

INTRODUCTION

Kounis Syndrome (KS) is an acute coronary syndrome (ACS) spectrum first described in 1991 by Kounis and Zavras as "allergic angina" or "allergic myocardial infarction," resulting from excessive mast-cell activation during allergic reactions [1]. Current studies indicate that the incidence of KS among patients presenting to the emergency department may be as low as 1 in 10,000, increasing to 3–4% among those with a history of allergy [2]. The clinical presentation often mimics acute myocardial infarction (MI); differential diagnosis is difficult in the presence of findings such as electrocardiogram (ECG) changes, chest pain and elevated cardiac enzymes [3,4].

Three types of KS have been defined in the literature [5,6]:

Type 1 KS: Vasospastic angina in normal coronary arteries.

Type 2 KS: Myocardial infarction triggered by an allergic reaction, with or without a history of coronary artery disease.

Type 3 KS: Stent thrombosis and ACS due to allergic reaction in patients who previously had a coronary stent.

Hysterosalpingography (HSG) is an invasive radiological procedure used in infertility investigations to assess the patency of the uterine cavity and fallopian tubes. The patency of the tubes and any possible deformities within the uterus are revealed by the administration of contrast medium through the cervix and sequential X-ray imaging [7]. Allergic reactions are rare in HSG; however, if sedation or general anaesthesia is required (e.g., propofol), multiple potential triggers may come into play, increasing the risk of KS [8,9].

This case report describes a rare case of KS that developed during HSG after propofol sedation and iodinated contrast administration, presenting with ACS-like symptoms. Since both agents were administered within a short procedural interval, the exact causative trigger could not be definitively determined.

CASE PRESENTATION

A 28-year-old woman with no known chronic disease, no history of drug, food, or environmental allergy, and no previous anaphylactic reaction was scheduled to undergo hysterosalpingography (HSG) because of unexplained infertility persisting for more than one year. The procedure was performed under intravenous sedation with propofol 1 mg/kg. Subsequently, 10 mL of iopromide 300 mg I/mL was administered into the intrauterine cavity. The procedure lasted approximately 5 minutes. The patient had no known previous exposure to either propofol or iodinated contrast medium. Propofol was administered before the iodinated contrast agent.

During HSG, the patient developed severe chest pain, diffuse cutaneous erythema, dyspnoea, and pain radiating to the left arm. An allergic reaction was initially suspected, and pheniramine 45.5 mg IV and dexamethasone 8 mg IV were administered. As the clinical findings did not improve, prednisolone 40 mg IV was administered, and adrenaline 0.5 mg IM was administered twice as two separate doses. Owing to haemodynamic instability, with a blood pressure of 90/60 mmHg and a pulse rate of 120/min, together with a rapid decline in peripheral oxygen saturation to 60%, the patient was transferred to the emergency department by ambulance. On admission to the emergency department, the patient exhibited fluctuating consciousness and marked dyspnoea. Acute myocardial infarction was initially suspected because of ST-segment elevation on electrocardiography (Figure 1) and an elevated troponin level of 1163 pg/mL. Before coronary angiography, the patient was intubated using midazolam 10 mg IV and rocuronium 40 mg IV. During intubation, marked hyperaemia of the laryngeal mucosa was observed, and approximately 200 mL of frothy pulmonary secretion was aspirated through the endotracheal tube.

Coronary angiography revealed no significant coronary occlusion or thrombotic lesion (Figure 2). In view of the allergic manifestations, elevated cardiac biomarkers, ECG changes, and the absence of obstructive coronary artery disease on angiography, the final clinical diagnosis was considered to be Kounis syndrome rather than isolated anaphylactic shock. Echocardiography performed by the cardiologist showed normal cardiac findings, with no significant structural or functional abnormality. Serum tryptase and IgE levels could not be evaluated; IgE testing was not available in our hospital. The eosinophil count was $0.01 \times 10^9/L$. The patient was transferred to a third-level intensive care unit for close monitoring and ongoing mechanical ventilatory support. The initial posteroanterior chest radiograph demonstrated diffuse pulmonary infiltration (Figure 3). Haemodynamic and respiratory stabilisation was achieved with sedation and supportive treatment, including intravenous corticosteroids, antihistamines, fluid therapy, and diuretics.

