Potential association between fentanyl, propofol-induced acute heart failure and Kounis syndrome: A case report and review of the literature

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Abstract

Propofol is a widely used anesthetic agent that is generally considered safe and well-tolerated. However, rare reports of propofol-induced acute heart failure have been reported, especially in patients with underlying cardiovascular disease. Propofol infusion syndrome (PRIS) is a rare but severe complication associated with prolonged use of propofol infusion. Kounis syndrome is a rare acute allergic reaction that can lead to inflammation of the coronary arteries, reduced blood flow to the heart, and damage to heart cells, potentially leading to symptoms of heart failure. The exact relationship between propofol-induced acute heart failure and Kounis syndrome is not yet fully understood and requires further investigation. Here, we present a case of propofol-induced acute heart failure in a previously healthy adolescent female who underwent nasal breathing surgery. The patient developed acute pulmonary edema during the procedure and was diagnosed with acute heart failure in the cardiology intensive care unit. Laboratory findings were consistent with an allergic reaction, and the patient received treatment for acute heart failure and supportive care. We review the literature on the potential association between propofol-induced acute heart failure and Kounis syndrome, discuss the possible underlying mechanisms, and highlight the importance of early recognition and prompt management to prevent adverse outcomes and improve patient outcomes. Further studies are needed to elucidate the relationship between these two conditions and guide clinical management.

Introduction

Kounis syndrome is a rare acute allergic reaction that can lead to the inflammation of the coronary arteries, reduced blood flow to the heart, and damage to heart cells, potentially leading to symptoms of heart failure. The condition is typically triggered by an allergic or hypersensitivity reaction to an external stimulus, such as medications, insect bites, or environmental allergens [1]. Kounis syndrome can present with a wide range of clinical features, depending on the severity and location of the coronary artery spasm and the degree of cardiac dysfunction. Common symptoms include chest pain, shortness of breath, palpitations, hypotension, and cardiac arrhythmias. Diagnosis of Kounis syndrome requires a high index of suspicion and may involve electrocardiography, laboratory testing (such as cardiac biomarkers and allergy testing), and coronary angiography [2]. Propofol is an intravenous anesthetic agent that is widely used for induction and maintenance of anesthesia during

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surgical procedures. While generally considered safe and well-tolerated in healthy patients, rare reports of propofol-induced acute heart failure have been reported, especially in patients with underlying cardiovascular disease. Propofol infusion syndrome (PRIS) is a rare but severe complication associated with the prolonged use of propofol infusion. PRIS is characterized by metabolic acidosis, rhabdomyolysis, hyperkalemia, lipemia, cardiac failure, and multi-organ failure [3]. The exact mechanism of PRIS is not yet fully understood, but it is believed to be related to the inhibition of mitochondrial fatty acid oxidation and uncoupling of oxidative phosphorylation, leading to the accumulation of fatty acids, lactate, and other metabolites. Rhabdomyolysis and hyperkalemia can result from muscle tissue breakdown, while lipemia arises from the release of fatty acids from adipose tissue. Propofol-induced acute heart failure may share some common mechanisms with Kounis syndrome, particularly in the context of an allergic or hypersensitivity reaction [4]. The release of inflammatory mediators and vasoactive substances during the reaction may lead to coronary artery spasm, decreased blood flow to the heart, and cardiac dysfunction. The exact relationship between propofol-induced acute heart failure and Kounis syndrome is not yet fully understood and requires further investigation. Management of propofol-induced acute heart failure typically involves discontinuation of propofol infusion, supportive measures to correct metabolic disturbances (such as acidosis, electrolyte imbalances, and fluid overload), and specific interventions to manage cardiac dysfunction (such as inotropic agents, mechanical circulatory support, and revascularization procedures). The prognosis of propofol-induced acute heart failure depends on the severity and duration of the cardiac dysfunction and the effectiveness of the treatment. Early recognition and prompt management are essential to prevent adverse outcomes and improve survival [5]. In conclusion, there appears to be a potential association between propofol-induced acute heart failure and Kounis syndrome, although the exact relationship is not yet fully understood. Healthcare providers should be aware of the potential risk of propofol-induced acute heart failure in all patients receiving propofol, particularly those with a history of allergies or cardiovascular disease, and should closely monitor patients for signs of cardiac dysfunction. Early recognition and prompt management of propofol-induced acute heart failure are essential to prevent adverse outcomes and improve patient outcomes. Further studies are needed to elucidate the relationship between these two conditions and guide clinical management.

