Case Report

HIV Infection Complicated by Autoimmune Hemolytic Anemia (AIHA): A Case Report

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Abstract:

Anemia in HIV-positive patients is one very common problem. Among its various causes, autoimmune hemolytic anemia (AIHA) is unusual where the degree of anemia may be moderate, severe or even fatal. It is more frequently mentioned among blacks than Asians. Herein we report a case of a 39-year-old Thai man presenting fever and fatigue due to marked anemia for 3 days. Before admission, he received a diagnosis of HIV and was treated with Kaletra (Lopinavir + Ritonavir) and Zilavir (AZT + Lamivudine) for a few years. His blood tests indicated Hb 6.1 g/dL, WBC 7x10^{9}/L, corrected WBC 6.7x10^{9}/L, platelet count 314x10^{9}/L, MCV 116.5 fL, MCH 40.2 pg, NRBC 4/100 WBC, direct antiglobulin test 1+, indirect antiglobulin test 2+, reticulocyte 2.3%, CD4 12%, CD4 count 463/mm^{3}, viral load 304 copies/mL and blood VDRL was negative but TPHA was reactive. He received a diagnosis of AIHA and late latent syphilis with underlying HIV during treatment and was treated with prednisolone 60 mg daily and benzathine penicillin, while zilavir was changed to lamivudine and tenofovir. Within 4 weeks, his Hb rose to 7.8 g/dL without blood transfusion, otherwise unremarkable, and then prednisolone was gradually tapered. In general, the lowered CD4 count in patients with HIV results in numerous autoantibody formations and rheumatologic syndrome, which may include AIHA. However, the CD4 count in our case is not low and the pathogenetic mechanism cannot be properly explained. Because relative reticulocytopenia is found in AIHA with HIV, AIHA may be simply overlooked, so the direct antiglobulin test should be performed in any case of anemia in patients with HIV.

Keywords : ● *Autoimmune hemolytic anemia* ● *HIV infection*

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รายงานผู้ป่วย

HIV Infection Complicated by Autoimmune Hemolytic Anemia (AIHA): A Case Report

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บทคัดย่อ:

ภาวะโลหิตจางในผู้ป่วยติดเชื้อเอชไอวีนับเป็นปัญหาหนึ่งที่พบได้บ่อยๆ ซึ่งเกิดได้จากหลายสาเหตุ และในบรรดาสาเหตุที่หลากหลายนี้ โลหิตจางจากการที่เม็ดเลือดแดงแตกด้วยภูมิต่อต้านตนเอง นับว่าเป็นหนึ่งในบรรดาสาเหตุที่พบน้อย แต่ก่อให้เกิดอาการโลหิตจางได้แตกต่างกัน อาจจะเป็นเพียงปานกลาง รุนแรง หรือ ถึงขั้นเสียชีวิตก็ได้ ในผู้ป่วยติดเชื้อเอชไอวี และมักมีรายงานพบโรคนี้ในกลุ่มคนผิวดำมากกว่าคนเอเชีย ในรายงานนี้เป็นของผู้ป่วยชายไทย อายุ 39 ปี มีอาการไข้ อ่อนเพลียเนื่องจากโลหิตจาง เป็นเวลา 3 วัน ก่อนหน้านี้ผู้ป่วยติดเชื้อ เอชไอวีและได้รับการรักษาด้วยยา Kaletra (Lopinavir + Ritonavir) และ Zilavir (AZT + lamivudine) ได้หลายปีแล้วตรวจเลือดครั้งนี้พบว่า Hb 6.1 กรัม/ดล., WBC 7x10^{9}/L, corrected WBC 6.7x10^{9}/L, platelet 314x10^{9}/L, MCV 116.5 เฟมโตลิตร, MCH 40.2 พิโคกรัม, NRBC 4/100 WBC, direct antiglobulin test 1+, indirect antiglobulin test 2+, reticulocyte 2.3%, CD4 12%, CD4 count 463/มม^{3}, viral load 304 copies/มล. VDRL ในเลือดให้ผลลบ แต่ TPHA ให้ผลบวกให้การวินิจฉัยว่าเป็น โลหิตจางจากการที่เม็ดเลือดแดงแตกด้วยภูมิต่อต้านตนเอง และซิฟิลิสระยะแฝงตอนปลาย โดยมีโรคเดิมคือการติดเชื้อเอชไอวีในระหว่างการรักษา และ ให้การรักษาด้วย prednisolone 60 มก.ต่อวัน ร่วมกับ benzathine penicillin ในขณะที่ zilavir ได้รับการปรับเปลี่ยนเป็น lamivudine กับ tenofovir แทน ภายใน 4 สัปดาห์ Hb เพิ่มขึ้นเป็น 7.8 กรัม/ดล. โดยไม่ต้องเติมเลือดให้ผู้ป่วย ผลเลือดส่วนอื่นๆ ยังไม่มีการเปลี่ยนแปลงชัดเจน จึงค่อยลด prednisolone ลงเรื่อยๆ โดยทั่วไปภาวะ CD4 ค่อนข้างต่ำในผู้ป่วยติดเชื้อเอชไอวี ทำให้มีการสร้าง autoantibodies หลากหลายชนิด รวมทั้งอาจก่อให้เกิดกลุ่มอาการทางรูมาโต ซึ่งรวมทั้ง โลหิตจางจากการที่เม็ดเลือดแดงแตกด้วยภูมิต่อต้านตนเองด้วยก็ได้แต่ผู้ป่วยของเรา CD4 ไม่ต่ำ (463/มม^{3}) โดยยังไม่มีคำอธิบายในเชิงกลไกทางพยาธิกำเนิดที่เหมาะสม และเนื่องจากพบภาวะ reticulocytopeniaในผู้ป่วยโลหิตจางจากการที่เม็ดเลือดแดงแตกด้วยภูมิต่อต้านตนเองในผู้ป่วยติดเชื้อเอชไอวี ได้เรื่อยๆ AIHA จึงอาจจะถูกมองข้ามไปได้ง่ายๆ ดังนั้นจึงควรตรวจ direct antiglobulin test ผู้ป่วยติดเชื้อเอชไอวีทุกรายที่มีภาวะโลหิตจาง

