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CASE REPORT

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MDMA("Ecstasy") abuse leading to delayed onset rhabdomyolysis: A case report and literature review

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Key Clinical Message

MDMA and cocaine can result in acute onset rhabdomyolysis. However, delayed onset rhabdomyolysis and its pathophysiology is of concern Early therapeutic intervention improves prognosis. Such cases should be promptly referred and managed in centers equipped with critical care and renal replacement therapy.

KEYWORDS

AKI, creatine kinase, MDMA, rhabdomyolysis

1 | INTRODUCTION

Recreational drug use and its overdose is increasing exponentially in the United States.[1] One of the commonly abused drugs, MDMA, is a party drug among adolescents and young adults in so-called 'raves'.[2] MDMA has a varying range of toxicities ranging from irritability, muscle cramps, and chills to life-threatening conditions such as Disseminated Intravascular coagulation, hyperthermia, rhabdomyolysis and AKI.[3] Rhabdomyolysis has been reported to be caused by several drugs with MDMA being one of the major contributors.[4] Several cases have been reported of mortality due to AKI and hyperkalemia caused by rhabdomyolysis and hyperkalemia in acute settings.[5] However, delayed rhabdomyolysis has not been reported widely. We present one such case of delayed onset AKI due to rhabdomyolysis.

2 | CASE PRESENTATION

A 37 years male with a history of Molly (MDMA) abuse, the amount not known 8 days back with no prior past medical commodities with a BMI of 35.78 (obese), former smoker, alcohol- 10 cans of beer per week presented to our hospital with complaints of lower back pain of 1-week duration, worsened 2 days before presentation to the hospital, mainly over the left back, burning/stabbing in nature, radiating to the abdomen and left thigh, partially relieved by lying on the right side, worse with movement, 9/10 in severity. The pain was associated with nausea without vomiting. No fever, chills, or saddle anesthesia. The patients hadn't passed urine for 2 days before presentation. On examination, he was lethargic but oriented, dry mucous membrane with left paraspinal tenderness and left thigh tenderness on examination. On neurological examination, power was 5/5 in all extremities, and motor and sensory exams were normal.

3 | METHODS

The patient's labs revealed normal electrolytes with a bicarbonate of 13 and an anion gap of 28. BUN was 119, creatinine 13.36, calcium 5.2, phosphorus 12.7, and eGFR

4.4. Liver function tests showed AST 2376, ALT 563, and lipase 265, with normal bilirubin and ALP. Mild leukocytosis was present with hemoglobin 11.4. Creatine kinase was exceptionally high at 307,570 (confirmed by dilution). Inflammatory markers showed ESR 71 and CRP 100.40. TSH was normal, hepatitis panel negative, as well as ethanol, salicylates, and urinary drug screen. Urinalysis indicated glucose 2+, blood 3+, protein 3+, RBC 12, and WBC 7. PTH was elevated at 148 (normal range 12–88 pg/mL), with calcium at 5.2, ionized calcium at 0.87, and vitamin D at 7.0 (Table 1). Noncontrast CT Abdomen and pelvis showed loss of cortical medullary differentiation in the kidneys bilaterally no hydronephrosis or nephrolithiasis was appreciated (Figures 1 and 2).

In the Emergency, foley catheterization was tried 2 times with no urine output. However, a bladder scan showed 125 mL of urine. The patient was anuric despite 5 L of crystalloid resuscitation. The patient was then taken to ICU, temporary catheterization was done and hemodialysis was initiated with a 125 mL/h of bicarbonate drip.

TABLE 1 Laboratory tests at the time of admission.

Test	Result
Electrolytes	
Bicarbonate	13
Anion gap	28
Calcium	5.2
Ionized calcium	0.87
Phosphorus	12.7
Lactic acid	Normal
Renal function tests	
BUN	119
Creatinine	13.36
eGFR	4.4
Liver function tests	
AST	2376
ALT	563
Lipase	265
Bilirubin	Normal
ALP	Normal
Complete blood count	
Hemoglobin	11.4
Leukocytosis	Mild
ESR	71
Urinalysis	
Urinary drug screen	Negative
Glucose	2+
Blood	3+
Protein	3+
RBC	12
WBC	7
Toxins	
Ethanol	Negative
Salicylates	Negative
Hormone panel	
TSH	Normal
PTH Intact	148 (N-12-88 pg/mL)
Vit D	7.0
Others	
Hepatitis Panel	Negative
CRP	100.40
Creatine kinase	307, 570 (rechecked by dilution)

4 | OUTCOME AND FOLLOW-UP

After 10 days of alternate-day dialysis, the patient has improved symptomatically with lab values of Creatinine Kinase-795; BUN-29; Cr-7.49; the patient is oliguric now and is making around 1.2 L of urine, with Hemoglobin stable at 10.1 g/dL.

