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Case Report

Unwashed Platelet-Specific Acute Pain Transfusion Reactions in One Patient from Three Unwashed Platelet Transfusions but Not from Eleven Washed Platelet Transfusions or Eight Unwashed Red Blood Cell Transfusions

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Abstract

Acute pain transfusion reactions (APTRs) are extremely rare and poorly understood reactions that are characterized by severe, otherwise unexplained pain from the transfusion of a blood product. Prior case studies have suggested it is associated with leukoreduced blood products, although there has been no consensus on the pathophysiology. We report a 4-year-old female patient with acute myeloid leukemia (AML) who had three acute pain transfusion reactions from transfusions of unwashed platelets. Various premedications and treatment plans were attempted, and the patient finally tolerated washed platelets. Most notably, the patient did not have any pain reactions from eleven transfusions of washed platelets or from eight transfusions of unwashed red blood cells, as her APTRs appeared to be specific to unwashed platelets only.

Introduction

An acute pain transfusion reaction (APTR) is a rarely reported reaction. The literature on the topic is scarce, and the pathophysiology is poorly understood. Prior case reports have characterized APTR as an acute severe pain involving the joints, back, and trunk seen immediately after initiation of transfusion. Additional features of this condition include tachycardia, dyspnea, and hypertension. The pain is occasionally disseminated or potentially only in the limb used for transfusion. Because it is a diagnosis of exclusion, other types of transfusion reactions including febrile non-hemolytic reaction (FNHTR), hemolytic transfusion reaction (HTR), transfusion-associated circulatory overload (TACO), transfusion-related acute lung injury (TRALI), and transfusion-associated sepsis (TAS) must be ruled out before clinical diagnosis may be made. APTR is usually a self-limited reaction and typically requires symptoms management only. So far, literature and case reports have not proposed an underlying mechanism for this reaction; however, cytokines and use of leukoreduction filters have been noted as associated causes. **[**1,2,3**]**

Our case patient is a 4-year-old female patient with a history of AML who suffered from an acute pain transfusion reaction solely from platelets. This case is unusual because when transfused with other types of blood products such as red blood cells, the patient did not have any acute pain episodes. The hospital course and treatment plan offer possible value to the already sparse literature on this topic.

Case

A 4-year-old female patient presented with relapsed acute myeloid leukemia. She had low platelets with bleeding along her gums, prompting the medical team to order a transfusion of platelets. Shortly after starting the platelet transfusion and increasing the transfusion rate, she developed pain in the chest, back, and bilateral lower extremities along with flushing and coughing. Vitals were stable except mild tachycardia with heart rate of 153. No fever, rash, SOB, facial swelling, swallowing difficulty, urine discoloration, nausea, vomiting, or other symptoms were reported.

Platelet transfusion was immediately paused, and the reaction stopped shortly after. Further investigation showed the platelets received by the patient was a partial unit with the other half being given to another patient without a reported transfusion reaction, decreasing the likelihood of a contaminated sample. Post-transfusion urinalysis was negative for hemoglobinuria. Visual hemolysis check of her post-transfusion plasma was negative, and DAT was negative. These findings ruled out a hemolytic transfusion reaction. Additionally, an allergic transfusion reaction, septic transfusion reaction, TACO, and TRALI were all deemed unlikely considering her lack of skin manifestations, otherwise normal vital signs, and absence of other symptoms. The plan for future transfusions included slowing the infusion rate, reducing the platelet volume, and premedicating with IV Tylenol and IV Benadryl. Interestingly, the patient did not have APTR with the transfusion of red blood cells during this episode or any of the following episodes. This led the clinicians to believe this was a unique case of APTR solely due to platelets.

About one month later, the patient needed another platelet transfusion, and the platelets were run at half rate (5ml/kg) with volume reduction. Benadryl was offered as a premedication to the patient's father for the patient, but he declined. The patient subsequently developed similar symptoms of extreme pain during the transfusion. She was crying, thrashing, and generally uncomfortable. The transfusion was immediately stopped, and the patient was given IV Tylenol with improvement. Her lungs were clear to auscultation bilaterally with no facial swelling, rash, or breathing changes. Her vitals were also stable. After stabilization, she subsequently tolerated the transfusion at half rate. Following the Tylenol infusion and secondary transfusion, the patient's pain had dissipated but wasn't gone, and she was discharged with routine primary follow up.

