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A Rare Case of Acute Hemolysis After Rasburicase Infusion

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Abstract

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is a genetic X-linked recessive disorder that results from mutations in the *G6PD* gene, which provides instructions for manufacturing the G6PD enzyme. G6PD deficiency primarily impacts red blood cells. This deficiency can result in hemolytic anemia (HA), in which rapid destruction of red blood cells occurs due to the vulnerability of erythrocytes to reactive oxygen species. It is most commonly found in males and affects 1 in 10 Black males in the United States. Persons with G6PD deficiency may exhibit symptoms such as pallor, jaundice, dark urine, fatigue, tachycardia, shortness of breath, and splenomegaly. Exposure to certain medications such as rasburicase, sulfonamides, nitrofurantoin, antimalarials, dapsone, chloramphenicol, high-dose aspirin, methylene blue, and phenazopyridine may trigger a hemolytic crisis in those with G6PD deficiency. Tests used in the diagnosis of HA include the Coombs test, haptoglobin, complete blood count, urinalysis, lactate dehydrogenase, bone marrow tests, and a peripheral blood smear. This article summarizes the case of a patient who developed HA after an infusion of rasburicase and offers management strategies.

CASE STUDY

A 58-year-old White man with relapsed chronic lymphocytic leukemia (CLL) was being treated on a clinical trial with a venetoclax-containing regimen due to disease progression. Venetoclax is a BCL-2 inhibitor that carries a high risk of tumor lysis syndrome. Therefore, many patients receiving treatment with venetoclax are prophylactically prescribed allopurinol or other antihyperuricemic agents to help lower uric acid levels and avert kidney injury. In general, patients starting venetoclax should be risk stratified and, for those at moderate to high risk, provided with prophylactic hydration and uric acid–lowering agents prior to initiating therapy. This is due to the anticipated rapid breakdown of CLL cells within the first 6 hours of dosing.

Afterward, the patient returned to the clinic for day 2 of dose escalation and was found to have an elevated serum creatinine level of 1.26 mg/dL (baseline 0.9 mg/dL) and an elevated uric acid level of 8.8 mg/dL (baseline 6.5 mg/dL). Although asymptomatic, he was given 1 liter of normal saline intravenously and 3 mg of intravenous rasburicase to lower his uric acid level in the acute cancer care center of the facility. Following discharge, the patient traveled about 6 hours to his home state.

Within 24 hours of receiving rasburicase, the patient began to pass dark brown urine. In response, he increased his water intake to improve hydration. The following day, the dark brown urine persisted, and he experienced increased fatigue, mild shortness of breath, and noticeable jaundice. He presented to his local emergency department (ED). His vital signs were stable and within normal range (pulse at 83 beats per minute, blood pressure at 123/73 mmHg, oxygen saturation at 98%, respiratory rate at 16 breaths per minute, and temperature at 98°F [36.7°C]).

Upon physical exam, the patient was noted to be jaundiced with scleral icterus present. The remainder of the physical exam was reported as unremarkable. Based on the patient's positive urine bilirubin test (Table 1), elevated total serum bilirubin level of 9.6 mg/dL (Table 2), and anemia with a hemoglobin of 10.7 g/dL (Table 3), it was concluded that the patient was experiencing hemolysis, likely induced by the administration of rasburicase. At this point, the patient had an undiagnosed G6PD deficiency with no prior history of autoimmune hemolysis. As a result, the study treatment was temporarily withheld during the hemolytic episode. The patient was admitted to the medical floor at his community hospital where he was treated with intravenous fluids and high-dose steroids at a dose of 1 mg/kg.

The patient was admitted for a 2-day stay, during which his total bilirubin and hemoglobin levels were closely monitored. Table 4 illustrates pertinent laboratory data during the management of hemolysis. Total bilirubin was 9.6 mg/dL upon admission but had already fallen to 6.5 mg/dL by the following morning. By the

Table 1. Urinalysis

Specimen UA	Urine, Clean Catch
Color, UA	Orange !
Appearance, UA	Clear
pH, UA	6.5
Specific gravity	1.02
Protein, UA	1+ !
Glucose, UA	Negative
Ketones, UA	Negative
Bilirubin (UA)	1+ !
Occult Blood UA	2+ !
Nitrite, UA	Positive !
Urobilinogen, UA	1.0
Leukocytes, UA	1+ !