On 3 months follow-up, the patient had persistently elevated creatinine levels. The patient is currently on Amlodipine 10; Carvedilol, Gabapentin; Hydralazine. On long-term follow-up, the patients' renal parameters had improved with creatinine and BUN within normal range. The lab parameters along the course of the disease are mentioned in Table 2.

5 | DISCUSSION

Acute tubular necrosis induced by pigment as a result of nontraumatic rhabdomyolysis (myocyte necrosis brought on by a sharp increase in intracellular calcium) is the most significant cause of acute kidney damage. In such cases, creatinine phosphokinase concentrations can exceed 100,000 U/L. Rhabdomyolysis is diagnosed when the measured CK reaches five times the upper limit of normal. MDMA has been postulated to cause rhabdomyolysis in acute settings via hyperpyrexia (aggravated by ambient temperature, motor activity, metabolic regulation, autonomic vascular changes, and central disturbances in thermoregulation), increased activity such as dancing and crush injury, as the patients are prone to being unconscious.[6,7] These processes can be split into traumatic or nontraumatic. This case present nontraumatic cause of rhabdomyolysis. These adverse effects resulting in rhabdomyolysis are usually acute in onset. Thus,

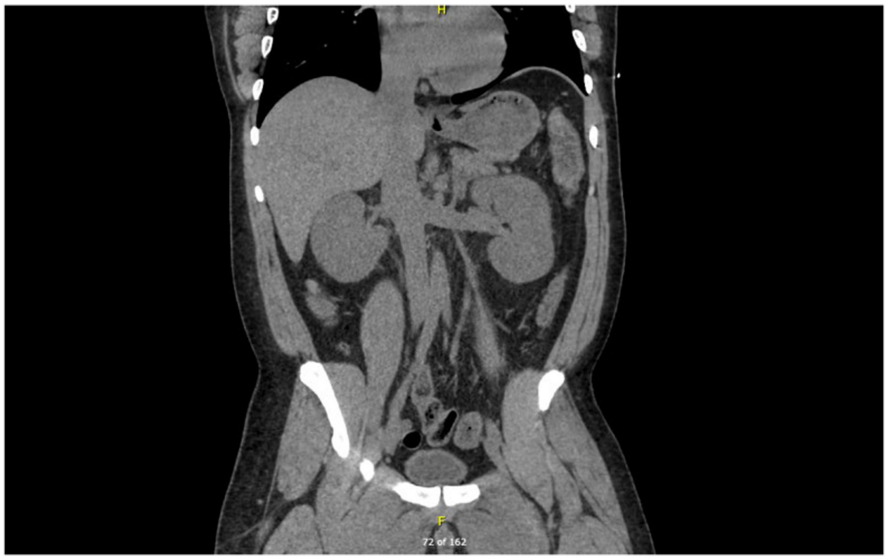

FIGURE 1 Noncontrast CT abdomen and pelvis.

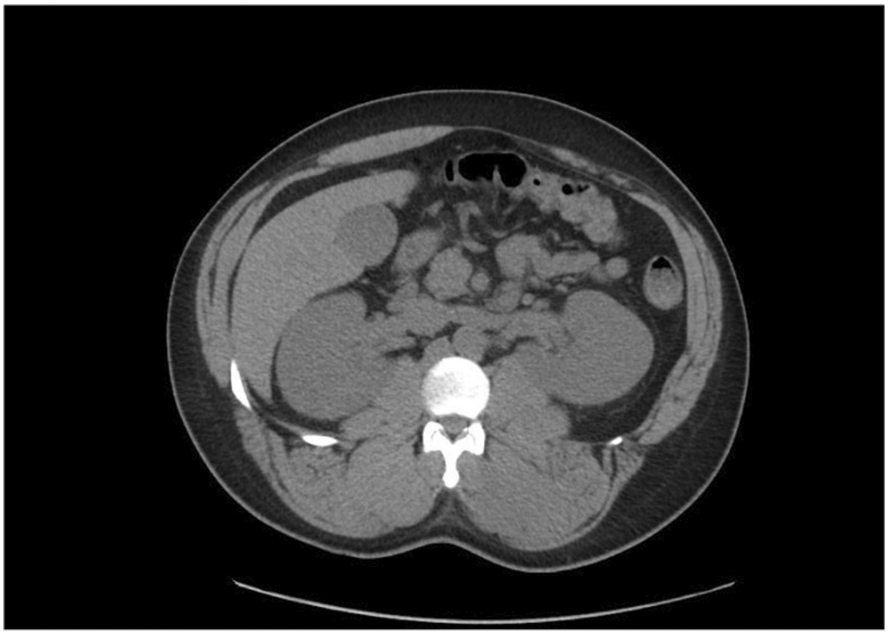

FIGURE 2 Noncontrast CT abdomen and pelvis.

