Human Parvovirus Infection and Pure Red cell Aplasia in an AIDS Patient: A Case Report

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Abstract: Although anemiais the very common presentation in AIDS patients but the pure red cell aplasia (PRCA), the normocytic normochromic anemia due to the decreased production of only the erythroid progenitor cells, has been rarely mentioned. Herein, onecase of PRCA is recognized in an AIDS patient who also has the evidence of human parvovirus infection. He was a 25-year-old Thai patient who was referred to the hematologist because of the progressive anemia and weight loss. Except for severe anemia, he had no hepatosplenomegaly, no other abnormality on the physical examination. His blood tests were: Hb 3.6 g%, MCV 65.6 fL, MCH 22.7 pg, WBC 4,800/mm^3, platelet 216,000/mm^3, CD4 count 4/mm^3, reticulocyte 0.9 %, serum ferritin 1,738.0 ng/mL. The bone marrow study showed the markedly decreased erythroid series despite normocellularity. The PCR for human parvovirus (HPV), HIV Ag/Aband VDRL werefound positive. The HIV viral load was less than 20 copies/ml. Therefore, he was diagnosed as having PRCA, HPV infection, full blown AIDS and late latent syphilis, and treated with ARV regimen containing nevirapine, lamivudine and stavudine, prednisolone 60 mg a day and benzathine penicillin. His Hb concentration as well as MCV was gradually raised to be normal within 2 yearswhereas prednisolone was tapered. Besides anemia of chronic infection, PRCA should be excluded in any HIV-infected patient who had severe normochromic normocytic anemia because it needed some specific therapy such as prednisolone.

Key words: Human Parvovirus Infection, Pure Red Cell Aplasia, AIDS

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บทคัดย่อ: **การติดเชื้อ human parvovirus และโลหิตจางจากเม็ดเลือดแดงฝ่อในผู้ป่วยภูมิคุ้มกันบกพร่อง: รายงานผู้ป่วย 1 ราย**

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แม้ว่าภาวะโลหิตจางจะพบบ่อยมากในผู้ป่วยโรคภูมิคุ้มกันบกพร่อง แต่โลหิตจางจากเม็ดเลือดแดงฝ่อซึ่งเป็นโลหิตจางชนิดเม็ดเลือดแดงขนาดปกติ ติดสีปกติ เนื่องจากการลดการสร้างเซลล์ต้นกำเนิดของเม็ดเลือดแดง ยังพบน้อยมากในรายงานนี้ เป็นผู้ป่วยโลหิตจางจากเม็ดเลือดแดงฝ่อร่วมกับการติดเชื้อ human parvovirus ในผู้ป่วยที่เป็นโรคภูมิคุ้มกันบกพร่อง ซึ่งเป็นชายไทย อายุ 25 ปี ถูกส่งมาพบโลหิตแพทย์เพราะมีโลหิตจางมากขึ้นเรื่อย ๆ ร่วมกับน้ำหนักลด นอกจากภาวะโลหิตจางอย่างรุนแรงแล้วการตรวจร่างกายก็ไม่พบสิ่งผิดปกติอื่น ตับม้ามไม่โต ตรวจเลือดพบ: Hb 3.6 กรัม%, MCV 65.6 เฟมโตลิตร, MCH 22.7 พิโครกรัม, WBC 4,800/มม^3, platelet 216,000/มม^3, CD4 count 4/มม^3, reticulocyte 0.9 %, serum ferritin 1,738.0 นาโนกรัม/มล. ตรวจชิ้นเนื้อไขกระดูกก็พบว่าเซลล์ต้นกำเนิดเม็ดเลือดแดงลดลงจำนวนมาก ทั้งที่เซลล์โดยรวมปกติ ตรวจ PCR สำหรับเชื้อ human parvovirus (HPV), HIV Ag/Ab และ VDRL ให้ผลบวกตรวจปริมาณเชื้อเอชไอวี พบน้อยกว่า 20 copies/มล. ฉะนั้น จึงให้การวินิจฉัยว่าเป็นโลหิตจางจากเม็ดเลือดแดงฝ่อร่วมกับการติดเชื้อ HPV โรคภูมิคุ้มกันบกพร่องและซิฟิลิสแฝงระยะสุดท้าย และให้การรักษาด้วยชุดยาต้านไวรัสซึ่งประกอบด้วย nevirapine, lamivudine และ stavudine, prednisolone 60 มก. ต่อวัน และ benzathine penicillin ความเข้มข้นฮีโมโกลบิน เช่นเดียวกับขนาดเฉลี่ยของเม็ดเลือดแดงค่อยตอบสนองอย่างช้า ๆ ต่อการรักษาจนเป็นปกติภายใน 2 ปีขณะที่ prednisolone ก็ค่อยลดลงเรื่อย ๆ ดังนั้นภาวะโลหิตจางชนิดขนาดเม็ดเลือดแดงปกติ การติดสีปกติในผู้ป่วยติดเชื้อเอชไอวี นอกจากโลหิตจางจากภาวการณ์ติดเชื้อเรื้อรังแล้วโลหิตจางจากเม็ดเลือดแดงฝ่อ ก็ต้องระลึกถึงด้วยเช่นกันเพราะโรคนี้ต้องการการรักษาบางอย่างที่จำเพาะ เช่น prednisolone เป็นต้น

