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Intraoperative acute hematuria: Sole clue to mismatch transfusion

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Abstract:

Hemolytic transfusion reactions (HTRs) remain one of the dreaded complications of transfusion-related morbidity and mortality. Here, we describe the diagnosis and management of acute HTR following transfusion of ABO-incompatible packed red blood cell under general anesthesia which manifested solely as acute intraoperative hematuria. A 65-year-old, diabetic male was scheduled for emergency re-exploratory laparotomy in view of suspected anastomotic leak following subtotal gastrectomy. One unit of packed cell was transfused intraoperatively. Toward the end of surgery, hematuria was noted by the attending anesthesiologist, and the accidental bladder injury was ruled out by the surgeon. Transfusion of ABO-incompatible blood was spotted; direct Coombs test became positive. To mitigate the impact of incompatible blood, 1 L of 0.9% normal saline was administered. Mannitol 0.5 g/kg and furosemide 20 mg were administered every 8th hourly, and 1 ml/kg/h of urine output was targeted. Sodium bicarbonate (7.5%) 20 meq was administered intravenously to alkalinize the urine.

Keywords:

Hemolytic transfusion reactions, intraoperative acute hematuria, mismatch transfusion

Introduction

Hemolytic transfusion reactions (HTR) remain one of the dreaded complications of transfusion-related morbidity and mortality.^[1,2] HTR can be acute (AHTR) or delayed. Here, we describe the diagnosis and management of AHTR following transfusion of ABO-incompatible packed red blood cell (PRBC) under general anesthesia (GA) which manifested solely as acute intraoperative hematuria in the absence of other common manifestations.

Case Report

A 65-year-old, diabetic male was scheduled for emergency re-exploratory laparotomy in view of suspected anastomotic leak following subtotal gastrectomy. His vital signs were as follows: heart rate – 130/min and noninvasive

blood pressure – 100/60 mmHg. He was clinically pale with the hemoglobin (Hb) of 8.5 g/dl. Under GA, anastomotic site leak repair was done. Due to the preexisting anemia and intraoperative blood loss, one unit of PRBC (volume: 300 ml) was transfused after checking the blood compatibility form and the blood bag. Toward the end of surgery, hematuria was noted by the attending anesthesiologist. Accidental bladder injury was ruled out by discussing with the surgeon. The blood compatibility form was rechecked which had documented the patient's blood group and that of blood bag as A1 positive and compatible. As there was acute-onset hematuria without other signs of bleeding, a fresh blood sample was sent to blood bank again to check the blood group and compatibility which was found to be O positive, and direct Coombs test became positive. To mitigate the impact of incompatible blood, 1 l of 0.9% normal saline was administered. A central venous access was secured in the right internal jugular

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vein, and fluids were administered to maintain central venous pressure between 12 and 14 mmHg. Mannitol 0.5 g/kg and furosemide 20 mg were administered every 8th hourly, and 1 ml/kg/h of urine output was targeted. Sodium bicarbonate (7.5%) 20 meq was given intravenously to alkalinize the urine. Throughout the resuscitation, the patient's airway pressure remained normal, and arterial blood gas (ABG) did not reveal any metabolic acidosis. After the surgery, he was shifted to the intensive care unit (ICU), and elective ventilation was planned. Postoperative investigations showed elevated serum lactate dehydrogenase (LDH), unconjugated bilirubin, and decreased level of haptoglobin [Table 1]. Peripheral smear revealed schistocytes. Serum creatinine was elevated on the next day, and urine was persistently reddish in color for 2 days. Urine microscopic examination was suggestive of hemoglobinuria with very few red blood cells (RBCs); the supernatant fluid was transparent and reddish. Diuretics were continued till urine became clear. The sample which was sent in preoperative period was analyzed again and it was found to be A1 positive. Four patients' samples were sent for grouping and cross-matching in the preoperative period from the same ward. Mislabeling of the blood sample would have led to HTR. The probable cause for incompatible transfusion could be wrong blood in tube. There was no clinical evidence of bleeding, except hemoglobinuria despite deranged coagulation parameters. Hemoglobinuria persisted for 3 days after which urine became straw colored. The patient was hemodynamically stable throughout the ICU stay. He was extubated on the 3rd postoperative day (POD) and discharged from hospital on the 15th POD.

Discussion

The most common reason for transfusion of incompatible blood is human error.^[3] Patients with blood group A have preformed anti-B antibodies, group B have anti-A antibodies, group O have both, and group AB have neither.^[2] The antibodies present in the recipient adhere to donor RBCs, thereby activating the complement system leading to intravascular hemolysis.^[4] The extent of hemolysis depends on the amount of transfused RBCs, the titer of preformed antibodies, immunoglobulin class and subclass of the involved antibody, and avidity of antibody to bind with antigen.^[2] AHTR can present

