

Drug Hypersensitivity: A Case Report

AIU 2026 – Ramtin Lichtenberger



Patient History

Admission:

- 43-year-old male admitted on 26.12.2023 for out-of-hospital cardiac arrest due to anterior STEMI.
- Hospitalized in the IMC unit from 26.12.2023 to 06.02.2024.

Complicated Medical History:

- Colon ischemia requiring extensive surgical management
- Thrombosis of both left and right internal jugular veins and thrombus at the level of the inferior vena cava bifurcation
- AKI stage 3 following resuscitation and septic shock, abdominal compartment syndrome
- Complete AV block
- Severe therapy-refractory hyperactive delirium
- Normochromic anemia

Known Comorbidities:

- Polytoxicosis, ADHD, arterial hypertension, atopic dermatitis

Patient History

Postoperative Course:

- Complicated postoperative course following extensive abdominal surgery
- Partial abdominal wall closure and fascial dehiscence due to large abdominal wall hematoma

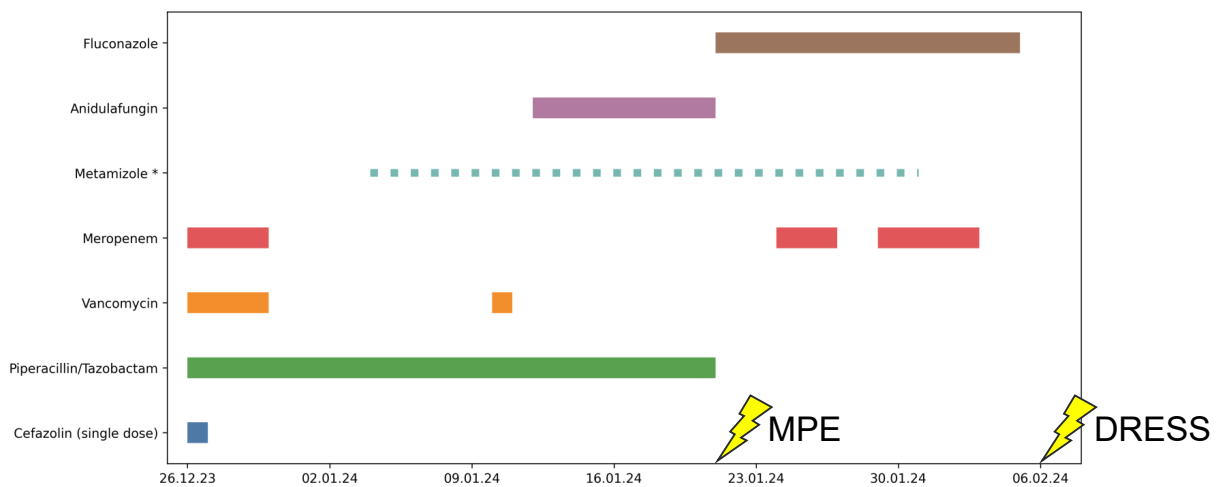
Sepsis Episodes:

- Twice during hospitalization, likely due to abdominal infection with intraabdominal candidiasis (Candida species confirmed).

Anti-infective Treatment:

- 26.12.2023 - 02.02.2024: Broad-spectrum antibiotics and antifungal therapy

Timeline of Medication Exposure



Development of Cutaneous and Systemic Reactions

21.01.2024: Development of a generalized maculopapular exanthema

- rapid clinical improvement after adjustment of therapy and initial symptomatic treatment

06.02.2024: Recurrent exanthema with systemic involvement

- fever
- elevated inflammatory markers
- marked eosinophilia (up to 9.68 G/L)

Evolution of Eosinophilia

Referenzbereich/-einheiten		EOSINOPHILE MASCHINELL	
		0.02 - 0.40 G/l	
30.09.2025	09:17	0.46	▲
29.07.2025	14:14	0.25	
30.06.2025	08:49	0.37	
21.02.2025	08:47	0.42	▲
27.01.2025	09:25	0.28	
17.05.2024	10:14	0.78	▲
19.02.2024	07:00	0.01	▼
17.02.2024	07:45	0.08	
14.02.2024	07:45	2.57	▲
10.02.2024	07:00	5.32	▲
09.02.2024	07:00	1.45	▲
08.02.2024	07:00	9.68	▲
07.02.2024	07:00	5.58	▲
30.01.2024	04:34	6.43	▲

