Evans Syndrome in the Co-infection of HIV and Hepatitis C Virus: A Case Report

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Abstract

Evans syndrome (ES) which consists of the autoimmune hemolytic anemia (AIHA) and autoimmune thrombocytopenia (ITP) has rarely been reported in cases of co-infection of HIV and hepatitis C virus (HCV). Herein we report a case of the 31-year old woman who presents with acute gastroenteritis and fever for a few days. The physical examination reveals marked pallor without jaundice, no lymphadenopathy / hepatosplenomegaly. Her blood tests show: Hb 4.9 g%, WBC 6,000/mm^3, platelet 105,000/mm^3, MCV 65.3 fL, MCH 21.0 pg, reticulocyte 1.2 %, ferritin 4,610 ng/mL, direct Coombs' test, anti-HCV and HIV Ag/Ab are all positive. The CD4 count is 409.3/mm^3. Hb electrophoresis reveals Hb E disease. She is diagnosed as ES with co-infection of HIV and HCV, hemosiderosis and Hb E disease and she is treated with antiretroviral therapy and subsequently corticosteroid for ES. She can maintain her hemoglobin concentration without blood transfusion. It is not clear whether there is any association between ES and co-infection of HIV and HCV but at least ES and HIV-infected patients have one immune derangement in common, viz. the decrease of the CD4 cell activity. They are different for the CD8 cell count that is decreased in HIV-infected patients but increased in ES.

Key words: Evans syndrome, Co-infection of HIV and Hepatitis C virus

บทคัดย่อ: **กลุ่มอาการอีแวนส์ในผู้ป่วยติดเชื้อร่วมระหว่างไวรัสเอชไอวี กับไวรัสตับอักเสบซี: รายงานผู้ป่วย 1 ราย**

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กลุ่มอาการอีแวนส์ (Evans syndrome หรือ ES) ซึ่งประกอบด้วยภาวะเม็ดเลือดแดงแตกและเกล็ดเลือดต่ำจากการถูกภูมิคุ้มกันตนเองทำลายยังมีรายงานน้อยในผู้ป่วยติดเชื้อร่วมระหว่างไวรัสเอชไอวีกับไวรัสตับอักเสบซี ในรายงานนี้เป็นผู้ป่วยหญิงอายุ 31 ปี มีอาการท้องร่วงและไข้เฉียบพลันเป็นเวลา 2-3 วันตรวจร่างกายพบว่าซีดมากแต่ไม่มีดีซ่านไม่พบต่อมน้ำเหลืองหรือตับม้ามโต ตรวจเลือดพบ Hb 4.9 g%, WBC 6,000/มม^3, platelet 105,000/มม^3, MCV 65.3 เฟมโตลิตร, MCH 21.0 พิโครกรัม, reticulocyte 1.2 %, ferritin 4,610 ng/mL, direct Coombs' test, anti-HCV และ HIV Ag/Ab ต่างให้ผลบวกค่า CD4 409.3/มม^3 ตรวจแยกชนิดของฮีโมโกลบินพบว่ามีโรคฮีโมโกลบิน อี ให้การวินิจฉัยว่าเป็น ES ร่วมกับการติดเชื้อร่วมระหว่างไวรัสเอชไอวีกับไวรัสตับอักเสบซี, มีภาวะเหล็กเกินและโรคฮีโมโกลบินอีด้วย ให้การรักษาด้วยยาต้านไวรัสเอชไอวี และต่อมาให้สเตอรอยด์สำหรับรักษากลุ่มอาการอีแวนส์ ผู้ป่วยสามารถคงระดับความเข้มข้นเลือดได้ดีโดยไม่ต้องได้รับเลือดเพิ่ม กลุ่มอาการอีแวนส์มีความเกี่ยวข้องกับการติดเชื้อร่วมระหว่างไวรัสเอชไอวีกับไวรัสตับอักเสบซีหรือไม่ไม่เป็นที่แน่ชัด แต่ทั้งกลุ่มอาการอีแวนส์กับการติดเชื้อเอชไอวีมีการรบกวนระบบภูมิคุ้มกันอย่างหนึ่งที่เหมือนกันนั่นคือการลดระดับลงของกิจกรรมของ CD4 แต่ไม่เหมือนกันในเรื่องของจำนวนเซลล์ CD8 เพราะ CD8 ลดลงในผู้ป่วยที่ติดเชื้อเอชไอวีแต่กลับเพิ่มขึ้นในผู้ป่วยที่เป็นกลุ่มอาการอีแวนส์

คำสำคัญ: กลุ่มอาการอีแวนส์, การติดเชื้อร่วมระหว่างไวรัสเอชไอวี กับไวรัสตับอักเสบซี

Introduction

The main target of HIV infection is the helper T lymphocyte (CD4). Without treatment, CD4 will be destroyed and decreased gradually, leading to the alteration of the immune system and subsequently various clinical manifestations, including the opportunistic infections, lymphoid malignancies and hematologic complications. And the common hematologic manifestations comprise anemia due to multifactorial etiologies including the hematopoietic stem cell dysplasia, anemia of chronic diseases, drugs, blood loss, pure red cell aplasia[1], autoimmune hemolytic anemia (AIHA)[2] and immune thrombocytopenia (ITP)[3].

