Received: 8 March 2017 | Revised: 17 March 2017 | Accepted: 18 March 2017

DOI: 10.1002/jca.21540

LETTER TO THE EDITOR

WILEY Journal of Clinical Apheresis ASFA

Brisk clinical response to erythrocytapheresis in a G6PD-deficient patient with rasburicase-induced methemoglobinemia

Correspondence
Laura Cooling MD, MS, 2F225 UH-Blood Bank, 1500 E Medical Cntr Drive, Ann Arbor, Michigan, United States.
Email: lcooling@med.umich.edu

Dear Editor,

We read with interest the recent report by Montgomery and Booth, who described a case of methemoglobinemia in a 50-year-old, G6PD-deficient African American man with newly diagnosed T-cell lymphoblastic leukemia being treated with rasburicase for tumor lysis syndrome.[1] Due to ongoing hemolysis and refractory hypoxia, the authors performed a one blood volume erythrocytapheresis with a 45% decrease in methemoglobin (14.6%–8%). Surprisingly, the patient continued to be hypoxic with subjective dyspnea, bilateral pleural effusions, and mildly elevated methemoglobin levels (7.5–11%) for 36 h post-exchange. We would like to share our experience in a nearly identical patient several years ago, in whom we observed an immediate improvement in symptoms following erythrocytapheresis.

The patient was a 64 kg, 15-year-old African-American male with a 2-week history of fever, Bell's palsy, lymphadenopathy, nausea, and abdominal pain due to new T-cell lymphoblastic leukemia. His initial laboratories showed a mildly elevated WBC count (11.6 K/μL, range 13.7–17) with 40% circulating blasts, anemia (hemoglobin 11.4 g/dL), elevated lactate dehydrogenase ([LDH] 8375 IU/L, range 120–240 IU/L), hyperuricemia (29.5 mg/dL, range 3.5–7.8), and acute renal failure (creatinine 4.8 mg/dL, range, 8–20). While in the emergency room, he received 6 mg rasburicase for tumor lysis syndrome. Within 3 h of receiving rasburicase, he became hypoxic with O_2 saturation 70-80% despite escalating O_2 supplementation, accompanied by falling hemoglobin and methemoglobinemia (16%, range 0–1.5%). The patient was transfused 1 unit RBC and given a 25% test dose of methylene blue with no clinical improvement, worsening anemia, tachypnea (21–27 breaths/minute), and ongoing methemoglobinemia. Within 12 h of admission, the patient required intubation with O_2 saturations = 60% on 100% FiO_2, methemoglobin = 23%, lactate = 5 mmol/L (range, 0.4–2.2), hemoglobin = 7.9 g/dL, LDH = 12,699 IU/L, and acidosis (pH = 7.2). The patient subsequently underwent emergent erythrocytapheresis for methemoglobinemia and presumed G6PD-deficiency. The procedure was performed on a COBE Spectra at a whole blood: anticoagulant ratio of 7:1, 30% fraction cell remaining, an end hematocrit of 30%, and 8 units group O RBC (2693 mL) for replacement. The patient had a brisk clinical response to erythrocytapheresis with O_2 saturations >90% by the end of the procedure. He was extubated approximately 4 h post-procedure with a methemoglobin = 5% and O_2 saturation = 95% on 2 L supplemental oxygen. By day 3, the patient had normal O_2 saturation on room air and a methemoglobin = 2.3%. Subsequent testing confirmed that the patient was G6PD-deficient.

This is the fifth report of refractory methemoglobinemia treated by either whole-blood exchange or erythrocytapheresis,[1–4] and the third case following rasburicase administration in G6PD-deficient patients.[1,2] Like carbon monoxide poisoning, methemoglobinemia causes a left-shift in the O_2 dissociation curve, leading to a progressive and refractory hypoxia that is exacerbated and amplified in the setting of anemia.[5] Patients with symptomatic methemoglobinemia are typically treated with supplemental oxygen, RBC transfusion, and methylene blue, which helps restore glutathione levels. In G6PD-deficient patients, however, methylene blue can independently precipitate hemolysis and methemoglobinemia. This case shows a prompt improvement in oxygenation with erythrocytapheresis in the setting of methemoglobinemia and G6PD-deficiency,[2,4] in whom methylene blue is contra-indicated.

Laura Cooling
Department of Pathology, University of Michigan
Ann Arbor, Michigan

REFERENCES

[1] Montgomery KW, Booth GS. A perfect storm: tumor lysis syndrome with rasburicase-induced methemoglobinemia. *J Clin Apher.* 2017;32:62–63.

[2] Bhat P, Sisler I, Collier AB. Exchange transfusion as treatment for rasburicase-induced methemoglobinemia in a glucose-6-phoshate dehydrogenase deficient patient. *Pediatr Blood Cancer.* 2008;51:568.

[3] Golden PJ, Weinstein R. Treatment of high-risk, refractory acquired methemoglobinemia with automated red blood cell exchange. *J Clin Apher.* 1998;13:28–31.

[4] Dasararaju R, Adamski J. Transfusion medicine illustrated: an unusual case of near-fatal hemolytic anemia treated with erthryocytapheresis and therapeutic plasma exchange. *Transfusion.* 2015; 475–444.

[5] Wright RO, Lewander WJ, Woolf AD. Methemoglobinemia: etiology, pharmacology and clinical management. *Ann Emerg Med.* 1999;34:646–656.