

“The Red Rebellion: How Lactagard Broke the Blood’s Oath”

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ABSTRACT:

LACTAGARD is the brand of CEFOPERAZONE +SULBACTUM is a third-generation cephalosporin antibiotic, beta-lactamase inhibitor. Usually gastrointestinal, hematologic, hepatic, hypersensitivity, local, and coagulation-related is common Adverse drug reaction caused by this drug, In this case, Hemolytic anemia is caused for the elder patient and it should be monitored closely; if it is not recognized/managed promptly, it can progress to life-threatening multiorgan complications. A 94-year-old male patient was admitted with complaints of Fever on &off for 4 days, h/o Breathlessness for 4 days, and h/o Cough with sputum. He has a past history of valvular heart disease - S/P AVR and known case of Systemic hypertension on regular treatment with T.ECOSPIRIN 150 mg , T. ATROVASTATIN 10mg, T.METOPROLOL 25 mg, T.LOSARTAN 25 mg. The Red blood cell

Haemoglobin, Packed cell volume, and Red cell distribution width level was normal in level and after administration of LACTOGARD, the Haematology level was decreased in level .The Haematology level was decreased day by day so the drug stopped and the drug was changed to CEFUROXIME AXETIL.A Probable relationship was indicated by the causality score of , which was determined by applying the Naranjo scale.This LACTOGARD is the brand of CEFOPERAZONE +SULBACTUM might result from the rare adverse effects because it destroy the Red blood cell before fully matured by its own immune system it leads to

Hemolytic anemia. Optimizing patient safety requires ongoing re-evaluation of therapy

INTRODUCTION:

Lower respiratory tract infections are the leading cause of illness and death among elderly patients.⁽¹⁾ In this case, a broad-spectrum antibiotic, specifically cefoperazone and sulbactam, was prescribed as a combined treatment.⁽¹⁾ Cefoperazone is a third-generation cephalosporin, while sulbactam acts as a beta-lactamase inhibitor.⁽¹⁾ The combination of cefoperazone and sulbactam was chosen for its effectiveness against resistant organisms.⁽³⁾ Although cephalosporins are generally deemed safe for such conditions, they can

infrequently lead to drug-induced immune haemolytic anaemia (DIIHA). (3) Haemolytic anaemia is caused when red blood cells are destroyed prematurely by the immune system. (3) Here, a 94-year-old male patient who was diagnosed with a lower respiratory tract infection was given the cefoperazone/sulbactam antibiotic intravenously as a drug therapy, which caused haemolytic anaemia, a rare condition, and it was diagnosed through haematological data. (2)

CASE DESCRIPTION:

A 94 years old male patient was admitted to the general medicine department with complaints of fever on and off x4 days. history of breathlessness x4 days, cough with sputum (+). no history of chest pain/orthopnea/palpitation/vomiting. On physical examination the patient was conscious, oriented, and febrile. His past medical history was found to be a known case of valvular heart disease - S/P AVR feb 2020, SHTN on regular treatment. his family history was found to be Nil. past medication history was found to be TAB.ECOSPIRIN 50mg, TAB.ASTIN 10mg, TAB.METOPROLOL 25mg, TAB.LOSARTAN 25mg. On the examination of vital sign, The blood pressure was slightly decreased for the first 2 days (110/70, 100/60mmHg) and increased for the next 2 days (130/80, 150/60mmHg), The pulse rate was found to be normal for all days, The SPO2 was found to be normal for all days, temperature was increased for the first day (102F) and normal for the next 3 days was given in the table 1. ON laboratory investigation the RBC was normal on 1st days and decreased in 3rd day (3.85gm/dl), Haemoglobin was decreased for the 1st (12.5gm/dl), 3rd day (11.78gm/dl), Packed cell volume was decreased for 1st & 3rd day (36.5%, 34.3%), Total WBC count was found to be increased for the 1st & 3rd day (13350 cells/cumm, 16710 cells/cumm), Red cells distribution width was found to be increased in the 3rd day of admission (14.9%), Neutrophils was found to be increased (87.85%, 86.81%), lymphocytes (7.13%), (9.45%), Eosinophils (0.34%), (0.67%) and Basophil (0.18%), (0.08%) was decreased was given in the table 2. on biochemical investigation the renal function test Uric acid (3.2mg/dl), Phosphorous (1.9 mg/dl), Sodium (133mmol/l) was decreased was given in the table 3. The serology test, C-Reactive protein (24.0 mg/l) was increased was given in the table 4. the patient was treated with INJ.

