

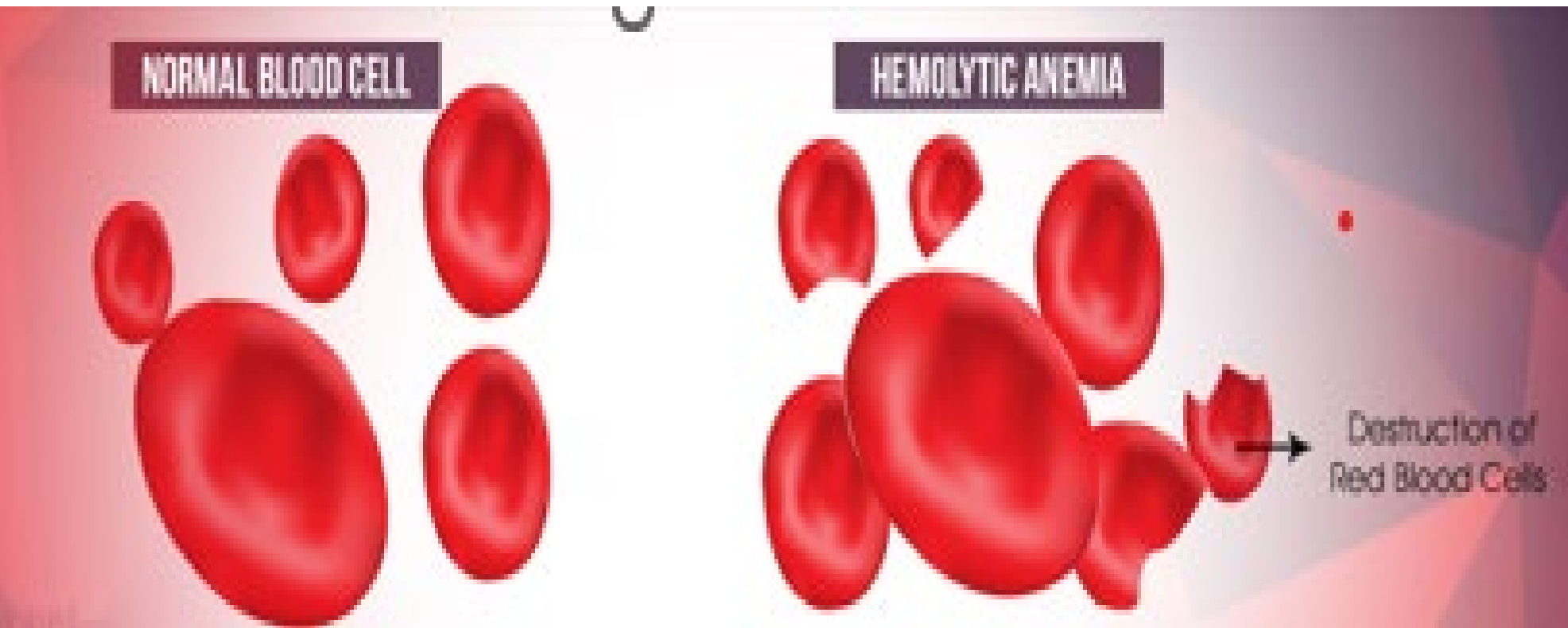
Breaking Bad Blood: Hemolysis post N-Acetylcysteine initiation for an acetaminophen overdose

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Background

- N-Acetylcysteine (NAC) is the antidote for acetaminophen induced hepatotoxicity.
- It is generally well tolerated with occasional rate-related anaphylactoid reactions.
- Hemolysis can result from genetic disorders, autoimmune conditions, infections, medications or other causes; however, hemolysis associated with NAC is exceedingly rare.



- We report a case of a previously healthy 17-year-old female who showed evidence of hemolysis during NAC administration.

Case Report

- A 17-year-old female with a history of mild chronic anemia presented to the emergency department with nausea, vomiting, fever, dyspnea, chills, and extremity numbness, and a history of ingestion of an unknown amount of acetaminophen and ibuprofen over several days for a dental abscess.
- Initial laboratory findings were significant for acute kidney and liver injury, and she was started on vitamin K and standard dosing intravenous NAC, leading to improvement in her LFTs.

