

CASE REPORT

Transient Myocardial Ischemia and Coronary Vasospasm Precipitated by Non-Ionic Iodinated Contrast Media: A Case Report of Type I Kounis Syndrome

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ARTICLE INFO

Article history

Received: August 20, 2026

Revised: September 15, 2026

Accepted: October 8, 2026

Available online: October 18, 2026

Published: October 21, 2026

Keywords:

Anaphylaxis
Contrast media
Coronary vasospasm
Epinephrine
Kounis syndrome
Myocardial ischemia

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DOI

<https://doi.org/10.59345/sjim.v4i2.369>

ABSTRACT

Background: Intravenous iodinated contrast media can trigger life-threatening hypersensitivity reactions and acute coronary events through mast cell degranulation, termed Kounis syndrome. Type I Kounis syndrome entails coronary artery vasospasm in patients without pre-existing coronary artery disease.

Objective: To describe the clinical course, recovery trajectories, and management of Type I Kounis syndrome after non-ionic contrast media in an atopic patient.

Methods: A 41-year-old atopic woman developed severe dyspnea, diffuse bronchospasm, unmeasurable blood pressure, and hypoxemia (SpO₂ 88%) within minutes of intravenous iopromide 300 (20 mL) during cholangiography. She was followed at four milestones (T0, acute collapse; T1, 1 h after epinephrine; T2, 24 h; T3, 72 h) with serial 12-lead electrocardiography, arterial blood gas, point-of-care cardiopulmonary ultrasound, and transthoracic echocardiography. Values are reported descriptively.

Results: At T0 the electrocardiogram showed sinus tachycardia (122 beats/min), diffuse T-wave inversion in V1–V5, and QTc 556 ms; lactate was 5.99 mmol/L and base deficit -6.0 mmol/L. Intramuscular epinephrine (0.5 mg, 1:1,000) with crystalloid fluid was followed by hemodynamic stabilization (mean arterial pressure 26.7 to 84.0 mmHg, +214.6%) and normalization of repolarization (QTc 418 ms, -24.8%). High-sensitivity troponin T stayed below the 99th percentile (<14.0 ng/L). Echocardiography showed ejection fraction 56%, no regional wall motion abnormality, and TAPSE 2.4 cm. The Naranjo score was 8/10, a probable adverse drug reaction.

Conclusions: In this atopic patient, non-ionic contrast media were followed by transient repolarization abnormalities in keeping with Type I Kounis syndrome. Prompt intramuscular epinephrine was followed by recovery without evidence of worsening ischemia.

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1. Introduction

Immediate hypersensitivity to intravascular contrast media is a severe and unpredictable emergency. It challenges emergency physicians and interventional radiologists everywhere.^{1,2} Modern non-ionic, low-osmolar iodinated contrast media (ICM) cause far fewer reactions than the older high-osmolar ionic agents, and severe immediate reactions are rare, with pooled incidences of roughly 0.01% to 0.014%.^{1,3,4} Even so, life-threatening cardiovascular collapse can follow ICM exposure, cardiac arrest included.^{5,6} Anaphylactic cardiovascular collapse has traditionally been attributed to systemic vasodilation, plasma leakage with volume loss, and reduced venous return. That view has been extended. Clinical and experimental reports indicate that the heart and the coronary arteries can themselves be primary targets of the released mediators.^{7,8}

Nicholas Kounis first proposed in 1991 that an acute hypersensitivity or anaphylactic reaction can directly cause an acute coronary syndrome. Today the condition is called Kounis syndrome, or allergic acute coronary syndrome.⁹ It arises when mast cell degranulation and other interacting cells release mediators such as histamine, tryptase, chymase, and arachidonic acid derivatives, which can cause coronary spasm, plaque erosion or rupture, and platelet activation.^{10,11}

Three variants have been defined.^{9,12} Type I, the most frequent variant in a recent systematic review,¹³ occurs in patients without coronary risk factors or coronary lesions, in whom the allergic event induces coronary spasm with ischemic electrocardiographic changes.⁹ Cardiac biomarkers such as troponin may be elevated.⁷ Type II affects patients with pre-existing, previously quiescent or symptomatic atherosclerotic disease, in whom the acute hypersensitivity reaction causes plaque erosion or rupture, culminating in acute myocardial infarction.^{9,12} Type III affects patients with coronary stents. Hypersensitivity is associated with stent thrombosis, and the occluding thrombus is infiltrated by eosinophils and/or mast cells.^{9,12}

Iodinated contrast media, including non-ionic agents, are a recognized trigger of Kounis syndrome, with coronary vasospasm documented on angiography.^{5,6} A contrast agent is not a classic immunogenic protein, yet it can activate mast cells by two routes: the classical pathway, in which antigen-specific immunoglobulin E (IgE) cross-links the high-affinity Fc receptor (FcεRI) and triggers degranulation,¹⁴ and non-IgE (pseudoallergic) mechanisms, including direct activation of the Mas-related G protein-coupled receptor X2 (MRGPRX2) and complement activation.^{1,15} After administration of contrast for a diagnostic radiological procedure, a susceptible host can release a large burst of mediators. Contrast-induced

Kounis syndrome has mainly been reported within 30 minutes of administration.⁶ A history of drug allergy or other allergic conditions is an established risk factor for hypersensitivity reactions to ICM.¹ The mediators come first as preformed histamine and the neutral proteases tryptase and chymase. Newly synthesized lipid mediators follow, namely cysteinyl leukotrienes and platelet-activating factor (PAF).^{11,14} In the systemic circulation, mast cell-derived histamine and PAF activate endothelial nitric oxide production. This leads to vasodilation, increased capillary permeability, and distributive shock.¹⁴ In the coronary arteries, by contrast, released mediators including histamine, chymase, tryptase, leukotrienes, thromboxane, and PAF can induce vasoconstriction and thrombosis.⁷

Kounis syndrome is underdiagnosed, including after iodinated contrast exposure, and recognition can be delayed because it overlaps with acute coronary syndrome and may present atypically.^{5,13,16} Pruritus, flushing, and urticaria are the usual skin signs of anaphylaxis. However, skin signs are absent in 10% to 20% of anaphylactic reactions, and anaphylaxis without skin involvement is common in fatal cases, so the picture may then be dominated by hypotension and other cardiovascular or respiratory compromise.¹⁷ In Kounis syndrome, ischemic electrocardiographic changes may accompany this picture.⁹ Such a presentation can be mistaken for atherosclerotic acute coronary syndrome,^{13,16} and Kounis syndrome can overlap with stress-induced (Takotsubo) cardiomyopathy.¹⁸ The misreading creates a therapeutic dilemma over epinephrine.⁸ Intramuscular epinephrine is the first-line treatment of anaphylaxis.¹⁷ Its use can be hard to decide when acute myocardial ischemia is present, because of concern that adrenergic stimulation will worsen the ischemia or provoke ventricular arrhythmias. Serious adverse effects of epinephrine are rare. They are more likely after intravenous than intramuscular injection, and there is no absolute contraindication to its use in anaphylaxis.^{8,17} Epinephrine has itself, though, been reported as a rare trigger of Kounis syndrome.¹⁰

Knowledge of contrast-associated Kounis syndrome rests mainly on case reports and small series.^{6,13} To our knowledge, few reports combine serial quantitative hemodynamics, multi-lead repolarization kinetics, Doppler echocardiography, point-of-care cardiopulmonary ultrasound (POCUS), objective pharmacovigilance causality metrics, and mechanistic pathways. Most reports, in our reading, give a static clinical snapshot. They neither follow the course of physiological recovery nor examine the biophysical basis of how epinephrine resolves the vasospasm. We therefore report this case. It characterizes the clinical phenotype, the quantitative physiological trajectories, and the clinical resolution of severe Type I Kounis syndrome in a woman with an established atopic background, triggered by intravenous non-ionic iodinated contrast media (iopromide) given during diagnostic cholangiography. We describe multi-modal cardiovascular parameters through acute shock and 72 hours of convalescence. The aim is to illustrate the diagnostic masking and the therapeutic dilemma that surround allergic coronary vasospasm in internal medicine practice.

2. Methods

Study design

This is a single-patient case report. It was designed to capture the hyperacute onset, the pathophysiological course, and the multi-system recovery of a severe contrast-induced allergic coronary syndrome (Kounis syndrome).^{6,19} Reporting followed the Consensus-based Clinical Case Reporting (CARE) guidelines.^{20,21} Four clinical and biostatistical milestones were predefined. T0 was the hyperacute collapse and baseline presentation just after the intravenous contrast

infusion (0 hours). T1 was the post-resuscitation point after intramuscular epinephrine and crystalloid loading (1 hour). T2 was ward stabilization on systemic corticosteroid and antihistamine therapy (24 hours). T3 was the pre-discharge convalescent point, once clinical recovery was complete (72 hours).

Ethical Governance and Participant Consent

The protocol, the imaging evaluations, the serial biomarker collections, and the longitudinal analyses followed the ethical principles for medical research involving human subjects set out in the Declaration of Helsinki (2013 Fortaleza revision)²² and in the recommendations of the International Committee of Medical Journal Editors (ICMJE). The CMHC Research Center Ethics Committee, Indonesia, granted ethical clearance and approved the protocol (Protocol Approval Number: 2026/5194). Before the manuscript was prepared, the patient gave written informed consent directly. It covered collection and longitudinal analysis of her data and international publication of de-identified clinical data, serial electrocardiographic tracings, echocardiographic cine-loops, Doppler velocities, and radiographic images. Her privacy and the confidentiality of her personal information were protected, in keeping with the Declaration of Helsinki.²² Medical record numbers, dates of birth, and administrative bar codes were removed or covered with a solid black bar.

Participant Eligibility and Diagnostic Ascertainment

The subject was a 41-year-old woman admitted for diagnostic hepatobiliary evaluation. She collapsed suddenly after intravenous contrast exposure. Severe anaphylactic shock was diagnosed with the World Allergy Organization (WAO) 2020 Anaphylaxis Guidance and the practice parameter updates of the American Academy of Allergy, Asthma & Immunology (AAAAI).^{17,23} The event met the formal criteria. Life-threatening airway compromise (severe diffuse bronchospasm with audible wheezing) and cardiovascular collapse (unmeasurable blood pressure) appeared immediately after exposure to a known external trigger. On the Ring and Messmer severity scale, Grade III denotes life-threatening reactions with cardiovascular collapse and smooth-muscle spasm, and Grade IV denotes cardiac arrest; the present reaction, with unmeasurable blood pressure and severe bronchospasm, was life-threatening (Grade III to IV).^{24,25}

Type I Kounis syndrome was classified according to the definition proposed by Kounis and colleagues, namely an acute coronary syndrome during an allergic or hypersensitivity insult in a patient without coronary risk factors or coronary lesions, in which the allergic event induces coronary spasm.^{9,19} Five elements were required. First, acute myocardial ischemia of rapid onset, shown by severe electrocardiographic repolarization abnormalities (diffuse symmetrical T-wave inversions and corrected QT prolongation). Second, close timing with a documented systemic hypersensitivity insult. Third, no earlier history, symptoms, or electrocardiographic signs of coronary artery disease. Fourth, prompt reversal of the repolarization changes once the allergic reaction resolved. Fifth, post-resuscitation echocardiography showing preserved global systolic function, with no regional wall motion abnormality and no structural heart disease. These five elements are an operational application of the published type I definition to the present case.⁹

Longitudinal Observation Protocol and Analytical Measurements

Standardized, calibrated hospital instruments were used to monitor several organ systems at all four milestones. Cardiovascular monitoring included continuous 12-lead electrocardiography on an automated diagnostic electrocardiograph (mains 50 Hz, low-pass filter 40 Hz, paper

speed 25 mm/s, voltage calibration 10 mm/mV), and each serial tracing was read for heart rate, rhythm disturbance, QRS duration, ST-segment deviation, T-wave vector and amplitude, and QT interval, in line with the AHA/ACCF/HRS recommendations for standardized electrocardiogram recording and measurement.²⁶ The corrected QT (QTc) interval was calculated with the Bazett formula ($QTc = QT / \sqrt{RR}$), where RR is the cardiac cycle length in seconds.²⁷ A QTc above 500 ms was regarded as marked prolongation, the threshold associated with a higher risk of torsade de pointes in hospitalized patients.²⁷