CEFOPERAZONE+SULBACTAM 1.5gm, INJ.PANTOPRAZOLE 4mg, INJ.PARACETAMOL 1g, TAB.MONTELUKAST SODIUM AND LEVOCETIZINE 10/5mg, TAB.DOXYFYLLINE 400mg, TAB.ACEBROPHYLLINE+ACE TYL CYSTEINE 100/600mg, NEB.IPRATROPIUM BROMIDE+LEVOSALBUTAMOL 1 NEB, NEB.BUDESONIDE 1 NEB, TAB.ASPIRIN 50mg, TAB.ATORVASTATIN 10mg, TAB.METOPROLOL 25mg, TAB.LOSARTAN 25mg, TAB.VITAMIN C CHEWABLE 1 CAP, CAPSULES OSELTAMIVIR 75mg, TAB.AZITHROMYCIN 500mg was given in the table 5. In this case the patient HAEMOGLOBIN level was decreased in level known as hemolytic anemia caused by INJ. CEFOPERAZONE+SULBACTAM 1.5gm so physician stopped the drug. the patient treated with the stat medication on his admission INJ.PANTOPRAZOLE 40mg, INJ.ONDANSETRON 4 mg, INJ.HYDROCORTISONE 100mg, PARACETAMOL 1gm, NEB.IPRATROPIUM BROMIDE+LEVOSALBUTAMOL 1 resp, NEB.BUDESONIDE 1 resp, INJ.CEFOPERAZONE+SULBACTAM 0.5ml, INJ. MVI 500ml,

INJ MVI500ml was given in the table 6.the patient was discharged with improved patient compliance and discharged with the medication TAB.CEFIXIME500mg,TAB.MONTELUKAST SODIUM AND LEVOCETRIZINE10/5mg,TAB.PANTOPRAZOLE+DOMPERIDONE40mg,TAB.ACEBR OPHYLLINE+ACETYLCYSTEINE100/600mg,TAB.DOXYFOLLINE400mg,TAB.DEXTR OMETHORPHAN10ml was given in the table 7.

TABLE 1 - VITAL SIGN:

PARAMETER	DAY 1	DAY 2	DAY 3	DAY 4	NORMAL VALUE
BLOOD PRESSURE	110/70mmHg	100/60mmHg	130/80mmHg	150/60mmHg	120/80mmHg
PULSE RATE	91 beats per minute	74 beats per minute	74 beats per minute	78 beats per minute	60 to 100 beats per minute
SPO2	98%	97%	93%	96%	95-100 %
TEMPERATURE	102F	97F	96.4F	98.6F	97.7F-99.5F

TABLE 2 - LABORATORY INVESTIGATION: HAEMATOLOGY

S.NO	PARAMETER	OBSERVED VALUE DAY 1	OBSERVED VALUE DAY3	NORMAL VALUE
1	RED BLOOD CELLS	4.10gm/dl	3.85gm/dl	4.7-6.2million/cu mm ₅
2	HAEMOGLOBIN	12.5gm/dl	11.78gm/dl	14-17g/dl
3	PACKED CELL VOLUME	36.5%	34.3%	42-52%
4	TOTAL WBC COUNT	13350cells/cum	16710cells/cum	5000-10000/mm

		m	m	3.5
5	RED CELLS DISTRIBUTION WIDTH	13.8%	14.9%	11.6-14%
6	NEUTROPHILS	87.85%	86.81%	40-80%
7	LYMPHOCYTES	7.13%	9.45%	20-40%
8	EOSINOPHILS	0.34%	0.67%	1.0-6%
9	BASOPHIL	0.18%	0.08%	1.4-4.5%

TABLE 3 -BIOCHEMISTRY (RENAL FUNCTION TEST):

S.NO	PARAMETER	OBSEVERED VALUE	NORMAL VALUE
1	URIC ACID	3.2mg/dl	3.5-8.5
2	PHOSPHOROUS	1.9mg/dl	2.5-4.5
3	SODIUM	133mmol/l	135-145