About 3 weeks later, the patient continued to have refractory acute undifferentiated leukemia and was started on various complex chemotherapy regimens. She required further platelet transfusions and was given Tylenol, Benadryl, and hydrocortisone for pre-medications.

She was also given 1mg morphine at the start of transfusion with an additional 0.5mg 15 minutes into the infusion. Despite this intervention, the patient continued to have an APTR. The subsequent transfusion, she was started on lidocaine infusion beginning 60 minutes prior to platelets and running for the duration of platelet transfusion, which alleviated some but not all the pain.

The next day, the decision was made to transfuse washed platelets as a trial. Despite the logistical challenges of washing platelets, the rationale was that this was worth a try because she kept having pain reactions despite significant lidocaine infusions and because very few other relatively safe options were available. She received 1 unit of washed platelets with Tylenol and morphine premedication and did not have an acute pain reaction.

As a result, washed platelets were subsequently used in future transfusions. She received a total of 11 washed platelet units over 4 weeks without any pain reactions. These transfusions were administered both with and without morphine premedication, thereby reducing the likelihood of a confounding analgesic masking the pain. Interestingly, over the course of the entire 16 weeks described above, the patient was transfused with 8 units of unwashed red blood cells and had no noticeable adverse effect or pain reaction during these transfusions. The patient was not transfused with any plasma or other blood products beyond those described above. No other infusions, medications, clinical states, donor factors, or patient factors were identified as present in her 3 APTRs and absent in her other transfusions. Thus, her acute pain transfusion reactions appeared to be associated solely with unwashed platelets.

Discussion

An acute pain transfusion reaction is rare complication of blood transfusions with sparse literature and research regarding its etiology. Prior studies and case reports of APTR are rare, but the few that are published describe symptoms succinctly in line with our case; however, our patient intriguingly has only had these pain episodes after the transfusion of platelets and not any other blood products. Orton et al. (2001), was a large retrospective study of 29,814 patients receiving blood transfusions. Transfusion reactions occurred in 146 patients, with 12 reports identified specifically as APTRs. This represented 8% of all transfusion reactions and .04% of all transfusions. In this study, all APTR cases experienced severe extremity, back, or chest pain, while some had symptoms of tachypnea, dyspnea, hypertension, chills, and tachycardia.**[**6**]** A study by Alvarado-Ramy et al. (2006) noted 29 patients had back pain during the

transfusion of red blood cells while one by Schonegevel et al. (2008) reported on two patients with severe pain to the lower back and hips, contributing more data to the qualities of this reaction.**[**4,7**]**

Although these rare findings have been recorded, a review of these case reports describing APTR provides no further analysis of the mechanism or possible treatment modalities for this reaction. Because APTR is a diagnosis of exclusion, prior reported cases were negative for hemolysis, infection, or other causes of acute reaction like our presented case. Some authors proposed a potential association between leukoreduced blood products and APTR, especially when using the Baxter® or HemaSure® filter. However, the increased use of leukoreduced blood products without a corresponding increase in APTRs weakens this association.**[**5**]**

Most prior cases of documented APTR have been in transfusions with red blood cells. Uniquely, our case is a 4-year-old patient who developed pain solely after each of 3 platelet transfusions. In attempting to find a prophylactic treatment, premeditations including Tylenol, Benadryl, and hydrocortisone failed to prevent the APTR. Additionally, infusion of morphine and lidocaine before and during the transfusion helped but did not completely resolve or prevent the symptoms. A solution was found when washed platelets were transfused without any pain symptoms. This may be a way to prevent platelet-specific-APTRs in other patients. Prior studies have not described details of treatments that were attempted for pain reactions. Thus, our report may help due to the details we provided. Additionally, because this patient appeared to have platelet-specific-APTR, our report may add to the scarce literature on the topic and may help describe this APTR subtype.

Conclusion

An APTR is a rare, transfusion-related adverse effect that can cause extreme pain in patients. This is unacceptable for its own sake and because it prevents completing necessary transfusions. We describe an unusual subtype of APTR that was associated solely with platelets and not red blood cells. Washing platelets appeared to prevent such reactions in this patient, as she had an APTR to each of 3 unwashed platelet transfusions (separated by a month between the first and second and then by 3 weeks between the second and third) but no reactions to 11 washed platelets and no reactions to 8 unwashed red blood cell transfusions during the same general time period.

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