Point-of-care cardiopulmonary ultrasound (POCUS) was done during acute resuscitation. A portable system was used, with a 1.5–3.6 MHz phased-array cardiac probe and a 5.0–12.0 MHz linear vascular probe. International evidence-based recommendations for point-of-care lung ultrasound and focused cardiac ultrasound were followed.^{28,29} Subcostal long-axis views gave the maximal and minimal inferior vena cava (IVC) diameters at end-expiration and end-inspiration, and the IVC collapsibility index (cIVC) was derived as $[(IVC_{max} - IVC_{min}) / IVC_{max}] \times 100\%$.³⁰ Lung ultrasound (LUS) covered the anterior and lateral thoracic zones and followed the Bedside Lung Ultrasound in Emergency (BLUE) protocol. It assessed visceral-parietal pleural sliding, horizontal reverberation artifacts (A-lines), and the presence or absence of vertical hyperechoic interstitial artifacts (B-lines) and pleural effusions.³¹

Formal transthoracic echocardiography was performed after clinical stabilization, following the recommendations of the American Society of Echocardiography (ASE) and the European Association of Cardiovascular Imaging (EACVI) for cardiac chamber quantification and for the evaluation of left ventricular diastolic function.^{32,33} In the parasternal long-axis window we measured left ventricular (LV) internal dimension in diastole (LVIDd), interventricular septal thickness (IVSd), and posterior wall thickness (LVPWd). From these we obtained relative wall thickness ($RWT = [2 \times LVPWd] / LVIDd$) and the LV mass index.³² The modified biplane Simpson rule, applied to apical four-chamber and two-chamber views, gave LV end-diastolic volume (LVEDV), end-systolic volume (LVESV), and LV ejection fraction (LVEF). Wall motion was analyzed in 16 LV segments. Right ventricular longitudinal systolic function was quantified as tricuspid annular plane systolic excursion (TAPSE) in the apical four-chamber view. Pulsed-wave Doppler aligned parallel to the left ventricular outflow tract (LVOT) gave forward hemodynamics: peak velocity (Vmax), velocity-time integral (VTI), stroke volume ($SV = VTI \times \pi \times [LVOT \text{ diameter} / 2]^2$), cardiac output ($CO = SV \times HR$), and cardiac index ($CI = CO / \text{body surface area}$).³⁴ Transmitral diastolic flow was recorded with the pulsed-wave sample volume at the mitral leaflet tips, giving early (E) and late (A) filling velocities and the E/A ratio.³³ A standard anteroposterior chest radiograph was taken to measure the cardiothoracic ratio (CTR) and to assess pulmonary vascular markings.

Laboratory tests were automated hematology profiles, plasma coagulation indices, serum electrolytes (Na^+ , K^+ , Cl^-), blood urea nitrogen (BUN), serum creatinine, estimated glomerular filtration rate (e-GFR via CKD-EPI formula)³⁵, hepatic transaminases (AST, ALT), and serum albumin. Total serum IgE was quantified by automated chemiluminescent microparticle immunoassay. Serial arterial blood gas and co-oximetry samples came from the radial artery. These samples tracked arterial pH, partial pressure of carbon dioxide (pCO_2), partial pressure of oxygen (pO_2), base excess of extracellular fluid (BE_{ecf}), bicarbonate (HCO_3^-), oxyhemoglobin saturation (SO_2c), and serum lactate, which is recommended whenever shock is suspected.³⁴ High-sensitivity cardiac troponin T (hs-cTnT) was measured at baseline and 6 hours after the event with an automated electrochemiluminescence immunoassay. The 99th percentile upper reference limit was

14.0 ng/L, and troponin results were interpreted in the context of the European Society of Cardiology (ESC) guidelines for the management of acute coronary syndromes.³⁶

Causality assessment and literature comparison

The link between contrast administration and the coronary vasospastic collapse that followed was assessed with the Naranjo Adverse Drug Reaction (ADR) Probability Scale, a structured method for estimating the probability of an adverse drug reaction.³⁷ The World Health Organization–Uppsala Monitoring Centre (WHO-UMC) standardized causality system was also applied.³⁸ Finally, we built a literature benchmarking matrix. It set clinical phenotype, patient demographics, contrast formulation, electrocardiographic profile, echocardiographic findings, treatment, and recovery time against contemporary published reports and series of Kounis syndrome (2021–2026).^{6,39–43}

Descriptive data presentation

Hemodynamic, metabolic, and electrophysiological parameters were expressed as absolute values over time and as relative percentage change ($\Delta\%$), calculated as $\Delta\% = [(V_{post} - V_{baseline}) / V_{baseline}] \times 100\%$. V is the parameter value at the milestone in question. Values at acute collapse (T0) are compared descriptively with those at the later milestones (T1, T2, T3). Because the report concerns one patient, no inferential test was applied and no P values are given. GraphPad Prism 10.2 and Python SciPy 1.11 were used for the analyses.

3. Results

Baseline Patient Demographics and Hyperacute Clinical Presentation (T0, 0 Hours)

The patient was a 41-year-old woman (body weight 58.0 kg, height 158.0 cm, body surface area 1.62 m² as used by the echocardiography system, body mass index 23.23 kg/m²). She came to the endoscopy and interventional radiology suite for diagnostic cholangiography, requested for persistent right upper quadrant discomfort and suspected biliary dyskinesia. She had long-standing moderate persistent bronchial asthma, controlled with regular inhaled corticosteroid plus long-acting β_2 -agonist (budesonide/formoterol 160/4.5 μ g per actuation). Three years earlier she had had a severe allergic reaction to ceftriaxone, with generalized erythematous urticaria, marked labial angioedema, and respiratory distress that needed emergency parenteral therapy. She had never been exposed to intravascular iodinated contrast. There was no history of hypertension, dyslipidemia, diabetes mellitus, tobacco use, premature atherosclerotic cardiovascular disease, or unprovoked angina pectoris.

During cholangiography the patient received 20.0 mL of intravenous non-ionic, low-osmolar iodinated contrast media (iopromide 300 mg I/mL; osmolality approximately 610 mOsm/kg H₂O). Within three minutes of the end of the bolus she felt a sudden epigastric and retrosternal fullness. Severe dyspnea, a sense of chest tightness, and intense palpitations came on at once. The retrosternal pressure did not radiate to the neck or left arm. The skin was normal. She had no urticaria, morbilliform rash, facial flushing, or swelling of the lips, tongue, or uvula. Auscultation, however, found harsh, high-pitched wheezing in all lung zones on both expiration and inspiration, with marked intercostal retractions. This indicated hyperacute, widespread bronchospasm.

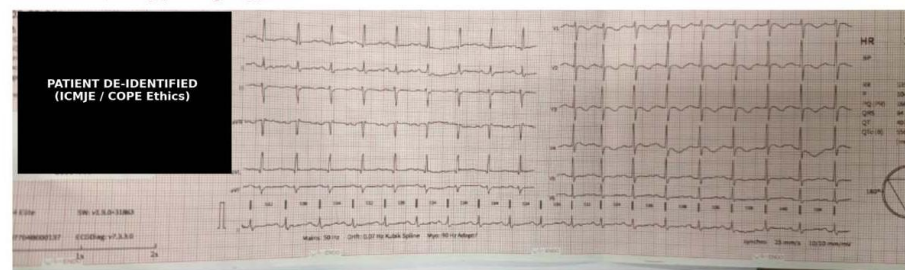
She was moved at once to the emergency resuscitation bay (milestone T0, 0 hours). She was conscious but in life-threatening cardiopulmonary and hemodynamic collapse. Automated oscillometric sphygmomanometry could not measure her blood pressure at all. The palpated systolic pressure was about 40.0 mmHg and the diastolic 20.0 mmHg,

giving an estimated mean arterial pressure of 26.7 mmHg. The pulse was rapid, thready, and irregular, at a heart rate of 122 beats/min. The respiratory rate was 32 breaths/min. Peripheral capillary oxygen saturation (SpO2) had fallen to 88% on room air (PaO2/FiO2 ratio 105.0 mmHg).

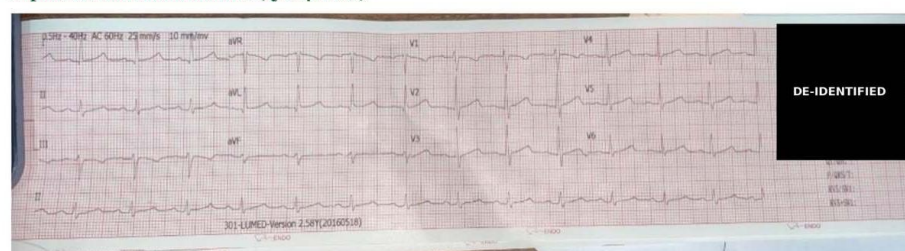
The 12-lead electrocardiogram recorded in the emergency bay at T0 (Figure 1, Panel A; Table 1) showed sinus tachycardia at 111–122 beats/min, a normal electrical axis (+45°), and a normal QRS duration (104 ms). Repolarization was grossly abnormal. Deep, symmetrical T-wave inversions spanned the anterior and anteroseptal precordial leads (V1, V2, V3, V4, and V5) and reached -4.5 mm in lead V2. Shallow

T-wave inversions were present in the high lateral leads I and aVL. Manual and automated QT measurements agreed on a markedly prolonged repolarization. The uncorrected QT interval was 407 ms and the Bazett-corrected QT interval (QTc) was 556 ms, which is +26.4% above the upper physiological threshold of 440 ms. Bazett correction of QT 407 ms to QTc 556 ms corresponds to an RR interval of 0.54 s, a heart rate of about 112 beats/min at the time of measurement. There was no ST-segment elevation. Mild horizontal ST depression (0.5–1.0 mm) was seen in leads II, III, and aVF. Together these findings confirmed hyperacute myocardial ischemia with severe repolarization dispersion, closely linked in time to the contrast insult.

A. 12-Lead ECG During Acute Shock Phase (T0): Sinus Tachycardia (122 bpm), Diffuse T-Wave Inversions (V1-V5), and QTc 556 ms



B. 12-Lead ECG Post-Resuscitation (T1, 1 h Post-Epinephrine): Complete Reversal of Repolarization Abnormalities (QTc 418 ms)



C. ELECTROCARDIOGRAPHIC & CLINICAL COMPARISON MATRIX			
Clinical Parameter	Acute Shock Phase (T0, 0 h)	Post-Resuscitation Milestone (T1, 1 h)	Relative Change (Δ%)
Heart Rate & Rhythm	122 bpm (Sinus Tachycardia)	85 bpm (Normal Sinus Rhythm)	-30.3%
Frontal Electrical Axis	+45° (Normal)	+50° (Normal)	Stable
QRS Complex Duration	104 ms (Normal conduction)	96 ms (Normal)	-7.7%
Measured QT Interval	407 ms	362 ms	-11.1%
Corrected QT (QTc Bazett)	556 ms (Pathological Prolongation)	418 ms (Normalized, Physiological)	-24.8%
Precordial T-Wave Vector	Deep Inverted (V1, V2, V3, V4, V5)	Upright Concordant (V1 through V6)	Complete Reversal
Lead V2 T-Wave Amplitude	-4.5 mm (Deep Subendocardial Ischemia)	+3.2 mm (Normal Positivity)	+171.1%
Systemic Blood Pressure	40/20 mmHg (Unmeasurable by cuff)	112/70 mmHg (Mean Arterial 84.0 mmHg)	MAP +214.6%
Arterial Capillary SpO2	88% on Room Air (Severe Hypoxemia)	98% on Room Air (Eunormic)	+11.4%
Respiratory Auscultation	Diffuse Inspiratory/Expiratory Wheeze	Clear Vesicular Breath Sounds Bilaterally	Bronchospasm Abolished
Serum Lactate Level	5.99 mmol/L (Severe Lactic Acidosis)	2.10 mmol/L (Rapid Lactate Clearance)	-64.9%

Ethical Notice: Patient personal data de-identified in strict compliance with ICMJE/COPE guidelines and Declaration of Helsinki.