TABLE 4- SEROLOGY

S.NO	PARAMETER	OBSERVED VALUE	NORMAL VALUE
1	C-REACTIVE PROTEIN	POSITIVE (24.0mg/l)	0.2-6

TABLE -5 THERAPUETIC CHART

S.NO	DRUG NAME	DOSE	ROUTE	
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				FREQUENCY
1	INJ.CEFOPERAZONE +SULBACTUM	1.5gm	IV	IV
2	INJ.PANTOPRAZOLE	40mg	IV	OD
3	INJ.PARACETAMOL	1g	IV	TDS
4	TAB.MONTELUKAST SODIUM AND LEVOCETRIZINE	10/5mg	P/O	HS
5	TAB.DOXYFYLLINE	400mg	P/O	BD
6	TAB.ACEBROPHYLLI NE+ACETYLCYSTEI NE	100/600mg	P/O	BD
7	NEB.IPRATROPIUM BROMIDE+LEVOSAL BUTAMOL	1 NEB	P/N	TDS
8	NEB.BUDESONIDE	1 NEB	P/N	TDS
9	TAB.ASPIRIN	50mg	P/O	OD
10	TAB.ATORVASTATIN	10mg	P/O	HS
11	TAB.METOPROLOL	25mg	P/O	BD
12	TAB.LOSARTAN	25mg	P/O	OD
13	TAB.VITAMIN C CHEWABLE	1 CAP	P/O	BD
14	CAPSULES OSELTAMIVIR	75mg	P/O	BD
15	TAB.AZITHROMYCI N	500mg	P/O	OD

TABLE- 6 STAT CHART

DATE	DRUG NAME	DOSE	ROUTE
DAY1	INJ.PANTOPRAZOLE	40mg	IV

DAY1	INJ ONDANSETRON	4 mg	IV
DAY1	INJ.HYDROCORTISONE	100mg	IV
DAY1	PARACETAMOL	1gm	IV
DAY1	NEB.IPRATROPIUM BROMIDE+LEVOSALBUTA MOL	1resp	P/N
DAY1	NEB.BUDESONIDE	1resp	P/N
DAY1	INJ.CEFOPERAZONE+SULB ACTUM	0.5ml	TDS
DAY1	INJ MVI	500ml	
DAY3	INJ MVI	500ml	

TABLE- 7 DISCHARGE CHART:

S.NO	DRUG NAME	DOSAGE	FREQUEN CY	BEFORE/A FTER FOOD	DURATION
1	TAB.CEFIXIME	500mg	BD	AFTER FOOD	5 DAYS
2	TAB..MONTELUKA ST SODIUM AND LEVOCETRIZINE	10/5mg	OD	AFTER FOOD	5 DAYS
3	TAB.PANTOPRAZO LE+DOMPERIDON E	40mg	BD	BEFORE FOOD	5 DAYS
4	TAB.ACEBROPHYL LINE+ACETYLCYS TEINE	100/600mg	BD	AFTER FOOD	5 DAYS
5	TAB.DOXYFOLLIN E	400mg	BD	AFTER FOOD	5 DAYS
6	TAB.DEXTROMET HORPHAN	10ml	10ml	AFTER FOOD	5 DAYS

NARANJO ADVERSE DRUG REACTION PROPABILITY SCALE^[9]

				TOTAL SCORE =7
QUESTION	YES	NO	DO NOT KNOW	SCORE
1. Are there previous conclusion reports on this reaction?	+1	0	0	+1
2. Did the adverse event appear after the suspected drug was administered?	+2	-1	0	+2
3. Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0	+1
4. Did the adverse event reappear when the drug was re-administered?	+2	-1	0	0
5. Are there alternative causes (other than the drug)that could, on their own, have caused the reaction?	-1	+2	0	+2
6. Did the reaction reappear when a placebo was given?	-1	+1	0	0
7. Was the drug detected in blood(or other fluids) in a concentration known to be toxic?	+1	0	0	0
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	0
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0	0
10. Was the adverse event confirmed by any objective evidence	+1	0	0	+1

CASE DISCUSSION:

In this case, a patient with Lower respiratory tract infection received cefoperazone-sulbactam which resulted in drug-induced immune hemolytic anemia.⁽⁵⁾ The hematological values indicate a sharp decrease in hemoglobin level from 17.2 g/dL to 11.8 g/dL, RBC declined from 4.6 to 3.8 million/microliter and Packed cell volume was decreased in level. Reduced circulating red blood cell survival is the hallmark of hemolytic anemia.⁽⁴⁾ An elevated reticulocyte count, positive RBC antibodies, and low hemoglobin levels identified as anemia are the main indicators of hemolytic anemia.⁽⁴⁾ Additionally, patients may exhibit lower haptoglobin levels. ⁽⁴⁾ (Chinese Medical Association, Chinese Society of Haematology, 2017)⁽⁴⁾

