Massive transfusion associated with a hemolytic transfusion reaction: necessary precautions for prevention

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CASE REPORT: A 45-year-old male presented in severe hypovolemic shock after a thoracoabdominal gunshot wound. The massive transfusion protocol (MTP) was activated and the patient was taken to the operating room. His major injuries included liver, small bowel, and right common iliac vein. Hemorrhage was stopped and a damage control laparotomy was completed. He received a total of 113 blood products. During his postoperative course he received a group B blood transfusion on Hospital Days 2 and 7 based on incorrect blood typing late in his massive transfusion and repeat testing on Day 4.

RESULTS: He succumbed to multiple organ failure on Day 8. MTPs are standard in most trauma centers during which universal donor red blood cells are initially used. As hemorrhage is controlled, the patient undergoes a complete type and cross according to blood banking protocols. These typing results are used to continue transfusions once the MTP is no longer needed. In contacting other blood banks servicing Level I trauma centers, the policy of when to switch from universal donor blood to crossmatched blood is variable.

CONCLUSION: Our case illustrates a potential blood typing problem that had a disastrous outcome. We identified changes in policy that will make MTPs safer.

CASE REPORT

Acute ABO hemolytic transfusion reaction with fatality is a rare event.[1] We discuss the case of a fatal acute ABO hemolytic transfusion reaction after a massive transfusion resuscitation in a trauma patient and provide recommendations for improving the safety of massive transfusion protocols (MTPs).

A 45-year-old male sustained a gunshot wound to the left chest located in the midclavicular line approximately 4 cm inferior to the nipple. Prehospital care included two upper-extremity intravenous (IV) lines and an intraosseous line in the left tibia. The patient had a patent airway and complained of left chest pain and difficulty breathing. His heart rate was 120 beats/minute and his Glasgow Coma Scale was 14. The patient initially had 2+ femoral pulses and thready radial pulses but quickly required intubation for worsening mental status and markedly deteriorated femoral pulse examination. The MTP was activated, and a left chest tube was placed, which returned less than 100 mL blood.

His chest x-ray showed no pneumothorax or hemothorax. A focused assessment with sonography for trauma was negative for pericardial fluid and positive for abdominal fluid. He received IV antibiotics and was taken to the operating room (OR) with his fifth unit of red blood cells (RBCs) infusing.

On arrival in the OR the patient had pulseless electrical activity prompting 30 seconds of chest compressions and administration of 1 mg IV epinephrine, which restored a

ABBREVIATIONS: MTP = massive transfusion protocol; OR = operating room.

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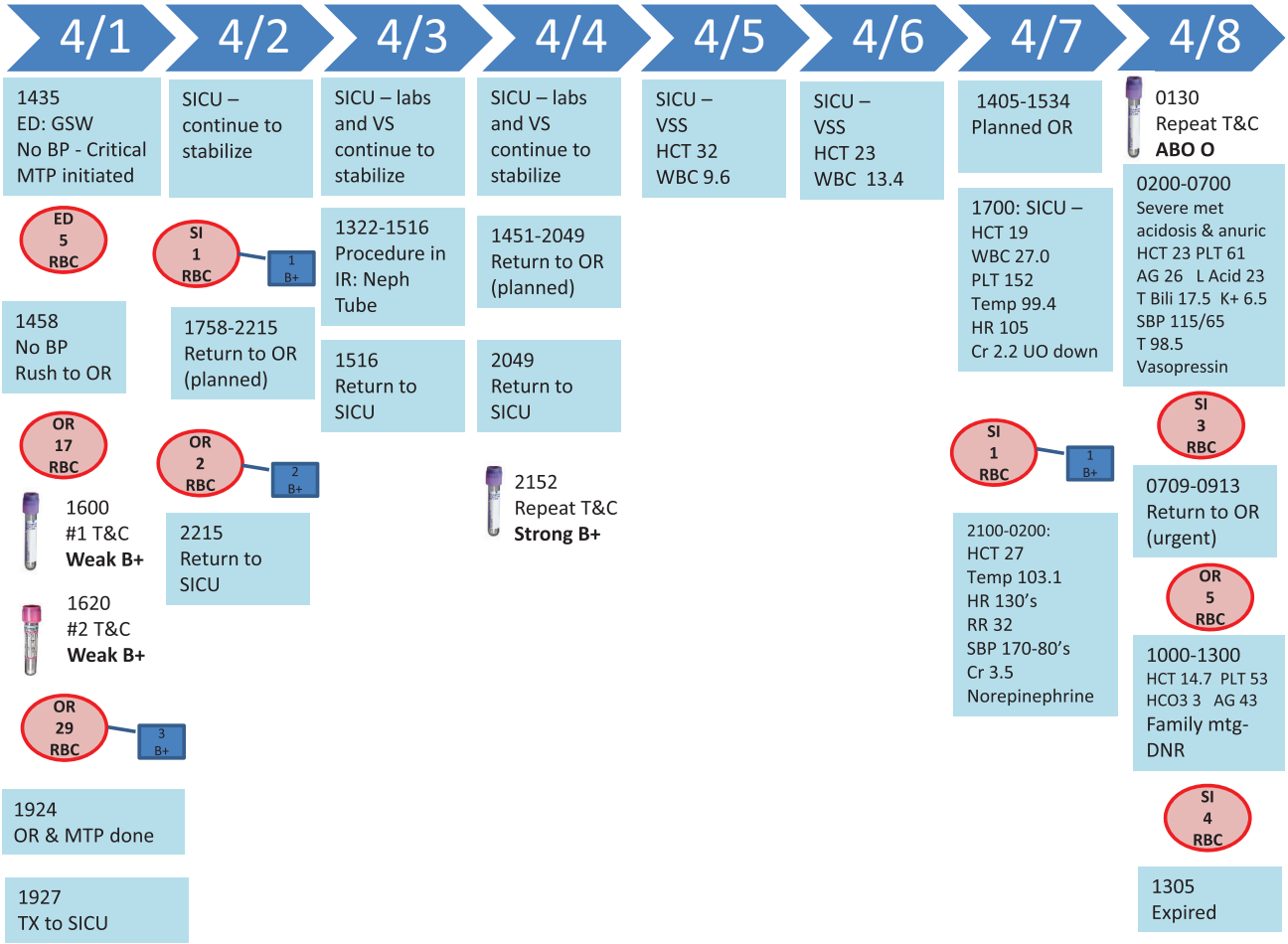