คำสำคัญ: การติดเชื้อ human parvovirus, โลหิตจางจากเม็ดเลือดแดงฝ่อ, โรคภูมิคุ้มกันบกพร่อง

Introduction

Anemia is commonly found in human immunodeficiency virus (HIV)-infected persons due to various causes, 71% of the population[(1)]. Its prevalence appears 2-fold more common than HIV-negative population (37% vs 17%)[(2)]. The main causes of anemia among this group are 40 % with iron deficiency, 23 % with vitamin B_{12} deficiency[(1)]. Other contributing factors includethe long history of HIV infection, CD4 count less than 200/mm^3, increased plasma viral load, women, black race, zidovudine therapy, increasing age, lower body mass index, history of bacterial pneumonia, oral candidiasis and historyof fever[(3)]. Although HIV itself can affect the hematopoietic stem cells in the bone marrow resulting in peripheral cytopenia, pure red cell aplasia (PRCA), the normocytic normocytic anemia with the reticulocytopeniadue to the decreased production of only the erythroid progenitor cells, has been rarely reported

in the HIV-infected persons[4,5]. Besides HIV, other viruses such as human parvovirus can also contribute to PRCA[6]. To recognize PRCA is important because it needs and responds well to the special treatment with corticosteroid. And herein, we report a case of PRCA and HPV infection in an AIDS Thai patient.

Case Report

A 25-year-old Thai man was referred to the hematologist because of progressiveanemia for a few months without any obvious blood loss. He lost his weight for a few kilograms but no fever. On the physical examination, he had marked pallor without jaundice, no oral thrush/lymphadenopathy/hepato-splenomegaly.

Blood tests: Hb 3.6g%, Hct 10.5%, MCV 65.6 fL, MCH 22.7 pg, MCHC 33.9 g%, RDW 14.1 %, WBC 4,800/mm^3, platelet 216,000/mm^3, N 74 %, L 12 %, CD41 % of lymphocyte, count 4/mm^3, reticulocyte 0.9 %, serum ferritin 1,738.0 ng/mL, serum iron 162 ug/dL, TIBC 383 ug/dL, G-6-PD enzyme-normal

Other blood tests such as liver function and kidney function tests were within normal limits.

The chest film showed unremarkable study whereas the ultrasonography of the upper abdomen showed only mild splenomegaly.

The bone marrow biopsystudy: normocellular marrow, cell: fat 50: 50, with relatively marked increase of the myeloid and markedly decreased erythroid cells, M: E 8: 1, increased hemosiderin pigment, no granuloma, no malignancy.

HIV Ag/Abwas positiveand the HIV viral load was <20 copies/ml, HBsAg and anti-HCV were negative, VDRL 1:4, the PCR for human parvovirus B19 was positive. The CSF showed no cell, no *Cryptococcus* antigen, negative for VDRL.

