Acute Pain Transfusion Reaction

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A 34-year-old woman with a diagnosis of hemophagocytic lymphohistocytosis (HLH) received a double umbilical cord blood transplantation following a myeloablative chemotherapy preparative regimen with busulfan and cyclophosphamide. HLH is a rare, potentially fatal hematologic disorder characterized by the overactivation of histocytes and T lymphocytes, leading to organ infiltration and acute illness. On day 25 post-transplantation, the patient required a platelet transfusion for a platelet count of 6,000 per ml (normal range = 150,000–450,000 per ml). The patient's blood type prior to the cord blood transplantation was B positive and, although both umbilical cord blood donors were O positive, the patient was still B positive per blood bank testing on that day. Although the recipient of an allogenic stem cell transplantation will eventually become the blood type of the donor, the time for this process to occur varies for each person. That process must be monitored by the blood bank for the purpose of cross-matching blood products to decrease hemolysis as much as possible. The patient was premedicated with the facility's standard for platelet transfusions: acetaminophen 650 mg and diphenhydramine 25 mg about 30 minutes prior to the platelet transfusion.

Baseline vital signs were heart rate, 108 bpm; blood pressure, 135/96; temperature, 97.2°F; respirations, 12; and O_2 saturation, 98%. The unit and patient identification was confirmed by a second RN for accuracy. The platelet transfusion was given through the patient's Port-a-Cath® via y-type, leukopoor-filtered tubing primed with 0.9% normal saline. An apheresed, leukocyte-reduced, cytomegalovirus (CMV)-negative, O-positive unit was transfused. Vital signs remained unremarkable throughout the 15-minute infusion. The patient was talkative and showed no visible signs or symptoms of a transfusion reaction.

About five minutes after transfusion completion, the patient called staff into her room and was visibly distressed, reporting excruciating pain in all of her joints, particularly the large joints of the hips and lower back. Erythema was noted in the face and neck. Vital signs were taken with blood pressure, 163/106; heart rate, 131 bpm; temperature, 97.9°F; and O_2 saturation, 97%. Blood pressure and heart rate remained consistently elevated during this 15-minute post-transfusion reaction and the patient remained afebrile. Meperidine 75 mg was given via IV push as well as a 1 mg IV bolus of hydromorphone. The patient was already receiving hydromorphone through a patient-controlled analgesia pump for severe mucositis at the time of the event. After about 15 minutes, the patient's vital signs returned to baseline and the severe, acute pain episode subsided, with complete resolution of lingering joint pain after several more hours. A complete post-transfusion analysis was conducted per hospital policy, beginning with bedside confirmation of correct product and patient identification. Blood samples and urine specimens were obtained. A direct antiglobulin test (DAT) also was performed showing 2+ reactivity. A positive DAT indicates that some degree of hemolysis of red blood cells has occurred and is measured on a range of minimally reactive to 4+ reactivity.

Reaction to Transfusion

The patient in the case study experienced what is known as an acute pain transfusion reaction (APTR). The current medical and nursing literature is limited regarding discussion of this type of transfusion reaction. APTR is rare, poorly understood, and can occur during or after the transfusion of blood products. The published reports on cases of APTR describe clinical manifestations consistent with those experienced by the patient in the case study. APTR is a diagnosis of exclusion, as other causes of blood transfusion reactions must be ruled out first based on negative laboratory analysis (Davenport, 2012). Although the positive DAT found in this case study is consistent with the minor hemolysis that likely occurred because of the ABO blood type mismatch of the transfused unit and patient, the pathology report and post-transfusion reaction analysis were otherwise negative.

Although APTRs are rarely documented, some studies have reported on this specific type of transfusion reaction. Orton et al. (2001) retrospectively studied 29,814 medical records of patients receiving blood transfusions in four large medical facilities. Transfusion reactions occurred in 146 patients, with 12 reports identified specifically as APTRs (representing 8% of all transfusion events). Of those 12 patients, all experienced severe chest, back, or proximal extremity pain. Other manifestations were tachypnea and/or dyspnea (n = 6), hypertension (n = 5), chills (n = 4), and one instance of tachycardia (Orton et al., 2001). Other authors who have published reports on this acute reaction describe similar manifestations. Alvarado-Ramy et al. (2006) evaluated 29 patients who experienced back pain during the transfusion of red blood cells. Schonegevel, McDonald, and Badami (2008) reported on two patients with acute and severe pain to the lower back and/or hips. One patient also experienced severe hypertension (blood pressure of 217/125) and another experienced dyspnea (Schonegevel et al., 2008).

- **Acute febrile reaction:** elevation in temperature by 2°F or more that occurs during or several hours after the transfusion; caused by cytokine-medicated reaction; prevented by leukocyte reduction and filtration
- **Acute hemolytic reaction:** from massive hemolysis after transfusion of ABO-incompatible red cells; life threatening; requires immediate emergent medical intervention
- **Acute pain transfusion reaction:** noted as severe pain soon after transfusion of blood product; most commonly pre-storage, leukocyte-reduced red blood cells; self-limited and requires only symptomatic management
- **Sepsis:** caused by transfusion of bacterially contaminated blood products; life threatening; requires prompt medical interventions
- **Transfusion-related acute lung injury:** caused by leukoagglutinins in transfused blood products with a possible increased incidence in patients with underlying lung injury; may be life threatening; difficult to prevent or predict

Figure 1. Acute Transfusion Reactions

Note. Based on information from Davenport, 2012; Wu et al., 2008.

