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Case Report

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Successful Use of Adjunctive Red Blood Cell Exchange Therapy for Treatment of an Acute Hemolytic Reaction After ABO-Incompatible Red Blood Cell Transfusion

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Abstract

An acute hemolytic transfusion reaction is a potentially fatal complication resulting from the transfusion of mismatched blood products. Symptoms vary from mild to severe depending on how much incompatible antigen was transfused and the nature of the recipient's antibodies. There is no consensus agreement of appropriate management other than discontinuing the transfusion and basic supportive methods including adjunctive pharmacologic agents. A 40-year-old male presented with a gunshot wound to the upper torso. During surgery, the O+ patient lost 1.3 L of blood and postoperatively was inadvertently given one unit of A+ packed red blood cells. The blood bank noticed the error and notified the floor within the hour. An acute hemolytic transfusion reaction had progressed to shock and disseminated intravascular coagulation within hours. The clinical course continued to decline despite a norepinephrine drip and a red blood cell exchange transfusion was implemented within 5 h of the mismatched transfusion. The patient's hematological parameters and clinical markers improved and he was eventually discharged in stable condition. An adjunctive red blood cell exchange transfusion may be useful when treating an ABO-incompatible acute hemolytic transfusion reaction if there has been a large volume mismatched transfusion and a poor clinical response to basic supportive methods.

Keywords: Acute hemolytic transfusion reaction; Red blood cell exchange therapy; ABO-incompatible red blood cell transfusion

Introduction

An acute hemolytic transfusion reaction (AHTR) is defined as a rapid destruction of red blood cells during a transfusion that occurs within 24 h of receipt [1]. AHTR can be either immune- or non-immune-mediated [2]. Immune-mediated AHTRs are caused by administration of red blood cells that are incompatible with the patient's anti-A, anti-B or, much less commonly, other red blood cell antibodies [2, 3]. The most common cause of immune AHTR is human error by improper identification of patient at time of administration [2, 3]. AHTR has a prevalence of 2.5 - 2.7 per 100,000 units transfused [2]. The presenting symptoms depend on how much incompatible blood was transfused, rate of administration and the nature of the recipient's antibodies. The symptoms can be abrupt in onset and usually develop within an hour of transfusion. Dyspnea, fever, chills, hematuria, facial flushing and severe pain especially in the lumbar area may occur. Although rare, AHTR can also result in lethal complications including hypotensive shock, disseminated intravascular coagulation, renal failure and death [3]. Red blood cell exchange therapy (RBCET) has been used to treat hemoglobinopathies such as sickle cell disease and thalassemia [4]. It has also been used to treat patients with malaria and babesiosis with heavy parasitemia [5]. To date, there are three previous reports [3, 6, 7] in the English-language literature of AHTR treated with adjunctive red blood cell exchange in an adult. In addition, there are two case reports [8, 9] in the Japanese literature where an RBCET was performed for AHTR. Nonetheless, the role of RBCET in an ABO-incompatible AHTR is not established and at this time there are no guidelines or recommendations from the American Society for Apheresis regarding the use of RBCET in patients with AHTR. We present a 40-year-old male who developed AHTR after receipt of misidentified red blood cells and was treated with adjunctive RBCET.

Case Report

A 40-year-old male with no past medical history was admitted as a trauma alert for a gunshot wound to the upper abdomen and chest. He arrived with a Glasgow coma score of 15 and was hemodynamically stable. A focused assessment with sonography was positive and the patient was taken emergently to the operating room (OR). An emergent exploratory laparotomy for repair of a ballistic gastric serosal tear, diagnostic pericardial window, complex hepatotrhaphy and liver debridement with argon beam coagulation, liver packing, repair of the dia-