Case Report continued

- Approximately 44 hours after NAC initiation, laboratory evidence of hemolysis emerged, prompting premature discontinuation of NAC at 48 hours.
- On hospital day 3, the patient had significant hyperbilirubinemia with a large indirect component compared to mild direct hyperbilirubinemia on admission.
- Labs were consistent with hemolysis with an elevated LDH at 2,745unit/L and haptoglobin <10.
- The Coombs test was negative.

Coags								
Lab	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8
PT(sec)	54.9H	47.1H	30.9H	21.7H	17.5H	16.3H	13.9H	12.9H
aPTT(sec)	29.6	28.7	28.9	23.8L	-	-	-	-
INR	5.04	4.32	2.83	1.99	1.61	1.5	1.28	1.18
Fibrinogen(mg/dL)	-	-	-	-	165L	-	-	-
CBC with Differential								
Lab	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8
WBCx10(3)/mcL	8.63	6.33	7.84	7.05	8.08	6.77	9.19	9.69
RBCx10(6)/mcL	3.83L	3.52L	3.08L	2.68L	2.62L	2.44L	2.69L	3.55L
HGB(gm/dL)	10.8L	10.4L	8.8L	7.8L	7.7L	7.0L	7.6L	10.4L
HCT(%)	35.5	31.7	27.1L	23.5L	22.6L	21.1L	23.2L	30.4L
Plateletx10(3)	215	197	162	124L	140	129L	167	154
LYMPHS(%)	6.5L	12.3L	16.6L	22.7L	26.0L	32.1L	30.9L	23.7L
RETICCOUNT(%)	1.77H	-	-	-	-	-	4.19H	4.81H
Hepatic Profile and Chemistry								
Lab	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8
TOTALPRO(gm/dL)	8.4	5.1L	4.7L	4.4L	4.8L	5.6L	6.1L	6.2L
ALTSGPT(unit/L)	9,260H	6,901H	4,993H	3,459H	2,618H	1,705H	1,389H	987H
ASTSGOT(unit/L)	10,335	6,198H	3,656H	1,097H	461H	215H	147H	124H
ALKPHOS(unit/L)	241H	241H	227H	193H	187H	160H	160H	159H
GGT(unit/L)	-	64H	63H	51H	49	44	59H	86H
BILITOTAL(mg/dL)	5.5H	14.0H	21.0H	25.3H	18.9H	14.5H	13.1H	12.8H
BILIDIRECT(mg/dL)	-	5.3H	9.5H	13.3H	9.9H	8.8H	8.8H	8.5H
BUN(mg/dL)	26H	20	17	13	10	8	9	7
Ceatinine(mg/dL)	1.27H	0.99	0.78	0.76	0.78	0.78	0.92	0.9
H= high value out of range; L= low value out of range								

- The patient received additional vitamin K and transfusion of packed red blood cells.
- A comprehensive workup for other causes of hemolysis, including glucose-6-phosphate dehydrogenase (G6PD) deficiency, was unremarkable
- She was subsequently diagnosed with Gilbert's syndrome, an inherited condition associated with benign, intermittent unconjugated hyperbilirubinemia.
- She was discharged on hospital day 8 with improving LFTs and ongoing outpatient monitoring. At a 46-day follow-up, her hemolytic anemia had resolved, and laboratory parameters had normalized.

Discussion

- This case highlights an association between NAC administration and hemolysis in a patient with pre-existing mild anemia and Gilbert's syndrome.
- While Gilbert's syndrome does not cause hemolysis, it may exacerbate hyperbilirubinemia in the setting of red blood cell breakdown.
- It is unknown if the drugs involved in the overdose: acetaminophen and/or ibuprofen may have contributed to the patient's hemolysis.
- The precise mechanism of hemolysis in this patient remains unclear, and a causal link to NAC cannot be definitively established.
- However, the temporal relationship between NAC initiation and onset of hemolysis raises the possibility of a NAC induced hemolysis effect.

Conclusion

- While NAC remains the cornerstone of treatment for acetaminophen toxicity, clinicians should be aware of the rare potential for hemolysis, particularly in patients with underlying hematologic or hepatic vulnerabilities.
- Further studies are warranted to elucidate the mechanisms, risk factors, and incidence of NAC-associated hemolysis.