

After the emergency: a case for the utilization of antibody registries and red cell exchange in the management of incompatible transfusions

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Disclosures

- None

Objectives

Through the lens of a representative case, we will...

- Describe the limitations of pre-transfusion testing and institutional records to prevent acute and delayed hemolytic transfusion reactions
- Discuss the benefits of integrated antibody registries and the barriers to widescale implementation
- Discuss the role of automated red cell exchange for the treatment of acute and delayed hemolytic transfusion reactions including treatment parameter considerations

Case presentation

- 77-year-old female
- CC: transfer for **subarachnoid/intraparenchymal hemorrhage** secondary to a fall with waning mental alertness and requiring **cerebral arteriogram**
- PMH: type 2 diabetes mellitus, **hemodialysis-dependent end-stage renal disease**, hypothyroidism, systemic hypertension, **coronary artery disease status post bypass grafting**, **aortic stenosis status post valve replacement**, **iron-deficiency anemia**, inflammatory arthritis
- Rx: chlorthalidone, clonidine, hydralazine, **325 mg aspirin daily**, trazadone, citalopram, levothyroxine

Case presentation

- Initial laboratory values:
 - Hemoglobin = 10.4 g/dL [12 – 15 g/dL]
 - Platelet count = 133 k/uL [150 – 400 k/uL]
 - Prothrombin time = 13.8 seconds [9.5 – 14.2 seconds]
 - INR = 1.2 [0.8 – 1.2]
 - Activated partial thromboplastin time = 31.5 seconds [24 – 36.5 seconds]
- Imaging:
 - Cerebral arteriogram = stable hemorrhage without evidence for aneurysm; no intervention indicated

Case presentation

- Days 1-2: Stable
- Day 3: progressive hypotension (mean arterial pressures 50-55 mmHg) requiring vasopressors
 - Hemoglobin = 7.1 g/dL
 - Lactate = 5.7 mmol/L [0.5 – 2 mmol/L]
 - PT/INR and aPTT = stable
 - Physical exam revealed firm right lower abdominal tenderness
 - Portable x-ray demonstrated asymmetric loss of bowel gas pattern
 - CT confirmed mixed retroperitoneal/intraperitoneal hemorrhage from right femoral pseudoaneurysmal rupture
 - Vascular repair and massive transfusion resuscitation

Blood loss evaluation

- Total blood volume = 3,856 mL (60 kg; 168 cm) at hematocrit 21.8 %
- Estimated blood loss = 3,000 mL (~0.8 TBVs)
- Blood transfused: ~0.4 TBVs auto + ~1.9 TBVs (~40% hematocrit excluding crystalloids)
 - 1,600 mL intraoperative salvage autotransfusion
 - 10 units uncrossmatched O(+) pRBCs
 - 10 units thawed plasma
 - 3 units apheresis platelets
 - 10 units cryoprecipitate
- Thromboelastography = single abnormal result of 35.4 mm maximum amplitude [>49.9 mm]

“Pre-transfusion” testing

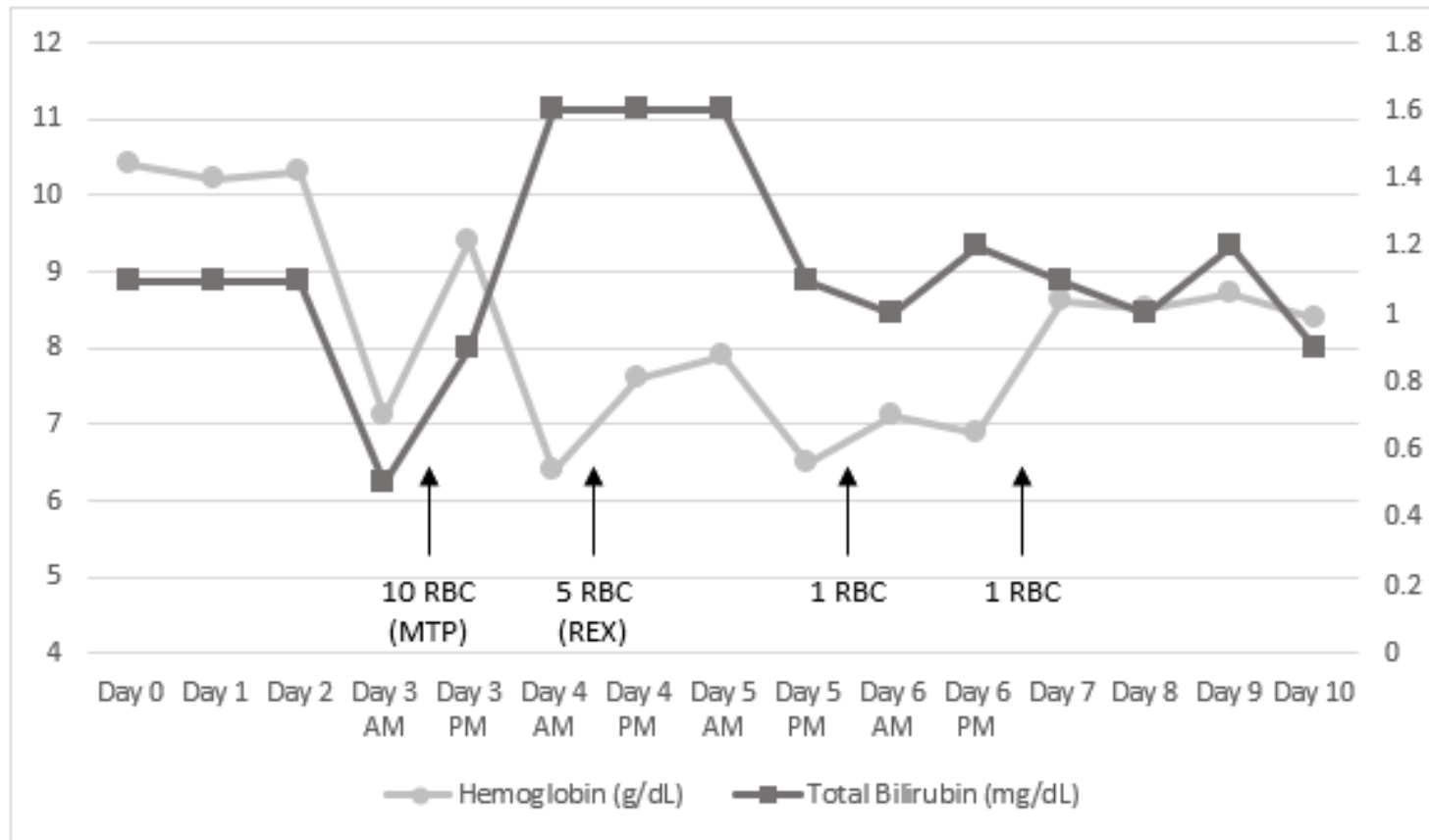
- Pre-transfusion sample received mid-MTP preparation
 - Type = A(+)
 - Antibody screen = inconclusive due to failed control (gel column agglutination; 2 cell phenotypes)
 - Registry search (expected prevalence) = historical anti-E (~20%), anti-Fya (~50%*), anti-Jka (~80%)
- Clinical teams contacted and antigen-negative units ordered
- Additional testing:
 - Repeat antibody testing = DAT IgG/Complement positive → eluate containing all 3 antibodies
 - Retrospective crossmatches = 10/10 incompatible (in vitro reactivity 1-3+)
 - Incompatible unit antigen typing:

Antigen	Packed red blood cell unit									
	1	2	3	4	5	6	7	8	9	10
E	+	-	-	+	-	-	-	-	-	-
<u>Fy(a)</u>	-	-	-	+	+	-	+	-	-	+
<u>Jk(a)</u>	-	+	+	+	-	+	+	+	+	+

Case presentation cont.

- Day 4: intubated; hemodynamically stable with titrated vasopressors
 - Hemoglobin = 6.4 g/dL
 - Total bilirubin = 1.6 mg/dL [0.3-1.2 mg/dL]
 - Haptoglobin = <30 mg/dL [16-200 mg/dL]
 - Automated red cell exchange: 5 units available → goal Hct 21 %; FCR 30 %
- Day 5: total bilirubin normalizes
- Day 6: haptoglobin normalizes

Hemolysis and Transfusion



Case presentation cont.

- Day 9: extubation
- Day 10: DAT and eluate remain positive
- Day 14: transfer out of ICU
- Day 23: discharge without need for transfusion since day 7
- No repeat admission for 6 months

Context/limitations

- One in every 9-10 inpatient encounters involve RBC transfusion
Karafin MS, et al., National Heart, Lung, and Blood Institute Recipient Epidemiology and Donor Evaluation Study-III (REDS-III). Demographic and epidemiologic characterization of transfusion recipients from four US regions: evidence from the REDS-III recipient database. *Transfusion*. 2017 Dec;57(12):2903-13.
- One in every 3 alloantibodies will be detected by routine testing (sensitivity, evanescence)
Tormey CA, Hendrickson JE. Transfusion-related red blood cell antibodies: induction and consequences. *Blood*. 2019;133:1821-30
- Testing is not always possible (emergent release, no sample obtained)
- Patient history is often incomplete (patient knowledge/memory, multi-institution care)
- In vitro reactivity does not equal in vivo activity (inaccurate semi-quantification of risk)

Antibody (+) registries

- They have been shown to be effective, nationally and regionally
 - van Gammeren AJ, et al. A national Transfusion Register of Irregular Antibodies and Cross (X)-match Problems: TRIX, a 10-year analysis. *Transfusion*. 2019 Aug;59(8):2559-66.
 - Mathur G, Wilkinson MB, Island ER, Menitove JE, Tilzer L. A case for a national registry of red blood cell antibodies. *Vox Sang*. 2022;117:738-40.
- There are significant barriers (LIS communication, coding/terminology, cost, etc.)
- There are efforts underway: <https://www.alloantibody.org/#about>

Red cell exchange for incompatibility

- ABO incompatibility

Wiener AS, Katz L. Hemolytic reaction caused by massive transfusion of incompatible blood, treated successfully by exchange transfusion. *Exp Med Surg.* **1950** May-Nov;8(2-4):390-401.

- Non-ABO incompatibility

Irani MS, Karafin MS, Ernster L. Red cell exchange to mitigate a **delayed** hemolytic transfusion reaction in a patient transfused with incompatible red blood cells. *J Clin Apher.* 2017;32: 59-61.

Tormey CA, Stack G. Limiting the extent of a **delayed** hemolytic transfusion reaction with automated red blood cell exchange. *Arch Pathol Lab Med.* 2013;137:861-4.

- Alternatives used (e.g. for patients with known antibodies to high-incidence antigens)

- Steroids, IVIG, and rituximab conditionally recommended based on case reports

Chou ST, et al. American Society of Hematology 2020 guidelines for sickle cell disease: transfusion support. *Blood Adv.* 2020;4: 327-55.

- No prospective comparisons for management decisions (cost, availability, side effects, etc.)

Questions or comments?

Thank you for your time!

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