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phragm and right chest tube placement was performed when he was found to have multiple ballistic perforations that injured the diaphragm, liver and gastric serosa. All of the identified tissue damage was repaired and the bleeding was surgically controlled. The estimated blood loss for the procedure was 1,300 mL. The patient was then transferred to the intensive care unit (ICU) still intubated with 5 cm H_2O positive end expiratory pressure (PEEP) and sedated as there were plans to return to the OR the following day for closure of the abdomen. He was transfused one unit of A+ packed red blood cells (PRBCs) after the procedure and serial labs were ordered (Supplementary Table 1, www.thejh.org). The initial hemoglobin on admission was 12.9 g/dL (12.6 - 16.7). Approximately 30 min after completion of the one unit of mismatched blood, the patient spiked a fever, developed hematuria and became hypotensive. The blood bank notified the floor that the patient had received a unit of A+ blood by mistake due to clerical error. Almost immediately, the patient was stabilized with intravenous (IV) hydrocortisone 100 mg, IV diphenhydramine 50 mg and intramuscular (IM) eipnephrine 1:1,000, 0.3 mL. As labs returned and his clinical deterioration became evident; he was given multiple liter IV fluid boluses without improvement. His labs revealed the direct Coombs test was positive (IgG interpretation), the haptoglobin was < 5.8 mg/dL (36.0 - 195.0) and lactate dehydrogenase was 1,193 U/L (140 - 271), suggesting a hemolytic reaction. His coagulation parameters were worsening and his hypotension eventually required a norepinephrine drip. His preoperative creatinine had been normal at 1.5 m/dL. At this point, it was determined that he was having an AHTR and it was decided to employ an urgent RBCET. The RBCET was started approximately 4.5 h after receiving the mismatched unit of PRBCs and consisted of five units of type O negative blood for a target hemoglobin goal of 9.0 g/dL (12.6 - 16.7). Over the next 2 days, he received five units of fresh frozen plasma (FFP), two units of PRBC and one unit of platelets. His creatinine peaked at 2.12 mg/dL 17 h after mismatched transfusion and his direct Coombs returned negative approximately 9 h after the RBCET. The norepinephrine was discontinued on day 2. Over the next 4 days, his clinical and lab parameters stabilized. He required no blood products after day 2. The patient's hospital course was prolonged due to surgical interventions to his abdomen, and was discharged in stable condition with no apparent long-term consequences from the transfusion or exchange.

Discussion

This case is important for three reasons. First, an ABO-incompatible AHTR is unusual and using RBCET as an adjunctive treatment is extremely rare. In fact, this case is only the fourth report in the English literature of an RBCET as a treatment for AHTR in an adult. Whether this is because RBCET has been tried and failed but simply not reported or the logistics to perform it are not widely available is uncertain. Nonetheless, the clinical recovery of a patient who suffered both a major trauma and a mismatched transfusion is compelling. The second important element to this case is the circumstances surrounding the RBCET and the timing. A case that is often referenced as an early RBCET for ABO-incompatible AHTR [10] actually describes the RBCET occurring 2 days after the mismatched transfusion in an asymptomatic patient. By definition this case does not represent an AHTR. The first genuine RBCET for ABO-incompatible AHTR was reported in 1949 [6] and described simply bleeding a patient and replacing his blood volume with properly matched blood within 16 h of the mismatched transfusion. The second case was in 1975 when Seager et al [7] reported a trauma case involving a 110-lb female who developed shock and disseminated intravascular coagulation (DIC) 1 h after an ABO mismatched transfusion. Within 2 h, the patient was under active hypothermia, hemodilution, cardiopulmonary bypass and was receiving an RBCET. The third report was in 2007 when Rose et al [3] described a massive transfusion of ABO-incompatible blood. An RBCET was performed within 11 h after the transfusion of the last incompatible unit. That RBCET was followed by a second RBCET 24 h later. Each RBCET consisted of eight units of type O Rh negative blood. The current report is the fourth English language case. These cases are difficult to compare since they differ over decades, technology, comorbidities and circumstances. One element they all have in common, however, is the AHTR secondary to an ABO mismatched transfusion was treated with an adjunctive RBCET. Also, they all survived a serious intravascular hemolytic event without reported sequelae. Theoretically, removing the offending intravascular substances as fast as possible can mitigate the effects of the hemolysis and reduce the likelihood of acute and long-term consequences [3, 6]. That is the very reasoning behind an urgent RBCET. Renal failure, DIC and systemic inflammatory response with shock are all known and expected complications of an ABO-incompatible AHTR [1], and, because these conditions have serious health implications, treatments that disrupt, delay or end the pathologic process are important and may be life-saving. The RBCET appears to be a method that safely and quickly ends the inflammatory cascade. In fact, the measureable effect of the adjunctive RBCET on our patient's organ system function is apparent. His renal involvement, DIC, pulmonary status and vitals stabilized and slowly improved over time after treatment. Most importantly, however, is the speed his direct antiglobulin IgG returned negative and his blood type resumed his natural O status. Admittedly, eventually the hemolytic process would end at some point in time without the RBCET, but if time exposed to the destructive elements of the AHR is important then rapid removal of the offending substance may be important to preserve organ function. The third important component to this case is the complicated traumatic injury and subsequent surgical insult resulting in significant blood loss. Naturally, the very fact that patients are receiving blood suggests an immediate comorbidity. In this and the previous three cases [3, 6, 7], the antecedent clinical insult has been blood loss from surgical or invasive trauma. Interpreting the postoperative and post-transfusion coagulation labs can be complicated even without a mismatched transfusion. Trends in coagulation factors, common blood parameters and vitals initially are similar between an AHTR and continued surgical bleeding or even sepsis. Consequently, rapid input from the blood bank is imperative to help differentiate. Complicating the events even more is the AHTR can result in DIC which can restart surgical bleeding. It is apparent that very quick identification of the mis-

