Confounding Case of Hemolysis in a Patient with Acute Leukemia

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CASE DESCRIPTION

A 12-year-old boy with refractory acute myeloid leukemia (AML)[2] was transferred to our hospital for compassionate treatment with gemtuzumab ozogamicin (GO; Mylotarg™). Before transfer, the patient had received 2 courses of salvage chemotherapy, after which bone marrow biopsy was negative for the disease. A plan for hematopoietic stem cell transplantation during his third cycle was halted because of disease recurrence.

On admission, the patient had leukemic infiltrates in his lungs, skin, distal esophagus, and gastric mucosa. He was profoundly immunocompromised, neutropenic, anemic, and thrombocytopenic. Despite persistent fever, daily blood cultures performed at an outside hospital and on admission at our hospital were negative. The patient was treated with a comprehensive panel of antibiotics without a significant change in his persistent fever.

A day after admission, the patient began a 15-day cycle of GO therapy. On day 5, the laboratory began receiving visibly hemolyzed specimens with increased hemolysis indices. Consequently, results from multiple biochemical tests were suppressed according to laboratory protocol (Table 1). The laboratory was contacted to help determine whether the hemolysis was in vivo or in vitro.

[2] Nonstandard abbreviations: AML, acute myeloid leukemia; GO, gemtuzumab ozogamicin.

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Table 1 Relevant laboratory testing performed during the patient's hospitalization.[a]

Analyte	Reference interval	Admission	Days after admission										
		0	1	2	3	4	5	6	7-13	14-20	21-27	28-End
K+, plasma, mmol/L	3.3-4.9	2.9	2.4	2.2	2.7	3.7	3.8	4.6	S[b]	S	S	S
K+, whole blood, mmol/L	3.3-4.9	–	–	–	–	–	–	3.2-3.6	2.5-3.6	3.1-8.3	2.6-4.0	2.3-6.9
AST[c], U/L	10-50	251	273	389	578	683	732	976	918, S	S	S	S
LDH, U/L	100-250	–	–	>2500	>2500	>2500	S	S	S	S	S	S
Bilirubin, mg/dL	0.0-1.2	0.3	0.3	0.5	0.2	0.2	0.2	0.2	0.2-0.6	0.2-0.4	0.2-0.3	0.3-0.5
μmol/L	0.0-20.5	5.1	5.1	8.6	3.4	3.4	3.4	3.4	3.4-10.3	3.4-6.8	3.4-5.1	5.1-8.6
Free plasma hemoglobin, mg/dL	<50	–	–	–	–	–	–	–	650	–	1020	370-640
mmol/L	<0.03	–	–	–	–	–	–	–	0.40	–	0.63	0.23-0.40
Haptoglobin, mg/dL	30-200	–	–	–	–	–	–	270	233	802	339	1115
g/L	0.3-2.0	–	–	–	–	–	–	2.70	2.33	8.02	3.39	11.15
hs-CRP, mg/L	<10	–	–	–	–	–	–	–	–	176.3	85.6	467.0
Ferritin, ng/mL	30-400	–	–	–	–	–	–	–	–	69243	56359	66263
μg/L	30-400	–	–	–	–	–	–	–	–	69243	56359	66263
Hemoglobin, g/dL	13.0-17.5	7.9	7.4	5.4	8.1	5.1	11.2	11	6.9-9.5	6.6-9.0	3.9-10	6.2-10.6
g/L	130-175	79	74	54	81	51	112	110	69-95	66-90	39-100	39-66
Hematocrit, %	38.9-50.3	20.1	19.8	14	21	13.3	29.2	29	16.9-24.7	15.2-26.9	10.5-38.6	19.1-25.6
MCV, fL	81.3-96.4	76.1	77.6	77.3	77.2	77.3	79.3	78.2	76.3-77.5	77.4-83.4	82.3-85.2	79.1-93.1
WBC, K/mm^3	3.8-9.9	0.3	0.4	0.1	0.1	0.1	0.2	0.2	0-0.2	0-0.2	0-0.2	0-0.3
Neutrophils, abs, K/mm^3	1.5-9.4	0	0	0	0	0	0	0	0	0	0	0-0.2
Monocytes, abs, Kl/mm^3	0.1-1.7	0	0	0	0	0	0	0	0	0	0	0
NRBC, abs, K/mm^3	0.0-0.01	0	0	0	0	0	0	0	0	0	0	0
Urine blood	Negative	–	–	–	–	–	–	–	3+	–	3+	–
Urine RBC	None/HPF	–	–	–	–	–	–	None to <5	–	–	None	–

[a] For simplicity, the final 33 days are grouped into weeks, and ranges of each test are shown for the week. GO treatment initiated on day 1 and completed on day 15.
[b] Result suppressed owing to hemolysis.
[c] Abbreviations: AST, aspartate aminotransferase; LDH, lactate dehydrogenase; hs-CRP, high sensitivity C-reactive protein; MCV, mean corpuscular volume; WBC, white blood cell; NRBC, nucleated red blood cell count; C, result reported with a "specimen hemolyzed" comment; abs, absolute; RBC, red blood cell; HPF, high power field.

QUESTIONS TO CONSIDER
• What is the fate of free hemoglobin released in vivo?
• What laboratory parameters are useful to distinguish in vivo from in vitro hemolysis?
• Is this patient's hemolysis likely in vivo or in vitro?
• How is GO involved with hemoglobin and haptoglobin clearance?

Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the December 2018 issue of *Clinical Chemistry*. To view the case and comments online, go to http://www.clinchem.org/content/vol64/issue12 and follow the link to the Clinical Case Study and Commentaries.

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