Referenzbereich/-einheiten		EOSINOPHILE visuell	
		0.02 - 0.40 G/l	
21.02.2025	08:47	0.43	▲
19.02.2024	07:00	0.00	▼
17.02.2024	07:45	0.10	
16.02.2024	07:45	0.30	
15.02.2024	07:45	1.72	▲
14.02.2024	07:45	2.84	▲
12.02.2024	07:00	3.27	▲
10.02.2024	07:00	4.39	▲
09.02.2024	07:00	0.95	▲
08.02.2024	07:00	11.15	▲
30.01.2024	04:34	5.08	▲
31.12.2023	06:00	0.89	▲

Histopathological Findings

Skin biopsy (08.02.2024):

- Epidermal spongiosis and acanthosis
- Subcorneal pustule formation with neutrophils
- Superficial and deep perivascular lymphohistiocytic infiltrates with eosinophils
- PAS staining negative for fungal elements

Interpretation:

- Findings compatible with a drug-induced eruption
- Histological features overlapping AGEP and DRESS
- Pure AGEP or DRESS cannot be reliably distinguished histologically

RegiSCAR Classification

No alternative cause identified, including negative serologies for EBV, CMV, HHV-6/7, and viral hepatitis.

Fever (≥38.5 °C)	No/Unknown	-1	Yes	0
Enlarged lymph nodes ≥2 sites, >1 cm	No/Unknown	0	Yes	+1
Atypical lymphocytes	No/Unknown	0	Yes	+1
Eosinophilia	0-699 cells or <10% (no eosinophilia)	0	700-1,499 cells or 10-19.9%	+1
	≥1,500 cells or ≥20%	+2		
Skin rash extent >50%	No/Unknown	0	Yes	+1
At least two of: edema, infiltration, purpura, scaling	No	-1	Yes	+1
	Unknown	0		
Biopsy suggesting DRESS	No	-1	Yes/Unknown	0
Internal organ involved	0	0	1	+1
			≥2	+2
Resolution in ≥15 days	No/Unknown	-1	Yes	0
Alternative diagnoses excluded (by ≥3 biological investigations)	No/Unknown	0	Yes	+1

4 points

RegiSCAR for DRESS

Probable case

Likelihood of DRESS diagnosis

Lymphocyte Transformation Test (LTT)

Test substances (ug/ml)		IL-5	IL-13	IFNg	GzB	GL
Meropenem	20	336.65	224.42	1.58	8.96	1.14
	100	838.34	579.03	4.26	112.15	5.18
	500	1000.00	979.54	8.29	387.10	12.17
Vancomycin	10	1.00	1.00	0.79	0.70	1.03
	100	15.37	10.82	0.71	3.41	1.06
	200	13.78	6.54	0.78	0.93	0.98
Piperacillin	100	1.00	1.00	0.92	0.82	0.98
	200	1.00	1.00	0.97	0.72	1.04
	500	1.00	1.00	1.05	0.70	0.92
Pokeweed Mitogen		241.88	411.01	1891.15	440.02	10.09
Tetanus Toxoid		7.69	8.95	5.21	22.30	0.72

Lymphocyte Transformation Test (LTT)

Test substances (ug/ml)		IL-5	IL-13	IFNg	GzB	GL
Metamizol	20	1.43	1.28	0.70	1.12	1.03
	100	13.28	9.95	0.69	2.76	1.21
	500	93.09	96.48	4.29	35.24	5.15
Cefazolin	10	4.49	1.71	0.69	0.77	1.15
	50	0.17	0.13	0.69	4.14	1.34
	100	0.17	0.13	0.69	0.15	1.51
Pokeweed Mitogen		59.12	123.21	2473.55	273.01	10.78
Tetanus Toxoid		3.68	2.37	1.23	8.30	0.96

Summary and Clinical Recommendations

Interpretation

- Likely trigger of **MPE**: vancomycin, with possible contribution of metamizole
- Trigger of **DRESS**: meropenem

