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KETAMINE INDUCED ACUTE SYSTOLIC HEART FAILURE

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ABSTRACT

Background: Studies have shown major cardiovascular effects associated with ketamine use disorder including dose-dependent negative inotropic effects. Preoperative ketamine use has been linked to ketamine-induced stress cardiomyopathy.

Case presentation: A 28-year-old female with a history of recurrent cystitis and ketamine use disorder (twice weekly for 14 years) presented with bilateral lower extremity oedema and shortness of breath for 3 months. She was tachycardic with a troponin level of 0.07 ng/ml and a B-type natriuretic peptide (BNP) level of 2511 pg/ml. Electrocardiogram showed normal sinus rhythm and transthoracic echocardiography (TTE) showed left ventricular ejection fraction (EF) of 15%, dilated left ventricle, and severe tricuspid and mitral regurgitation. Computed tomography (CT) scan of the chest and abdomen showed bilateral pleural effusions with congestive hepatopathy and ascites. The patient was started on intravenous furosemide, metoprolol, and sacubitril/valsartan. Rheumatological workup including complement levels, and antinuclear anti-double-stranded DNA was negative. A repeat TTE 2 weeks later revealed an EF of 25% and moderate tricuspid regurgitation. Four months later, the EF was 54% with normal left ventricular cavity size.

Conclusion: Although ketamine use disorder is increasing, data on long-term side effects is minimal. Screening for ketamine use disorders should be considered in patients presenting with acute systolic heart failure. Long-term studies are needed to evaluate the benefits of adding ketamine screening to standard urine toxicology.

KEYWORDS

Ketamine, heart failure, ketamine-induced disorder, systolic heart failure

LEARNING POINTS

- Ketamine use disorder can lead to severe cardiovascular complications, including acute systolic heart failure, likely due to its direct negative inotropic effects and dose-dependent impact on cardiac function.
- Clinicians should consider screening for ketamine use disorder in young adults presenting with acute systolic heart failure, especially when other common aetiologies have been ruled out.
- Early recognition and prompt treatment of ketamine-induced heart failure with diuretics and guideline-directed medical therapy can lead to significant improvement in cardiac function, but long-term management should also focus on ensuring cessation of ketamine use disorder.

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INTRODUCTION

The unauthorized non-medical use of ketamine has increased in the United States over the past two decades. In 2006, a US survey assessed that nearly 2.3 million adults and teenagers have used ketamine in their lifetime[1].

Known by its street name, "special K", the drug is typically used by young adults at parties and clubs for its psychotomimetic effects described as "K-hole". Ketamine is FDA-approved as an anaesthetic for short-duration procedures. It can be used in combination or as a single agent. Ketamine is also being used off-label to manage pain and multiple studies have reported it to be safe and effective[2]. Major side effects include nausea, vomiting, tachycardia, tachypnea, convulsion, temporary paralysis, and hallucinations[3].

Growing evidence shows that ketamine use disorder has multiple cardiovascular effects including but not limited to cardiac arrest. In some studies, ketamine had a dose-dependent negative inotropic effect[4]. A few cases of stress cardiomyopathy caused by preoperative ketamine administration have been reported[5]. Two case reports revealed a link between myocardial fibrosis and chronic ketamine poisoning[6]. Ketamine use disorder has also been associated with major lower urinary tract symptoms, such as bladder pain, haematuria, urinary urgency, and urinary frequency. These adverse effects can become irreversible and lead to chronic bladder dysfunction with poor compliance and capacity[7].

Heart failure in young adults is uncommon and known etiologies include familial cardiomyopathy, peripartum cardiomyopathy, and tachycardia-induced cardiomyopathy. Less frequently heart failure can be seen in spontaneous coronary artery dissection, malignant hypertension, or illicit drug use such as cocaine use disorder[8]. We report a case of acute systolic heart failure likely secondary to street ketamine use disorder.

CASE PRESENTATION

A 28-year-old female with a history of ketamine use disorder with multiple genitourinary complications presented with progressive bilateral lower extremity oedema that started 3 months prior. She also reported shortness of breath, orthopnoea, chronic cough, and decreased exercise tolerance. The patient had been abusing ketamine inconsistently since the age of 14 years. She reported using ketamine twice weekly along with smoking half a pack of cigarettes daily. She denied any family history of cardiac diseases and never experienced similar symptoms previously. On presentation, she was tachycardic with a heart rate of 118 bpm. Physical examination showed basal crackles on lung auscultation and 2+ bilateral lower extremity oedema. She had a troponin level of 0.07 ng/ml and a B-type natriuretic peptide (BNP) level of 2511 pg/ml. Electrocardiogram was normal sinus rhythm *(Fig. 1)* and transthoracic echocardiography (TTE) showed left ventricular ejection fraction (EF) of 15%, dilated left ventricle, and severe tricuspid and mitral regurgitation *(Fig. 2 and Fig. 3)*. Computed tomography (CT) scan of the chest and abdomen showed bilateral pleural effusions with congestive hepatopathy and ascites.

