Published in final edited form as:

J Pediatr Hematol Oncol. 2013 July ; 35(5): e226–e228. doi:10.1097/MPH.0b013e3182830c25.

Severe Thrombocytopenia in a Child Secondary to Passive Platelet Antibody Transfer from a Plasma Transfusion

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Abstract

Though rare, passive transfer of platelet antibodies through blood products can result in thrombocytopenia, acute transfusion reactions and death. We report a case of severe alloimmune thrombocytopenia from a plasma transfusion. A post-liver transplant patient with a normal platelet count received fresh frozen plasma (FFP) prior to liver biopsy. Post-biopsy she developed cardiorespiratory distress, petechiae and severe thrombocytopenia (platelet count 2,000/ μ L). Her platelet count recovered to normal over one week. This diagnosis should be considered whenever an unexpected drop in the platelet count occurs after a plasma-rich transfusion. Conservative transfusion practices and more targeted donor screening may prevent similar events.

Keywords

Thrombocytopenia; Transfusion; Fresh Frozen Plasma; Blood bank; Platelets

Introduction

Passive transfer of platelet antibodies through blood products can result in severe adverse events including thrombocytopenia, bleeding, acute transfusion reactions and death.^{1–3} Transfusion-associated alloimmune thrombocytopenia occurs when a platelet antigen-negative donor is exposed to a common platelet antigen, for example, through pregnancy or prior transfusion, and forms an antibody. Transfusion of plasma-containing product from the sensitized donor into an antigen-positive recipient can result in sudden, severe thrombocytopenia. There have only been 3 occurrences reported in the pediatric population.^{4–6}

Methods

Platelet antibodies were detected by a modified antigen-capture enzyme-linked immunosorbent assay (MACE[®] 1 and 2, Gen-Probe, San Diego, CA). Platelet antibody

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Conflicts of interest: The authors have no conflicts of interest to disclose.

testing and antigen genotyping performed by Platelet and Neutrophil Immunology Laboratory, Blood Center of Wisconsin.

Case Report

The patient was 3-year-old female status-post liver transplantation at 8 months of age admitted for liver biopsy for evaluation of acutely elevated liver aminotransferases: serum aspartate aminotransferase 85 IU/L and alanine aminotransferase 121 IU/L. Just prior to biopsy, prothrombin time (PT) was 16.3 seconds (normal 11.4–13.6), partial thromboplastin time (PTT) 41.4 seconds (normal 23.8–35.0), white blood cell (WBC) count 5,800/ μ L, hemoglobin 11.5 g/dL and platelet count 178,000/ μ L (Table 1). Fibrinogen level was low normal at 201 mg/dL (normal 200–400mg/dL). Due to the prolonged PT, she was transfused with 10 mL/kg of FFP from a single donor. The PT was not rechecked prior to the procedure. 4 hours after the procedure she developed tachycardia (heart rate 170/min) and tachypnea (respiratory rate 60/min), but oxygen saturation remained normal (98% on room air). A chest x-ray was consistent with pulmonary edema. Cardiorespiratory status returned to baseline after albumin 5% (10 mL/kg) and intravenous furosemide (1 mg/kg). At this time her platelet count was 2,000/ μ L (Figure 1). Repeat platelet count was 6,000/ μ L. WBC count (5,700/ μ L) and hemoglobin (11.6 g/dL) remained at baseline. Petechiae developed across her upper extremities but there were no other signs or symptoms of bleeding including no liver hemorrhage or subcapsular hematoma on ultrasound. She was transfused $\frac{1}{2}$ single-donor unit platelets (SDP) from a random donor; immediate post-transfusion platelet count was 41,000/ μ L. Six hours later, repeat platelet count was slightly lower at 31,000/ μ L. She received another $\frac{1}{2}$ SDP; immediate post-transfusion platelet count was 60,000/ μ L. Platelet counts gradually improved with no additional transfusions, becoming normal within one week.

Given the sudden, severe thrombocytopenia following FFP transfusion, we suspected a transfusion reaction secondary to passive transfer of platelet alloantibody from the FFP donor. Pre- and post-transfusion platelet antibody screen of the patient's serum was negative (Table 1), but testing of the donor's serum revealed antibody to HPA-1a-positive platelets. Genotyping of the patient's platelets revealed she was homozygous for HPA-1a. The plasma donor had had 3 pregnancies, the latest resulting in late-term pregnancy loss due to an unidentified, possible platelet problem in the fetus. This history was not captured on the blood donor screening form.