He was diagnosed as having PRCA associated with the concurrent HPV infection, full blown AIDS and the late latent syphilis. The ARV regimen consisting of nevirapine 200 mg, lamivudine 150 mg, stavudine 30 mg was initiated as well as oral prednisolone 60 mg a day. Other treatment was the multiple doses of intramuscular benzathine penicillin injection. He refused to be transfused. He was followed every two or three months. And he slowly responded to therapy while prednisolone was gradually tapered until two years later, his blood tests were found to be: Hb 15.3g%, Hct 47.1%, MCV 87.1 fL, MCH 28.3 pg, MCHC 32.6 g%, RDW 15.7%, WBC 9,400/mm^3, platelet 259,000/mm^3, CD4 91/mm^3, ferritin 2,691.0 ng/mL.

Discussion

The diagnosis of PRCA in our case is based on the combination of severe anemia and the marked decrease of erythroid progenitor cells in spite of the normocellularity of the bone marrow[7]. Likewise, HPV infection is documented based on the positive PCR for HPV B19 in the patient's serum. Theoretically, the MCV and MCH in cases of PRCA should be normal but they were found strikingly low in our case. Because the serum ferritin level was markedly increased, the iron deficiency anemia, one of the two common causes of the severe microcytosis of the red blood cells, can be excluded. Therefore, the other common cause of the microcytosismust bethalassemia that is highly prevalent in the northeastern part of the country[8]. However the presence of any form of the thalas-semiaswas not explored.

The basic pathogenesis of PRCA in HIV-infected patients[5] is mainly the autoimmune response from immune-dysregulation in AIDS due to the low CD4 count from the infection and destruction by HIV, and drugs in ARV regimen such as lamivudine[4] or zidovudine therapy[9]. However PRCA is also found associated with HPV B19 especially in HIV-infected patients which seems responsive to intravenous immunoglobulin (IVIG) in the majority of cases[10]. But IVIG is not offered to our case.

HPV B19 infection is usually asymptomatic or may have mild common cold-like symptom. It may trigger the cessation of the red blood cell production leading to aplastic crisis or pure red cell aplasia especially in the patients with formerly shortened red blood cell survival such as HIV-infected patients, thalassemia or sickle cell anemia[11]. HPV is found to be related with very low CD4 (<50 cells/mm^3) in 2 HIV-infected individuals with anemia[12]. Our case had extremely low CD4 (4 cells/mm^3) with anemia whereas the HIV viral load was also very low (<20 copies/ml). For the HIV-infected patients with syphilis, they were found to be associated with lower CD4 count but higher HIV viral load level than the HIV-infected patients without syphilis[13]. Therefore it seems to suggest the very low CD4 count may be associated with HPV rather than HIV in our case.

In fact, HPV B19 infection is believed to be active in the case of the presence of IgM without IgG of HPV B19 antibody[14]. HPV B19 can infect and replicate in the erythroid progenitor cells and this is believed to be the basis of bone marrow failure in cases of viral tropism and cytotoxicity and it needs antibody to neutralize and terminate it. However the virusitself may persist in case of immune-compromised hosts such as HIV-infected patients or the patients with the organ transplant[15-17].

PRCA in our case is treated with prednisolone while the ARV is continued and he responds to the treatment well. Steroid is shown not harmful for the HIV-infected patient[18]. His Hb concentration is gradually increased until it becomesnormal within 2 years. This suggests that the autoimmune process possibly contributed by HPV infection may play the major role as the underlying pathogenesis for PRCA in our case.

The low MCV or the microcytosis of the red blood cells as well as the MCH was found increased in the HIV-infected patients without thalassemia after ARV therapy for 6 or 12 months. Likewise, these RBC parameters could also become normal in individuals with beta thalassemia traitsfollowing the ARV therapy[19]. The MCV and MCH of our patient were found very low at the initial investigation, 65.6 fl and 22.7 pg, respectively but they could be raised until normal after ARV therapy for two years, 87.1 fL and 28.3 pg respectively.

Conclusion

When severe normochromic normocytic anemia in any HIV-infected patient was encountered, PRCA on top of the anemia of chronic infection should be excluded because it needed the special treatment and responded well to therapy.

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