Recommendations

- **Strict avoidance** of all carbapenems
- **Strict avoidance** of all glycopeptide antibiotics (including teicoplanin)
- **Strict avoidance** of all pyrazolones (metamizole, propyphenazone, phenylbutazone, aminophenazone, phenazone)

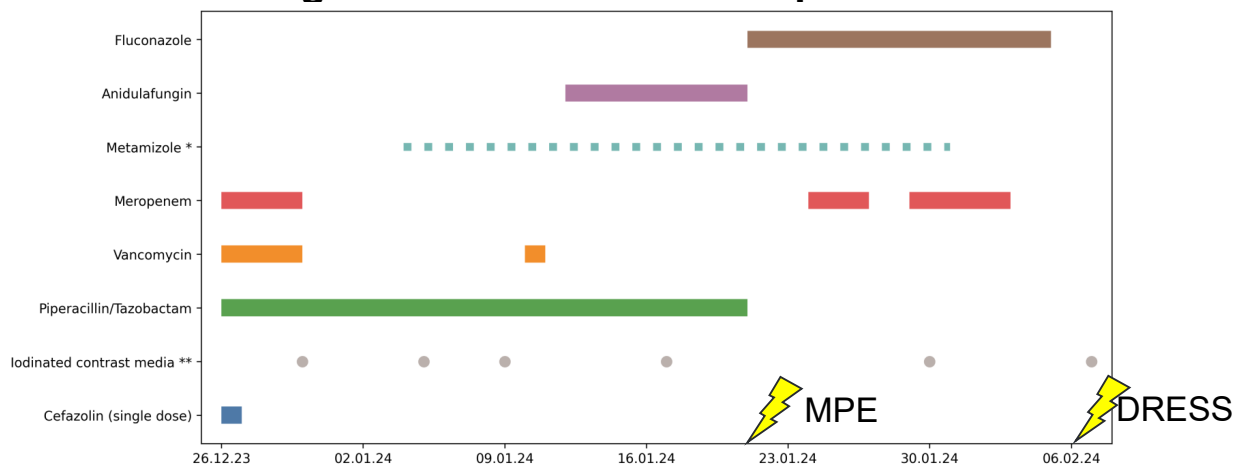
Drugs considered safe

- penicillins and aminopenicillins, cephalosporins, fluconazole

Clinical Follow-up

- Subsequent exposure to amoxicillin–clavulanate, cefazolin, cefuroxime, and fluconazole

Timeline of Drug and Contrast Media Exposure



* ≥ 3 administrations documented; exact number unknown.
 ** CT thorax-abdomen with iomeprol; last exposure with iopromide.

Patch Testing

Iodinated contrast agents	07.04.2025	09.04.2025 (48h)	10.04.2025 (72h)
Vaseline	-	-	-
Sodium lauryl sulfate	-	-	-
Iopamidol (Iopamiro®)	-	-	-
Iodixanol (Visipaque®)	-	-	++
Iopromide (Ultravist®)	-	-	-
Iobitridol (Xenetix®)	-	-	-
Iomeprol (Iomeron®)	-	++	+++
Ioversol (Optiray®)	-	+	+++
Amidotriazoate Natrium (Gastrografin®)	-	-	-

Lymphocyte Transformation Test (LTT)

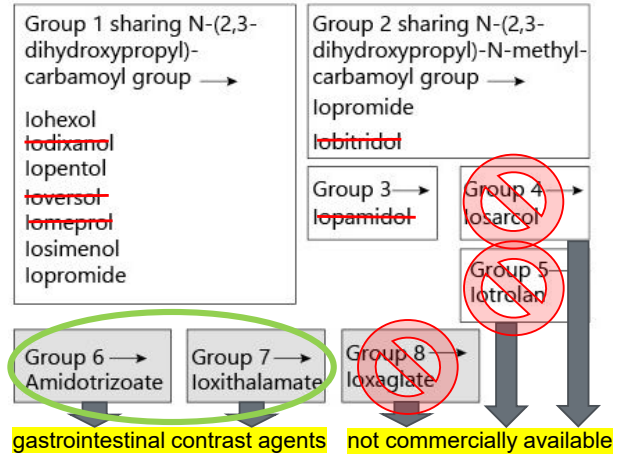
Test substances (ug/ml)		IL-5	IL-13	IFN γ	GzB	GL
Iomeprol (Iomeron®)	1000	187.03	142.12	9.71	144.55	5.47
	5000	239.27	185.26	40.98	144.55	5.47
	10000	244.76	159.61	33.82	144.55	5.47
Iobitridol (Xenetix®)	1000	0.45	0.93	1.76	1.57	1.00
	5000	3.48	5.33	1.15	2.76	1.04
	10000	1.25	2.02	2.23	1.88	1.11
Iopamidol (Iopamiro®)	1000	2.09	1.95	1.47	1.49	0.93
	5000	2.52	6.32	1.54	2.48	1.18
	10000	1.57	2.84	0.93	0.99	1.04
Pokeweed Mitogen		118.73	338.75	537.54	144.55	5.47
Tetanus Toxoid		6.76	5.34	10.00	24.71	1.31

