A rare transfusion reaction as the cause of thrombocytopenia in a young woman with sickle cell disease

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INTRODUCTION

- The differential for acute thrombocytopenia in hospitalized patients is broad.
- Two rare causes include post-transfusion purpura (PTP) and passive transfer of anti-platelet antibodies.

CLINICAL COURSE

HPI:
- 30 year-old G1 P[1-0-0-1] woman with sickle cell disease (HbSS)
- Admitted for acute vaso-occlusive pain crisis

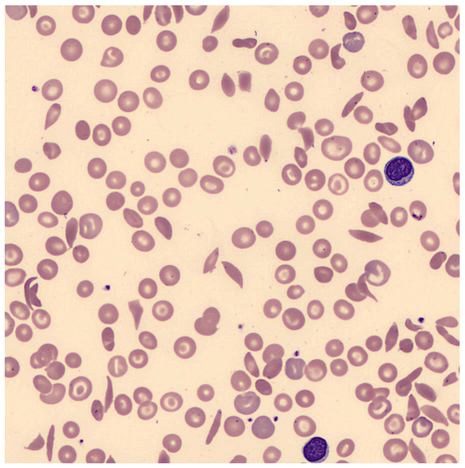
Initial Labs:
- Hgb 8.2 g/dL and Platelets 182,000/mL (Stable from baseline)

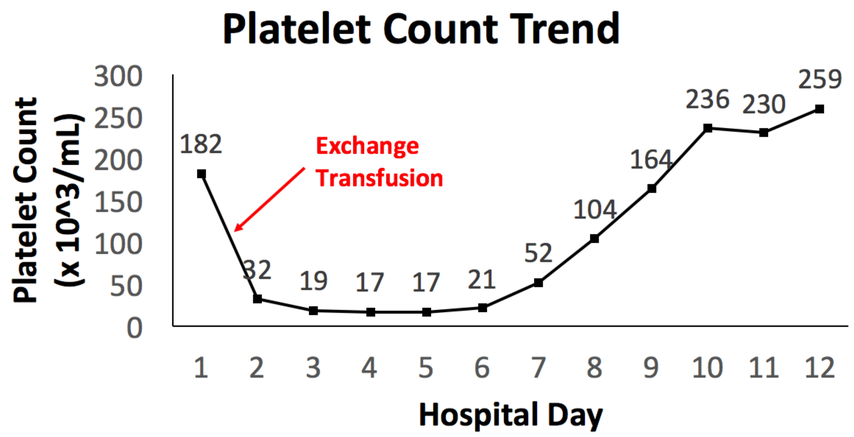
Day 1:
- Started on Ceftriaxone and IV fluids

Day 2:
- Developed fever, tachycardia, hypoxemia, and chest pain
- Worsening bilateral ground glass opacities on Chest XR
- Ceftriaxone transitioned to Piperacillin-Tazobactam
- Transferred to MICU for acute chest syndrome
- **Received 1U pRBC via simple transfusion**
- **Underwent red cell exchange transfusion of 8U pRBC**
- **POST-TRANSFUSION- Platelets 32,000/mL**

Day 3:
- Immature Platelet Fraction: 19.5%
- INR: 1.44
- Fibrinogen: 480 mg/dL
- Platelet Factor 4 ELISA: negative
- PTP Assay:
  Negative: Anti-HPA-1, 2, 3, 5, 15 Antibodies
  Positive: HPA-1a/1b, HPA-2a/2a, HPA-3a/3b, HPA-4a/4a, HPA-5a/5a, HPA-6a/6a, HPA-9a/9a, and HPA-15a/15a Platelet Antigens

Day 12:
- **DISCHARGE - Platelets 259,000/mL (Spontaneous recovery)**





DIFFERENTIAL DIAGNOSIS of Acute Thrombocytopenia in Critically Ill Patients

DIAGNOSIS	ONSET	SEVERITY	RISK FACTORS	DIAGNOSIS
Sepsis	Variable	Variable	Bacteremia, Fungemia	Clinical Diagnosis
Disseminated Intravascular Coagulation	Variable	Variable	Sepsis, Malignancy	High PT and aPTT Low Fibrinogen
Drug-Induced Immune Thrombocytopenia	Variable 1-14 days post-drug exposure	< 100,000	Drug induced: Penicillins, Cephalosporins, Linezolid, Vancomycin, Phenytoin, Valproate	Drug-Dependent Anti-Platelet Antibodies
Thrombotic Thrombocytopenic Purpura	Variable	20,000 – 50,000	Female sex, African American	Hemolysis (Low haptoglobin, High indirect bilirubin, High LDH), ADAMTS13 activity <10%
Hemolytic Uremic Syndrome	Variable	20,000 – 50,000	Complement/coagulation mutations Infection: Shiga-toxin producing E. coli, Strep. pneumoniae	Hemolysis (Low haptoglobin, High indirect bilirubin, High LDH), AKI
Heparin Induced Thrombocytopenia	5-10 days after heparin exposure	≥ 50% drop	Exposure to unfractionated heparin or low molecular weight heparin	Platelet Factor 4 ELISA Serotonin Release Assay
Post-Transfusion Purpura	5-10 days after transfusion	< 20,000	Female sex, Multiparity, Transfusion history	Positive Anti-HPA-1a Antibody Negative HPA-1a Platelets
***Passive Transfer of Anti-Platelet Antibodies**	Within hours of transfusion	< 20,000	DONOR - Female sex, Multiparity, Transfusion history	DONOR – Presence of Anti-Platelet Antibodies

DISCUSSION

- **Pathophysiology of PTP:** 1)Initial exposure to platelet antigen, usually during pregnancy or prior transfusion, ultimately leading to production of anti-platelet antibodies. 2) When re-exposed to the foreign platelet antigen, these antibodies cause destruction of both the transfused platelets and patient's own antigen-negative platelets.
- **Diagnosis of PTP:** Confirmed with serological testing showing the presence of anti-platelet allo-antibodies and the absence of the corresponding antigen on the individual's own platelets.
- **Treatment for PTP:** High-dose intravenous immunoglobulin (IVIG), usually for 5 days.
- Though a diagnosis of typical PTP was given in this case, the patient's negative serology and platelet drop within hours of transfusion makes the subtype of PTP involving passive transfer of anti-platelet antibody more likely. Confirmation of passive allo-antibody transfer requires testing donor blood for anti-platelet antibodies.

(1) In critically ill patients, it is important to keep a broad differential when considering the cause of acute thrombocytopenia.

(2) Post-transfusion purpura (PTP) should be considered in the differential for any patient with acute onset of thrombocytopenia after a blood transfusion.

REFERENCES

1. Ali N, Auerbach HE. New-onset acute thrombocytopenia in hospitalized patients: pathophysiology and diagnostic approach. Journal of Community Hospital Internal Medicine Perspectives. 2017; 7(3):157-167
2. Greinacher A and Selleng K. Thrombocytopenia in the Intensive Care Unit Patient. Hematology. 2010; 135-143.
3. McCrae KR, Herman JH. Posttransfusion purpura: two unusual cases and a literature review. American Journal of Hematology. 1996; 52:205
4. Mueller-Eckhardt C: Posttransfusion purpura. British Journal of Hematology. 1986; 64:4 I9-424.
5. Pavenski K, Webert KE, Goldman M. Conseq uences of transfusion of platelet antibody: a case report and literature review. Transfusion. 2008; 48(9):1981–1989.
6. Vogelsang G, Kickler TS, Bell WR. Post-transfusion purpura: a report of five patients and a review of the pathogenesis and management. American Journal of Hematology. 1986; 21:259.