TABLE 2 Laboratory parameters along the course of the disease.

Day of presentation	1st day	10th day (After alternate-day hemodialysis)	3 month follow-up	1 year follow-up
Creatininie kinase	307,570	795	841	
Serum urea	119	29	41	13
Serum creatinine	13.36	7.49	5.99	1.2
Serum calcium – total/ionized	5.2/0.87	–	9.3	
eGFR			12.7 mL/min/m^2	

very few instances of delayed rhabdomyolysis have been reported in cases of MDMA abuse. Previously reported delayed onset rhabdomyolysis had occurred at 30 h,[8] 35 h,[9] 55 h,[7] and 5[10] days. Other predisposing factors such as drugs, toxins, dehydration, chronic diseases were not present in this patient, thus MDMA was the likely suspect for rhabdomyolysis. However, in our case, the patient did not specify the amount of MDMA consumed, although he mentioned it was a small amount taken just once. As our patient presented after 8 days, a new study into the

mechanism of metabolism of MDMA and pathophysiology of rhabdomyolysis may be required.

Although MDMA generally causes tachycardia, enhanced energy, empathy, and euphoria, the onset of various severe consequences such as sudden death, multiorgan failure, rhabdomyolysis, and hyperpyrexia/hyperthermia are unpredictable. This unpredictability can be attributed to factors like polydrug use and adulterants in MDMA pills. Studies show varied MDMA content and contamination in tablets, affecting toxicity. Additionally, the enzymes metabolizing MDMA, particularly CYP2D6 and COMT, exhibit genetic polymorphisms affecting drug breakdown. A deficiency in CYP2D6, present in 5%–9% of Caucasians, leads to poor metabolism and increased toxicity. COMT polymorphisms, affecting 25% of Caucasians, can influence water retention and hyponatremia.[9] Other mutations such as a novel RYR1 mutation was detected in a case with delayed rhabdomyolysis and neuroleptic malignant syndrome.[10] It is also hypothesized that MDMA toxicity may be increased by an interaction of direct pharmacological effects of the drug and the prevailing environmental conditions at administration. Other factors (e.g., immune mechanisms, idiosyncrasy) cannot be excluded as influencers.[11] Our patient may have showed unusual response to MDMA, likely due to these enzyme polymorphisms. Chronic MDMA users may develop tolerance or reverse tolerance, leading to increased doses or polydrug use for desired effects. Our patient, despite claiming no dose increase and no previous use of MDMA, might have experienced reverse tolerance, escalated serotonergic adverse effects and resulted in delayed rhabdomyolysis and prolonged hyperthermia.

CT scan without IV contrast is preferred as contrast may further deteriorate the kidney injury Noncontrast CT scan of Abdomen and Pelvis showed loss of corticomedullary differentiation in our case. In another case report where rhabdomyolysis resulted in AKI, CT findings were striate nephrogram, perinephric collection and nephromegaly.[12] However, in other reported cases of rhabdomyolysis associated with illicit drug use, MRI and CT scan was primarily used to identify the muscles affected and the extent of disease. MRI was preferred over CT scan for early diagnosis of rhabdomyolysis.[13] Even though the MRI findings are nonspecific, the sensitivity in the detection of muscle involvement is higher than CT or US.[14]

Our patient also presented with significantly high creatinine kinase values in the range of 300,000 U/L. Similarly, high creatinine values were reported in another case ultimately requiring hemodialysis and high creatinine kinase value is indicative of the severity of renal injury.[15] Few cases have been reported where patients have survived a massive overdose.[11,16]