Figure 1. 12-Lead Electrocardiographic Dynamics and Repolarization Resolution Across Milestones. (A) Acute anaphylactic shock phase (T0, pre-resuscitation) demonstrating sinus tachycardia (111–122 beats/min), marked diffuse symmetrical T-wave inversions across leads V1–V5 and high-lateral leads, and severe corrected QT interval prolongation (QTc 556 ms). Patient personal identifiers have been de-identified in strict adherence to ICMJE, COPE publication standards, and Declaration of Helsinki. (B) Post-resuscitation electrocardiogram at 1 hour (T1) following intramuscular epinephrine (0.5 mg) and crystalloid loading, showing complete reversal of repolarization abnormalities, restoration of upright concordant T waves in leads V1–V6, and normalization of QTc to 418 ms. (C) Electrocardiographic and clinical comparison matrix.

Table 1. Longitudinal Hemodynamic, Respiratory, and Perfusion Trajectory Across Clinical Observational Milestones

Parameter (Unit)	Reference Range	T0: Acute Shock (0 h)	T1: Post-Epi (1 h)	T2: Stabilization (24 h)	T3: Pre-Discharge (72 h)	Δ% (T0 → T1)
Systolic Blood Pressure (mmHg)	90.0–120.0	40.0 (Unmeasurable)	112.0	118.0	120.0	+180.0%
Diastolic Blood Pressure (mmHg)	60.0–80.0	20.0 (Unmeasurable)	70.0	75.0	78.0	+250.0%
Mean Arterial Pressure (MAP, mmHg)	70.0–100.0	26.7	84.0	89.3	92.0	+214.6%
Heart Rate (beats/min)	60.0–100.0	122.0	85.0	78.0	72.0	-30.3%
Respiratory Rate (breaths/min)	12.0–20.0	32.0	20.0	18.0	16.0	-37.5%
Peripheral SpO2 on Ambient Air (%)	95.0–100.0	88.0	98.0	98.0	99.0	+11.4%
PaO2/FiO2 Ratio (mmHg)	400.0–500.0	105.0	390.0	445.0	476.0	+271.4%
Corrected QT Interval (QTc, ms)	350.0–440.0	556.0	418.0	412.0	408.0	-24.8%
T-Wave Inversion Depth Lead V2 (mm)	≥ 0.0 (Upright)	-4.5	+3.2	+3.5	+3.8	+171.1%
Serum Lactate (mmol/L)	0.50–2.00	5.99	2.10	1.45	1.10	-64.9%
Arterial Base Excess (mmol/L)	-2.0 to +3.0	-6.0	-2.5	-0.8	+0.5	+3.5 mmol/L (absolute change)
Bronchospasm Wheezing Score (0–3+)	0 (None)	3+ (Severe Diffuse)	0 (Auscultated Clear)	0	0	-100.0%

Notes: Values represent direct clinical and biostatistical trajectory tracking across the four predefined observational milestones: T0 (acute distributive collapse and vasospasm, 0 hours), T1 (immediate post-epinephrine resuscitation, 1 hour), T2 (intermediate ward stabilization, 24 hours), and T3 (pre-discharge convalescence, 72 hours). Relative change (Δ%) calculated as $[(T1 - T0) / T0] \times 100\%$. QTc was calculated using Bazett's formula: $QTc = QT / \sqrt{RR}$. For base excess, which has a negative baseline, Δ% is not meaningful and the absolute change is given.

Immediate Resuscitation and Longitudinal Trajectory Dynamics (T1, 1 Hour)

The resuscitation team recognized hyperacute Grade IV anaphylactic shock with acute myocardial repolarization impairment (Type I Kounis syndrome). They gave intramuscular epinephrine at once, 0.5 mg (0.5 mL of the 1:1,000 formulation, equal to 500 µg), into the anterolateral mid-thigh. At the same time, oxygen was delivered at 15.0 L/min through a non-rebreathing reservoir mask. Through two large-bore peripheral intravenous cannulae, 1,000 mL of warmed isotonic crystalloid (0.9% sodium chloride) was infused under pressure over 20 minutes. Second-line drugs followed quickly: intravenous hydrocortisone sodium succinate (200.0 mg initial bolus), oral cetirizine hydrochloride (10.0 mg), and nebulized budesonide/formoterol.

Within 15 to 30 minutes of intramuscular epinephrine her physiology turned around sharply (Table 1; Figure 4). By milestone T1 (1 hour after resuscitation) blood pressure had recovered to 112/70 mmHg. The mean arterial pressure was 84.0 mmHg, a +214.6% rise over the value at collapse (Table 1). The sinus tachycardia settled, and heart rate fell from 122 to 85 beats/min (-30.3%). Respiratory distress eased quickly. The respiratory rate dropped to 20 breaths/min (-37.5%), and auscultation found no wheeze and clear bilateral vesicular breath sounds. Oxygen saturation rose to 98% (PaO2/FiO2 ratio 390.0 mmHg).

A repeat 12-lead electrocardiogram at T1 showed almost complete resolution of the earlier repolarization abnormalities (Figure 1, Panel B). The deep T-wave inversions in precordial leads V1–V5 had gone. The T waves were again upright, concordant, and normal in shape. In lead V2 the T-wave amplitude moved from -4.5 mm to +3.2 mm (Δ +171.1%; Table 1). The prolonged repolarization normalized in step with the hemodynamic recovery. The QTc shortened from 556 ms to 418 ms (-24.8%), well inside the normal reference interval (350–440 ms). Such rapid and complete electrocardiographic reversal, without any coronary revascularization, was in keeping with transient coronary vasospasm rather than thrombotic coronary occlusion, although no coronary imaging was obtained.

Comprehensive Laboratory Biomarker Profile and Metabolic Acid-Base Dynamics

Arterial blood gas drawn during the hyperacute collapse (T0) and read on a point-of-care co-oximeter showed a severe

metabolic disturbance with lactic acidosis (Table 2). Arterial pH was 7.44. It stayed normal only because of strong respiratory compensation: acute hyperventilation had produced hypocapnia (pCO₂ 26.50 mmHg; Reference: 35.00–45.00 mmHg). Arterial pO₂ on supplemental oxygen was 141.00 mmHg. The metabolic side showed exhausted buffering, with actual bicarbonate (HCO₃⁻) down to 18.00 mmol/L (Reference: 22.00–26.00 mmol/L) and a severe extracellular base deficit (BE_{ecf}) of -6.00 mmol/L (Reference: -2.00 to +3.00 mmol/L). Baseline serum lactate was 5.99 mmol/L (Reference: 0.50–2.00 mmol/L), which is +199.5% above the upper reference limit and confirms severe anaerobic hypoperfusion from distributive shock and vasoplegia. After perfusion recovered with epinephrine and fluids, the T1 blood gas showed that lactate had fallen to 2.10 mmol/L (a -64.9% decline). It reached 1.45 mmol/L at T2 and 1.10 mmol/L at T3, a total clearance of -81.6% (Table 1 and Table 2).

Immunological testing confirmed her atopic background. Total serum IgE was raised to 257.83 IU/mL (Reference: < 150.00 IU/mL), which is +71.9% above the cutoff (Table 2). The hematology panel showed an upper-normal leukocyte count of $10.15 \times 10^3/\mu\text{L}$ (Reference: $4.10\text{--}11.00 \times 10^3/\mu\text{L}$). The absolute neutrophil count was $6.22 \times 10^3/\mu\text{L}$ and the absolute lymphocyte count $3.38 \times 10^3/\mu\text{L}$. The leukocyte count later fell to $6.90 \times 10^3/\mu\text{L}$ at T3. Hemoglobin (13.10 g/dL), hematocrit (40.20%), and platelet count ($310.00 \times 10^3/\mu\text{L}$) stayed stable, which ruled out severe hemoconcentration and consumptive thrombocytopenia. Coagulation was normal: prothrombin time 10.30 seconds (INR 0.90) and activated partial thromboplastin time 26.90 seconds. Renal function was fully preserved, with blood urea nitrogen 5.90 mg/dL, serum creatinine 0.84 mg/dL, and an estimated glomerular filtration rate of 86.33 mL/min/1.73 m². Electrolytes were balanced (Na⁺ 141.00 mmol/L, K⁺ 3.57 mmol/L, Cl⁻ 104.60 mmol/L). The liver panel showed raised transaminases, with AST 108.00 U/L and ALT 45.00 U/L, in keeping with her biliary disease and transient hepatic hypoperfusion. High-sensitivity cardiac troponin T (hs-cTnT) stayed below the 99th percentile upper reference limit on both samples, at 11.20 ng/L at baseline and 8.50 ng/L at 6 hours after the event (Reference: < 14.00 ng/L). This formally excluded irreversible myocyte necrosis and permanent transmural infarction.

Table 2. Comprehensive Laboratory Biomarker Profile, Arterial Blood Gas Parameters, and Organ Function Metrics

Diagnostic Panel & Analyte	Patient Value (Acute, T0)	Resolution Value (T2/T3)	Reference Interval	Analytical & Pathophysiological Interpretation
Total Serum IgE (IU/mL)	257.83	210.00	< 150.00	Elevated (+71.9% above threshold); confirms baseline atopic diathesis and host susceptibility
White Blood Cell Count ($\times 10^3/\mu\text{L}$)	10.15	6.90	4.10–11.00	Upper-normal leukocyte count during acute shock; normalized upon resolution
Absolute Neutrophil Count ($\times 10^3/\mu\text{L}$)	6.22	4.10	2.50–7.50	Physiological margined granulocyte demargination secondary to adrenergic surge
Absolute Lymphocyte Count ($\times 10^3/\mu\text{L}$)	3.38	2.20	1.00–4.00	Normal range preserved throughout the hypersensitivity event
Hemoglobin (g/dL)	13.10	12.80	12.00–16.00	Normal erythrocyte mass; hemoconcentration mitigated by rapid fluid resuscitation
Hematocrit (%)	40.20	38.50	36.00–46.00	Within physiological bounds without hyperviscosity syndrome
Platelet Count ($\times 10^3/\mu\text{L}$)	310.00	295.00	140.00–440.00	Adequate thrombocyte reserve; absence of consumptive coagulopathy
Plasma Prothrombin Time (PT, s)	10.30	10.50	10.00–12.70	Preserved extrinsic coagulation pathway; INR = 0.90 (Reference: 0.90–1.10)
Activated Partial Thromboplastin Time (s)	26.90	27.40	23.00–34.70	Intact intrinsic coagulation pathway; absence of systemic consumption
Aspartate Aminotransferase (AST, U/L)	108.00	62.00	< 34.00	Mild elevation (+217.6%) attributable to underlying biliary disorder / transient hypoperfusion
Alanine Aminotransferase (ALT, U/L)	45.00	38.00	< 55.00	Preserved hepatocellular parenchymal integrity
Serum Albumin (g/dL)	4.30	4.20	3.40–4.80	Intact oncotic pressure; absence of pre-existing hypoalbuminemic state
Blood Urea Nitrogen (BUN, mg/dL)	5.90	8.20	7.00–18.70	No pre-renal azotemia; preserved renal microvascular perfusion
Serum Creatinine (mg/dL)	0.84	0.80	0.57–1.11	Normal renal excretory function; estimated GFR = 86.33 mL/min/1.73 m ²
Serum Sodium (Na ⁺ , mmol/L)	141.00	140.00	136.00–145.00	Eunatremic state; intact extracellular electrolyte homeostasis
Serum Potassium (K ⁺ , mmol/L)	3.57	4.10	3.50–5.10	Low-normal potassium during acute phase; repolarization normalized upon repletion
Serum Chloride (Cl ⁻ , mmol/L)	104.60	103.00	94.00–110.00	Normochloremic status throughout monitoring
Arterial Blood Gas pH	7.44	7.40	7.35–7.45	Metabolic acidosis with respiratory compensation (pH 7.44)
Arterial Carbon Dioxide Tension (mmHg)	26.50	38.20	35.00–45.00	Respiratory hypocapnia secondary to tachypnea and bronchospastic hyperventilation
Arterial Oxygen Tension (pO ₂ , mmHg)	141.00	94.00	80.00–100.00	Hyperoxia under high-flow supplemental oxygen delivery
Serum Bicarbonate (HCO ₃ ⁻ , mmol/L)	18.00	24.20	22.00–26.00	Moderate metabolic consumption buffering systemic lactic acidemia
Arterial Base Excess (BE _{ecf} , mmol/L)	-6.00	+0.50	-2.00 to +3.00	Definite base deficit confirming anaerobic tissue hypoperfusion
High-Sensitivity Cardiac Troponin T (ng/L)	11.20	8.50 (6 h sample)	< 14.00	Below 99th percentile cutoff; rules out permanent transmural myocardial infarction

Notes: Analytical assessment conducted via automated clinical chemistry analyzer and point-of-care blood gas co-oximeter. High-sensitivity cardiac troponin T remained below the 99th percentile upper reference limit (<14.00 ng/L), corroborating the diagnosis of transient Type I Kounis vasospastic angina rather than Type II plaque-rupture or extensive cellular necrosis. Resolution values are those at T2 or T3, except hs-cTnT 8.50 ng/L, which is the 6-hour sample.