A review of these case reports describing APTR reveals no understanding regarding the pathophysiology underlying this reaction. As with the patient in the case study, post-transfusion laboratory studies in these documented cases are negative for infectious processes, major hemolysis, or other obvious causes of acute transfusion reaction. Others also have reported negative post-transfusion laboratory findings and acknowledged the likelihood of an unidentified process causing acute back pain (Alvarado-Ramy et al., 2006; Schonegevel et al., 2008). The reaction appears to occur in patients receiving blood products with any number of underlying diagnoses including, but not limited to, hematologic malignancy, solid tumors, and liver disease, as well as patients in a postoperative setting (Davenport, 2012).

However, an association seems to exist between pre-storage leukocyte-reduced blood products and APTR. Some authors have suggested that certain brands of filters have specifically been associated with APTR. In the Orton et al. (2001) study, all red blood cell products that resulted in an APTR were leukocyte reduced using either a Baxter® or HemaSure® filter. Alvarado-Ramy et al. (2006) also suggested an association between certain leukocyte-reduction filters and APTR. All transfused units leading to an APTR in that multistate investigation were leukocyte reduced with a HemaSure® filter prior to storage (Alvarado-Ramy et al., 2006). The platelet transfusion that resulted in an APTR in the current article's case study was leukocyte reduced prior to storage by a COBE® LRS filtration system. However, the unit was leukocyte reduced at the time of collection and did not occur within the authors' facility. Therefore, which brand of filter was used in the leukoreduction process was unknown.

Davenport (2012) noted, however, that leukoreduction was becoming a mainstay in blood transfusion protocols at the same time case reports of APTR began to occur. This may have led to a coincidental increase in incidence as opposed to identifying a causative factor. Davenport (2012) further explained that cases have been reported of APTRs stemming from red blood cell transfusions filtered by leukoreduction systems not previously referenced in the published studies. In addition, cases of APTR have been reported from nonleukoreduced platelet units. Although hard to ignore the possibility of an association between pre-storage leukocyte-reduced blood products and APTR, additional investigational studies are needed for better understanding of the etiology of this acute, severe blood transfusion reaction.

Implications for Nursing Practice

Increasing awareness of APTRs is the first step in identification of this rare phenomenon. If an APTR or any acute transfusion reaction is suspected, the transfusion should be immediately stopped. When considering a diagnosis of APTR, the treating team must not overlook the possibility of a more severe, life-threatening transfusion reaction such as ABO hemolytic reaction or sepsis. Figure 1 lists the various types of transfusion reactions. ABO hemolytic reaction and sepsis are possibly fatal reactions that may present with pain, particularly to the lower back, mimicking the most common symptom of an APTR. Unlike an APTR, however, ABO hemolytic reaction and sepsis can cause hypotension and fever, and will subsequently have a positive laboratory workup (Wu, Mantha, & Snyder, 2008). Commonality between the initial manifestations of these reactions and APTR can make diagnosis more difficult but should not alter the acute medical care provided. Once established that the patient is not experiencing a life-threatening complication, the team may recognize the reaction as APTR and should begin initiating the appropriate care.

Treatment for APTRs should focus on supportive care and symptom control. Medical management has been described as nonspecific because of the initial ambiguity between APTRs and other more common transfusion reactions (Schonegevel et al., 2008). Therefore, emergent treatment has included medications that may otherwise be indicated for suspected allergic, septic, and ABO hemolytic

Clinical Highlights

Acute Pain Transfusion Reaction Overview

- Acute pain transfusion reaction (APTR) is a syndrome of acute, severe pain seen soon after a blood transfusion in the context of lack of other causes of a transfusion reaction.
- Signs and symptoms of APTR include severe pain involving joints, particularly in and around the back or trunk, and may include hypertension, tachycardia, and dyspnea.
- Some patients experience pain located only in the specific limb used for the infusion.
- Exact etiology is unknown, but a high association has been noted with pre-stored, leukocyte-reduced red blood cells with a potential for an increased concentration of cytokines.
- APTR is typically self-limited and requires treatment of symptoms with pain control, supplemental oxygen, and emotional support.

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reactions, including a combination of antihistamines, acetaminophen, beta-blockers, albuterol, and narcotics (Alvarado-Ramy et al., 2006; Orton et al., 2001). The patient presented in the case study received a combination of IV meperidine for rigors and IV hydromorphone for reported "10 of 10" pain. She reported pain relief and an overall decrease in symptom severity through these immediate interventions, but continued to experience mild pain throughout the afternoon.

Medication is not the only treatment for this acute event. At the onset of pain, patients are likely to be extremely anxious and alarmed. To help alleviate symptoms, the nurse should attempt to reassure the patient in a calm manner as well as offer any information available. The patient also should be reassured that the transfusion has been stopped and that treatment of symptoms has been initiated through IV medications as appropriate. If a patient is experiencing dyspnea, it would be appropriate to use supplemental oxygen. Facilitating slow, deep breathing with the patient also can help alleviate anxiety in the acute phase of this rare phenomenon.

Like most transfusion reactions, APTR is a rare event. Orton et al. (2001) reported an incidence rate of three cases in 10,000 red blood cell unit transfusions. APTR may actually occur at a higher rate than other more commonly recognized life-threatening transfusion reactions because it has not been frequently reported in the literature and clinicians may not be aware of this complication. This may be particularly true in the case of delayed manifestations of pain after the transfusion of a blood product. An important consideration is that APTR may cause different degrees of pain on a spectrum of severity. Less severe pain may decrease the chances that APTR will be recognized. An increase in awareness of this phenomenon is needed for recognition to take place at the time of the event or retrospectively through analysis of the event. Nurses can play a vital role in the identification of APTR as awareness is increased. Patient outcomes during this acute reaction also can be positively affected by the nurse's prompt interventions, including the initiation of supportive medications as well as psychosocial support.

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