Case report

Transfusion-associated graft-versus-host disease: a case report

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Abstract:

Transfusion-associated graft-versus-host disease (TA-GVHD) is a rare complication of blood transfusion resulting from donor's T-lymphocyte engrafts, proliferates and attacks to recipient's cells. Clinical manifestations include fever, rash, hepatomegaly, liver dysfunction and pancytopenia occurring up to 6 weeks after transfusion. We present here a case of TA-GVHD in an infant with severe combined immunodeficiency (SCID).

A 3-month-old male infant at a province hospital presented fever, anemia and tachypnea and subsequently received a diagnosis of severe pneumonia. Non-irradiated leukocyte poor red cells (LPRC) was given for anemia correction. He was transferred to the King Chulalongkorn Memorial Hospital 2 days after the transfusion and symptoms deteriorated. Given the history of his two older brothers, who died of pneumonia at the age of 3 months, peripheral blood flow cytometry was performed showing the absence of B/T lymphocytes and NK cells. He was diagnosed with SCID at the age of 4 months. At six weeks after hospital admission, he developed hepatomegaly with elevated liver enzymes and pancytopenia. HLA typing from the patients' peripheral blood was made and the results showed a total mismatch with his parents. In addition, HLA typing from his buccal epithelial cells was matched with his parents. Subsequently, he was diagnosed with TA-GVHD and died of severe pneumonia and respiratory failure at age 6 months.

Clinical manifestations of the patient that occurred within 6 weeks after blood transfusion met the diagnostic criteria of TA-GVHD. The HLA typing result from his peripheral blood might have resulted from active T-lymphocytes in transfused nonirradiated LPRC. Transfusion with irradiated blood products can prevent the risk of TA-GVHD because radiation is used to deactivate T-lymphocytes in blood products.

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รายงานผู้ป่วย

ภาวะเซลล์ใหม่ต่อต้านร่างกายแทรกซ้อนจากการได้รับเลือด

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บทคัดย่อ

บทนำ *ภาวะสเต็มเซลล์ใหม่ต่อต้านร่างกาย เป็นภาวะแทรกซ้อนจากการได้รับเลือด ซึ่งเกิดจากเม็ดเลือดขาวชนิด ที ลิมโฟไซต์ ของผู้บริจาค เข้าไปเจริญเติบโต และทำลายเซลล์ของผู้รับบริจาค อาการแสดง ประกอบด้วย ไข้ ผื่น ตับโตและสูญเสียการทำงาน อีกทั้งพบจำนวนเม็ดเลือดทุกชนิดลดลงภายใน 6 สัปดาห์หลังการได้รับเลือด* ***รายงานผู้ป่วย*** *ผู้ป่วยเด็กชายอายุ 3 เดือนมาโรงพยาบาลด้วยไข้ ภาวะซีดและหายใจเร็ว ได้รับการวินิจฉัยเป็นโรคปอดติดเชื้อรุนแรง และได้รับผลิตภัณฑ์โลหิตแดงแบบปนเปื้อนเม็ดเลือดขาวน้อยที่ไม่ผ่านการฉายแสง หลังจากนั้นผู้ป่วยถูกส่งตัวมาที่โรงพยาบาลจุฬาลงกรณ์ และได้รับการวินิจฉัยเป็น ภาวะภูมิคุ้มกันบกพร่องรุนแรงแต่กำเนิด เนื่องจากตรวจไม่พบเม็ดเลือดขาว ชนิดลิมโฟไซต์ และเซลล์เอ็นเคในเลือด ต่อมาตรวจพบตับโต ระดับเอนไซม์จากตับเพิ่มขึ้นและเม็ดเลือดทุกชนิดต่ำภายใน 6 สัปดาห์ ผลตรวจ ตรวจเนื้อเยื่อจากเลือดผู้ป่วย ไม่เข้ากันกับผลจากบิดามารดา แต่ผลการตรวจเนื้อเยื่อจากเซลล์กระพุงแก้มของผู้ป่วยเข้ากันได้กับผลจากบิดามารดา อาการแสดงในช่วง 6 สัปดาห์หลังการรับเลือด ตรงกับเกณฑ์การวินิจฉัยภาวะสเต็มเซลล์ใหม่ต่อต้านร่างกาย เป็นภาวะแทรกซ้อนจากการได้รับเลือด ผลการตรวจเนื้อเยื่อจากเลือดผู้ป่วยอาจเป็นผลจากการได้รับ ผลิตภัณฑ์จากเลือดที่ไม่ผ่านการฉายแสง การให้เลือดที่ผ่านการฉายแสงป้องกันภาวะนี้ได้เนื่องจากการฉายแสงทำให้เม็ดเลือดขาวชนิดทีลิมโฟไซต์ในผลิตภัณฑ์โลหิตไม่สามารถแบ่งตัวได้*

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Introduction

Transfusion-associated graft-versus-host disease (TA-GVHD) is a rare complication of blood transfusion with viable lymphocytes containing blood products.[1] TA-GVHD occurs when donor's viable T lymphocytes from blood products are not rejected by the recipient. Furthermore, they engraft, proliferate and attack recipient's cells due to immunologic differences. Risk factors for TA-GVHD are congenital and acquired cellular immunodeficiency, newborns, intrauterine transfusion, bone marrow transplantation, Hodgkin's lymphoma, non-Hodgkin's lymphoma and acute leukemia.[1,2] Clinical manifestations include erythematous papulomacular rash, fever, nausea, vomiting, diarrhea, hepatomegaly, elevated liver enzymes and pancytopenia occurring up to 6 weeks after transfusion.[1,3] Because the clinical features may be nonspecific, a definitive diagnosis of TA-GVHD requires the documentation of the presence of donor-derived cells or DNA in recipient's blood or affected tissue.[2,3] The overall mortality of TA-GVHD is about 90 to 100%.[2,4] At present, no effective treatment exists for TA-GVHD. Prevention by identifying at risk patients and transfusion with irradiated blood products remain the best strategies to reduce the patient mortality rate from this disease.[4] We present here a case of TA-GVHD in an infant with severe combined immunodeficiency (SCID).

