

## Introduction

Takotsubo, or stress-induced cardiomyopathy, is characterized by transient left-ventricular ballooning and hypokinesis in the absence of obstructive coronary disease or plaque rupture. Occurring in the setting of significant emotional or physiologic stress, catecholamine excess is postulated to be a part of its mechanism for development.

Xylazine is a non-opiate sedative with central alpha-2-adrenergic agonism that is approved exclusively for veterinary use. It is emerging as a frequent adulterant with other drugs of abuse, particularly with heroin where there may be a synergistic toxic effect. We present a case of a patient with recreational xylazine and polysubstance use, who subsequently developed takotsubo cardiomyopathy in the course of intoxication and withdrawal.

## Case

A 30-year-old female with fetal alcohol syndrome and polysubstance use disorder presented with profound encephalopathy after being found disoriented and nonverbal. Vitals were labile over the first 24 hours. On admission, she had sinus bradycardia at 40-55 beats per minute, hypertension to 155/100, and 30-35 respirations per minute. On physical exam, she appeared severely cachectic with a BMI of 15.7. She was obtunded but protecting her airway, and exhibited significant sialorrhea, rhinorrhea, and sluggish pupils. Urine drug screen was positive for fentanyl and cocaine, with negative serum ethanol level. Within 24 hours of admission, mental status returned to baseline and she had signs and symptoms of opiate withdrawal.

On day 3 of hospitalization, an ECG incidentally revealed ST elevations in leads 1, aVL, and V3-V6 (Fig 2). She was hemodynamically stable without cardiac symptoms, only complaining of continued withdrawal-associated agitation and discomfort. Serial high sensitivity troponins T were 237 and 187. Echocardiogram revealed an ejection fraction of 40+/-5% with akinesia of the distal two-thirds of the left ventricle with relative preservation of the extreme apex, suggestive of a mid-ventricular variant takotsubo cardiomyopathy (Fig 1).

The patient was not taken for cardiac catheterization in the absence of symptoms and concern for poor follow-up. After several days of clinical stability, she was discharged with methadone maintenance and cardiology follow-up, but has since been lost to care.

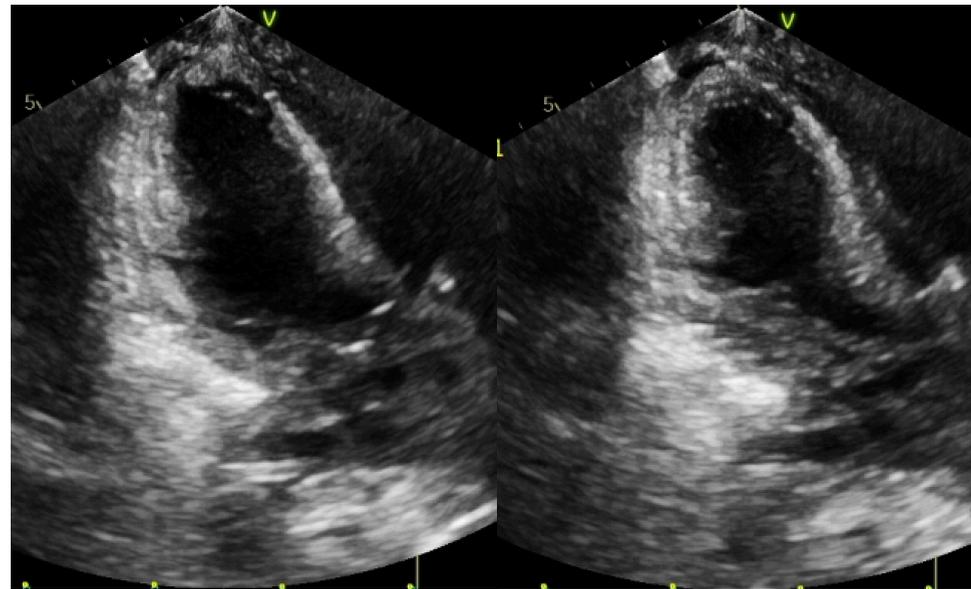


Figure 1: Echocardiogram suggestive of mid-ventricular variant takotsubo cardiomyopathy.



Figure 2: ECG with ST elevations in leads 1, aVL and V3-V6.

## Discussion

To our knowledge, this is the first case report of takotsubo cardiomyopathy associated with xylazine and polysubstance use. Xylazine is a potent central alpha-2-adrenergic agonist, causing sedation, anesthesia, respiratory depression, bradycardia, muscle relaxation, and transient hypertension followed by hypotension. Due to significant bradycardia and hypotension, it was never approved for human use.

Skin ulcerations and physical deterioration have been noted with chronic use, but other harms and toxic effects still remain unknown. In 2018, xylazine was detected in 152 drug intoxication deaths, compared to 15 in 2015. As xylazine continues to be used alongside opiates, further investigation into its adverse cardiac side effects is warranted, as demonstrated by this case.

## References

1. Lim S, Viner K. "National Drug Early Warning System (NDEWS) Philadelphia Sentinel Community Site Drug Use Patterns and Trends, 2019." NDEWS. <https://ndews.org/wordpress/files/2020/07/SCS-Report-2019-Philadelphia-FINAL.pdf>
2. Reyes, J.C., et al. "The Emerging of Xylazine as a New Drug of Abuse and its Health Consequences among Drug Users in Puerto Rico." *J Urban Health* (2012). <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3368046/>
3. Ruiz-Colón K, Chavez-Arias C, Díaz-Alcalá JE, Martínez MA. Xylazine intoxication in humans and its importance as an emerging adulterant in abused drugs: A comprehensive review of the literature. *Forensic Sci Int*. 2014;240:1-8. doi:10.1016/j.forsciint.2014.03.015
4. Silva-Torres L, Veléz C, Alvarez L, Zayas B. Xylazine as a drug of abuse and its effects on the generation of reactive species and DNA damage on human umbilical vein endothelial cells. *J Toxicol*. 2014;2014:492609. doi:10.1155/2014/492609
5. Wong SC, Curtis JA, Wingert WE. Concurrent detection of heroin, fentanyl, and xylazine in seven drug-related deaths reported from the Philadelphia Medical Examiner's Office. *J Forensic Sci*. 2008;53(2):495-498. doi:10.1111/j.1556-4029.2007.00648.x