Table 2. Complete Metabolic Panel

Component	11/9/2024
Sodium	137
Potassium	4.5
Chloride	105
CO2	29
Glucose	102
BUN	31 ↑
Creatinine	1.04
Calcium	9.1
Total protein	6.2
Albumin	4.1
Total bilirubin	9.6 ↑
Alkaline phosphatase	43
AST	41
ALT	17
Anion gap	3 ↓

Note. BUN = blood urea nitrogen; AST = aspartate aminotransferase; ALT = alanine aminotransferase.

afternoon of the second day, his total bilirubin had decreased to 4.0 mg/dL. His hemoglobin decreased to 9.5 g/dL on the morning of the second day but had risen to 10.4 g/dL by the end of the second day. As a result of decreasing bilirubin levels and recovering hemoglobin, the patient was discharged home with instructions to continue high-dose steroids for 4 days. The study treatment was resumed 4 days after the onset of the event.

The patient returned to the clinic for follow-up 5 days after the onset of his hemolysis. At that time, his hemoglobin was 10.2 g/dL, total bilirubin was 0.6 mg/dL, and uric acid was 5.6 mg/dL. Over the course of 3 weeks, his hemoglobin slowly returned to normal.

Table 3. Complete Blood Count

Component	11/10/2024	11/10/2024	11/9/2024
WBC	18 ↑	16.53 ↑	21.52 ↑
RBC	3.17 ↓	2.91 ↓	3.33 ↓
Hemoglobin	10.4 ↓	9.5 ↓	10.7 ↓
Hematocrit	32.1 ↓	29.1 ↓	34.3 ↓
MCV	101 ↑	100 ↑	103 ↑
MCH	32.8 ↑	32.6 ↑	32.1 ↑
MCHC	32.4	32.6	31.2 ↓
RDW	16.5 ↑	16.4 ↑	15.7 ↑
Platelets	173	162	159
MPV	10.7	11.8	11.2
Gran # (ANC)	12.5 ↑	10.6 ↑	7.5

Note. Trend of laboratory data during the admission for hemolysis over 24 hours of management. WBC = white blood cell count; RBC = red blood cell count; MCV = mean corpuscular volume; MCH = mean corpuscular hemoglobin; MCHC = mean corpuscular hemoglobin concentration; RDW = red cell distribution width; MPV = mean platelet volume; ANC = absolute neutrophil count.

Table 4. Laboratory Data During Management of Hemolysis

Lab	Day 1 at 1:48 pm	Day 2 at 5:12 am	Day 2 at 3:43 pm
WBC (K/µL)	21.52	16.53	18.00
Hemoglobin (g/dL)	10.7	9.5	10.4
Hematocrit (%)	34.3	29.1	32.1
Platelet count (K/µL)	159	162	173
Total bilirubin (mg/dL)	9.6	6.5	4.0
LDH	401	582	398

Note. WBC = white blood cell count; LDH = lactate dehydrogenase.

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is a genetic X-linked recessive disorder that results from mutations in the *G6PD* gene. This gene provides instructions for manufacturing the G6PD enzyme that is found in the cytoplasm of all cells in the body (Richardson & O'Malley, 2024). Deficiency may result in hemolytic anemia (HA) due to the rapid destruction of red blood cells (Barcellini, 2024). It can be triggered by infections, certain medications (nonsteroidal anti-inflammatory drugs, antimalarials, sulfonamides, etc.), stress, fatigue, dyspnea, abdominal pain, or foods such as fava beans (Mahfooz, 2023; National Institutes of Health, n.d.). G6PD deficiency affects between 400 million and 500 million people worldwide and is more prevalent among African Americans and persons of Middle Eastern descent.

CASE STUDY DISCUSSION

In this patient's case, tumor lysis syndrome (TLS) developed within 8 hours after initiating venetoclax at a dose of 20 mg. Venetoclax is a selective BCL-2 inhibitor that targets B-cell lymphoma 2. It induces rapid apoptosis in cancer cells and is indicated for the treatment of patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL). Generally, patients starting venetoclax should be risk stratified and provided prophylactic hydration (for those at moderate to high risk) and uric acid–lowering agents prior to the initiation of therapy due to the anticipated rapid breakdown of CLL cells within the first 6 hours of dosing (AbbVie, 2023).

This patient had a known allergy to allopurinol and was alternatively started on febuxostat to prevent kidney injury. Unbeknownst to his treatment team, he had missed several doses of febuxostat. For this reason, it is imperative for patients to inform their health-care providers of their current medications during each clinic visit. Due to the acute onset of TLS, the patient was given an infusion of rasburicase. Rasburicase is considered a safe and effective option in the management of TLS (Mahfooz, 2023). However, in this case, the patient developed HA due to an unknown G6PD deficiency.