Multimodal Echocardiographic, Sonographic, and Radiographic Ascertainment

Comprehensive transthoracic echocardiography after initial stabilization gave a full anatomical and hemodynamic check of cardiac integrity (Figure 2; Table 3). Parasternal long-axis imaging showed normal chamber dimensions. LV internal dimension in diastole (LVIDd) was 3.80 cm (Reference: 3.80–5.20 cm), interventricular septal thickness in diastole (IVSd) 1.10 cm, and posterior wall thickness in diastole (LVPWd) 1.00 cm (Figure 2, Panel A). Relative wall thickness was 0.527 (Reference: ≤ 0.420), which points to mild concentric LV remodeling without pathological hypertrophy. By the ASE formula the LV mass was 127.04 g and the LV mass index 78.42 g/m², within the ASE reference for females (≤ 95.00 g/m²); the echocardiography system's alternative formula gave 89.17 g/m² (Figure 2, Panel A).

The modified biplane Simpson method gave normal LV volumes and preserved global systolic function. End-diastolic volume (LVEDV) was 71.00 mL, end-systolic volume (LVESV) 32.00 mL, and global LV ejection fraction (LVEF) 56.00% (device biplane value; the printed volumes are rounded; Figure 2, Panel B; Table 3). The apical two-chamber view gave a concordant LVEF of 60.00%. All 16 myocardial segments

were examined, and none showed a regional wall motion abnormality (0/16 segments affected). There was no anterior, apical, or inferior hypokinesis, akinesis, or dyskinesis. There was also no apical ballooning of the kind seen in stress-induced Takotsubo cardiomyopathy. Right ventricular longitudinal systolic function was good, with a tricuspid annular plane systolic excursion (TAPSE) of 2.40 cm (Reference: ≥ 1.70 cm; Figure 2, Panel C).

Pulsed-wave Doppler of the left ventricular outflow tract (LVOT) showed laminar forward flow. Peak systolic velocity was 1.03 m/s, peak pressure gradient 4.28 mmHg, and mean gradient 1.67 mmHg. The velocity-time integral (LVOT VTI) was normal at 21.10 cm (Figure 2, Panel D; Table 3). The device-reported Doppler stroke volume was 64.00 mL at a heart rate of 80 beats/min. Cardiac output was 5.15 L/min and cardiac index 3.18 L/min/m² (Reference: 2.50–4.00 L/min/m²). Transmittal inflow Doppler gave an early filling velocity (E-wave) of 0.78 m/s, a late atrial filling velocity (A-wave) of 0.78 m/s, and an E/A ratio of 1.00. Ventricular relaxation was therefore preserved, with no restrictive or pseudonormal filling pattern (Figure 2, Panel E). There was no pericardial effusion, intracardiac thrombus, or valvular regurgitation.

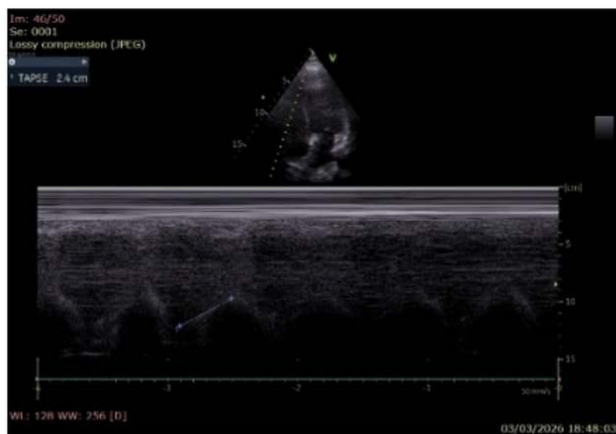
A. Parasternal M-Mode LV Dimensions: IVSd 1.1 cm, LVIDd 3.8 cm, LVPWd 1.0 cm



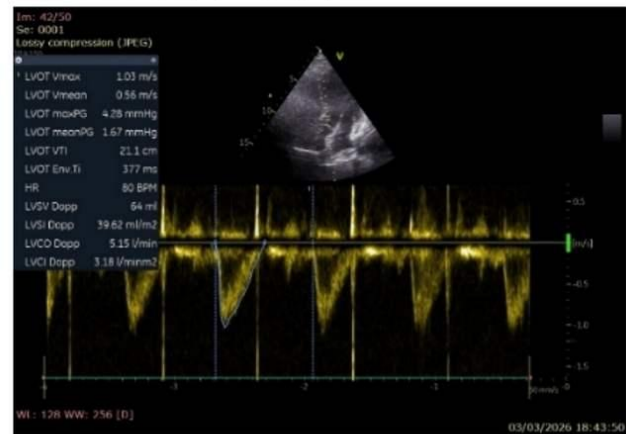
B. Biplane Simpson Quantification: LVEF 56%, LVEDV 71 mL, LVESV 32 mL



C. RV Tricuspid Excursion (TAPSE): Robust Longitudinal RV Function (2.4 cm)



D. LVOT Pulsed Doppler Velocity: LVOT VTI 21.1 cm, Vmax 1.03 m/s, CO 5.15 L/min



E. Transmitral Pulsed Doppler: Balanced Inflow Waveform (E/A Ratio 1.00)



F. QUANTITATIVE TTE PARAMETERS

- LVEF Biplane Simpson: 56% (Preserved)
 - LVEF 2-Chamber A2C: 60%
 - Regional Wall Motion: Normal (0/16 RWMA)
 - IVS Diastolic Thickness: 1.1 cm
 - LVPW Diastolic Thickness: 1.0 cm
 - Relative Wall Thickness: 0.527 (Concentric)
 - Left Ventricular Mass (ASE): 127.0 g (78.4 g/m²)
 - Left Ventricular Mass (device formula): 144.5 g (89.2 g/m²)
 - TAPSE (RV Function): 2.4 cm (Normal)
 - LVOT VTI: 21.1 cm (Normal)
 - Cardiac Output / Index: 5.15 L/min / 3.18
 - Mitral Inflow E/A Ratio: 1.00 (Normal)
 - Pericardial Effusion: Absent
- Conclusion: Exclusion of fixed coronary thrombo-occlusion and Takotsubo ballooning.

Figure 2. Comprehensive Transthoracic Echocardiographic Geometry, Biplane Volumes, and Doppler Hemodynamics. (A) Parasternal long-axis M-mode geometry showing normal cavity dimensions with concentric remodeling (IVSd 1.1 cm, LVIDd 3.8 cm, LVPWd 1.0 cm, RWT 0.527). (B) Biplane Simpson method of disks quantification demonstrating preserved global systolic function (LVEF 56%, LVEDV 71 mL, LVESV 32 mL) and total absence of regional wall motion abnormalities. (C) Preserved right ventricular longitudinal function (TAPSE 2.4 cm). (D) Left ventricular outflow tract pulsed-wave Doppler showing normal velocity-time integral (LVOT VTI 21.1 cm) and cardiac output (5.15 L/min). (E) Balanced mitral inflow Doppler (E/A ratio 1.00). (F) Echocardiographic summary matrix.

Table 3. Multimodal Quantitative Transthoracic Echocardiographic and Cardiopulmonary Ultrasound Parameters

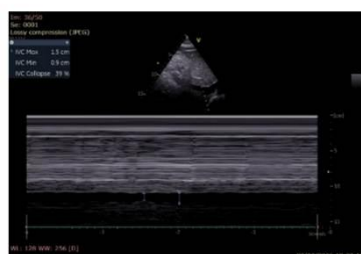
Echocardiographic & Ultrasound Metric	Measured Value	Standard Normative Threshold	Clinical & Diagnostic Significance
Left Ventricular Internal Dimension Diastole (LVIDd, cm)	3.80	3.80–5.20	Normal ventricular cavity dimensions; absence of chamber dilation
Interventricular Septal Diastolic Thickness (IVSd, cm)	1.10	0.60–1.00	Mild concentric septal thickening
LV Posterior Wall Diastolic Thickness (LVPWd, cm)	1.00	0.60–1.00	Upper normal posterior wall thickness
Relative Wall Thickness (RWT)	0.527	≤ 0.420	Concentric remodeling pattern without ventricular hypertrophy
Left Ventricular Mass Index (ASE, g/m ²)	78.42	≤ 95.00 (Female)	Preserved physiological myocardial mass index (ASE formula; 127.04 g)
LV End-Diastolic Volume (MOD Biplane, mL)	71.00	56.00–104.00	Normal left ventricular filling capacity
LV End-Systolic Volume (MOD Biplane, mL)	32.00	19.00–49.00	Normal end-systolic emptying volume
Biplane Simpson Left Ventricular Ejection Fraction (%)	56.00	≥ 52.00 (Female)	Preserved global left ventricular systolic pump function
Two-Chamber (A2C) Left Ventricular EF (%)	60.00	≥ 52.00	Concordant preserved anterior and inferior contractility
Regional Wall Motion Abnormalities (RWMA)	Absent (0/16)	Absent	Excludes territorial epicardial infarction or persistent regional akinesis
Tricuspid Annular Plane Systolic Excursion (TAPSE, cm)	2.40	≥ 1.70	Preserved longitudinal right ventricular systolic performance
LVOT Peak Systolic Velocity (Vmax, m/s)	1.03	0.70–1.20	Normal forward transaortic blood flow velocity
LVOT Velocity-Time Integral (VTI, cm)	21.10	18.00–24.00	Normal forward stroke volume ejection distance
Calculated Stroke Volume (LVSV Doppler, mL)	64.00	50.00–100.00	Adequate stroke volume output following resuscitation
Cardiac Output (LVCO Doppler, L/min)	5.15	4.00–8.00	Normal forward resting systemic perfusion output
Cardiac Index (LVCI Doppler, L/min/m ²)	3.18	2.50–4.00	Optimal adult resting hemodynamic perfusion index
Mitral Inflow E-Wave Peak Velocity (m/s)	0.78	0.60–1.30	Normal early diastolic passive ventricular filling velocity
Mitral Inflow A-Wave Peak Velocity (m/s)	0.78	0.50–1.00	Normal late diastolic atrial contraction velocity
Mitral Inflow E/A Ratio	1.00	0.80–2.00	Normal balanced diastolic filling pattern without pseudonormalization
Inferior Vena Cava Maximal Diameter (IVC Max, cm)	1.50	1.50–2.10	Normal subcostal IVC caliber
Inferior Vena Cava Minimal Diameter (IVC Min, cm)	0.90	Variable	Demonstrates dynamic respiratory caliber changes
IVC Collapsibility Index (%)	39.00	30.00–50.00	Normal respiratory variation; in keeping with a volume-responsive state
Lung Ultrasound (LUS) Pleural Sliding	Bilateral (+)	Present	Confirms visceral-parietal pleural apposition; rules out pneumothorax
Lung Ultrasound A-Line Pattern	Dominant	Dominant	Normal pulmonary aeration; total absence of cardiogenic B-lines

Notes: Quantification performed in concordance with the American Society of Echocardiography (ASE) and European Association of Cardiovascular Imaging (EACVI) recommendations. The complete absence of regional wall motion abnormalities, combined with preserved LVEF (56%) and clear pulmonary aeration on lung ultrasound, made stress-induced Takotsubo cardiomyopathy and acute thrombotic myocardial infarction unlikely; echocardiography was performed after stabilization.