It is evident that severe acute sickness is relatively rare despite widespread MDMA use. However, when difficulties do arise, they can be fatal, necessitating the execution of a well-thought-out plan based on the clinical situation and knowledge of the physiological effects and toxicity profile of MDMA.[17] Treatment modalities for MDMA overdose and rhabdomyolysis include hydration-force diuresis, monitoring and optimization of the fluid and electrolyte situation, including intake and removal, and kidney function tests.[18] For hyperkalemia, hemodialysis can be used. Urine alkalization is not recommended, as it would lessen the kidneys' ability to remove MDMA.[19] Specifically, in all cases of delayed rhabdomyolysis, including ours, rhabdomyolysis was managed with vigorous intravenous and oral hydration. However, unlike other cases of delayed rhabdomyolysis, our patient's CK peaked at 307,570 U/L, making it the third-highest reported CK in a survivor (after 555,000 and 409,440 U/L), and the second highest recorded CK for delayed rhabdomyolysis.[9,20] Notably, despite this extreme CK value, the patient returned to baseline health at discharge with no complications, including kidney damage.

Upon a 3-month follow-up, our patient demonstrated elevated serum creatinine levels, now qualifying as chronic kidney disease (CKD). The progression of acute kidney injury (AKI) to CKD in illicit drug users has not been extensively studied, with existing research presenting contrasting conclusions. In ICU patients with severe rhabdomyolysis, AKI develops in the majority, with renal replacement therapy (RRT) necessary in 35% of cases. Serum myoglobin and phosphate levels at admission are significantly linked to long-term renal prognosis, suggesting that eliminating these molecules could reduce the risk of AKI progressing to CKD. A large multicenter retrospective study evaluated 259 rhabdomyolysis patients for AKI and CKD, with 80 having eGFR data at 3 months. Among them, 28.8% had an estimated GFR below 60 mL/min/1.73 m^2 at 3 months (CKD KDIGO stage 3–5), compared to 11.2% before hospitalization, indicating rhabdomyolysis as a significant CKD risk factor.[21] In a study of 5861 CKD patients, 1202 reported illicit drug use, but CKD presence, kidney function, and albuminuria were not significantly associated with cocaine, methamphetamine, or heroin use.[22] Conversely, a study by Vupputuri et al.[23] documented a significant positive association between illicit drug use and the risk for mild kidney function decline.

On long-term follow-up, the patient's kidney function improved and the renal parameters were within normal range. This can be attributed to aggressive monitoring, early initiation of renal replacement therapy and a multidisciplinary team involvement in an intensive care set-up. Similar recovery was reported in other studies where it was found that early therapeutic intervention improves

prognosis, such cases should be promptly referred and managed in centers where aggressive supportive therapy can quickly be instituted.[3]

6 | CONCLUSION

MDMA, known as Ecstasy/Molly is a recreational drug that is widely used and can result in severe life-threatening complications. Delayed rhabdomyolysis is rarely reported as compared to the acute onset mechanism still unexplored. AKI and subsequently CKD is a common consequence of rhabdomyolysis in MDMA overdose although very few fatalities have been reported.

AUTHOR CONTRIBUTIONS

Swotantra Gautam: Conceptualization; writing – original draft; writing – review and editing. **Aakash Neupane:** Conceptualization; writing – original draft; writing – review and editing. **Ivonne De La Hoz Molina:** Writing – original draft; writing – review and editing. **Jhonny Bonilla Villarreal:** Writing – original draft; writing – review and editing. **Weiying Li:** Writing – original draft; writing – review and editing. **Tasnuva Anindita H. Mahmud:** Supervision; writing – review and editing.

FUNDING INFORMATION

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICAL APPROVAL

All methods were performed in accordance with the relevant guidelines and regulations. Written informed consent was obtained from the patient.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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REFERENCES