Cross-reactivity among iodinated contrast agents

Culprit ICM	lopentol	loversol	lomeprool	lohexol	loixanol	losimenol	lopromide	lobitridol	lopamidol	losarcol	lotrolan	Amidotrizoate	loxithalamate	loxaglate
lopentol	o	x	x	x	x	x	x							
loversol	x	o	x	x	x	x	x							
lomeprool	x	x	o	x	x	x	x							
lohexol	x	x	x	o	x	x	x							
loixanol	x	x	x	o	x	x	x							
losimenol	x	x	x	x	x	o	x							
lopromide	x	x	x	x	x	x	o	x						
lobitridol							x	o						
lopamidol									o					
losarcol										o				
lotrolan											o			
Amidotrizoate												o		
loxithalamate													o	
loxaglate														o

Schmid AA, Morelli JN, Hungerbühler MN, Boehm IB. Cross-reactivity among iodinated contrast agents: should we be concerned?. *Quant Imaging Med Surg.* 2021;11(9):4028-4041. doi:10.21037/qims-20-1325

Schmid AA, Böhm IB. Cross-Reactivity and Polyvalent Reactivity in Patients with Iodinated Contrast Medium Allergy: How to Use the Terms Correctly. *Int Arch Allergy Immunol.* 2021;182(8):725-727. doi:10.1159/000514974



Clinical Dilemma and Management Considerations

Recommendations

- **Strict avoidance** of iodinated contrast media (*precautionary approach given multi-drug hypersensitivity and diagnostic uncertainty*)
 - Exception: gastrointestinal contrast agents (e.g. amidotrizoate)
- Preference for non-contrast CT or MRI with gadolinium-based contrast agents, when feasible

Emergency Scenario

e.g. recurrent thrombosis or OHCA requiring CT angiography

- No evidence-based strategy to prevent recurrence of severe delayed NIHR/SCAR
- Switching to a non-cross-reactive iodinated contrast agent: *not feasible in this patient (broad sensitization pattern)*
- Systemic corticosteroid premedication: *not suitable for SCAR prevention*

Experimental Considerations

- Desensitization protocols: experimental / not established and generally not recommended in SCAR
- Targeted immunomodulation:
 - experimental use of IL-5 blockade (benralizumab)
 - rationale: marked IL-5-driven response in LTT

Torres MJ, Trautmann A, Böhm I, et al. Practice parameters for diagnosing and managing iodinated contrast media hypersensitivity. *Allergy.* 2021;76(5):1325-1339. doi:10.1111/all.14656
Lerondeau B, Trechot P, Waton J, et al. Analysis of cross-reactivity among radiocontrast media in 97 hypersensitivity reactions. *J Allergy Clin Immunol.* 2016;137(2):633-635.e4. doi:10.1016/j.jaci.2015.07.035

Take-Home Messages

- Severe drug hypersensitivity may involve multiple phenotypes and multiple culprit drugs.
 - DRESS and MPE can coexist in the same patient.
- Identification of the culprit drug requires integration of clinical course, laboratory findings, functional testing, and follow-up.
 - No single test is sufficient.
 - All relevant exposures, including anesthetic records and contrast media, must be considered in complex cases.
- In the absence of evidence-based strategies for SCAR, management must prioritize risk minimization.
 - Especially for iodinated contrast media in patients with multi-drug hypersensitivity.