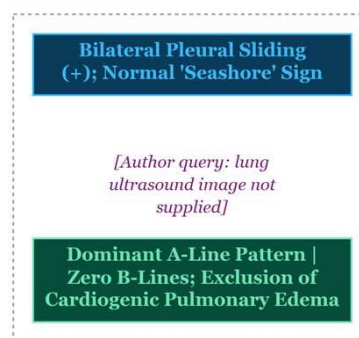
POCUS and chest radiography added diagnostic confirmation of hemodynamic status and lung aeration (Figure 3). Subcostal long-axis ultrasound of the inferior vena cava showed a maximal diameter of 1.50 cm and a minimal diameter of 0.90 cm, a collapsibility index of 39.00% (Figure 3, Panel A; Table 3). In a spontaneously breathing patient this degree of collapse excluded obstructive cardiac tamponade, massive right ventricular failure, and raised right atrial pressure. It pointed to volume-responsive distributive vasoplegia. Lung ultrasound (LUS) by the BLUE protocol showed clear bilateral pleural sliding (the 'seashore sign' on

M-mode) in all anterior and lateral intercostal spaces. Equidistant horizontal A-lines dominated (Figure 3, Panel B). Pathological B-lines (lung rockets), subpleural consolidations, and pleural effusions were absent on both sides. This argued strongly against acute cardiogenic pulmonary edema. The chest radiograph agreed with the ultrasound. It showed clear bronchovascular markings, sharp costophrenic sulci, and a cardiothoracic ratio of 56.00% on the anteroposterior projection, which magnifies the cardiac shadow (Figure 3, Panel C).

A. Inferior Vena Cava POCUS: IVC Max 1.5 cm, Min 0.9 cm (CI: 39%)



B. Focused Lung Ultrasound (LUS): Bilateral Sliding, Intact A-Line Pattern



C. AP Chest Radiography: Cardiopulmonary Silhouette (CTR 56%, AP projection)

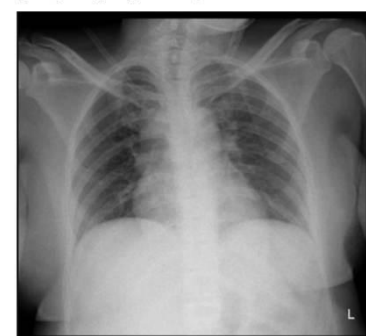


Figure 3. Focused Cardiopulmonary Ultrasound and Thoracic Radiography Findings Against Cardiogenic Congestion. (A) Subcostal long-axis ultrasound of the inferior vena cava (IVC) showing dynamic respiratory caliber variation (IVC Max 1.5 cm, IVC Min 0.9 cm; collapsibility index 39%), consistent with volume-responsive distributive vasoplegia. (B) Point-of-care lung ultrasound (LUS) demonstrating bilateral pleural sliding and clear horizontal A-lines without B-lines or effusions, arguing against pulmonary edema.

Intermediate Stabilization, Longitudinal Trajectory, and Convalescence (T2 and T3)

After acute resuscitation she was admitted to the intensive internal medicine intermediate care unit for continuous hemodynamic, rhythm, and respiratory monitoring. Anti-inflammatory and antiallergic treatment was continued. It comprised intravenous hydrocortisone sodium succinate (100.0 mg every 8 hours for 72 hours), oral cetirizine hydrochloride (10.0 mg every 24 hours), maintenance intravenous crystalloid (0.9% sodium chloride at 80 mL/h), and maintenance inhaled budesonide/formoterol.

At T2 (24 hours) and T3 (72 hours) she had no symptoms and walked comfortably, with no return of chest fullness, dyspnea, palpitations, or lightheadedness (Figure 4). Serial vital signs were stable. Blood pressure was 118/75 mmHg (MAP 89.3 mmHg) at T2 and 120/78 mmHg (MAP 92.0 mmHg) at T3. Resting heart rate was 78 beats/min at T2 and 72 beats/min at T3. Respiratory rate stayed at 16–18 breaths/min, and oxygen saturation at ambient air was 98% at T2 and 99% at T3 (Table 1). Continuous telemetry and serial 12-lead electrocardiograms showed a sustained normal sinus rhythm, intact atrioventricular conduction,

normal upright T waves, and a normal QTc interval of 408 ms at T3 (Figure 4, Panel C). There were no ventricular premature contractions, no non-sustained ventricular tachycardia, and no delayed repolarization abnormality.

Clinical surveillance throughout the 72-hour admission found no biphasic anaphylactic reaction. Laboratory tests before discharge showed full normalization of the acid-base parameters, with serum lactate 1.10 mmol/L and base excess +0.50 mmol/L (Table 1 and Table 2). She went home in stable condition on hospital day 3. At discharge she received detailed counseling and a medical emergency allergy passport recording severe, life-threatening hypersensitivity to non-ionic iodinated contrast media (iopromide) and to ceftriaxone. She and her primary physicians were told that any future imaging that would need intravascular contrast must use a non-contrast alternative (for example unenhanced magnetic resonance imaging or non-contrast computed tomography). If contrast cannot be avoided in an emergency, multi-agent oral corticosteroid and antihistamine premedication is required, under direct intensive care supervision.

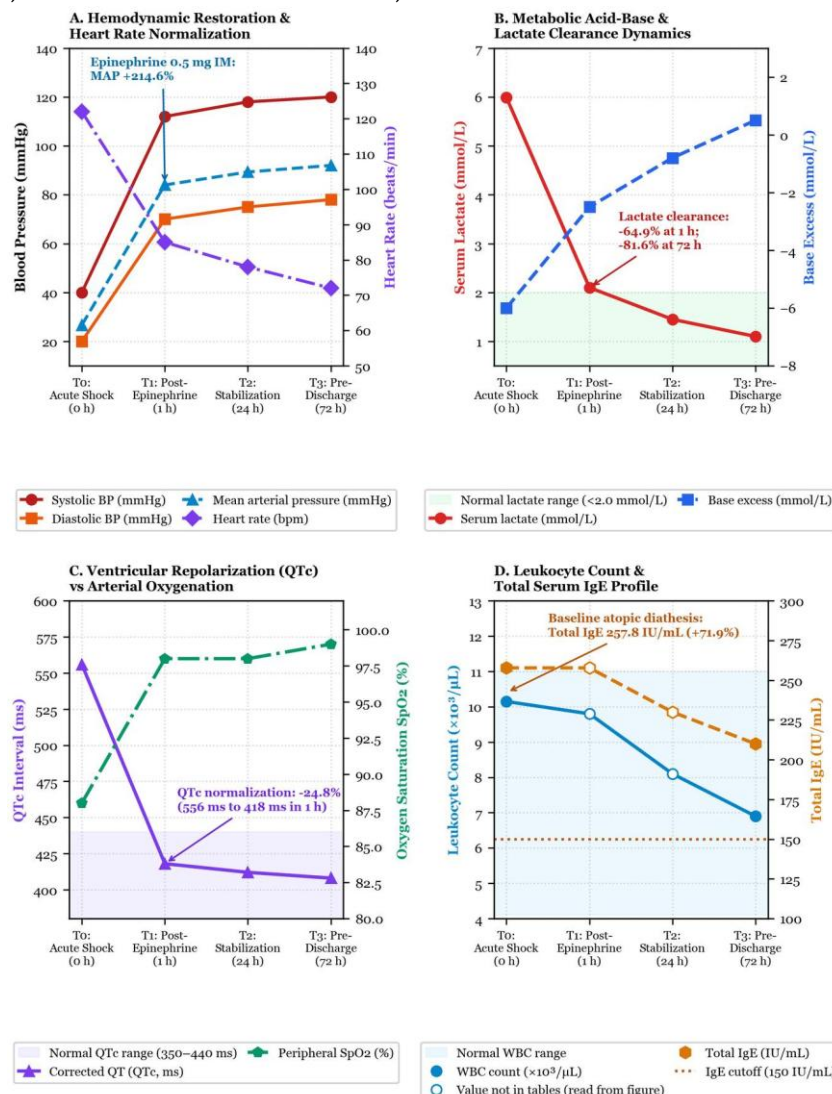


Figure 4. Longitudinal Trajectory Matrix of Hemodynamics, Arterial Blood Gas, and Allergic Biomarkers Across Follow-Up. (A) Serial blood pressure and heart rate dynamics across milestones T0 (0 h), T1 (1 h), T2 (24 h), and T3 (72 h), showing prompt surge in mean arterial pressure (+214.6%) and heart rate normalization (-30.3%) post-epinephrine. (B) Metabolic acid-base restoration with rapid serum lactate clearance (-64.9% at 1 h; -81.6% at 72 h) and base excess recovery. (C) Ventricular repolarization dynamics showing rapid QTc interval shortening from 556 ms to 418 ms (-24.8%) plotted against peripheral oxygen saturation (SpO₂). (D) Leukocyte count dynamics alongside elevated baseline total serum IgE (257.8 IU/mL), confirming atopic predisposition. Open markers in panel D are values read from the original figure that are not given in the tables.

4. Discussion

Immunobiological Cascades and Non-Ionic Contrast Media Reactivity

The course of this patient shows how non-ionic iodinated contrast media can cause acute cardiovascular collapse and transient coronary vasospasm through massive mast cell degranulation,^{44,45} a course that fits Type I Kounis syndrome.^{39,41} Intravascular contrast agents are everyday diagnostic tools in hospital medicine. Their immunobiological safety profile is complex.^{1,6} Reactions that cannot be traced to drug-specific IgE have traditionally been called 'anaphylactoid' or pseudoallergic. Current evidence points to more than one route. Immediate reactions to iodinated contrast can arise through classical IgE-mediated hypersensitivity and through non-IgE-mediated mechanisms, including direct mast cell activation through MRGPRX2 and complement activation.^{1,14,15,46}

Recent molecular work has identified the Mas-related G protein-coupled receptor member X2 (MRGPRX2) as a key receptor in non-IgE pseudoallergic drug reactions. The receptor is selectively expressed on mast cells.^{47,48} MRGPRX2 is activated directly by basic secretagogues and a range of small-molecule drugs, independently of IgE. For iodinated contrast media, iopamidol and iohexol have been shown to activate MRGPRX2-expressing mast cells, with intracellular calcium mobilization, degranulation, and release of histamine and cytokines, and serum MRGPRX2 levels were higher in patients with contrast-induced anaphylaxis than in those without.^{15,46–49} In patients with an atopic background, mast cells are thought to be primed and hyperresponsive. The evidence linking this state to Kounis syndrome is largely mechanistic. Asthma or severe atopy is also listed among the risk factors for immediate hypersensitivity reactions to iodinated contrast.^{50,51} Our patient had chronic bronchial asthma, a prior severe ceftriaxone allergy, and a raised baseline total serum IgE (257.83 IU/mL). In such individuals, contrast molecules may also cross-link existing cross-reactive IgE bound to FcεRI on mast cells, a classical IgE-dependent route that could add to degranulation (Figure 5).¹⁴ Together the two activation pathways may explain the hyperacute onset. Symptoms began within three minutes of exposure, even though she had no documented earlier contrast administration.

Coronary Arterial Vasospasm Mechanics in Type I Kounis Syndrome

The defining pathophysiological feature of Type I Kounis syndrome is acute epicardial and microvascular coronary vasospasm in anatomically normal vessels (Figure 5).^{9,16,19} To understand it, one has to look at the receptor architecture and mast cell density of the human coronary circulation.¹⁹ In the human heart, mast cells lie between myocardial fibers, around vessels, and in the intima and adventitia of the coronary arteries, where they express high-affinity IgE receptors; they are also found in the shoulder regions of coronary atheroma, and increased adventitial mast cell density has been reported in coronary spasm.^{44,45,52} Systemic

degranulation exposes these cells. Circulating triggers, including radiocontrast media, can readily reach the perivascular mast cells, which then release histamine, cysteinyl leukotrienes, prostaglandin D₂, and platelet-activating factor that act on the adjacent vessel wall.^{11,44}

Histamine is a major preformed mediator released from mast cells in anaphylaxis.¹⁴ Its vascular effects differ between territories. Different receptor subtypes mediate divergent vascular responses.⁴⁵ In the systemic circulation, mast cell-derived histamine and PAF act on endothelial cells and activate endothelial nitric oxide synthase (eNOS); the resulting nitric oxide production causes vasodilation, while endothelial barrier dysfunction increases capillary permeability and fluid extravasation, contributing to hypovolemia and distributive shock.¹⁴ In coronary arteries the action can be the opposite. H1 receptor activation predominantly induces contraction of coronary smooth muscle and vasoconstriction, whereas H2 receptor activation mediates relaxation, usually to a lesser extent.⁴⁵ In patients with vasospastic angina, selective H1 stimulation by histamine infusion was followed by angina with reduced coronary blood flow in a subset of patients. In patients with normal coronary arteries, it lowered coronary vascular resistance.⁴⁴ Coronary smooth muscle contraction in vasospasm depends on a rise in intracellular calcium and calcium/calmodulin-dependent myosin light chain kinase (MLCK) phosphorylation of myosin light chain. Sustained spasm involves Rho-kinase inhibition of myosin light chain phosphatase.⁵³ During massive mast cell degranulation this receptor imbalance may favor focal or diffuse coronary spasm, while concomitant systemic vasodilation and increased permeability lower coronary perfusion pressure.⁴⁵ Endothelial dysfunction, with reduced nitric oxide-mediated vasodilation, further predisposes to vasospasm. Histamine can provoke it.⁵³

Histamine is not the only mediator. Degranulating mast cells also release the neutral proteases tryptase and chymase, and newly synthesized lipid mediators: cysteinyl leukotrienes (such as LTC₄), platelet-activating factor (PAF), and prostaglandins, with thromboxanes also implicated in coronary vasoconstriction.^{11,14,45} Cysteinyl leukotrienes also act on the human coronary circulation. In patients with normal coronary arteries, small doses of LTD₄ produced a transient fall in mean arterial pressure followed by a later rise in coronary arteriolar resistance.⁴⁴ Chymase from human heart mast cells converts angiotensin I into angiotensin II, and angiotensin II generated through chymase is one of the vasoconstrictors implicated in the coronary spasm of Kounis syndrome.^{44,45} In atherosclerotic plaque, tryptase and chymase also activate matrix metalloproteinases. This mechanism is relevant mainly to plaque erosion or rupture in type II disease.⁴⁵ In our patient, intense coronary vasospasm in the left anterior descending and circumflex distributions is the likely mechanism of the severe myocardial hypoperfusion that appeared on the electrocardiogram as diffuse anterior T-wave inversions and a marked QTc prolongation (Figure 1, Table 1).