Hemolytic anemia is defined as premature destruction of circulating red blood cells (Barcellini, 2024). It may be inherited or acquired, and acute or chronic. In this case, the hemolysis was acute as it occurred within 24 hours of receiving rasburicase (Hammami et al., 2024). The diagnosis of HA is made by a compilation of data including a detailed history and physical examination, and laboratory findings.

Pertinent laboratory tests include a reticulocyte count, haptoglobin, complete blood count, comprehensive metabolic panel, lactate dehydrogenase (LDH), and peripheral blood smear. Findings that indicate active hemolysis may include reticulocytosis, decreased haptoglobin, decreased hemoglobin, increased bilirubin, and elevated LDH. Several of these findings were present in the patient's laboratory results; however, neither a reticulocyte count nor direct antiglobulin test was identified in the laboratory workup from the outside facility.

The patient denied any prior hemolytic episodes and had no history of hematologic disorders other than CLL. Rasburicase, or recombinant urate oxidase, is contraindicated for use in patients with G6PD deficiency (Lakra et al., 2022). A G6PD assay was not ordered prior to or during his hospital admission, as the enzyme level will often appear normal during a hemolytic episode. However, a G6PD enzyme activity assay was obtained 4 weeks after the episode, which confirmed the diagnosis of G6PD deficiency. His level was 1.3 U/g Hb (normal: 8.0–11.9 U/g Hb). The patient has continued his venetoclax dose escalation without incident since consistently taking febuxostat. His laboratory results have remained within normal limits during weekly laboratory reviews.

CONCLUSIONS AND IMPLICATIONS

Advanced practice providers (APPs) are at the forefront of oncology patient management. In this case, the patient's G6PD deficiency was unknown to providers. Current BCL-2 inhibitors may increase the risk of TLS (AbbVie, 2023). Since venetoclax is known to cause a rapid breakdown of tumor cells, APPs need to be aware of drugs that are used prophylactically to prevent TLS such as rasburicase and possible underlying interactions