Fig. 1. Hospital course of trauma patient succumbing to ABO hemolytic transfusion reaction after MTP. BP = blood pressure; Cr = creatinine; ED = emergency department; GSW = gunshot wound; HR = heart rate; IR = interventional radiology; PLT = platelet count; RR = respiratory rate; SBP = systolic blood pressure; SICU = surgical intensive care unit; T&C = type and crossmatch; TX = transfer; UO = urine output; VS = vital signs; VSS = vital signs stable; WBC = white blood count. [Color figure can be viewed at wileyonlinelibrary.com]

perfusing rhythm. A laparotomy was performed identifying a nearly complete transection of the right common iliac vein at the junction of the inferior vena cava. This was ligated. Liver bleeding responded to sutures and packing. The two gastric and numerous small bowel holes were oversewn. A temporary vacuum closure of the abdomen was accomplished, at which time 113 blood product units had been given (57 RBC units, 43 fresh-frozen plasma [FFP] units, 5 cryoprecipitate units, and 8 apheresis platelet units). In the surgical intensive care unit he opened his eyes to voice and followed simple commands. He was taken back to the OR for reexploration on Hospital Day 2. Bowel continuity was established. He remained intubated, but responsive postoperatively.

Our MTP protocol calls for two blood samples to be sent as soon as possible for crossmatching. Our samples were sent 60 minutes after arriving in the OR and a second sample sent 20 minutes later. The initial sample was sent after 22 units of blood were transfused. The two samples were tested by protocol and tested weakly positive as group B. Subsequently, he was given 3 more units of group B blood. On Hospital Day 4 he was crossmatched again by protocol and tested as a strong B+.

On Day 7 he was transfused with 1 unit of B+ blood for a hematocrit (Hct) level of 19%, whereas on Day 6 the Hct was level 23%. Notably, the pretransfusion complete blood count on Day 7 could not determine a hemoglobin (Hb) level secondary to lipemia and icteria. Immediately after this transfusion the patient became acutely febrile and oliguric. He developed a severe acidosis prompting a return trip to the OR on Day 8 for suspected bleeding. No bleeding was found, but his omentum was ischemic and his liver was very pale. On this date his bilirubin was 17.5 mg/dL despite being normal on Day 3. Liver function tests were not serially followed as there was no routine clinical reason to do so. The patient progressed to liver failure and despite maximal support he died on Day 8 within 14 hours of his fever spike. The patient's overall hospital course is summarized in Fig. 1.