PROPOSED MULTI-TIER PATHOPHYSIOLOGICAL & IMMUNOBIOCHEMICAL CASCADE OF TYPE I KOUNIS SYNDROME

Triggered by Non-Ionic Iodinated Contrast Media (Iopromide) in an Atopic Patient

TIER 1: INTRAVENOUS NON-IONIC IODINATED CONTRAST INSULT & MAST CELL RECEPTOR ACTIVATION

- Antigenic Trigger: Intravenous administration of 20 mL iopromide 300 non-ionic contrast during diagnostic cholangiography.
- Predisposing Host Diathesis: Chronic bronchial asthma, previous severe ceftriaxone hypersensitivity, and elevated baseline IgE (257.83 IU/mL).
- Dual Activation Cascades: Direct non-IgE mast-cell activation via MRGPRX2 receptor engagement and hyperosmolar chemotoxic membrane perturbation, synergistic with classic IgE-dependent FcεRI cross-linking in a hyperreactive immune substrate.

↓ **Massive Explosive Mast Cell & Basophil Degranulation**

TIER 2: SYSTEMIC DEGRANULATION & VASOACTIVE INFLAMMATORY MEDIATOR STORM

- Pre-Formed Primary Mediators: Immediate release of Histamine (acting on H1, H2, and H3 receptors) and Neutral Proteases (Tryptase, Chymase).
- De Novo Synthesized Mediators: Activation of phospholipase A2 generating Platelet-Activating Factor (PAF), Leukotrienes (LTC4, LTD4, LTE4), and Thromboxane A2 (TXA2); rapid mobilization of Endothelin-1 and Pro-inflammatory Cytokines (TNF-α, IL-6).
- Proteolytic Cascades: Tryptase directly activates matrix metalloproteinases (MMPs) and converts angiotensin I to angiotensin II.

TIER 3A: CORONARY ARTERIAL VASOSPASM (TYPE I KOUNIS SYNDROME)

- Coronary H1 Receptor Engagement: Histamine-induced profound vascular smooth muscle contraction.
- Leukotriene & Thromboxane Synergy: LTC4/D4 and TXA2 induce epicardial coronary vasospasm.
- Transient Transmural/Subendocardial Ischemia: Absence of prior CAD (Type I variant); diffuse T-wave inversion (V1–V5) and severe QTc prolongation (556 ms).
- Preservation of Myocardial Structure: Preserved LVEF (56%), no RWMA, resolving upon spasm relief.

TIER 3B: DISTRIBUTIVE SHOCK & RESPIRATORY CRISIS (GRADE IV ANAPHYLAXIS)

- Endothelial Nitric Oxide & Prostacyclin Surge: Profound systemic vasodilation via vascular H2 & H1 activation.
- Microvascular Hyperpermeability & Third-Spacing: Hypovolemia and vasoplegia; unmeasurable BP (palpated about 40/20 mmHg).
- Bronchial Smooth Muscle Spasm: H1 & cysteinyl leukotriene receptor activation driving diffuse bronchospasm, refractory wheezing, and hypoxemia (SpO2 88%).
- Severe Tissue Hypoperfusion: Marked hyperlactatemia (5.99 mmol/L) & metabolic base deficit.

TIER 4: TARGETED PHARMACOTHERAPEUTIC REVERSAL & COMPLETE CLINICAL RESTORATION

- First-Line Intramuscular Epinephrine (0.5 mg 1:1,000):
 - α1-Adrenergic Agonism: Rapid arteriolar vasoconstriction restores systemic vascular resistance, diastolic BP, and coronary perfusion.
 - β2-Adrenergic Agonism: Stimulates adenylate cyclase, elevating intracellular cAMP in mast cells to halt ongoing degranulation; reverses bronchospasm.
- Multimodal Supportive Regimen: Aggressive isotonic crystalloid fluid resuscitation (0.9% NaCl), intravenous hydrocortisone (200 mg loading, then 100 mg q8h), oral cetirizine (10 mg q24h), and high-flow oxygen, achieving full repolarization recovery and 72-hour relapse-free discharge.

Figure 5. Proposed Multi-Tier Pathophysiological and Immunobiochemical Cascade of Type I Kounis Syndrome. Schematic of the proposed mechanisms (not measured in this patient), illustrating the four sequential mechanistic disease tiers: Tier 1, intravenous non-ionic iodinated contrast insult (iopromide) triggering dual MRGPRX2 and IgE/FcεRI receptor activation on primed perivascular mast cells in an atopic host; Tier 2, explosive systemic mast cell degranulation discharging primary mediators (histamine, neutral proteases, chymase, tryptase) and synthesizing eicosanoids (leukotrienes C4/D4/E4, PAF, thromboxane A2); Tier 3A, high-affinity coronary H1 receptor engagement and leukotriene-mediated vasoconstriction inducing profound epicardial coronary vasospasm with diffuse T-wave inversion and extreme QTc prolongation (Type I Kounis syndrome); Tier 3B, concurrent endothelial H1/H2-mediated peripheral vasodilation and hyperpermeability causing severe distributive shock and respiratory bronchospasm; and Tier 4, immediate first-line intramuscular epinephrine administration mediating α1 arteriolar vasoconstriction (restoring coronary perfusion pressure), β1 inotropic support, and β2-adrenergic mast cell membrane stabilization (halting ongoing mediator release), resulting in rapid ischemia reversal and complete clinical recovery.

Electrocardiographic Repolarization Derangements and Arrhythmogenic Risk

The electrocardiogram of this patient showed sinus tachycardia, diffuse symmetrical T-wave inversions in precordial leads V1–V5, and a marked prolongation of the corrected QT interval (QTc 556 ms; Figure 1). ST-segment elevation is the dominant electrocardiographic pattern of Kounis syndrome. It is reported in approximately 43% to 76% of mixed cohorts. Repolarization abnormalities occur less often, in up to 38% of reported cases. They include ST-segment depression, T-wave inversion, and non-specific ST–T changes, and completely normal tracings are uncommon.⁴⁵ T-wave inversion has also been reported in Type I Kounis syndrome with angiographically normal coronary arteries.⁵⁴ Deep, symmetrical anterior T-wave inversions without QRS widening or bundle branch block, as seen here, resemble the Wellens pattern, which, besides severe left anterior descending artery stenosis, can be produced by coronary vasospasm in the absence of obstructive coronary disease.⁵⁵

A QTc above 500 ms is a recognized risk marker for Torsades de Pointes. A QTc of 556 ms is therefore of considerable clinical importance.^{27,56} Ventricular repolarization is regulated by the balance between outward potassium currents, chiefly the rapid delayed rectifier current (IKr), and inward sodium and calcium currents.⁵⁶ The mechanism of QT prolongation was not measured in this patient. QT prolongation has been reported in anaphylactic shock complicated by myocardial ischemia,⁵⁷ and myocardial infarction and electrolyte disturbances are recognized risk factors for Torsades de Pointes.⁵⁶ When repolarization is delayed, early afterdepolarizations and increased dispersion of repolarization across the myocardium predispose to Torsades de Pointes.^{27,56} Life-threatening ventricular arrhythmias, including ventricular fibrillation, have been reported in Type I Kounis syndrome.^{45,58} The QTc shortened quickly after resuscitation, from 556 ms to 418 ms (Table 1; Figure 4). Such rapid normalization fits a transient, functional disturbance of repolarization rather than a structural one, in line with the reversibility of ST–T changes in Kounis syndrome once the allergic reaction is controlled.⁵⁹

The Epinephrine Paradox in Kounis Syndrome

Drug treatment of Kounis syndrome raises a recognized dilemma, known as the 'epinephrine paradox'. Epinephrine, the first-line treatment of anaphylaxis, may itself aggravate myocardial ischemia or coronary vasospasm.^{45,60,61} In patients with acute coronary syndromes, it is traditionally used with caution. The concern is that its α 1-adrenergic vasoconstrictor and β 1-adrenergic positive inotropic and chronotropic actions may aggravate myocardial ischemia, increase myocardial oxygen consumption, provoke arrhythmias, or worsen coronary vasospasm.^{8,45,62} Emergency medicine and allergy guidelines take the opposite view. Epinephrine given intramuscularly into the anterolateral thigh is the first-line, life-saving treatment of anaphylaxis, including anaphylaxis to contrast media.^{17,45,63,64} Delayed administration has been associated with fatal outcomes. Current reviews find no absolute contraindication to epinephrine in a life-threatening reaction.^{8,64,65}

The use of epinephrine is controversial when anaphylaxis is complicated by myocardial ischemia (Kounis syndrome).^{45,62} Some authors propose coronary vasodilators such as calcium channel blockers or α 1-adrenergic blockers, which may also stabilize mast cells, as alternative or adjunctive agents.⁶⁶ Others caution against hesitation: physicians should give epinephrine when anaphylaxis is life-threatening.^{45,67} Our patient was in severe Grade IV anaphylactic shock with unmeasurable blood pressure. We treated her with intramuscular epinephrine (0.5 mg, 1:1,000), in keeping with guideline advice that epinephrine be given immediately once anaphylaxis is suspected. The recommended adult

intramuscular dose is 0.5 mg of the 1 mg/mL (1:1000) solution.^{17,45} The physiological rationale is as follows:

1. Restoration of Coronary Perfusion Pressure: In anaphylaxis, systemic vasodilation, plasma leakage, and reduced venous return can lower coronary perfusion pressure and cause myocardial hypoperfusion.^{45,59} Our patient had a blood pressure of 40/20 mmHg and a mean arterial pressure of 26.7 mmHg. Coronary perfusion was presumably severely compromised, and this alone may have produced myocardial ischemia. Through α 1-adrenergic vasoconstriction, epinephrine counteracts the peripheral vasodilation of anaphylaxis and raises blood pressure, and it has been reported to enhance coronary blood flow.^{8,45}

2. Arrest of Ongoing Degranulation: Epinephrine inhibits mast cell degranulation in experimental studies, an effect mediated mainly by β 2-adrenergic receptors.⁶⁸ Suppressing further release of histamine and other mediators would be expected to remove part of the biochemical stimulus behind the coronary vasospasm (Figure 5).⁴⁵

3. Airway and Oxygenation Rescue: Epinephrine produces bronchodilation. It counteracts the bronchospasm and respiratory compromise of anaphylaxis.⁴⁵ Restoring ventilation and oxygenation is expected to improve oxygen delivery to the ischemic myocardium.