1. Nicholson T, Duncan DF, White JB. Is recreational drug use normal? *J Subst Use*. 2002;7(3):116-123. doi:10.1080/14659890209169340
2. Shannon M. Methylenedioxymethamphetamine (MDMA, "Ecstasy"). *Pediatr Emerg Care*. 2000;16(5):377-380. doi:10.1097/00006565-200010000-00022
3. Walubo A, Seger D. Fatal multi-organ failure after suicidal overdose with MDMA, "Ecstasy": case report and review of the literature. *Hum Exp Toxicol*. 1999;18(2):119-125. doi:10.1191/096032799678839707
4. Coco TJ, Klasner AE. Drug-induced rhabdomyolysis. *Curr Opin Pediatr*. 2004;16(2):206-210. doi:10.1097/00008480-200404000-00017
5. Vanden EH, Montenij LJ, Touw DJ, Norris EM. Rhabdomyolysis in MDMA intoxication: a rapid and underestimated killer. "Clean" ecstasy, a safe party drug? *J Emerg Med*. 2012;42(6):655-658. doi:10.1016/j.jemermed.2009.04.057
6. Cunningham M. Ecstasy-induced rhabdomyolysis and its role in the development of acute renal failure. *Intensive Crit Care Nurs*. 1997;13(4):216-223. doi:10.1016/S0964-3397(97)80056-0
7. Halachanova V. Delayed rhabdomyolysis after ecstasy use. *Mayo Clin Proc*. 2001;76(1):112-113. doi:10.4065/76.1.112
8. Lehmann ED, Thom CH, Croft DN. Delayed severe rhabdomyolysis after taking "Ecstasy". *Postgrad Med J*. 1995;71(833):186-187. doi:10.1136/pgmj.71.833.186-a
9. Ghaffari-Rafi A, Eum KS, Villanueva J, Jahanmir J. Protracted hyperthermia and delayed rhabdomyolysis in ecstasy toxicity: a case report. *Medicine*. 2020;99(41):E21842. doi:10.1097/MD.0000000000021842
10. Russell T, Riazi S, Kraeva N, Steel AC, Hawryluck LA. Ecstacy-induced delayed rhabdomyolysis and neuroleptic malignant syndrome in a patient with a novel variant in the ryanodine receptor type 1 gene. *Anaesthesia*. 2012;67(9):1021-1024. doi:10.1111/j.1365-2044.2012.07226.x
11. Ramcharan S, Meenhorst PL, Otten JMMB, et al. Survival after massive ecstasy overdose. *J Toxicol Clin Toxicol*. 1998;36(7):727-731. doi:10.3109/15563659809162623
12. Mangano FA, Zaontz M, Pahira JJ, et al. Computed tomography of acute renal failure secondary to rhabdomyolysis. *J Comput Assist Tomogr*. 1985;9(4):777-779. doi:10.1097/00004728-198507010-00021
13. Nakahara K, Tanaka H, Masutani K, et al. The value of computed tomography and magnetic resonance imaging to diagnose rhabdomyolysis in acute renal failure. *Nephrol Dial Transplant*. 1999;14(6):1564-1567. doi:10.1093/ndt/14.6.1564
14. Moratalla MB, Braun P, Fornas GM. Importance of MRI in the diagnosis and treatment of rhabdomyolysis. *Eur J Radiol*. 2008;65(2):311-315. doi:10.1016/j.ejrad.2007.03.033
15. Luckoor P, Salehi M, Kunadu A. Exceptionally high creatine kinase (CK) levels in multicausal and complicated rhabdomyolysis: a case report. *Am J Case Rep*. 2017;18:746-749. doi:10.12659/AJCR.905089
16. Danis DM, McIntyre RT. Gamma hydroxybutyrate overdose: two cases illustrate the unique aspects of this dangerous recreational drug. *J Emerg Nurs*. 1995;21(5):374-376. doi:10.1016/S0099-1767(05)80087-X
17. Hall AP, Henry JA. Acute toxic effects of 'Ecstasy' (MDMA) and related compounds: overview of pathophysiology and clinical

management. *Br J Anaesth*. 2006;96(6):678-685. doi:10.1093/bja/ael078
18. Bora F, Yılmaz F, Bora T. Ecstasy (MDMA) and its effects on kidneys and their treatment: a review. *Iran J Basic Med Sci*. 2016;19(11):1151-1158. doi:10.22038/ijbms.2016.7813
19. Ricaurte GA, McCann UD. Recognition and management of complications of new recreational drug use. *Lancet*. 2005;365(9477):2137-2145. doi:10.1016/S0140-6736(05)66737-2
20. Hall AP, Lyburn ID, Spears FD, Riley B. An unusual case of ecstasy poisoning. *Intensive Care Med*. 1996;22:670-671. doi:10.1007/BF01709744
21. Candela N, Silva S, Georges B, et al. Short- and long-term renal outcomes following severe rhabdomyolysis: a French multi-center retrospective study of 387 patients. *Ann Intensive Care*. 2020;10(1):27. doi:10.1186/s13613-020-0645-1
22. Akkina SK, Ricardo AC, Patel A, et al. Illicit drug use, hypertension, and chronic kidney disease in the US adult population. *Transl Res*. 2012;160(6):391-398. doi:10.1016/j.trsl.2012.05.008
23. Vupputuri S, Batuman V, Muntner P, et al. The risk for mild kidney function decline associated with illicit drug use among hypertensive men. *Am J Kidney Dis*. 2004;43(4):629-635. doi:10.1053/j.ajkd.2003.12.027

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