Case Report

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Transfusion-Associated HIV Infection in Pediatric Leukemia Patients (Two Case Reports)

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Abstract

Background: Leukemia is the second most malignant tumor in children. The chemotherapy induced anemia (CIA) and hemorrhage are the most popular side-effects due to the myelosuppression of chemotherapy. So far, multitransfusion is still the timely and effective measure in curing these complications. The acquisition of HIV infection and subsequent development of AIDS by component transfusion from donors at risk is well known, and prognosis of HIV infection is particularly severe in patients with leukemia.

Case Presentation: We report two leukemic cases that were infected with HIV through transfusion. The first patient was totally transfused with 16 U RBC, 20 U platelets and 820 ml fresh frozen plasma, and later test showed that his first used FFP carried the HIV. For the second 2 U RBC, 5 U platelets and 1500 ml fresh frozen plasma were transfused to her. Late test of her used blood products showed that the fourth RBC carried the HIV. Both results were confirmed by the local Center for Disease Control (CDC). They were not transfused before the diagnosis of leukemia. Their parents were healthy with negative HIV-Ab

Conclusion: Since the two leukemic patients suffered transfusion-associated HIV with poor prognosis, we must take more efforts to utilize blood products judiciously, manage blood donors, test blood samples etiologically, shorten HIV testing "window periods" and develop preventive vaccination against HIV to reduce the incidence as low as possible.

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Key Words: HIV; Blood Treansfusion; Leukemia; AIDS

Introduction

Leukemia is the second most malignant tumor in children. Approximately 30 new-onset leukemic patients yearly during the recent 5 years are referred to our hospital, the only tertiary and comprehensive teaching hospital for children in Zhejiang Province. Anemia and hemorrhage were the most observed side-effects during chemotherapy. Although the humanized erythropoietin (EPO) and thrombopoietin (TPO) are used in clinic, component transfusion is still the timely and effective modality. Thus, the infection risk of HIV through transfusion still threatens children's health[1], although it has been documented that mother-to-baby is the most common way for children to be infected by HIV[2]. Transfusion-related HIV infection has been reported repeatedly since the first case report in 1982[3]. In fact, the World Health Organization (WHO) estimates that 5% to 10% of all HIV infections worldwide have been acquired through

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transfusions of infected blood and its products. The risk of transfusion-associated HIV exceeds that of any other risk exposure, 90% of recipients transfused with HIV antibody-positive blood are found to be HIV infected at follow-up. But there were few cases reported about transfusion-related HIV infection in leukemia. Prognosis of HIV infection is particularly severe in patients with leukemia and other cancers[4].

In 2009, the first pediatric patient infected with HIV in our hospital was identified and the second HIV positive child was identified in May, 2010. Both of them suffered from leukemia, and had underwent multi-transfusions. In this report, we aimed to discuss the safety of transfusion, scientific use of blood and blood products in hospital, accurate and timely HIV screening in laboratory and the right measures that doctors and nurses should take to decrease the incidence of transfusion-associated HIV infection as much as possible, and combat HIV infection more efficiently later.

Case Presentation

Case 1: A 13-year-1-month old boy weighing 50.5 kg was admitted to our hospital on September 15, 2008 because of 2 weeks of fatigue and pallor associated with 1 week of chest distress. Bone marrow aspiration was carried out immediately. The complete blood count (CBC) of emergency showed white blood cells (WBC) 16.2×10^9/L, N 11.4%, Hb 75 g/L, Plt 79×10^9/L. The diagnosis was acute lymphocyte leukemia (ALL) with L_2, common-B and middle risk according to the results of bone marrow cytomorphology examination, flow cytometry immunophenotyping (FCMI) and CBC. From September 17 to December 17, 2008, the chemotherapy was carried out sequentially. During the chemotherapy, when the hemoglobin was below 70g/L and/or platelets below 20×10^9/L, red blood cells (RBC) and/or platelets were transfused respectively, and fresh frozen plasma was used when dysfunction of blood coagulation was detected. He was multi-transfused with 16 U RBC, 20 U platelets and 820 ml fresh frozen plasma. During each hospitalization, screen tests of rapid plasma reagin (RPR), antibody of HIV (HIV-Ab) and hepatitis viruses were carried out. On February 1, 2009, he was admitted again for consolidation chemotherapy. Before transfusion, his blood sample was positive for HIV antibody [human immunodeficiency virus antibody diagnosis reagents (double antigen-binding enzyme-linked immunosorbent assay), INTEC (Xiamen) technology Ltd. LOT: 2008066607]. The result was confirmed by the Center for Disease Control (CDC) (HIV 1/2 Antibody Immunoblot Kit, MP Biomedicals Asia Pacific Pte. Ltd. Lot: AE8034). After retesting of blood products that this patient had received before, it was confirmed that the first used FFP carried the HIV. There was no transfusion before the diagnosis of ALL, no operation and infectious disease in his past history. The history of preventive vaccinations was normal. His parents and elder brother were healthy, with negative HIV screen tests .