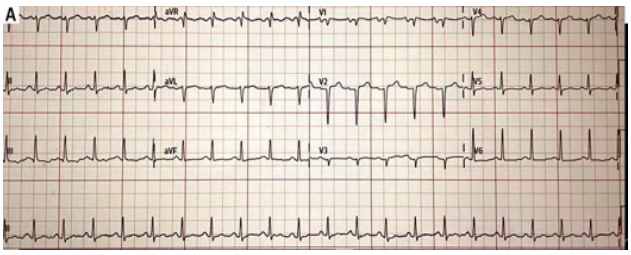

Figure 1. Electrocardiogram on presentation showing normal sinus rhythm and no ischemic changes.

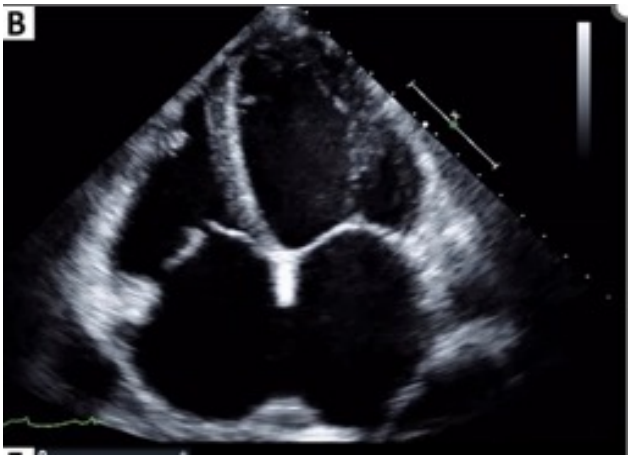

Figure 2. Initial transthoracic echocardiogram showing dilated global cardiomyopathy.

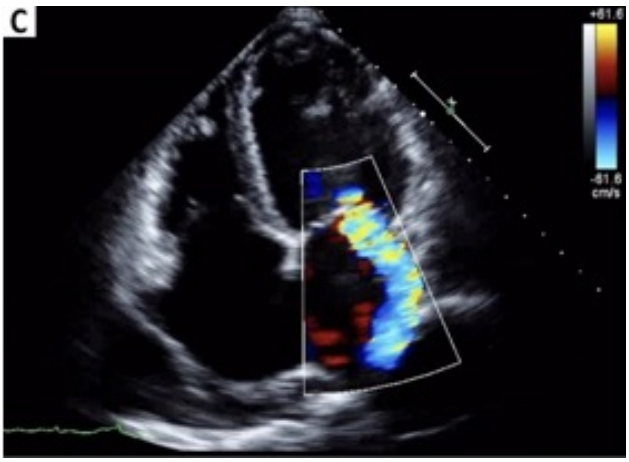

Figure 3. Initial transthoracic echocardiogram showing mitral regurgitation.

She was started on intravenous furosemide drip as well as guideline directed medical therapy (GDMT), which she tolerated well and had adequate urinary output. Ischemic workup was negative. Repeated echocardiography 2 weeks later revealed an improved EF of 25% along with a decrease in tricuspid regurgitation grade from severe to moderate. Four months later, the EF was 54% with normal left ventricular cavity size.

Rheumatology was consulted and autoimmune workup including C3, C4, total complement (CH50), antinuclear antibody (ANA), anti-double stranded DNA (anti-dsDNA) antibody, cytoplasmic and perinuclear-antinuclear