Case presentation

In our hospital, a female adolescent with no prior medical history, no family medical history, and no history of substance abuse required surgical treatment for correction of nasal breathing difficulties. Prior to surgery, the anesthesiologist assessed all of the patient's vital signs, ordered a cardiology evaluation that included an electrocardiogram (ECG) and an echocardiogram, both of which showed normal results. The patient also tested negative for COVID-19 by polymerase chain reaction (PCR). An allergy test was performed for anesthesia medications, which showed normal results.

During surgery, the anesthesiologist observed an increase in heart rate and a decrease in oxygen saturation levels on the monitor. Upon clinical examination, acute pulmonary edema was identified. The surgical procedure was immediately interrupted, and the anesthesiologist administered diuretic medication and adjusted the ventilator settings. A cardiology re-evaluation was promptly requested, and the patient was transferred to the cardiology intensive care unit (ICU) to address this emergency situation.

In the cardiology ICU, cardiac ultrasound revealed a diminished ejection fraction (EF) of 25%, with mitral valve regurgitation (1-2/4), tricuspid valve regurgitation (1/4), and a right ventricular systolic pressure (RVSP) of 33 mmHg, indicating acute heart failure. Laboratory admittance findings showed elevated levels of high-sensitive troponin (maximum of 2000 pg/mL), WBC (maximum of 20,000 K/μL), Neutr./Lymph.: 86,7/7,5%, Eosinophil 0,00 K/μl, slightly elevated B-type natriuretic peptide (BNP) levels (110 pg/mL). All other laboratory tests, including creatine phosphokinase (CPK), potassium (K), sodium (Na), thyroid-stimulating hormone (TSH), pH (7.44), blood lactate (1.3 mmol/L), bicarbonate (HCO3- : 19.5 mmol/L), urea (21 mg/dL), C-reactive protein (CRP), creatinine (0.5 mg/dL), immunoglobulin (Ig)/light chain kappa, cholesterol levels, and hepatic function tests, were within normal limits. We transferred the patient in the coronary angiography laboratory where we performed an angiography which was without evidences of occlusion. Later, the patient received oxygen supplementation and treatment for heart failure with angiotensin-converting enzyme (ACE) inhibitors, beta-blockers, loop diuretics, and potassium-sparing diuretics during hospitalization. The patient's clinical status improved, and subsequent blood tests showed normal results with troponin levels got to normal range as well the complete blood count. A follow-up evaluation by the same physician revealed improved cardiac muscle function, with an increase in the EF to 40%. The patient was discharged with medication for heart failure and an appointment for re-evaluation in the near future.

The patient visited the cardiology outpatient department, where a cardiologist performed an evaluation of the heart function with an ultrasound. The results were normal. The medication for heart failure was discontinued,
and a heart magnetic resonance imaging (MRI) was recommended by the cardiologist. The MRI was performed one month after discharge and showed normal results.

**Discussion**

Propofol-induced acute heart failure is an infrequent yet severe complication associated with prolonged propofol infusion. The precise underlying mechanism remains unclear; however, it is hypothesized to be related to the inhibition of mitochondrial fatty acid oxidation, which results in the accumulation of fatty acids, lactate, and other metabolites. The clinical presentation of this condition encompasses metabolic acidosis, rhabdomyolysis, hyperkalemia, lipemia, cardiac failure, and multi-organ failure [6].