During intensive care follow-up, the patient was initially managed with mechanical ventilation in SIMV mode at an FiO₂ of 0.9. Medical treatment included prednisolone 40 mg IV twice daily, pheniramine 45.5 mg IV twice daily, furosemide 20 mg IV four times daily, intravenous fluid replacement, low-molecular-weight heparin 0.4 mL subcutaneously twice daily, N-acetylcysteine intravenously three times daily, pantoprazole 40 mg IV twice daily, and noradrenaline infusion when required. Ceftriaxone 1 g IV twice daily was initiated following infectious diseases consultation because the patient was intubated and required mechanical ventilation. Arterial blood gas parameters and vital signs were monitored

closely. Despite intensive symptomatic and supportive treatment, the patient remained relatively unstable during the first 12–24 hours.

On the second day, partial regression of interstitial oedema was observed on chest radiography, while the troponin level reached a peak value of 3840 pg/mL. Sedation was gradually reduced, and ventilatory support was transitioned to SIMV-CPAP mode. Following reduction of FiO₂ to 0.4, the patient's haemodynamic status became stable. By the third day,

arterial blood gas values had improved and troponin levels had decreased markedly to 1063 pg/mL. As the patient fulfilled extubation criteria, she was extubated uneventfully with a Glasgow Coma Scale score of 15 and oxygen saturation above 96% under nasal cannula oxygen support. On the fourth day, both chest radiography (Figure 4) and electrocardiography (Figure 5) were normal. The patient was transferred to the ward without further complication and was discharged after a short period of observation.

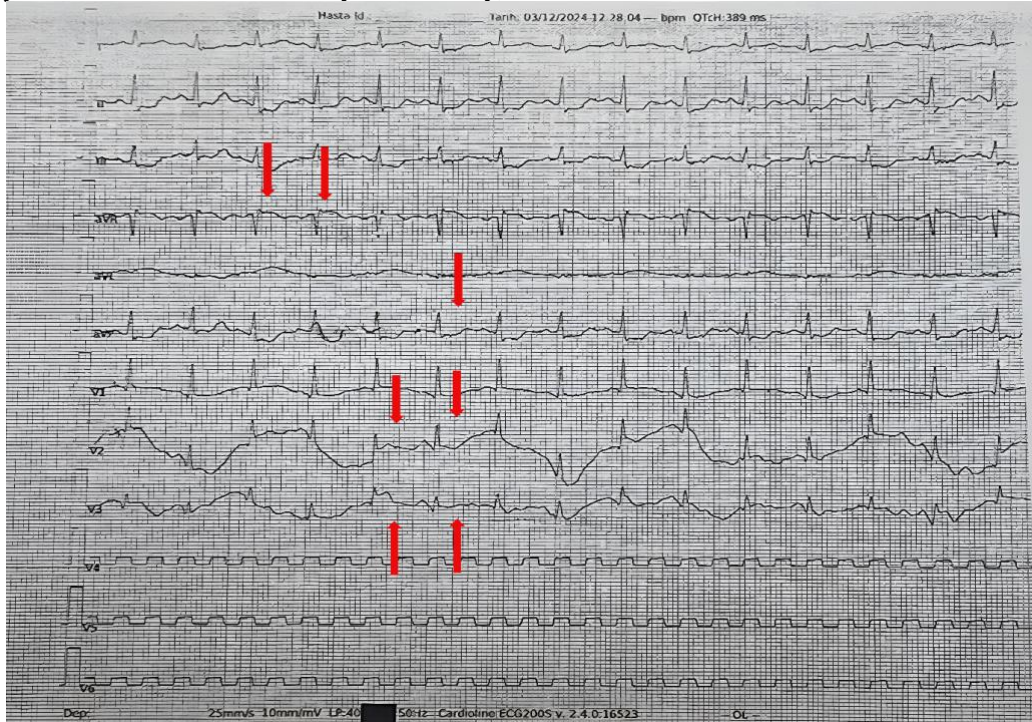


Figure 1. Admission ECG in the emergency department

Note: The arrows indicate ST-segment elevation on the admission ECG.