Case 2: A 4-year-9-month old girl weighing 21 kg was admitted to hematology department of our hospital on December 8, 2009 because of 20 days of abdominal discomfort and anorexia. The initial CBC showed WBC 0.83×10^9/L, N 7.2%, Hb 90 g/L, Plt 202×10^9/L. The diagnosis was ALL (L_2, common-B, low risk) according to the results of bone marrow cytomorphology examination, FCMI and CBC. During the first hospitalization from December 8, 2009 to January 22, 2010, she formally underwent chemotherapy. During the second hospitalization from February 16, 2010 to April 3, 2010, sequential chemotherapy was carried out. Totally, 2 U RBC, 5 U platelets and 1500 ml fresh frozen plasma were transfused during the two hospitalizations. During the third hospitalization, her blood test for HIV-Ab was positive [human immunodeficiency virus antibody diagnosis reagents (double antigen-binding enzyme-linked immunosorbent assay), INTEC (Xiamen) technology Ltd. LOT: 2010046607]. The result was also confirmed by CDC (HIV 1/2 Antibody Immunoblot Kit, MP Biomedicals Asia Pacific Pte. Ltd. Lot: AE9015). Later, tests of blood products transfused showed that the fourth RBC carried the HIV. There was no transfusion before her diagnosis of leukemia, no operation and infectious disease in her past history. Her history of vaccinations was normal. Her parents were healthy, and their blood sample was negative for HIV-Ab.

Discussion

Chemotherapy-induced anemia (CIA) and hemorrhage are common problems in leukemic patients. During tackling the complications, component transfusion is still the effective and timely modality. When anemia becomes severe (generally hemoglobin below 70-80g/L) transfusions are often used to quickly raise hemoglobin levels to a normal range and reduce symptoms like significant fatigue and dizziness[5,6]. Prophylactic platelets transfusion during chemo-therapy for leukemia using a threshold of 10×10^9/L and during the pre engraftment phase of stem cell transplantation using a threshold of 20×10^9/L is widely practiced[7]. In our hospital, when the hemoglobin falls below 70 g/L and/or platelets below 20×10^9/L, RBC and/or platelets are transfused.

So far, totally 2 transfusion-related HIV infected cases were reported in the history of our hospital, also there were few transfusion-related HIV infected leukemic patients reported in other countries and regions, but the transfusion-related infection risks still exist in leukemia[1,8], and that really deteriorates the patients' conditions[4]. Since the unnecessary blood products transfusion will further increase the risk of infection, the guideline for judicious use of blood products should be developed and performed strictly.

In China, an estimation showed that 740,000 people living suffered from HIV in 2007, including about 105,000 cases of AIDS[9]. HIV can be transmitted through three main routes: unprotected vaginal, anal and oral sex; direct blood contact; mother to baby before or during birth or through breast milk[10,11]. In China, all blood collected is now screened for alanine aminotransferase (Alt), HIV-1/2, hepatitis B virus, hepatitis C virus and syphilis[12]. All potential donors are interviewed before donation, if they had a risk factor for HIV they should not donate. Every unit of donated blood with a positive result from HIV antibody testing is discarded, and future donations are not accepted from those persons. Despite these procedures, HIV transmission may still occur for four theoretical reasons: (1) Donations may be collected during the window period of infection. (2) The possible existence of a long term HIV chronic carrier state in which the individual never develops (or loses) HIV antibody. (3) Infection with variant strains of HIV that may escape detection by current serologic assays. (4) Testing or clerical errors. In America, it was estimated that 1 in every 360,000 donations was made during the window period, and 1 in 2,600,000 donations was HIV-seropositive but was not identified because of an error in the laboratory[13]. In children, it has been documented that mother-to-baby was the most common way to cause children infected by HIV[2]. However, these two children were infected from the donated blood which was provided and screened "negative" (maybe within "window period"). Our later retrospective investigation demonstrated that both of the donors were volunteers and had sex with other men (MSM), but they did not declare it during interview. Obviously, it is important to carefully interview donors to decrease infectious risks of blood transfusion.

Healthcare workers in hospitals and CDC have to timely update and pay more attention to HIV prevention, transmission and treatment, and have to follow strictly the protocols of HIV problems from local CDC. Laboratory staff must receive professional training for HIV screening test and get licensed. If a positive result of HIV screening test is found, a strict protocol has to be followed including specimen taking and transporting and confirmation by local CDC. Doctors have to reduce transfusion of blood products as much as possible. Nowadays the supportive therapy for the myelosuppressive chemotherapy is developing rapidly, such as EPO, G-CSF and TPO. The recombinant humanized EPO (rHuEPO) therapy has provided substantial clinical benefits and been practiced widely for the CIA, but it also faces the challenge of human anti mouse or human anti rabbit disease due to the repeated use[14-16]. Compared to the rHuEPO, the TPO remains a therapeutic reagent for the thrombocytopenia, but the application encounters a number of obstacles, the clinic effect and side-effect have to be carefully studied[17-19]. On the side, nurses have to know how to take care of the HIV-infected children, such as psychological comforting and eliminating stigma and discrimination[20,21].

At last, facing the challenges of HIV infection, different level governments have taken different measures to fight against the terrible disease. Currently, China provides free medical care, compensation to HIV-positive blood recipients due

to undetectable infectious blood transfusion within the “window period”, therefore, how to shorten the “window period” is especially important to the scientist. Now Blood center of Zhejiang province of China has substituted polymerase chain reaction (PCR) for enzyme linked immunosorbent assay (ELISA) to screen HIV since August first, 2010. The development of a preventive vaccine against HIV has been a major goal. Significant progress toward that goal has been made recently. But the clinic effect and long term side-effects of the vaccines remain to be explored[22].

Conclusion

The morbidity of leukemia is getting higher and higher, although the researchers and clinic doctors have made significant achievement in reducing chemotherapeutic side-effects and supportive therapies, but the CIA and platelet associated hemorrhage still hamper the procedure of chemotherapy, and till now, component transfusion is still the most effective step. To avoid this event in the future, we must make all-out efforts on the development of judicious clinic usage of blood products, management of blood donors, etiological testing of blood samples, shortness of HIV testing "window periods" and preventive vaccination against HIV.

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