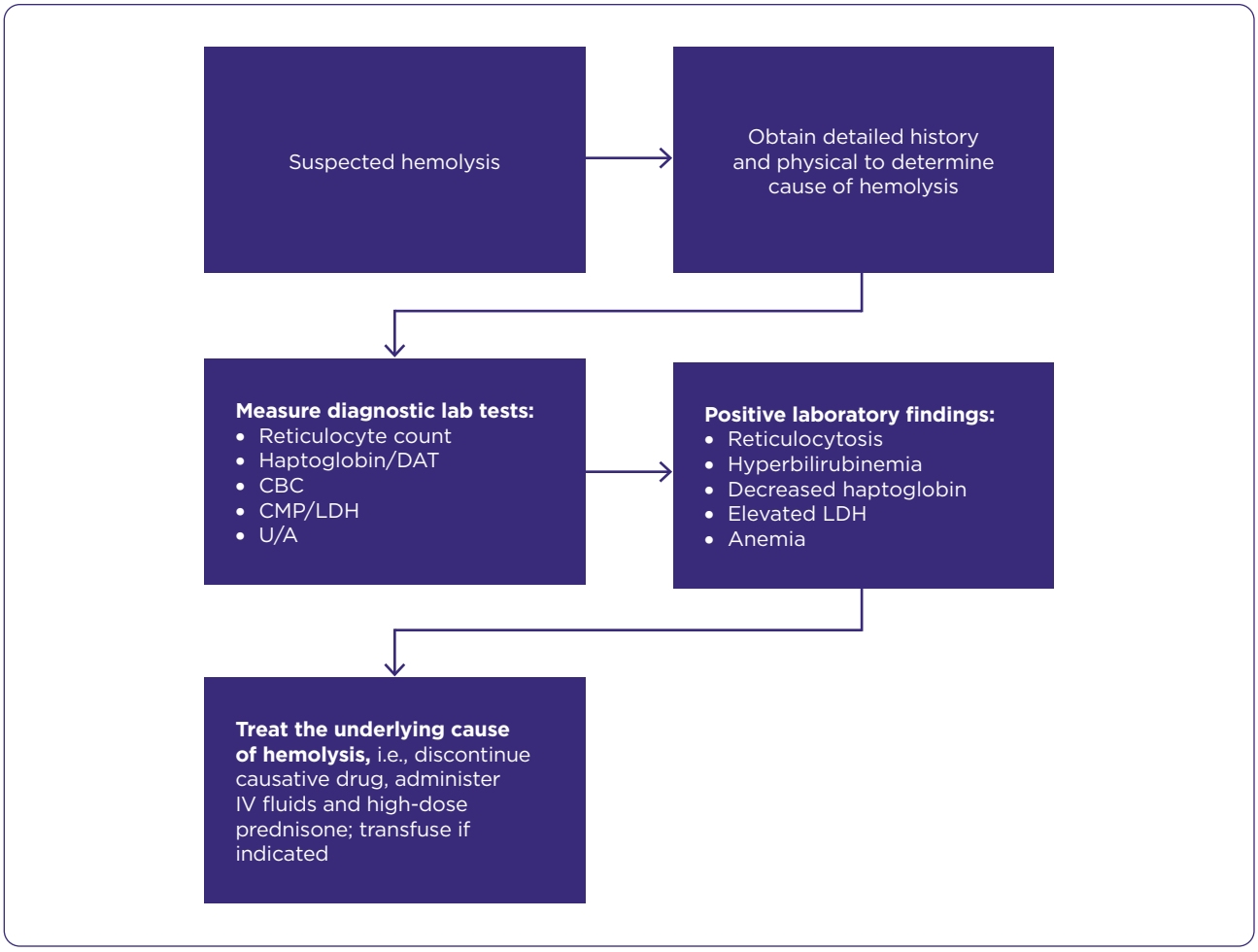

Figure 1. A diagnostic algorithm for hemolysis. Adapted from Shroff & Maddur (2020). DAT = direct antiglobulin test; CBC = complete blood count; CMP = comprehensive metabolic panel; LDH = lactate dehydrogenase; U/A = urinalysis.

with other medications. It is imperative that APPs be cognizant of early recognition of complications such as acute HA and provide rapid intervention to prevent poor outcomes. According to the National Comprehensive Cancer Network (NCCN) Guidelines (2024), the initial management of acute hemolysis is to identify the underlying cause and intervene with appropriate treatments. If the hemolysis is determined to be drug induced, the drug should be discontinued.

A vital role for the APP is comprehensive physical assessment and assessment of laboratory tests to guide treatment strategies. The APP should work collaboratively with the interprofessional team, including the physician and clinical pharmacist, to provide the best overall outcomes for patients. In collaboration with the physician, APPs should consider preemptively ordering G6PD screening in patients with CLL or SLL, particularly in high-risk populations such as African Americans and those of Middle Eastern descent. Predetermining the presence of G6PD deficiency may improve patient outcomes for those at risk.

Figure 1 shows a diagnostic algorithm designed to assist APPs in the prompt recognition and diagnosis of hemolysis. This algorithm can be used to help increase the survival rate of patients and prevent organ dysfunction through early intervention.

Disclosure

The authors have no conflicts of interest to disclose.

References

AbbVie. (2013). Venclexta (venetoclax) package insert. https://www.rxabbvie.com/pdf/venclexta.pdf

Barcellini, W. (2024). *Diagnosis of hemolytic anemia in adults*. https://www.uptodate.com/contents/diagnosis-of-hemolytic-anemia-in-adults

Mahfooz, K., Sohail, H., Gvajaia, A., Arif, U., Grewal, D., Muppidi, M. R., Vohra, V., Tarique, A., & Vasavada, A. (2023). Rasburicase in treating tumor lysis syndrome: An umbrella review. *Cancer Pathogenesis and Therapy, 1*(4), 262–271. https://doi.org/10.1016/j.cpt.2023.07.001

National Comprehensive Cancer Network. (2024). NCCN guidelines for patients: Anemia. https://www.nccn.org/patients/guidelines/content/PDF/anemia-patient-guideline.pdf

National Institutes of Health. (n.d.). *G6PD deficiency*. MedlinePlus. https://medlineplus.gov/g6pddeficiency.html

Hammami, M. B., Qasim, A., Thakur, R., Vegivinti, C. T. R., Patton, C. D., Vikash, S., & Kumar, A. (2024). Rasburicase-induced hemolytic anemia and methemoglobinemia: A systematic review of current reports. *Annals of Hematology, 103*(9), 3399–3411. https://doi.org/10.1007/s00277-023-05364-6

Lakra, R., Grewal, U. S., Dhaliwal, L., Gaddam, S. J., Master, S. R., & Ramades, P. (2022). Patients receiving rasburicase for treatment and prophylaxis of tumor lysis syndrome are undertested for glucose-6-phosphate dehydrogenase (G6PD) deficiency: A single center retrospective analysis. *Blood, 140*, 11054–11055. https://doi.org/10.1182/blood-2022-170490

Richardson, S. R., & O'Malley, G. F. (2024). Glucose-6-phosphate dehydrogenase deficiency. In *StatPearls*. StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK470315/

Shroff, H., & Maddur, H. (2020). Isolated elevated bilirubin. *Clinical Liver Disease, 15*(4), 153–156. https://doi.org/10.1002/cld.944