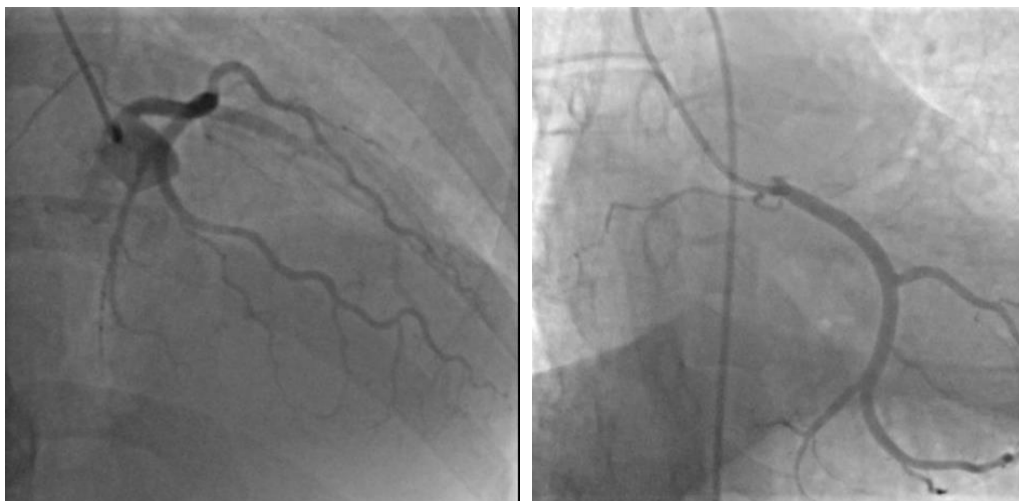


Figure 2. The patient's coronary angiography image

Note: Coronary angiography showing no significant obstructive coronary artery disease or thrombotic lesion.

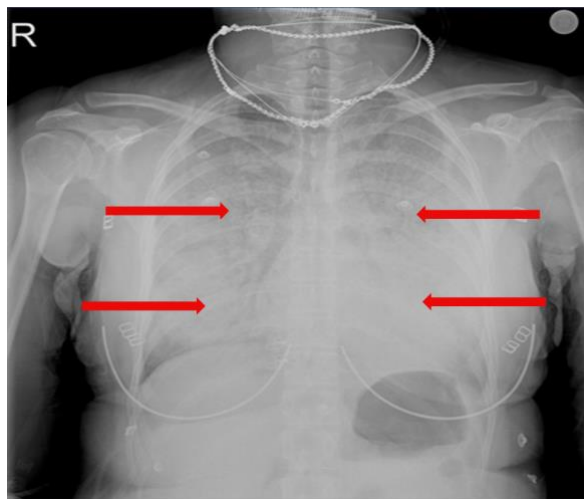


Figure 3. PA chest X-ray at the time of the patient's initial presentation

Note: The arrows indicate bilateral diffuse pulmonary infiltrates consistent with acute pulmonary edema.

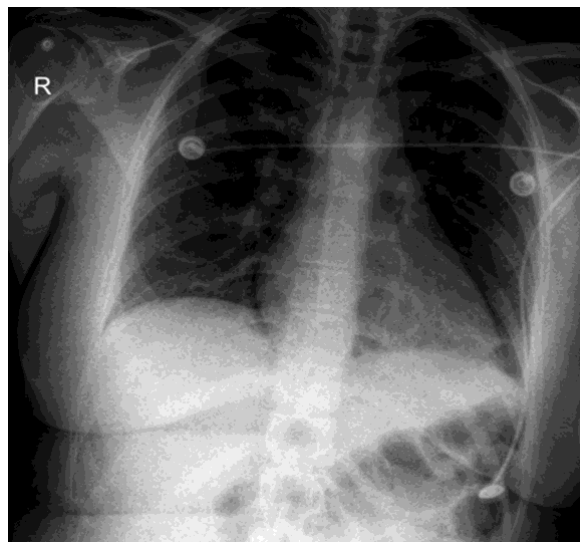


Figure 4. Patient's PA chest X-ray on Day 4

Note: PA chest X-ray on day 4 showing marked regression of the previously observed bilateral pulmonary infiltrates.

