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Case Report

Primary Hypotensive Reaction: A Case Report

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Abstract

Primary hypotensive reaction is a rare type of transfusion reaction caused by excess bradykinin in the blood product, which is typically not screened for during packed red blood cell preparation. Here, we describe a patient who experienced hypotension during blood transfusion that could not be attributed to other life-threatening reactions such as acute hemolytic reaction, anaphylaxis, transfusion-related acute lung injury, or sepsis. He had received several blood transfusions in his lifetime and had previously never experienced any adverse effects. This case report details a rare complication of blood transfusions and provides insight for providers who respond to suspected transfusion reactions.

Keywords: Hypotension; Transfusion; Bradykinin; ACE inhibitor

Case Presentation

A 67-year-old man presented to the hospital with chest pressure, abdominal pain, and lightheadedness after doing yardwork. His medical history included myocardial infarctions, coronary artery bypass graft, atrial fibrillation with defibrillator placement, Congestive Heart Failure (CHF), remote gastric cancer, gastric ulcers, gastroesophageal reflux disease, diabetes mellitus type 2 and hypertension. His medications included lisinopril, amlodipine, apixaban, aspirin, clopidogrel, digoxin, dofetilide, metoprolol, torsemide, spironolactone, atorvastatin, levothyroxine, insulin, tamsulosin, and pantoprazole. Initial concern for myocardial infarction was evaluated, however electrocardiogram showed no acute changes and troponins were negative for ischemia. His chest pressure resolved with nitroglycerin. He was seen by Cardiology who did not recommend further ischemic workup.

He continued to report abdominal pain, which had been occurring for the past 3 weeks and was associated with lightheadedness and vomiting. He endorsed melena and denied hematemesis. His hemoglobin and hematocrit were 6.3/25. The patient was consented for transfusion and two units of leukoreduced O+ packed Red Blood Cells (pRBC) were ordered. He reported being transfused several times during his lifetime and denied previous adverse effects. His blood pressure was 110/59 prior to transfusion.

Approximately thirty minutes into transfusion of the first unit, the primary medical team was called to assess the patient for a blood pressure of 88/58. The transfusion was stopped, EKG showed no acute changes, and blood glucose was normal. The patient reported feeling lightheaded and itchy but denied fever, shortness of breath, or throat swelling. He was not given fluids initially due to concern that fluids would exacerbate his anemia and lead to fluid overload in the setting of severe CHF. His systolic blood pressure spontaneously improved to 106 mmHg. His hypotension was attributed to symptomatic anemia secondary to ongoing GI bleed, and the transfusion was restarted. His pruritis resolved with diphenhydramine.

Twenty minutes later, the medical team was again called to assess the patient for a blood pressure of 86/48. His transfusion was again stopped. His systolic blood pressure dropped further to the 70's despite being placed in the supine position and receiving a bolus of 250cc normal saline. Transfusion reaction labs were obtained, specifically the direct antiglobulin test to detect incompatibility and urine to detect hemoglobinuria. He was transferred to the intensive care unit.

Upon arrival to the ICU the patient's systolic blood pressure improved to the 130's with complete resolution of his symptoms. His direct antiglobulin test was negative, and his urine did not show hemoglobinuria, ruling out acute hemolytic reaction. He tolerated a subsequent transfusion of a different blood product well without pre-medication. After review with the Transfusion Service Medical Director, it was determined that the patient had experienced a primary hypotensive reaction.

Discussion

Primary hypotensive reaction is a rare type of transfusion reaction defined as a decrease in systolic blood pressure by at least 30mmHg during transfusion that spontaneously resolves after the transfusion is stopped without symptoms to suggest other life-threatening transfusion reactions [1].

Excess bradykinin in the transfused blood product causes primary hypotensive reaction, and the risk of experiencing one is increased in patients taking Angiotensin-Converting Enzyme (ACE) inhibitors. Bradykinin is a polypeptide that causes vasodilation by activating bradykinin 2 receptors on vascular endothelium, leading to the release of nitric oxide and prostacyclin [2]. Bradykinin is a byproduct of Factor XII, which is activated by negative charges on tubing surfaces, blood storage bags, and leukoreduction filters [3]. ACE inactivates bradykinin via hydrolysis and ACE inhibitors increase both the amount of bradykinin and risk of primary hypotensive reaction. Currently, bradykinin is not measured during routine blood product preparation.

In addition to native B2 receptors, bradykinin also acts on cytokine-inducible bradykinin-1 (B1) receptors[3]. Patients with medical conditions that increase cytokines and upregulate B1 receptors are predisposed to primary hypotensive reactions. One proposed method of preventing hypotensive reactions is to "wash" the blood product prior to transfusion. Crews et al demonstrated in

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2014 that washing pRBC with normal saline prevented recurrence of primary hypotensive reaction in a patient with a history of end-stage liver disease admitted with sepsis. They concluded that this patient was predisposed to primary hypotensive reaction due to poor liver synthetic function of angiotensinogen and increased cytokines secondary to sepsis.

It is important to note that primary hypotensive reaction is a diagnosis of exclusion. The recommended approach to evaluating hypotension during transfusion is to first stop the transfusion, then evaluate for symptoms that indicate a life-threatening reaction. For example, fever may be caused by sepsis or acute hemolytic reaction. If bacterial contamination of the blood product is suspected, blood cultures should be obtained, and antibiotics administered. Fever accompanied by pain, bleeding, hemoglobinuria, and/or disseminated intravascular coagulation is concerning for acute hemolytic reaction. Intramuscular epinephrine should be given to patients who develop urticaria, pruritis, and/or throat swelling concerning for anaphylaxis [4]. These patients may have underlying IgA deficiency [5]. Respiratory distress may be secondary to sepsis, Transfusion-Associated Circulatory Overload (TACO), or Transfusion-Related Acute Lung Injury (TRALI). TACO occurs when excessive infusion of blood products leads to fluid overload and left ventricular failure. TRALI is characterized by pulmonary edema without circulatory overload and the mechanism most likely involves activation of recipient neutrophils by donor antibodies [6]. In all cases of suspected life-threatening reaction, the blood product should be sent to the blood bank for additional testing. For example, if there is concern for sepsis the blood product can be cultured for bacterial contaminants. In cases of suspected hemolytic reaction, the patient ID and unit ID should first be checked to ensure the patient did not receive the wrong blood product[5] and then the direct antiglobulin test should be conducted to assess for incompatibility.

Conclusion

Primary hypotensive reaction is a rare type of transfusion reaction characterized by hypotension that cannot be attributed to another life-threatening reaction such as sepsis, anaphylaxis, acute hemolytic reaction, TACO, or TRALI. The systolic blood pressure drops by at least 30 mmHg early in transfusion and resolves spontaneously after transfusion is stopped. Primary hypotensive reaction is caused by excess bradykinin in the blood product, and patients on ACE inhibitors or with conditions that increase cytokine production are at greater risk. This case study provides insight into an uncommon condition and a general approach to evaluating suspected transfusion reactions.

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