take is important, preferably before the patient develops serious symptomatology. In two previous cases [3, 7], the mismatched transfusions were noted during the surgical procedure. In the current case, the blood bank notified the floor within 5 h.

In summary, classic AHTR is defined as an intravascular hemolytic event occurring within 24 h of a mismatched transfusion usually an ABO incompatibility. The cause is typically the result of a clerical error. Because AHTR is an emergency and can be potentially life-threatening, there should be no delay in treatment [11]. Current treatment guidelines of suspected transfusion reaction include immediately discontinuing infusion of blood product and maintaining venous access by IV saline (0.9% NaCl) [1, 11]. Supportive care using IV steroids, antihistamine and anti-pyretics may also be used, as was used in our patient [1]. Currently, the American Association of Blood Banks (AABB) does not have any recommendations regarding the use of RBCET as an option for use in AHTR. Other sources have identified RBCET as a possibility of treating acute, life-threatening AHTR unresponsive to other options [1]. The pathophysiology of its use includes removal of damaged red blood cell products of donor blood and intact red blood cells that are covered with antibodies and re-infusing cells that are compatible with the recipient that can simultaneously act as oxygen carriers [1]. Appropriate labeling and prevention remains the gold standard. Nonetheless, RBCET could be considered in cases of high-volume and severe reactions. Mortality rate of ABO-incompatible transfusions has been reported as 5.5% and 14% by two different sources [11]. Mortality approaches 17% in patients transfused > 50 mL of blood [11]. RBCET may be an important and life-saving option to consider in patients with AHTR after receiving ABO-incompatible blood.

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Conflict of Interest

The authors declare that they have no conflict of interest.

Informed Consent

Written informed consent was obtained from the patient for publication of this case report.

Authors Contributions

SM was the primary housestaff provider and wrote the initial drafts. JS was one of the attending physicians and contributed to writing the clinical case section. SC wrote the final manuscript versions, coordinated the flow of information between the different services and was corresponding author. JK was critical in obtaining, interpreting and adding the serial labs and vitals. NS coordinated the hematologic data and wrote elements of the treatment phase. MM provided the oversight, direction and guidance on the treatment elements to this case and wrote the section pertaining to new management. All coauthors made substantial contributions to the design of the case report and revisions. Also all approved of the versions and are agreeable to be accountable for all aspects of the work. All authors read and approved the final manuscript.

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