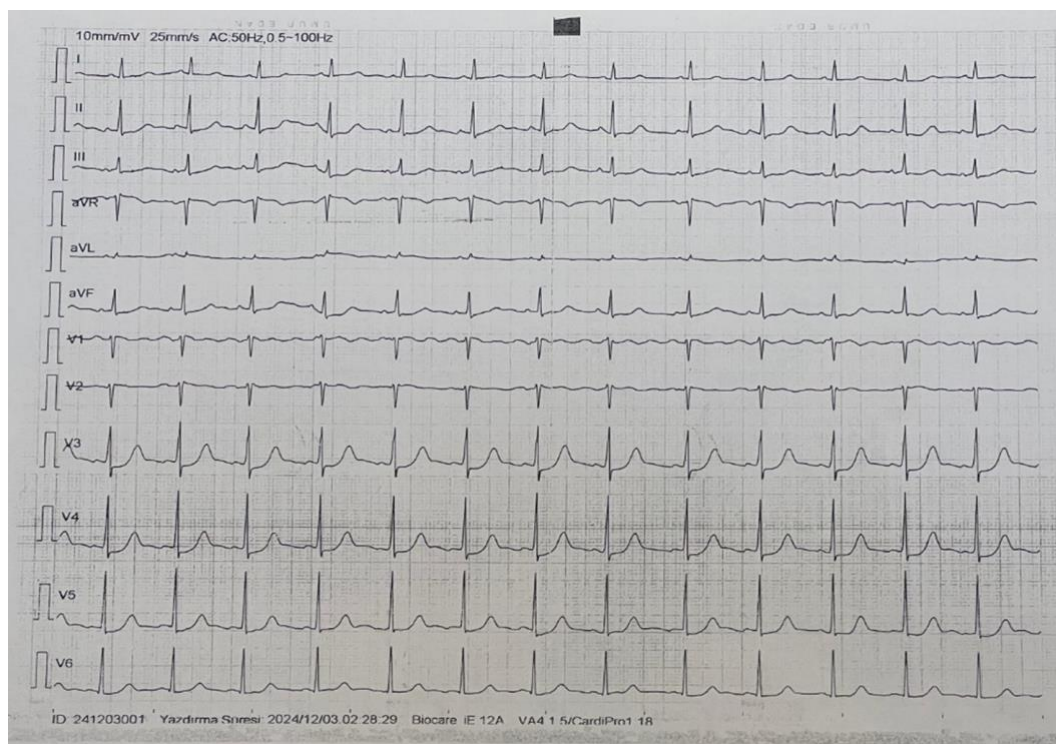


Figure 5. Patient's ECG image on Day 4

Note: ECG on day 4 showing resolution of the previously observed ischemia-like changes.

DISCUSSION

Kounis syndrome (KS) is a rare but serious condition in which allergic or anaphylactic reactions trigger acute coronary syndrome (ACS) through the release of histamine, tryptase, and other inflammatory mediators from mast cells [1–3]. Accordingly, the present case was interpreted as KS occurring in the setting of a severe allergic/anaphylactic reaction, rather than as isolated anaphylactic shock. It typically presents with a combination of allergic manifestations, chest pain, dyspnoea, and cutaneous findings, and is supported by coronary angiography and elevated cardiac biomarkers [4–6].

Hysterosalpingography (HSG) is widely used in the evaluation of infertility, particularly for assessing tubal patency and the uterine cavity. Although allergic reactions during this procedure are uncommon, the concomitant use of anaesthetic agents such as propofol in sedated patients may pose additional risks [8–10]. In the present case, both propofol and the iodinated contrast agent iopromide were considered potential triggers, as KS associated with both agents has previously been reported in the literature [11,12]. However, the patient had no known previous exposure to either propofol or iodinated contrast medium. Propofol was administered before the iodinated contrast agent; nevertheless, because both agents were used within a short procedural interval, the exact causative trigger could not be definitively identified. Therefore, both agents should be interpreted as possible triggers rather than one being conclusively identified as the sole cause. Similar to previous KS cases associated with contrast agents or anesthetic drugs, the present case showed the coexistence of allergic manifestations and ACS-like findings. However, unlike cases in which a single culprit agent can be identified, the exact trigger in our patient remained uncertain because propofol and iodinated contrast medium were administered within a short procedural interval.