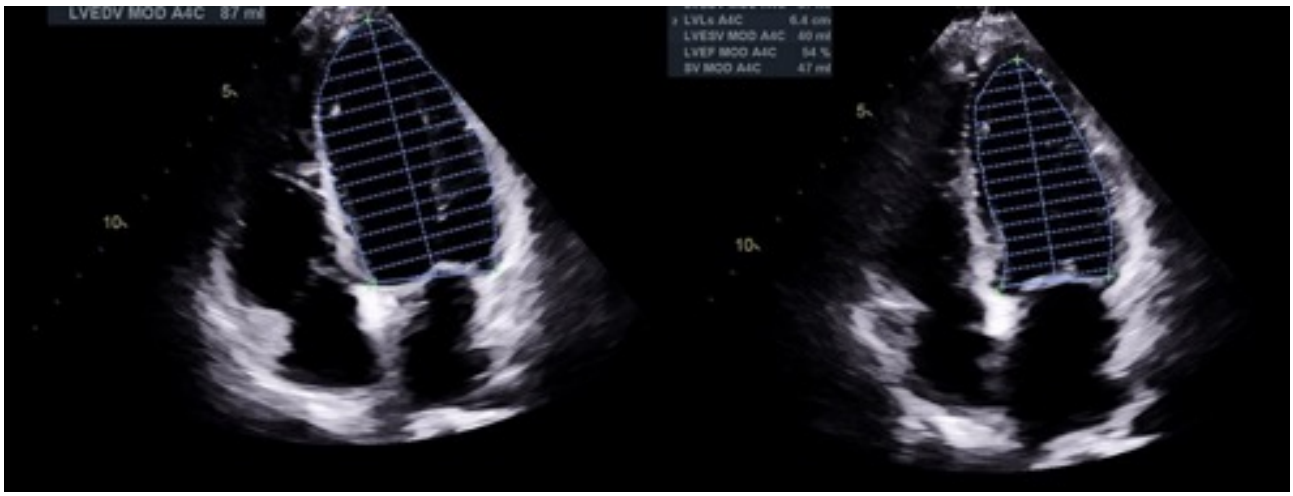

Figure 4. Follow-up transthoracic echocardiogram showing left ventricular ejection fraction of 54% using the biplane Simpson method with normal left ventricular size.

cytoplasmic autoantibodies (C- and P-ANCA), were negative. The patient was discharged on GDMT and a follow-up echocardiogram showed an improvement in EF to 50%. *(Fig. 4)*.

DISCUSSION

Ketamine's effect on the cardiovascular system has been mentioned in the literature on multiple occasions. Tao et al. described a case of chronic ketamine poising and myocardial fibrosis with hyaline degeneration of small arteries in a 34-year-old woman[6]. To our knowledge, this is the first case describing an association of ketamine with acute systolic heart failure.

Ketamine has direct negative inotropic effects, central sympathetic stimulation effect, and neuronal catecholamine uptake inhibition effect. In patients with left ventricular dysfunction, sympathetic stimulation may not be adequate to overcome the negative inotropic effects, leading to decreased cardiac performance[9]. Christ et al. reported that patients receiving ketamine infusion had a decrease in the cardiac index by 21% (p=0.01)[5]. Another study stated that ketamine exerted a dose-dependent negative inotropic effect on human cardiac myocytes[10]. Li. et al. showed that in rabbits, ketamine can cause decreased left ventricular EF through myocardial apoptosis and fibrosis, also leading to electrophysiological disturbance causing malignant arrhythmia and sudden cardiac death[11].

A study by Goddard et al. showed that ketamine might cause electrocardiogram (ECG) changes consistent with new-onset ischemia during sedation[12]. However, a recent study showed variability in cardiovascular contractility secondary to ketamine use. S-ketamine increased cardiac output in contrast to its metabolite S-nor-ketamine which reduced cardiac excitation in a dose-dependent manner[13]. A similar case report to ours showed that upon administration of intravenous (IV) ketamine, a patient experienced delusions, tachycardia, hypertension, and 1 mm ST depression in V3-V6 on ECG with elevated troponins. Cardiac catheterization showed no significant coronary artery disease, and the echocardiogram showed a left ventricular EF of 45% with moderate apical hypokinesis which improved to 60% the following day[14].

In our case, the patient had elevated troponins along with an EF of 15% which improved in 2-4 weeks. Ischemic workup was negative. The transient nature of acute systolic heart failure along with ruling out other possible etiologies leaves ketamine-induced heart failure as the most plausible explanation. The data on the management of ketamine induced heart failure is sparse and is mainly driven by similar case reports. In our case, the patient improved with adequate diuresis and GDMT. Close follow-up and monitoring are required, and steps should be taken to ensure cessation of ketamine use.

CONCLUSION

Ketamine use disorder is becoming a major concern in the United States and very little long-term data on its cardiovascular side effects is available. Individuals should be counselled on these potential side effects and screening should be considered in patients with a history of ketamine use presenting with acute systolic heart failure. Large-scale studies are required to establish this association and formulate management strategies.

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