Evans syndrome (ES) consists of the AIHA, ITP and/or immune neutropenia and they may develop simultaneously or sequentially. Half cases of ES develop primarily while the other half develop secondarily following various disease groups including SLE, lymphoproliferative disorders and common variable immunodeficiency[4]. ES that happens in HIV-infected persons has been rarely reported[5] although isolated anemia, leucopenia or thrombocytopenia can be more commonly found[6]. Herein, we report one case of ES in the case of the co-incidence of HIV and hepatitis C virus infection.

Case Report

A 31-year old Thai female was admitted because of acute diarrhea, nausea, vomiting and fever for 3 days. Her stool did not contain any tint of mucus or blood. Prior this acute illness, she did not have any complaint, not take any drug. On admission, she was found to have severe anemia and dehydration, no fever/jaundice/hepatosplenomegaly/ petechia/ lymphadenopathy.

Her blood tests included: Hb 4.9 g%, WBC 6,000/mm^3, platelet 105,000/mm^3, MCV 65.3 fL, MCH 21.0 pg, RDW 15.4%, N 58 %, L 30 %, M 10 %, reticulocyte 1.2 %, albumin 3.0 g%, globulin 3.1 g%, AST 105 IU/L, ALT 8 IU/L, alkaline phosphatase 56 IU/L, total bilirubin 0.9 mg%, indirect bilirubin 0.5 mg%, creatinine 0.9 mg%, cholesterol 216 mg%, triglyceride 412 mg%.

Direct Coombs' test 3+, indirect Coombs' test 1+, Hb electrophoresis: Hb E disease

Ferritin 4,610 ng/mL, serum iron 76 mcg/dL, TIBC 268 mcg/dL

HIV Ag/Ab and anti-HCV antibodies-positive, TPHA and HBsAg-negative

Absolute lymphocyte 984/mm^3, T helper (CD4) 30%, absolute CD4 409.3/mm^3

The stool examination revealed E. histolytica cyst, no RBC or WBC. Urinalysis and the chest film were unremarkable.

She was diagnosed as ES with the underlying co-infection of asymptomatic HIV and HCV, hemosiderosis and Hb E disease. She was firstly treated with ceftriaxone and metronidazole and then with the antiretroviral therapy including tenofovir 300 mg, efavirenz 600 mg and lamivudine 300 mg a day. And her ES was treated with intravenous dexamethasone 40 mg a day x 4 days and later oral prednisolone 60 mg a day. Because the least incompatible blood was not available, she was not transfused at all. During admission, she could keep her Hb level stable until she could be discharged on the seventh day of admission.

She lost follow-up after discharge.

Discussion

In fact, direct antiglobulin or Coombs' test is found highly prevalent in HIV-infected patients, 21% of seropositive patients without or with minimal disease and 55% of AIDS patients without clinical AIHA[7]. But our case had the positive direct Coombs' test while she had severe anemia with an increased serum AST but normal ALT level, so she was believed to have active AIHA although the reticulocyte was not rising. AIHA in combination with thrombocy-topenia, our case was diagnosed as ES with the co-incidence of asymptomatic HIV and HCV. So far few cases of ES have been occasionally reported associated with some viral infections including HBV[8], HCV(9), HIV[5] and co-infection of HIV and HCV[10].

ES and chronic HIV infection have an immune derangement in common, viz, the decrease of CD4 activity. In HIV infection, there is a progressive loss of CD4 cells, furthermore the function of CD4 is relatively weak or even absent before its loss[11]. And the patients with AIDS who develop AIHA have the lower CD4 than the HIV-infected patients without AIHA (161.0±37.6/mm^3 vs. 230.2±120.0/mm^3)[12]. On contrary, the cytotoxic T lymphocytes (CTL) which are specific to HIV decline while the HIV-infected persons progress to AIDS because the HIV-specific CTL has shorter life span than CTL with specificities for other viruses[11], whereas the CD8 cell is increased in ES leading to the persistently decreased CD4/CD8 ratio in the peripheral blood[13].

AIHA usually responds well to steroid even in cases with AIDS[14], therefore our case is treated with steroids without transfusion while ARV is also

initiated because the patient has CD4 lower than 500/mm3 and simultaneous HCV infection[15]. And she can maintain her Hb level well during steroid therapy.

In spite of active hemolysis and severe anemia, the reticulocyte is quite low (reticulocyte 1.2 %). Sangle et al[5] found the corrected reticulocyte in cases of ES in HIV-infected patients was not high (2%). This relatively low reticulocyte and low platelet may probably be due to the altered stem cell differentiation by HIV[16]. Therefore, when anemia with thrombocy-topenia among HIV-infected persons is encountered, ES cannot be overlooked even though the reticulocyte is not increased and direct Coombs' test should be considered as one of the imperative investigations[17].

Conclusion

A 31-year old woman presents with acute gastroenteritis. She is found to have anemia, thrombocytopenia, positive direct Coombs' test, anti-HIV and anti-HCV antibodies, but no reticulocytosis. She is diagnosed as ES with co-infection of HIV and HCV and treated with steroid and antiretroviral therapy. In case of anemia and thrombocytopenia in co-infection of HIV and HCV, ES cannot be excluded although the reticulocyte is not increased and direct Coombs' test should be included as one of the essential investigations.

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