คำสำคัญ : ● *Autoimmune hemolytic anemia* ● *HIV infection*

วารสารโลหิตวิทยาและเวชศาสตร์บริการโลหิต 2560;27:159-63.

Introduction

Anemia is commonly found among patients with HIV, viz., the 1-year incidence for anemia among individuals with HIV is 36.9% and could shorten the survival of patients regardless of the CD4 level[1]. Its pathogenesis may involve either inadequate production or increased destruction (or hemolysis) of red blood cells or a combination of both. For hemolytic anemia, various diseases have been found among patients with HIV, including autoimmune hemolytic anemia (AIHA), hemophagocytic syndrome, DIC, thrombotic thrombocytopenic purpura, G-6-PD deficiency and drug usage[2]. AIHA has rarely been reported among patients with HIV; its prevalence ranges from 2 of 350 (0.6%) in Nigeria[3] to 3 of 98 patients (3.1 %) in Ghana. However, 11.2% of patients with HIV had only a positive direct antiglobulin test without obvious anemia. The severity of anemia regarding AIHA in the HIV group is mainly moderate, Hct 24.7±3.3% as compared with 32.1±5.8% of patients with HIV without AIHA[4], but it can be severe or even fatal in some cases[5]. Because of its severity and need of specific treatment, distinguishing AIHA from other anemias in patients with HIV is necessary although it has been hardly ever reported among Asians, as compared with blacks. The aim of this report was to describe a case of AIHA in a Thai patient with HIV during ARV regimen.

Case Report

A 39-year-old Thai man was referred to our hospital presenting high grade fever with cough and fatigue for three days. The physical examination revealed a body temperature of 37.3° Celsius, marked pallor, an icterus, no oral thrush and no lymphadenopathy.

He was positive for HIV and daily treated with 4 tablets of Kaletra (Lopinavir 200 mg + Ritonavir 50 mg) and 2 tablets of Zilavir (zidovudine 300 mg + 3TC 150 mg) for a few years. During this period, he had one episode of CMV retinitis and was treated with ganciclovir injection.