Discussion

This case highlights a rare cause of alloimmune thrombocytopenia caused by passive transfer of platelet-specific antibody from a transfusion. The clinical course in our case mirrors that of other published reports.^{1–9} In these cases, the time to nadir was rapid (<12 hours from transfusion), and platelet recovery occurred over a few days to a week, often without any specific therapy. Our patient demonstrated this characteristic response with a nadir 4 hours post-transfusion and steady normalization of the platelet count over 7 days. In this setting, post-transfusion reactions range from no symptoms to death from bleeding or severe anaphylaxis. Our patient manifested a moderate transfusion reaction with

tachycardia, tachypnea and mild pulmonary edema, which resolved with diuresis. Clinically it can be difficult to differentiate between transfusion-associated circulatory overload (TACO) and transfusion-related acute lung injury (TRALI). The rapid improvement of her symptoms following diuresis was more suggestive of TACO, although the possibility of mild TRALI was not ruled out.¹⁰

The negative platelet antibody screen on the recipient's pre- and post-transfusion samples has been described, and is thought to be due to rapid adsorption of the antibody to recipient platelets with minimal free antibody in the circulation.⁷ Thus, a negative recipient platelet antibody screen does not preclude this diagnosis and suggests examining the donor's sera is warranted when the antibody screen is negative.

In other published cases, the donors were female with a history of pregnancy and often with pregnancy losses. In cases where the antibody was identified, it was most often against HPA-1a. In the Caucasian population, HPA-1a is the most common allelic variant, with only 2% homozygous for HPA-1b. Platelet antigen typing of the patient confirmed she was homozygous for HPA-1a. We were able to detect high titers of anti-HPA-1a antibody in the donor's serum; the donor was negative for the platelet antigen HPA-1a. The plasma donor in this case was likely sensitized to HPA-1a antigen through her previous pregnancies. Her late-term pregnancy loss was probably a result of neonatal alloimmune thrombocytopenia.

The donor's history of a pregnancy loss was not discovered during initial donor screening. The current FDA-approved Donor History Questionnaire asks potential female donors if they have been pregnant in the last 6 weeks or are currently pregnant, but it does not ask information regarding past pregnancies. In a study of 500 women with a history of pregnancy, 21 (4.2%) tested positive for platelet-specific antibodies.¹¹ In some centers only males may donate plasma-containing products. In our center we test female donors with a history of pregnancy for the presence of human leukocyte antigen (HLA) antibodies and defer those testing positive. The donor in this case had previously tested negative for HLA antibodies and was allowed to donate. In women with a history of pregnancy, also testing for the presence of platelet alloantibodies and deferring those testing positive may be a strategy; however, the risk-benefit ratio of this approach would need to be evaluated. Alternatively, more detailed screening regarding a history of known fetal loss may be warranted.

Although our patient did not suffer any long-term sequelae, the severe thrombocytopenia put her at risk for bleeding. In addition, she experienced symptoms consistent with TACO or mild TRALI (tachycardia, tachypnea and pulmonary edema), which required medical intervention. In light of these potentially serious consequences, it is prudent to examine the indications for transfusion.

Our patient was transfused with FFP to correct a mild, asymptomatic coagulopathy prior to liver biopsy. The coagulopathy was likely secondary to poor synthetic function of the liver from rejection of the transplanted organ. Evidence suggests that transfusion of FFP will not correct mild elevations of the PT.¹² In addition, a study of 200 patients undergoing percutaneous liver biopsy, the PT did not correlate with bleeding symptoms post-biopsy.¹³ Despite these data, empiric transfusion of FFP in patients with coagulopathy is still a

common practice. This case serves as a reminder that there are potential life-threatening consequences of transfusion.

In summary, transfusion-associated alloimmune thrombocytopenia is a rare but life-threatening entity. The diagnosis requires a high-degree of suspicion, and should be considered whenever a patient experiences an unexplained, sudden drop in the platelet count following transfusion of a plasma-containing product. The diagnosis can be confirmed by testing of the donor's serum for the presence of antiplatelet antibodies. Treatment is supportive with care provided for the symptoms of a transfusion reaction in addition to platelet transfusion for bleeding or severe thrombocytopenia until the antibody clears. Platelet counts should slowly rise over the next few days to a week without further intervention. By altering transfusion practices, possibly avoiding FFP transfusion for mild, asymptomatic coagulopathy, another occurrence similar to our case could be prevented. There may be rationale for revising the donor screening process to best prevent the transfusion of allosensitized blood products.

Acknowledgments

sources of funding: No source of funding contributed to this work.

The authors would like to thank Dr. Brian Curtis and the Platelet and Neutrophil Immunology Laboratory at the Blood Center of Wisconsin, Milwaukee, WI.

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Figure 1.
Platelet count over time after transfusion of FFP

Table I

Pre- and post- FFP transfusion laboratory values

	Pre-FFP transfusion	4 hours post-FFP transfusion
Platelet count (/μL)	178,000	2,000
Hemoglobin (g/dL)	11.5	11.6
White blood cell count (/μL)	5,800	5,700
Prothrombin time (sec)	16.3	15.7
Partial thromboplastin time (sec)	41.4	39.4
Platelet antibody screen	Negative	Negative