DISCUSSION

Increasingly rare, death from an ABO hemolytic transfusion reaction is required by the federal government to be reported to the Food and Drug Administration (FDA). From 2011 to 2016 there were only 16 deaths reported from ABO-incompatible transfusions.[1–6] These cases typically involved errors in labeling, transfusion to an incorrect patient by way of improper nonadherence to patient verification procedures, transfusion of ABO-incompatible plasma in plateletpheresis products, and incorrect manual entry of crossmatching results. Upon review of FDA archives, there has been only one ABO-incompatible transfusion fatality since 2005 associated with an MTP.[6]

Ours is a case of a fatal acute hemolytic transfusion reaction secondary to a blood group O patient receiving several units of group B blood. The following is the transfusion services evaluation. Hospital and transfusion service policy requires that a new patient to the hospital who may need blood be ABO and Rh typed by two different technologist using samples collected at two different times. Group O RBCs are given until both samples are confirmed ABO identical to one another. At that time the patient is switched to ABO group-specific RBCs. In this case the first sample was obtained after the patient had already received 22 units of group O RBCs. The sample was initially typed as indeterminate using our automated technology. When that occurs the technologist proceeds to using a manual, tube typing method. The initial sample's forward type was weak B+. Forward typing detects the presence of ABO antigens present on the patient's RBCs. A weak result is the least strong a result can be to be called a blood type. Accordingly, to confirm the forward type a back type is done. The back type detects the presence of ABO antibody in the patient's plasma. The forward type and the back type must match to correctly identify the ABO type. In this case the back type was 2+ strong against A cells and negative against B cells, confirming the patient's blood as ABO group B. A second sample was drawn from the patient 20 minutes after the first sample was obtained. A second technologist obtained identical results as the first technologist. The patient was listed in the transfusion services records as ABO group B. This result was arrived at using existing blood-banking policies. As the MTP was stopped, the patient received 3 units of group B RBCs and an additional 3 units of group B RBCs over the next 12 hours in the intensive care unit. These units were tolerated without any signs of an acute hemolytic transfusion reaction. On Day 4, a new sample was obtained for type and crossmatch and confirmed that the patient was ABO group B. The patient's Hb level decreased over the next several days and 1 unit of RBCs was given on Day 7 based on the crossmatch from Day 4. He deteriorated and new crossmatch on Day 8 confirmed that he was ABO group O alerting to the possibility of an ABO hemolytic transfusion reaction. His future transfusions were group O. After the patient's demise two separate already in-laboratory samples were obtained and sent for ABO typing by molecular methods. Both samples confirmed the patient to be ABO blood group O.

A retrospective review was done to explain our typing results that led to this fatal transfusion reaction. First, a sample should have been sent for type and crossmatch earlier in the MTP, however difficult the procedure or massive transfusion was. Second, both technologists followed transfusion service policy and obtained identical results. This raised our concern over our policy of allowing "weak" forward type results to be used for ABO interpretation. This policy was implemented many years ago to better service our marrow transplant program in detecting early RBC engraftment in ABO-nonidentical transplants. This worked without incident for many years; however, in retrospect, it was a flawed policy. We were unable to ascertain why each technologist detected small agglutinates when adding anti-B reagent to the patient's sample. The failure to detect anti-B in the patient's samples was likely due to the dilution of the anti-B from the volume of fluids and massive transfusion the patient had received before the care team procuring the initial two blood samples. Anti-A was detectable most likely because group O patients generally have higher anti-A titers than anti-B titers. On Day 4 the patient forward typed as a B, reflecting the 6 units of B RBCs transfused in the first 12 hours of hospitalization. Between Day 4 and Day 7 the patient's Hct level began to decrease. This likely indicates an unaccounted-for delayed hemolytic transfusion reaction with an increasing anti-B in the patient's plasma beginning to destroy the previously transfused B cells. After the transfusion of the unit of B RBCs on the evening of Day 7 the patient suffered a classic ABO hemolytic transfusion reaction with the development of hypotension, acute renal failure, anemia, and disseminated intravascular coagulation. A new sample obtained within 4 hours of the end of transfusion failed to detect any circulating B cells, indicating the complete hemolysis of all B RBCs. The acute hemolysis almost certainly is from a rapidly increasing anti-B titer between Day 4 and Day 7.

CONCLUSION

This case identified an opportunity for further improvement in our MTP and potentially other similar protocols at other institutions. Our review identified a number of areas where potential safety issues can occur, which are: 1) It is imperative to obtain the initial blood samples early in any patient's treatment course when the MTP is activated; 2) all MTP patients who are resuscitated with uncrossmatched group O blood will now continue to receive group O blood throughout their resuscitation; 3) plasma for resuscitation will be group A or AB until an appropriate sample is obtained for typing at which time the patient will be converted to group-specific plasma for transfusion; and 4) patients will not be switched

to type-specific RBCs until approved by the transfusion service attending. These changes in our MTP should avoid any temporary disturbances in massively transfused patient's ABO compatibility testing. We will continue to refine our guidelines and protocols as more data on the topic emerge.

CONFLICT OF INTEREST

The authors have disclosed no conflicts of interest.

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