Blood tests revealed Hb 6.1 g/dL, Hct 17.7%, WBC $7x10^9$/L, corrected WBC $6.7x10^9$/L, platelet count 314 $x10^9$/L, MCV 116.5 fL, MCH 40.2 pg, MCHC 34.5 g/dL, RDW 19.6%, NRBC 4/100 WBC, N 52%, L 20%, M 20%, normal liver and kidney function tests and reticulocyte, 2.3%.

In addition, tests indicated ferritin 297.9 ng/mL, serum iron 207 mcg/dL, TIBC 452 mcg/dL, CD4 12%, CD4 count 463/mm^3 and viral load 304 copies/mL.

Moreover, his Hb electrophoresis was AE, HbE 27.3% and HbF 3.7%.

The VDRL, HBsAg, and anti-HCV were all negative but TPHA was reactive. The direct antiglobulin test was positive 1+ and indirect antiglobulin test positive 2+.

The bone marrow biopsy revealed marked hypercellularity especially erythroid series, negative for AFB and fungus.

He received a diagnosis of AIHA and late latent syphilis and was treated with oral prednisolone 60 mg daily and benzathine penicillin injection while kaletra was still continued. However, zilavir was changed to 2 tablets of lamivudine 150 mg and one tablet of tenofovir daily. Within 4 weeks, his Hb concentration was markedly increased to 7.8 g/dL, otherwise-unremarkable. Prednisolone was gradually tapered off.

Discussion

The main target of HIV is the T helper cell or CD4 lymphocyte, the longer the period of infection, the lower the CD4 level. Therefore, its usual role is facilitating B cells to produce deranged antibodies resulting in forming various autoantibodies such as anti-cardiolipin and anti-denatured DNA among patients with HIV. Moreover, rheumatologic syndromes such as SLE, immune thrombocytopenic purpura, are also more commonly found, 1-60% among patients with HIV[7]. Likewise, the CD4 count in patients with AIHA in the

HIV group was found lower (161.0±37.6/mm^3) than 230.2±120.0/mm^{3}of the nonAIHA group[4]. In another group of AIHA among patients with HIV, the CD4 ranged from 10/mm^3 to 120/mm^3, mean 49.5±51.3/mm^3 while Hb level was 3.6±1.2 g%[5]. However, the CD4 in our case was 463/mm^3 in a normal range, 415 to 1,189/mm^3; its pathogenesis cannot be properly explained, so far[8].

In the study of four cases with patients with HIV developing AIHA, three were receiving various ARV regimens. All three were treated with 3TC as a common drug and zidovudine, ritonavir and saquinavir was received by two. As compared with this study, our case also received 3TC as well as zidovudine, lopinavir and ritonavir. In one case control surveillance, 3TC, lopinavir and tenofovir were in the list of suspected drug-induced immune hemolytic anemia[9] as well as zidovudine[10]. Furthermore, zidovudine can cause as much as 34% of patients with HIV to become anemic with predominantly macrocytosis[11], so, zidovudine was promptly withheld and tenofovir was prescribed instead. The patient dramatically responded well to corticosteroid despite the continuation of 3TC, lopinavir and ritonavir.

Our case was a male, like most cases of AIHA among patients with HIV. He differed from patients of AIHA negative for HIV where the male to female ratio is 40:60[12].

Because reticulocytopenia may be found in AIHA with[10] or without HIV[13] and anemias from other causes are much more common among patients with HIV, AIHA may be easily overlooked. Therefore, the direct antiglobulin test should be performed in any case of anemia in patients with HIV because AIHA requires special treatment.

To diagnose syphilis among patients with HIV, some authorities recommend using TPHA instead of VDRL because they found only 37.5% of TPHA reactive patients were positive for VDRL, but only 0.3% of VDRL reactive patients had negative test results for TPHA[14]. Our case also confirmed this recommendation because his blood tested positive for TPHA in spite of negative VDRL.

Summary

A 39-year-old Thai man had a diagnosis of AIHA while being treated with zidovudine, 3TC, lopinavir and ritonavir for HIV. He responded well to corticosteroid whereas zidovudine was replaced with tenofovir. He had no reticulocytosis, so AIHA should be ruled out when anemia among any patient with HIV is encountered.

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