KS may present as coronary vasospasm (Type 1), allergic myocardial infarction (Type 2), or stent thrombosis (Type 3) [5,6]. In this case, the coexistence of allergic manifestations, chest pain, ST-segment elevation, elevated troponin levels, and the absence of obstructive coronary artery disease or thrombotic lesion on coronary angiography strongly supported the diagnosis of Type 1 KS. Although direct angiographic evidence of coronary vasospasm was not documented, the transient ischemia-like ECG findings and biomarker elevation in the setting of an acute allergic/anaphylactic reaction were considered compatible with Type 1 KS. The differential diagnosis included acute myocardial infarction, isolated anaphylactic shock, pulmonary edema, stress-induced cardiomyopathy, and drug- or contrast-related hypersensitivity reactions. Acute myocardial infarction was initially suspected because of chest pain, ECG changes, and elevated troponin levels. However, the absence of obstructive coronary artery

disease on coronary angiography, together with simultaneous allergic manifestations, supported the diagnosis of KS rather than isolated myocardial infarction or isolated anaphylactic shock.

In KS accompanied by allergic or anaphylactic manifestations, prompt management of the allergic reaction, including adrenaline when indicated, corticosteroids, and antihistamines, is essential [2,4]. In cases of respiratory failure, early intubation and mechanical ventilation are of vital importance, particularly when airway and pulmonary findings are prominent. In this case, pharmacological management was directed at controlling the allergic/anaphylactic component, maintaining hemodynamic stability, supporting respiratory failure, and excluding ACS until coronary angiography clarified the diagnosis.

In patients with suspected ACS accompanied by an allergic reaction, rapid ECG and troponin assessment, together with coronary angiography when indicated, play a critical role in excluding potentially fatal occult coronary artery disease [1,3]. In Type 1 KS, where no coronary lesion is present, treatment is mainly based on avoidance of the triggering allergen, antiallergic and anti-inflammatory therapy, and symptomatic management. However, in Type 2 and Type 3 cases, standard ACS treatment protocols should also be implemented [6]. In addition, drugs with high allergenic potential should be avoided as much as possible in the management of KS [13].

Although KS-related deaths are rarely reported in the literature, post-mortem examinations in some unexplained fatal ACS cases have demonstrated anaphylactic immune cell activation and inflammatory mediators in the coronary arteries and myocardial tissue [14]. This finding highlights the importance of rapid diagnosis and appropriate treatment planning in severe forms of KS.

Even in procedures considered minor, such as HSG performed under sedation, the simultaneous use of contrast media and anaesthetic agents may lead to serious and unexpected complications such as KS. Therefore, even in the absence of a known allergy history, a detailed pre-procedural assessment should be performed before any interventional procedure. The choice of anaesthetic and contrast agents should be made carefully, and premedication protocols should be considered when necessary [9,10]. Early elective intubation and prompt intensive care support may prevent a potentially fatal course, particularly in patients with rapidly declining oxygen saturation and severe allergic manifestations.

A limitation of this case is that the exact trigger of KS could not be definitively determined. Although propofol was administered before the iodinated contrast agent, both agents were used within a short procedural interval, and the patient had no known previous exposure to either agent. In addition, confirmatory allergy testing could not be performed during the acute phase. Therefore, causality should be

interpreted with caution. Another limitation is that serum tryptase and IgE levels were not available, and direct angiographic documentation of coronary vasospasm could not be obtained. However, the diagnosis was supported by the clinical presentation, ECG changes, elevated troponin levels, normal coronary angiography, and normal echocardiographic findings.

CONCLUSION

KS is a rare but extremely serious clinical condition that may occur after exposure to anaesthetics or contrast media and can progress rapidly. Even in procedures considered relatively low risk, such as HSG, the possibility of KS developing in association with accompanying sedation and contrast media use should not be overlooked. Early diagnosis, cessation of contact with the allergen, appropriate and rapid pharmacological interventions (corticosteroids, antihistamines, adrenaline if necessary) and intensive care follow-up can significantly reduce mortality and morbidity. This case contributes to the literature by presenting a rare but important example of KS developing after propofol sedation and iodinated contrast administration during HSG, while emphasizing that the exact causative trigger could not be definitively identified.

Informed Consent

Written informed consent was obtained from the patient for publication of this case report. All personal information that could reveal the patient's identity was kept confidential, and the data were anonymized in accordance with ethical principles.

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