

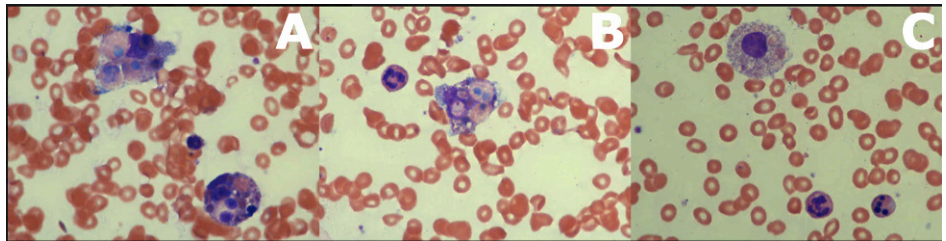
# Post-Transfusion Hemophagocytosis Without Evidence of Hemophagocytic Lymphohistiocytosis (HLH)

MATTHEW J. HADFIELD, DO; CHARLES J. MILROD, MD; ANDREW HSU, MD; NANCY FREEMAN, MD

A 68-year-old male with atrial fibrillation on anticoagulation, coronary artery disease (CAD) status post bypass surgery, chronic kidney disease, alcohol use disorder, type II diabetes, and intermittent gastrointestinal bleeding for which an outpatient work-up was ongoing was admitted for acute on chronic anemia with a hemoglobin of 6.6 g/dL (baseline 10.0 g/dL) and hypotension. Initial work-up revealed positive fecal occult blood testing. He was transfused one unit of packed red blood cells with an increase in hemoglobin to 7.2 g/dL. Three days following his initial transfusion he developed a leukocytosis to 17,400 k/mm, prompting a peripheral smear which revealed mild rouleaux formation and significant (29% of WBC) hemophagocytosis of red blood cells (RBC), polymorphonuclear leukocytes (PMN), and platelets, with necrobiosis/pyknosis of WBC (11%). (See **Figure 1.**) Review of smears pre-transfusion and days 1 and 2 post-transfusion were largely unremarkable with mild anisocytosis, poikilocytosis, elliptocytes, and burr cells. A repeat CBC 12 and 24 hours after the elevated WBC revealed a normal WBC count and differential. A repeat smear performed at both time points was largely unremarkable. Physical exam revealed stable and known splenomegaly but otherwise he did not meet other criteria for hemophagocytic lymphohistiocytosis (HLH) with normal triglycerides, low ferritin level, no other cytopenias, and no fever.

Removal of senescent RBCs by macrophages is not completely understood. Aged, transfused RBCs undergo phagocytosis to a greater extent when compared to fresh transfused RBCs, primarily by macrophages of the spleen and marrow. Rarely, transfusion with senescent RBCs have been reported to show peripheral blood hemophagocytosis.<sup>1</sup> In this case the RBCs were donated only one week prior to the transfusion. Thus, he appeared to have unexplainable, asymptomatic, transient hemophagocytosis without significant clinical consequences. Given the delayed onset of hemophagocytosis this was felt not to be secondary to an effect from the transfused blood. There have been previous reports of hemophagocytosis noted on bone marrow biopsy

**Figure 1:** (A) Hemophagocytosis of red blood cells (RBC), (B) polymorphonuclear leukocytes (PMN), and platelets, with (C) necrobiosis/pyknosis of WBCs.



without clinical evidence of HLH.<sup>2</sup> To our knowledge this is the first reported case of hemophagocytosis by neutrophils in the peripheral blood with no clear evidence of HLH.

## References

- Hess JR. "Red cell changes during storage." *Transfusion and Apheresis Science* 43.1 (2010): 51-59.
- McGinnis E, Medvedev N, Richards MJ, Chen LYC, Wong MP. Post-Transfusion Hemophagocytosis Without Hemophagocytic Lymphohistiocytosis. *Mayo Clin Proc Innov Qual Outcomes*. 2019 Oct 16;3(4):517-522. doi: 10.1016/j.mayocp.iqo.2019.07.001. PMID: 31993572; PMCID: PMC6978597.

## Authors

Matthew J. Hadfield, DO, Division of Hematology/Oncology, Warren Alpert Medical School of Brown University, Providence, RI.

Charles J. Milrod, MD, Division of Hematology/Oncology, Warren Alpert Medical School of Brown University, Providence, RI.

Andrew Hsu, MD, Division of Hematology/Oncology, Department of Medicine, Warren Alpert Medical School of Brown University, Providence, RI.

Nancy Freeman, MD, Division of Hematology/Oncology, Department of Medicine, Warren Alpert Medical School of Brown University; Providence Veterans Affairs Medical Center, Providence, RI.

## Disclosures

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## Correspondence

Andrew Hsu, MD  
593 Eddy Street, Providence, RI 02903  
401-444-2330  
andrew\_hsu1@brown.edu