Kounis syndrome is a rare acute hypersensitivity reaction that can culminate in reduced blood flow to the heart, thereby predisposing to heart failure. The inciting factor can vary and includes hypersensitivity reactions to environmental allergens, insect bites, or medications. The release of inflammatory mediators and vasoactive substances can induce coronary artery spasm, ultimately leading to decreased blood flow to the heart and associated cardiac dysfunction. The clinical presentation of Kounis syndrome can vary depending on the severity of the coronary artery spasm and associated cardiac dysfunction. The exact relationship between propofol-induced acute heart failure and Kounis syndrome is not yet fully understood and requires further investigation. However, there appears to be a potential association between these two conditions, particularly in the context of an allergic or hypersensitivity reaction. The release of inflammatory mediators and vasoactive substances during an allergic reaction may contribute to coronary artery spasm, decreased blood flow to the heart, and cardiac dysfunction, which can result in acute heart failure [7].

The two contexts of discussion are related to the adverse cardiovascular effects of general anesthesia, particularly the combination of propofol and fentanyl, and the risk of propofol-induced acute heart failure. The use of propofol and fentanyl can lead to significant reductions in blood pressure and cardiac function, even in young and healthy patients, and can be particularly dangerous for patients with pre-existing heart conditions. The mechanisms by which these agents produce cardiovascular depression are multifactorial, including vasodilation and baroreceptor response alterations [8].

In a systematic review and meta-analysis of 32 studies involving 170,906 patients, propofol administration was associated with a higher risk of cardiovascular adverse events compared to other intravenous anesthetics. The analysis reported a pooled odds ratio of 1.28 (95% CI, 1.17-1.40) [9,10]. The risk of propofol-induced cardiovascular adverse events was even higher in patients with pre-existing cardiovascular disease or risk factors, such as advanced age, hypertension, diabetes, and obesity. The review suggested that the hemodynamic effects of propofol, such as decreased myocardial contractility, vascular smooth muscle relaxation, or sympathetic activity, may be the underlying mechanisms leading to the decrease in cardiac output, systemic blood pressure, or heart rate variability [11,12]. A number of case reports have also reported the occurrence of acute heart failure following propofol use in patients with pre-existing cardiovascular disease or risk factors. These reports have proposed that the hemodynamic effects of propofol, such as decreased afterload, increased preload, and decreased contractility, may contribute to the development of acute heart failure [13].

In this case report, the patient did not exhibit any known cardiovascular disease or risk factors, and the pre-surgical preparation, which included a cardiology checkup with an electrocardiogram and echocardiogram, revealed normal results. Thus, the mechanism behind propofol-induced acute heart failure in this patient may differ from those observed in patients with pre-existing cardiovascular disease or risk factors. One plausible explanation is that the patient experienced an idiosyncratic reaction to propofol, which triggered an acute hypersensitivity or immune-mediated response, ultimately resulting in acute heart failure. However, this hypothesis requires further investigation, and additional cases and studies are necessary to elucidate the mechanism of propofol-induced acute heart failure in otherwise healthy patients.

**Conclusion**

Propofol-induced acute heart failure is an uncommon yet serious complication that may arise during surgical procedures, especially in individuals with underlying cardiovascular disease or hypersensitivity reactions. Kounis syndrome may share some pathophysiological mechanisms with propofol-induced acute heart failure, particularly in the context of an allergic or hypersensitivity reaction. Further investigations are warranted to explore the interplay between these two conditions and offer clinical guidance. Medical professionals should be cognizant of the potential hazard of propofol-induced acute heart failure in all patients receiving propofol, particularly those with a history of allergies or cardiovascular disease, and should vigilantly monitor patients for indications of cardiac dysfunction. Early recognition and management of propofol-induced acute heart failure are crucial to prevent unfavorable outcomes and optimize patient prognosis.


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