as hypotension, tachycardia, increase in temperature, perspiration, flushing, rashes, bronchospasm, nausea, breathlessness, and palpitation, but in an anesthetized patient, it may present as hypotension, increase in airway pressure, hematuria, and diffuse bleeding due to disseminated intravascular coagulation (DIC) either in combination or alone.^[2,5] In this case, the presence of hematuria was the only clue that led to the suspicion of mismatch transfusion and further evaluation in that direction. Intravascular hemolysis leads to release of Hb which is bound by haptoglobin, hemopexin, and albumin; when the binding capacity of free Hb is exhausted, it will be secreted and reabsorbed in glomeruli; when the absorptive capacity by the glomeruli is exceeded, hemoglobinuria ensues.^[6] Acute kidney injury (AKI) following AHTR can be prevented by treating hypotension, maintaining intravascular volume status, thereby maintaining adequate renal perfusion and alkalization of urine. Soon after the suspicion of incompatible transfusion, the patient's blood sample and the remaining blood in donor blood bag should be sent to blood bank to repeat the cross-matching; blood sample should be sent for direct Coombs test, peripheral smear examination, LDH, haptoglobin, serum bilirubin (total, direct, and indirect), prothrombin time, activated partial thromboplastin time, blood urea nitrogen, serum creatinine, urine sample for microscopy, to detect hemoglobinuria, and sample for ABG.^[6]

The management of mismatch transfusion is primarily supportive. The ongoing transfusion should be stopped and crystalloids should be administered to maintain intravascular volume and perfusion to kidneys. Steroid suppresses the immune system, thereby reducing the release of inflammatory mediators. Diuretics should be administered to flush out hematin casts which can block the renal tubules. The acidic pH of urine in tubules converts free Hb from intravascular hemolysis into acid hematin. Alkalinization of urine with sodium bicarbonate increases the solubility of the acid hematin, thereby preventing AKI.^[7,8] Fresh frozen plasma (FFP), platelets can be considered if there is clinical evidence of bleeding or any invasive procedure is planned.^[6] Vasopressors and inotropic support may be needed to correct the hypotension. Mechanical ventilation can be considered for patients with pulmonary edema or severe metabolic acidosis. Hemodialysis or continuous

Table 1: Laboratory investigations following acute hemolytic transfusion reaction

Day/test	Hb (g %)	S. Cr (mg %)	Blood urea (mg %)	S. K ⁺ (meq/l)	PT/INR	Platelet	Total bilirubin/direct (mg %)	LDH (IU/l)	Haptoglobin (mg/dl)	FDP
POD 1	7.5	1.2	46	3.8	35.3/2.99	126,000	5.4/1.5	1202	20	
POD 2	6.8	1.0	30	3.5	22.2/1.76	120,000	9.3/1.3			Negative
POD 3	6.7	0.9	30	3.4	15/1.2	110,000	5.8/2.0	1090		

Hb=Hemoglobin, S. Cr=Serum creatinine, S. K⁺=Serum potassium, PT/INR=Prothrombin time/international normalized ratio, LDH=Lactate dehydrogenase, FDP=Fibrinogen degradation product, POD=Postoperative day

renal replacement therapy can be considered for AKI [Figure 1]. Plasmapheresis is an option to remove the circulating antibodies which can cease ongoing hemolysis.^[9] However, removing the plasma and exchanging with albumin during plasmapheresis can deplete the clotting factors which can aggravate DIC. Instead of albumin, FFP which belongs to AB group can be utilized for exchange in this patient, but due to unavailability of AB group FFP, plasmapheresis was deferred.

Performing blood grouping and typing as a routine investigation for all surgical patients who might need perioperative blood transfusion and documentation of the same on the first page of patient's case record should be made mandatory. The blood group should be documented in the preanesthetic assessment record after confirmation with the patient. Similarly, counter-checking the patient's details and blood group with the compatibility form before transfusion of blood products can prevent this never event.

Conclusion

AHTR can present as acute-onset hematuria in an anesthetized patient. A high index of suspicion and

vigilance for signs of transfusion reactions after taking aforementioned precautions are essential for early diagnosis and management of this life-threatening complication.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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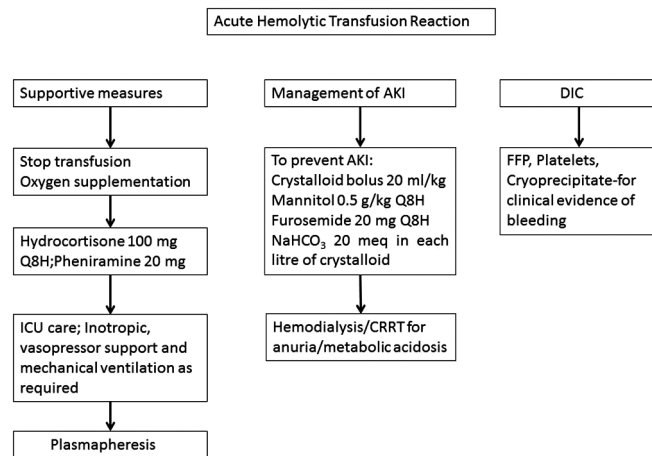


Figure 1: Treatment algorithm for acute hemolytic transfusion reaction.

ICU=Intensive care unit, AKI = Acute kidney injury, NaHCO₃ = Sodium bicarbonate, CRRT = Continuous renal replacement therapy, DIC = Disseminated intravascular coagulation, FFP = Fresh frozen plasma