH 34.0 pg, N 11.4 %, L 83.2%, serum ferritin 3,377 ng/ml, serum ery-thropoietin >200 mIU/ml, normal liver and kidney function tests.

HIV antigen/antibody-positive, CD4 21 %, CD4 count 437/$mm^3$, viral titer 57,720

HBsAg, anti-HCV, VDRL, ANA and Cryptococcus antigenwere all negative.

The bone marrow biopsy was pathologically found to be diffuse medullary aplasia whereas it was dry tap on the aspiration.

He was definitely diagnosed ashaving severeaplastic anemia withconcomitant asymptomatic HIV infection and hemosiderosis. He was initially treated with oral oxymetholone 150 mg. a day. The highly active antiretroviral therapy (HAART) was not initiated because the CD4 count was still more than 350/$mm^3$. Other regular treatments includedoral deferiprone 1,500 mg a day for the hyperferritinemia and quinine sulfate tablet 300 mg. at bed time for the frequent night cramp.

He regularly attended our hematology and infectious disease clinics every month for the physical examination and the CBC test. He would be transfused with the packed red blood cell if his Hb concentration was found to be less than 7.0 g%. The liver and kidney function tests and the serum ferritin were checked every three months. The CBCs and CD4 count of each year were shown in the table.

The table showed the serial Hb (g%), WBC (/$mm^3$), platelet (/$mm^3$) and CD4 (/$mm^3$) every year from 2012 to 2016.

| | **Nov 2012** | **Nov 2013** | **Aug 2014** | **Aug 2015** | **Apr 2016** |
|---|---|---|---|---|---|
| Hb | 6.6 | 9.3 | 10.6 | 13.8 | 13.2 |
| WBC | 2,500 | 5,500 | 4,600 | 4,400 | 4,000 |
| platelet | 10,000 | 14,000 | 22,000 | 27,000 | 30,000 |
| CD4 | 437 | 443 | 470 | 497 | 526 |

During 4-yearfollow-up, he had no side effects such as transaminitis/cholestasis/kidney impairment/ gynecomastia/impotence/opportunistic infection. His body weight was slightly gained from 60 to 62 kg.

**Discussion**

Our case was definitely diagnosed as having severe AA based on the combination of neutrophil <500/$mm^3$, platelet <20,000/$mm^3$, and cellularity <20 % in the bone marrow[6] and asymptomatic HIV infection. In HIV-infected persons, AA can be more commonly found because the HIV can infect and damage the pleuri potential hematopoietic stem cells in the bone marrow, leading to the decreased production of all cell lines resulting in the peripheral pancytopenia and AA. However in some cases, the hematopoietic stem cells may act as the reservoir of the HIV organism[7].

After oxymetholone therapy, the hematological parameters and the CD4 count in our case are

gradually increased every year. The effect of oxymetholone100 mg a day used to be found to augment the CD4 count in HIV-infected patients from 417 to 520x106 cells/L with statistical significance but not found in the oxymetholone 150 mg. a day group-probably because of the frequent interruption due to the side effects of oxymetholone in the latter group although it did not affect the HIV RNA viral load[8]. Oxymetholone is documented to improve the pancytopenia or even the aplastic anemia by its stimulating effect upon the hematopoietic stem cells[7,9].

As the target of HIV infection, the CD4 cell will be destroyed by the virus and gradually decreased since the starting of HIVinfection until it is less than 200/$mm^3$ in less than 2 years for the rapid progressors and as long as 15 years for the slow progressors[10]. When HAART is commenced and continued, the CD4 will be gradually increased such as average increase of 102 CD4 cells within around one year[11]. In contrast, the CD4 cells in our case are yearly increasedinstead of decrease, along with the hematological parameters during the regular oxymetholonetherapy without HAART.

Oxymetholonecan significantly increase the body weight of 3.0±0.5 and 3.5±0.7 kgin the 150 mg and 100 mg. a day groups, respectively ($P < 0.05$ for each treatment versus placebo), compared with 1.0±0.7 kg. in the placebo group because of the improvements in the appetite, food intake, and increased well-being[12]. But our case gains the body weight only of 2 kg inthe 4 years of oxymetholonetherapy.

Apart from oxymetholone, our case had been also treated with quinine for a very long term forthe frequent night cramp. Althoughthe long effect of quinine has not been mentioned, its effect upon CD4 level in the 7-day treatmentfor P. falciparum in HIV-infected patients is found not eventful[13].

**Conclusion**

A 46-year old Thai man was definitely diagnosed as severe aplastic anemia with concurrent HIV infection. After treatment with oxymetholone 150 mg. a day without HAART, his pancytopenia and the CD4 count have been much improved with in 4 years with minimal side effect.

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