In our patient 0.5 mg of intramuscular epinephrine did not worsen the coronary vasospasm. Recovery was immediate. Mean arterial pressure rose from 26.7 to 84.0 mmHg (+214.6%). The bronchospasm stopped. Arterial lactate fell by -64.9%, and the electrocardiogram almost normalized, with upright T-waves fully restored within 1 hour (Figure 1, Table 1). Intravenous bolus epinephrine carries a much higher risk of cardiovascular adverse events and overdose than intramuscular injection,^{64,65} and the intravenous route is not recommended for the initial treatment of anaphylaxis.¹⁷ Intramuscular injection into the anterolateral thigh is generally well tolerated. It remains the first-line treatment of anaphylaxis, and current evidence does not support withholding it when Kounis syndrome is suspected in a life-threatening reaction.^{17,45,69}

Differential Diagnosis and Multimodal Echocardiographic Exclusion

Diagnosing Type I Kounis syndrome requires that other cardiovascular emergencies presenting with acute collapse and repolarization abnormalities be excluded, because Kounis syndrome overlaps clinically with acute coronary syndrome.^{9,16} The main differential diagnoses in our patient were these:

1. Atherosclerotic Acute Coronary Syndrome (Type II Kounis or Classic Plaque Rupture): Plaque rupture or erosion with coronary thrombosis, whether as a classic acute coronary syndrome or as Type II Kounis syndrome,^{9,45} is expected to produce ischemic ECG changes, myocardial injury detectable by serial high-sensitivity troponin, and regional wall motion abnormalities on echocardiography.^{36,45} Here, high-sensitivity troponin T stayed negative (<14.0 ng/L). The 12-lead ECG changes were diffuse. They spanned the precordial and high-lateral leads. Echocardiography showed entirely normal wall motion in all 16 myocardial segments, with a preserved LVEF (56%; Figure 2, Table 3). These findings argued against acute atherothrombosis. They fit the Type I variant better than the Type II variant.⁹ Normal biomarkers or a normal echocardiogram do not exclude Type I Kounis syndrome by themselves. In this type, coronary vasospasm may be transient.⁴⁵

2. Stress-Induced Takotsubo Cardiomyopathy: Takotsubo syndrome is usually precipitated by an emotional or physical trigger, including intravenous catecholamines and, as described in the ATAK complex, anaphylaxis and adrenaline.^{18,70} It typically presents with acute chest pain or

dyspnea together with new ECG abnormalities such as ST-segment changes, T-wave inversion, and QTc prolongation.⁷⁰ Its defining feature, however, is transient left ventricular dysfunction (hypokinesia, akinesia, or dyskinesia) presenting as apical ballooning or as midventricular, basal, or focal wall motion abnormalities.⁷⁰ In our patient, echocardiography done right after stabilization showed completely normal apical and regional contractility, a preserved biplane ejection fraction (56%), and no apical dyssynergy. Takotsubo cardiomyopathy was therefore considered unlikely. Echocardiography was, however, performed only after stabilization (Figure 2, Table 3).

3. Obstructive Shock and Massive Pulmonary Embolism: Obstructive shock from massive pulmonary embolism also had to be excluded in a patient with acute collapse and respiratory distress. In our patient, POCUS and echocardiography showed a normal right ventricle without dilation, a preserved TAPSE (2.4 cm), and no McConnell's sign or pulmonary hypertension (Figure 2, Table 3).⁷¹ In a series of 511 patients with confirmed pulmonary embolism, all hemodynamically unstable patients showed an enlarged, hypokinetic right ventricle and at least one typical echocardiographic sign.⁷² Lung ultrasound also showed bilateral pleural sliding and clear A-lines without subpleural consolidations. The chest radiograph was normal (Figure 3).^{28,31}

4. Cardiogenic Pulmonary Edema: Point-of-care lung ultrasound found no vertical B-lines in any anterior or lateral lung zone (Figure 3). Lung sliding was preserved, A-lines

were present, and B-lines were absent. This pattern argued against cardiogenic pulmonary edema and pointed to a bronchospastic mechanism of the respiratory distress rather than raised left atrial pressure.^{28,31,73}

Objective Pharmacovigilance, Causality Assessment, and Global Literature Benchmarking

The causal link between iopromide and the cardiovascular collapse that followed was assessed with standardized pharmacovigilance algorithms (Table 4).^{37,74} The Naranjo Adverse Drug Reaction Probability Scale gave a cumulative score of +8 out of 10. This classifies the reaction as a 'Probable' adverse drug reaction (score 5 to 8).^{37,74} Points were scored for earlier conclusive reports in the literature (+1), onset within minutes of administration (+2), rapid recovery after contrast stopped and treatment began (+1), no alternative explanation (+2), a documented earlier severe drug allergy to ceftriaxone (+1), and objective electrocardiographic and metabolic confirmation (+1). Rechallenge scored 0. Deliberate re-exposure was ethically and medically contraindicated after Grade IV anaphylaxis. The WHO-UMC system likewise classed causality as 'Probable / Likely', given the clear temporal plausibility, a positive dechallenge, and no confounding medication.⁷⁴ No rechallenge was performed. The 'Certain' category, which requires a satisfactory rechallenge when necessary, therefore could not be assigned.⁷⁴ The close temporal relation and the biological plausibility of mast cell activation, with release of vasoactive mediators that can provoke coronary vasospasm, support a causal role of the contrast agent.⁴⁵

Table 4. Objective Pharmacovigilance, Causality Assessment, and Adverse Drug Event Attribution Matrix

Assessment Framework	Evaluated Domain / Question	Case Verification Finding	Algorithm Score	Attribution Classification
Naranjo ADR Probability Scale	1. Previous conclusive reports on this reaction?	Yes, iodinated contrast is a documented trigger of Kounis syndrome	+1	—
Naranjo ADR Probability Scale	2. Event appeared after suspected drug administered?	Yes, symptoms appeared within 3 minutes of iopromide injection	+2	—
Naranjo ADR Probability Scale	3. Adverse reaction improved when drug was discontinued?	Yes, rapid resolution following cessation of contrast infusion	+1	—
Naranjo ADR Probability Scale	4. Adverse reaction reappeared upon readministration?	Not re-challenged (medically contraindicated in Grade IV anaphylaxis)	0	—
Naranjo ADR Probability Scale	5. Alternative causes that could solely cause the reaction?	No alternative triggers; echocardiogram normal; no prior CAD history	+2	—
Naranjo ADR Probability Scale	6. Reaction appeared after placebo was administered?	No placebo administered	0	—
Naranjo ADR Probability Scale	7. Drug detected in blood/fluids in toxic concentrations?	Not assayed (immunological rather than concentration-toxic event)	0	—
Naranjo ADR Probability Scale	8. Reaction more severe with increased dose / lower with decreased?	Single bolus administered during cholangiography	0	—
Naranjo ADR Probability Scale	9. Patient had similar reaction to same/similar agents?	Yes, documented prior severe anaphylaxis to ceftriaxone	+1	—
Naranjo ADR Probability Scale	10. Adverse event confirmed by objective evidence?	Yes, ECG repolarization shifts, severe hypotension, hyperlactatemia	+1	Score: 8 (Probable ADR)
WHO-UMC Causality System	Temporal Relationship	Acute onset within minutes post-iopromide administration	Plausible	Probable / Likely
WHO-UMC Causality System	Dechallenge Outcome	Rapid clinical and ECG resolution post-epinephrine and cessation	Positive	Probable / Likely
WHO-UMC Causality System	Absence of Confounders	No concurrent pharmacological agents or baseline coronary disease	Confirmed	Probable / Likely

Notes: Cumulative Naranjo Adverse Drug Reaction Probability Scale score of 8/10 classifies the relationship between iopromide administration and the occurrence of Type I Kounis syndrome as 'Probable' (scores ≥ 9 are definite; 5–8 are probable). Rechallenge was deliberately avoided due to the life-threatening severity of Grade IV anaphylaxis.

Benchmarking against published case reports and small case series of contrast-induced Kounis syndrome from 2019 to 2026 (Table 5) shows features that overlap with those of our patient, together with considerable heterogeneity. Our patient's presentation fits Type I Kounis syndrome. In this type, hypersensitivity is accompanied by coronary vasospasm in the absence of obstructive coronary disease, as described after iodinated contrast in patients without known coronary disease.^{75–77} Across published Kounis syndrome cases, contrast-related cases occurred at older ages than those triggered by cephalosporins or nonsteroidal anti-inflammatory drugs. Male patients predominated (approximately 75%), and recovery was the predominant

outcome (94%; mortality 4%).³⁹ In a review of 26 contrast-induced cases, the median age was 60 years (range 30–83). Of these, 12 cases involved iodine-containing media and 7 gadolinium-based agents. 24 patients recovered completely. The other 2 died.⁶ She is thus much younger than the typical reported patient. A documented allergic history was present in 4 of 11 contrast-induced cases (36%) in an earlier review,⁷⁸ and individual reports describe patients with prior allergic reactions, such as bee-sting anaphylaxis or acetylcysteine allergy,^{75,76} as well as patients without any known allergic history.^{77,79} Atopy, although present in our patient, was therefore not a uniform feature. The agents in the cases of Table 5 were iopromide, iopamidol, and iodixanol, that is,

low-osmolar or iso-osmolar iodinated media.^{75,76,78–81} The earlier review listed iopromide (3 cases), iohexol (3 cases), and iopamidol (1 case) among the triggers.⁷⁸ Electrocardiographic presentations were not uniform. ST-segment elevation predominated in the pooled analyses and in most individual reports,^{6,39,75–77,80,82} sometimes accompanied by ST-segment depression^{75,82} or conduction abnormalities.⁸⁰ Diffuse T-wave inversion with QT prolongation, as in our patient, was not described in Table 5. Troponin was elevated in some reports (peak 266 ng/L and 8,000 ng/L)^{75,77} but biomarkers were not elevated in others,^{76,82} so the normal troponin of our patient corresponds to only part of the published spectrum. Management varied widely. Recovery of ECG, echocardiographic, and clinical findings within minutes of 0.3 mg intramuscular adrenaline was described in one hemodialysis patient.⁸⁰ In two other patients the circulation did not recover after intramuscular

adrenaline, and cardiopulmonary resuscitation, intracoronary nitrates, or extracorporeal support was needed.^{76,81} Epinephrine has itself been discussed as a possible aggravator of coronary vasospasm in Kounis syndrome.^{75,76,81} For anaphylaxis in general, however, intramuscular epinephrine is the recommended first-line treatment, and the potential harm of delaying it is considered to outweigh the risk of adverse events.⁶⁴ None of these sources compares prompt with delayed epinephrine in contrast-induced Kounis syndrome. The rapid recovery of our patient after intramuscular epinephrine therefore cannot be generalized from the published reports. Within these limits, her rapid reversal of electrocardiographic changes resembles the transient changes described in Type I reports,^{75–77} although her electrocardiographic pattern and normal troponin differ from most of them.

Table 5. Published Cases of Contrast-Induced Kounis Syndrome Compared with the Present Case.