Case report

A 3-month-old male infant presented fever, cough and tachypnea for 1 week at a province hospital 22 September 2018. He received a diagnosis of severe pneumonia with respiratory failure and was admitted to the hospital for antibiotic treatments. Initial laboratory testing revealed marked anemia. Subsequently, he received a transfusion of nonirradiated leukocyte poor red cells. He was transferred to King Chulalongkorn Memorial Hospital (KCMH) 2 days after the transfusion and symptoms deteriorated.

Hematologic testing on the first day in KCMH included white blood cell counts (WBC) 1.86 x 10^9 /L (normal range : 6-17 x 10^9 /L) with 43.5% neutrophil, hemoglobin (Hb) 10.4 g/dL (normal range : 11.0-13.5 g/dL), hematocrit (Hct) 33% (normal range : 34-41%), and platelets 104 x 10^9/L (normal range : 150-450 x10^9/L) (Table 1). Liver function testing revealed aspartate transaminase levels of 1,187 IU/L (normal range: 18-92 IU/L) and alanine transaminase levels of 194 IU/L (normal range: 0-41 IU/L). Chest X-ray showed bilateral alveolar infiltration. Fungal culture of the tracheal suction catheter implied Aspergillus infection and urine culture results revealed *Candida albicans* infection. Cytomegalovirus (CMV) viral load was 4,887,336 copies (Log 6.69). Given the family history of early death from severe infection in his two older brothers, he was suspected of severe primary immune deficiency. Peripheral blood flow cytometry was performed. The results were CD3 1% (normal range: 65-88%), CD4 1% (normal range: 26-62%), CD8 1% (normal range: 14-44%) and CD56 3% (normal range: 2-27%) with the absence of T lymphocyte and NK cells. He was diagnosed with SCID.

He was treated with antibiotics but the fever persisted. CBC showed progressive pancytopenia (Table 1). Thereafter, he developed an erythematous rash at the groin and forehead, and hepatomegaly within 6 weeks after the transfusion. The HLA typing from his peripheral blood was performed to compare with HLA typing from the parents' blood. The results showed a mismatch with both parents (Table 2). However, HLA typing from his buccal epithelial cells was matched with HLA typing of his parents. From these results no relationship was found between his blood samples and tissue, confirming the diagnosis of TA-GVHD. Finally, he developed respiratory failure and died of severe infection during the following 3 months.

Table 1 Patient's laboratory results on admission

Parameters (normal range)	Date (days after transfusion)		
	27 Sep 2018 (2)	30 Sep 2018 (5)	2 Oct 2018 (7)
Hemoglobin (11.0-13.5 g/dL)	10.4	9.5	8.2
Hematocrit (34-41%)	33	31	25
White blood cells (6-17 x 10^9 /L)	1.86 x 10^9/L	5.05 x 10^9/L	2.3 x10^9/L
Platelet (150-450 x 10^9/L)	104 x 10^9/L	72 x 10^9/L	51 x10^9/L
Aspartate transaminase (18-92 IU/L)	1,187	353	307
Alanine transaminase (0-41 IU/L)	194	64	49

Table 2 HLA Typing results of specimen from patient and his parents

Person (type of specimen)	Father (peripheral blood)	Mother (peripheral blood)	Patient (peripheral blood)	Patient (buccal epithelial cell)
HLA-A	A*11, A*11	A*11, A*11	A*02, A*33	A*11 , A*11
HLA-B	B*15, B*48	B*13, B*13	B*44, B*46	B*48 , B*13
HLA-DRB1	DRB1*09, DRB1*12	DRB1*15, DRB1*16	DRB1*07, DRB1*12	DRB1*09, DRB1*16

Discussion

Clinical manifestations of the patient that occurred within 6 weeks after blood transfusion met the diagnostic criteria of TA-GVHD.[3] The HLA typing resulting from his peripheral blood might have resulted from active T-lymphocytes in the transfused non-irradiated LPRC. Skin or liver biopsy was not performed. Therefore, he was diagnosed with probable TA-GVHD with definite imputability from transfusion, following definition by NHSN Biovigilance Component Protocol.[3] The risk factor for TA-GVHD in this patient was SCID. Because of his underlying disease, he could not reject the T-lymphocytes which came from the blood product but was suitable to receive irradiated blood products. The irradiated blood product inhibited T-cell proliferation and showed no adverse effect on red blood cells, platelets and granulocytes.[2] But at provincial hospitals, no evidence exists to support regarding his underlying disease. Although TA-GVHD is a rare complication, the mortality rate is high and no effective treatment is available. Transfusion with irradiated blood products can prevent the risk of TA-GVHD, especially in an immunocompromised host. Therefore, it was important to identify the risk of TA-GVHD in the patient requiring an allogeneic blood transfusion and to prevent TA-GVHD using irradiated blood product.

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