Clinical signs of hemolysis linked to medication therapy indicate DIIHA, which is caused by immunization against the medication and/or RBCs.⁽⁵⁾ Drugs are tiny molecules that, when combined with a carrier molecule, have the potential to become immunogenic.⁽⁴⁾ Drugs are

haptens that require carriers to elicit an antibody response, such as proteins, red blood cells, or the platelet membrane.[\(5\)](#)

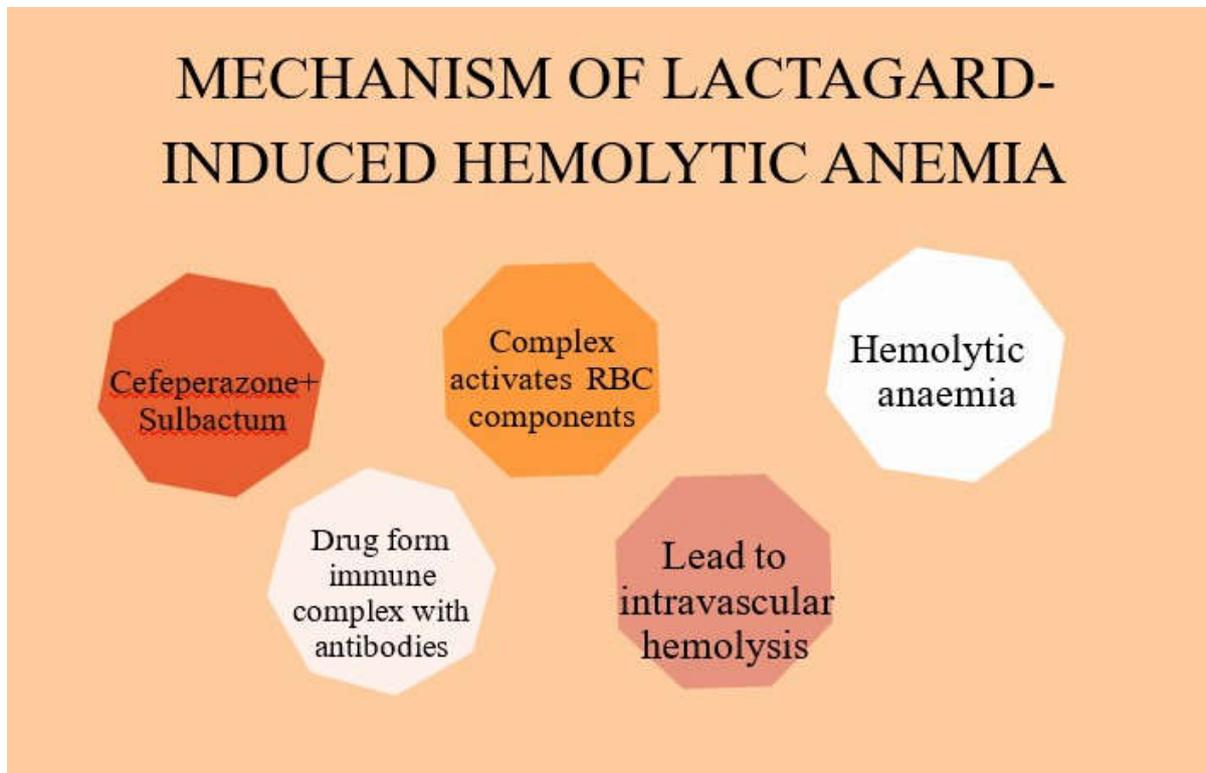


FIGURE 1: MECHANISM OF LACTAGARD INDUCED HEMOLYTIC ANEMIA[\(5\)](#)

The drug-independent DIIHA mechanism that has been documented in the literature.[\(5\)](#) The medication loosely interacts with the red blood cell membrane in the circulation, changing RBC surface antigens and its normal structural components .[\(5\)](#) When the inciting substance is not present, DIABs may interact, bind to the RBC membrane, and cause extravascular hemolysis . [\(5\)](#)

CONCLUSION:

This case emphasises that even widely used antibiotics such as cefoperazone/sulbactam can rarely cause life-threatening adverse reactions like haemolytic anaemia. Early identification through clinical and laboratory data, discontinuation of the offending drug and initiation of supportive care are essential to prevent serious outcomes.

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