Study & Year	Age / Sex	Contrast Media & Procedure	Underlying Allergic Diathesis	ECG Presentation	Troponin & Echo/Coronary Findings	Therapeutic Intervention	Clinical Outcome
Present Study (2026)	41 / F	Iopromide 300 (20 mL, Cholangiography)	Bronchial asthma; ceftriaxone allergy; IgE 257.8 IU/mL	Sinus tachycardia, diffuse T-wave inversion (V1–V5), QTc 556 ms	Troponin normal (<14 ng/L); LVEF 56%, no RWMA	Epinephrine 0.5 mg IM, hydrocortisone, cetirizine, crystalloids	Rapid complete resolution in 1h; uneventful discharge
Zmolik et al. (2025) ⁷⁵	60 / F	Iopromide 370 mg/mL (95 mL via Port-a-Cath); contrast-enhanced CT of thorax and abdomen	Known acetylcholine allergy (urticarial reaction); no prior reaction to CT contrast media	Tachycardia; ST-segment elevation in II, III, aVF; ST-segment depression in V2–V4 (normalized the next day)	hs-Troponin T 8 ng/L at baseline, peak 266 ng/L at 4 h after intervention, normal within 2 days; echocardiography not reported; angiography: no significant stenosis or plaque rupture, right coronary vasospasm (iodixanol used for angiography) resolved with intracoronary nitroglycerin	IV Ringer's lactate, clemastine and methylprednisolone; intracoronary nitroglycerin; molsidomine, later switched to diltiazem	ICU overnight; uneventful inpatient stay; at 2 weeks ECG unremarkable and hs-troponin T undetectable
Kurokawa et al. (2025) ⁷⁶	77 / M	Iopamidol (about 100 mL); contrast-enhanced CT (gastric cancer follow-up)	Anaphylaxis after two bee stings	After return of spontaneous circulation: ST-segment elevation in inferior leads and V1–V3 (normalized after intracoronary isosorbide dinitrate)	Cardiac biomarkers not elevated; transthoracic echocardiography: normal systolic function, no regional wall motion abnormality; angiography (iohexol): spasms of the right and left coronary arteries	Adrenaline 0.5 mg IM, then CPR with IV adrenaline; IV methylprednisolone, chlorpheniramine, famotidine; intracoronary isosorbide dinitrate	Three episodes of pulseless electrical activity; spasms resolved; discharged on day 7 with intact neurological function
Deb et al. (2026) ⁷⁷	45 / F	Iodinated contrast (agent not reported); contrast-enhanced CT of the thorax	No prior allergic history stated; myasthenia gravis (anti-acetylcholine receptor antibody positive)	"Shark-fin" ST-segment elevation in I, aVL and V2 ("South African flag sign"); complete resolution on repeat ECG	Troponin I 8,000 ng/L; echocardiography: anterolateral hypokinesia, LVEF 40%; angiography: no obstructive coronary disease	IV hydrocortisone 100 mg and pheniramine 22.75 mg; supportive care	ST-segment elevation resolved; completed immunoglobulin therapy uneventfully; asymptomatic at 6 weeks
Nakamura et al. (2024) ⁸⁰	58 / M	Iopamidol; contrast-enhanced CT (kidney tumor work-up) in a patient on weekly hemodialysis	Not reported (no urticaria or skin swelling during the event)	Complete atrioventricular block; ST-segment elevation in II, III, aVF and V3–V6; ST-segment depression in aVL	Troponin not reported (creatinine kinase did not rise); echocardiography: asynergy of the lateral wall and part of the septum; coronary angiography not performed	Adrenaline 0.3 mg IM; hydrocortisone and chlorpheniramine maleate; high-care unit monitoring	ECG, echocardiogram and symptoms improved 3 min after adrenaline; ECG normal the next day; discharged the next day
Chien et al. (2019) ⁸²	81 / F	Iodinated contrast (agent not reported); emergency contrast-enhanced CT of chest and abdomen	Not reported	Progressive bradycardia; ST-segment elevation in II, III, aVF; ST-segment depression in V1–V6 (resolved during ICU stay)	Cardiac enzymes normal; bedside echocardiography: adequate LVEF, no dyskinesia; coronary angiography withheld because of the risk of recurrent anaphylaxis	Atropine, betamethasone, CPR (pulseless electrical activity), dopamine; corticosteroid and antihistamine; ICU monitoring	Spontaneous circulation after 2 min of CPR; extubated; no ST-segment change on ECG at 1 month
Yano et al. (2026), Case 2 ⁸¹	79 / M	Iopamidol; percutaneous coronary intervention (standby) in a patient with chronic kidney disease	Not reported (itching of the back during the event); prior multiple PCI	ST-segment elevation in II, III, aVF, followed by pulseless electrical activity and ventricular fibrillation; ST elevation disappeared after sinus rhythm was restored	Maximum troponin T 0.16 ng/mL and CK-MB 3.8 ng/mL (ICU day 2); LVEF 27.1% before the procedure; angiography: coronary spasm mainly in the right coronary artery (authors: likely Type I)	Adrenaline 0.5 mg IM; ACLS, ECMO, IABP; hydrocortisone 300 mg; intracoronary isosorbide nitrate; amiodarone, defibrillation	ECMO and IABP weaned on day 5, extubated on day 8; died 39 days after ICU transfer from an ECMO-site infection (bypass surgery not performed)
Shibuya et al. (2019) (Type II variant) ⁷⁸	60 / M	Iopamidol 370 (80 mL); contrast-enhanced CT (hepatocellular carcinoma work-up); prior myocardial infarction treated with PCI	Hypotension during earlier angiography with iopamidol; allergy-like reactions during earlier chemoembolization; no history of atopy	ST-segment elevation in II, III, aVF; acute T waves in precordial leads; ST elevation improved within minutes	Only a slight rise in myocardial enzymes; no new asynergy on echocardiography; coronary angiography not performed (PCI avoided because of the risk of anaphylaxis)	Adrenaline 0.3 mg IM (twice), IV fluids, hydrocortisone 300 mg, heparin, nicorandil	ST elevation reversed without coronary intervention; stable after 2 days in ICU and transferred to the ward; the authors report that all patients in their review, including this one, recovered and were discharged
Zhang et al. (2025) (Type II variant) ⁷⁹	77 / F	Iodixanol; coronary angiography (multivessel coronary artery disease, type 2 diabetes, hypertension)	No history of food or drug allergies	Not reported (bradycardia to 38 beats/min, hypotension 60/40 mmHg, convulsions)	Troponin not reported; bedside echocardiography: ejection fraction about 50%, no pericardial effusion; angiography: severe spasm and stenosis of the left coronary artery	CPR; repeated intracoronary nitroglycerin 5 mg; atropine, norepinephrine, epinephrine 1 mg, dexamethasone, sodium bicarbonate; intra-aortic balloon pump	Hemodynamics stabilized after IABP; IABP removed after 10 h, discharged 17 days later in good recovery; no significant sequelae at 3-year follow-up

Notes: Published cases of contrast-induced Kounis syndrome are listed as described by their authors; fields the source does not state are shown as “Not reported”, and Type II variants are marked. The present case differs from the listed reports in its electrocardiographic pattern (diffuse T-wave inversion with QT prolongation).

Preventive Paradigms, Patient Safety, and Pre-Procedural Risk Stratification

Preventing a recurrence of life-threatening hypersensitivity and allergic coronary vasospasm takes a multi-tiered safety strategy across the health care system. It combines structured risk assessment before the procedure, preparedness to treat a reaction, and a deliberate choice of the contrast strategy in patients with a previous reaction.^{2,63,83} Every patient scheduled for a diagnostic or interventional procedure with intravascular contrast media should undergo a standardized pre-procedural risk assessment, with documentation of any previous reaction to contrast media.⁶³ A previous hypersensitivity reaction to contrast media is the most consistent predictor of a future reaction. A history of other allergic diseases or of uncontrolled asthma is a weaker and less consistent predictor.⁶³ Patients at increased risk call for closer vigilance. Resuscitation equipment should be kept ready, with intramuscular epinephrine 1 mg/mL (1:1,000) at hand in the radiological suite.^{17,63}

Once contrast-induced Kounis syndrome has been documented, re-exposure to the culprit contrast agent should be avoided. Strict avoidance of the trigger remains the most effective measure against recurrence in Type I Kounis syndrome.⁴⁵ Further intravascular iodinated contrast should be considered only when imaging is essential and no alternative exists. The decision should rest on an individual risk-benefit analysis after allergological evaluation.² Non-contrast techniques should therefore be preferred whenever they can answer the clinical question, such as non-contrast CT, unenhanced magnetic resonance imaging (MRI), or diagnostic ultrasonography.^{2,45} If iodinated contrast cannot be replaced, a different agent should be used, chosen after allergological evaluation with skin testing. Skin tests can help identify a tolerated alternative, and changing the agent was associated with a lower risk of recurrent reactions.^{2,83,84} The American College of Radiology recommends oral corticosteroid premedication started 12 to 13 hours before exposure (for example, oral methylprednisolone 32 mg at 12 and 2 hours, with an optional antihistamine such as diphenhydramine 50 mg). European guidance does not recommend premedication.^{85,86} Its efficacy is uncertain. Steroid premedication did not prevent recurrent reactions in several cohorts and was less effective than switching the agent, and breakthrough reactions occur despite tailored premedication.^{84,87,88} Recent guidance describes the supporting evidence as weak and outdated. No strategy eliminates reactions.^{89,90} Any unavoidable re-exposure should therefore take place where continuous cardiac and hemodynamic monitoring and immediate resuscitation capability are available.^{63,89} Kounis syndrome remains underdiagnosed because of limited awareness, particularly in emergency settings where it mimics acute coronary syndrome.^{16,45} It should be better known across interventional radiology, cardiology, allergy, and internal medicine. Better awareness would support prompt diagnosis and early intramuscular epinephrine for anaphylaxis, which is first-line treatment.^{17,63}

5. Limitations

This report has limitations. It describes a single patient, so nothing can be inferred beyond this case. The close temporal relation between epinephrine and recovery does not establish the effect of the drug. No coronary angiography or other coronary imaging was performed, and serum tryptase, allergen-specific IgE, and skin testing are not reported. The diagnosis of Type I Kounis syndrome therefore rests on the timing after contrast administration, the electrocardiographic changes, a normal high-sensitivity

troponin T, and preserved function on echocardiography. It is best regarded as probable rather than confirmed.

Echocardiography was performed after initial stabilization. A transient regional wall motion abnormality at the time of collapse therefore cannot be excluded, and takotsubo cardiomyopathy is made unlikely rather than ruled out. Hypotension, hypoxemia, acidosis, and catecholamine exposure may also have contributed to the repolarization changes. Troponin was sampled only at baseline and at 6 hours. The mechanisms discussed above are taken from the literature. They were not measured in this patient, and the patient has not been re-exposed to a contrast agent or tested for cross-reactivity.

6. Conclusion

This case report shows that intravenous non-ionic iodinated contrast media (iopromide) can trigger severe Grade IV anaphylactic shock with acute, transient myocardial ischemia and coronary vasospasm (Type I Kounis syndrome). The patient was atopic. She had no pre-existing coronary artery disease. The hyperacute picture was profound distributive vasoplegia, refractory bronchospasm, severe lactic acidosis, and extensive repolarization abnormalities on the electrocardiogram: diffuse symmetrical T-wave inversions in leads V1–V5 and an extreme QTc prolongation (QTc 556 ms). High-sensitivity cardiac troponin T stayed normal. Immediate first-line intramuscular epinephrine (0.5 mg, 1:1,000), given with aggressive crystalloid resuscitation, brought rapid and complete hemodynamic stabilization, marked lactate clearance, and fast normalization of repolarization, without aggravating myocardial ischemia. Transthoracic echocardiography and point-of-care cardiopulmonary ultrasound argued against fixed atherothrombotic coronary occlusion, stress-induced Takotsubo cardiomyopathy, and cardiogenic pulmonary edema. They also showed preserved systolic performance, in keeping with functional vasospasm. The Naranjo algorithm (score 8/10) and the WHO-UMC criteria indicated a probable causal relationship. Acute allergic reactions must be recognized as possible triggers of acute coronary syndromes. Skin signs may be entirely absent in life-threatening anaphylaxis. Intramuscular epinephrine remains first-line treatment of anaphylactic shock.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki (2013 Fortaleza revision) and the ICMJE publication ethics guidelines. Ethical approval and protocol registration were formally granted by the CMHC Research Center Ethics Committee, Indonesia (Protocol Approval Number: 2026/5194). Written informed consent was obtained directly from the patient for the collection and academic analysis of clinical, laboratory, and imaging data.

Consent for publication

The patient provided written informed consent for the publication of this article and any accompanying diagnostic images, electrocardiographic tracings, and ultrasound recordings. All personal identifiers have been removed or obscured with solid black anonymization bars in accordance with ICMJE and COPE privacy regulations.

Use of artificial intelligence

None.

Author contributions

A.A.N.S.P.: Conceptualization, Investigation, Data curation, Writing – original draft. K.S.: Validation, Supervision, Writing – review & editing. D.F.E.: Methodology, Validation, Project administration. All authors critically reviewed, revised, and approved the final manuscript for publication.

Funding

None.

Conflict of interest

The authors declare that they have no competing financial, personal, commercial, or professional interests that could inappropriately influence or bias the work reported in this paper.

Data availability

The clinical, hemodynamic, laboratory, and imaging datasets analyzed during the current investigation are available from the corresponding author upon reasonable academic request, subject to institutional ethical review and patient confidentiality agreements.

Acknowledgements

The authors express their sincere appreciation to the clinical nursing, diagnostic imaging, and intensive care staff at Prof. I.G.N.G. Ngoerah General Hospital and the Faculty of Medicine, Universitas Udayana, Denpasar, Bali, Indonesia, for their dedicated multidisciplinary collaboration and patient care.

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