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Fulminant Hepatitis Associated with Chronic Consumption of 3,4-Methylenedioxy-Methamphetamine; Case Report

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Abstract

The amphetamine derivative 3,4-methylenedioxymethamphetamine (MDMA), also called ecstasy, is a neurotoxin widely consumed among young people that has increased in recent years because it is a recreational drug, of which immediate effects are known such as a greater sensation of well-being, extroversion, increased sensory perception. However, its long-term effects have been described very little in the medical literature, including damage to the heart, central nervous system, kidney, etc. One of its little-known effects is hepatotoxicity, of which few cases are known associated with fulminant hepatitis, which is a rapidly deteriorating condition that is generally associated with a syndrome of multiple organ dysfunction and death. Therefore, it is very important to know this type of damage in the short and long term. The following case is of a 39-year-old man who came to our service due to jaundice syndrome and the only history of MDMA consumption, who as the days went by met the criteria for fulminant liver failure, with damage to multiple organs (organ dysfunction syndrome).

Keywords

Fulminant Hepatitis, Acute Liver Failure, Methamphetamine, Severe Acute Liver Failure in a User of Drugs of Abuse, Hepatology

1. Introduction

Amphetamines are designer drugs, among the best known today, which are known

to have originally been widely used in academic, industrial and medical settings [1]. Of these compounds, the most used is 3,4-methylendioxy-methamphetamine (MDMA) and 3,4-methylenedioxy-amphetmine (MDA), MDMA was first synthesized in 1914 as an appetite suppressant, but it was not until 1960 that it began to be used as a recreational drug in the US. And in 1990 in the rest of the world [2]. With the passage of time, its long-term adverse effects such as damage to the central nervous system, heart, kidney and hepatotoxicity began to be discovered. Hepatotoxicity, although the exact mechanism is unknown, is believed to be due to multiple mechanisms, among the most investigated is the interaction of amphetamines and monoaminergic receptors, mainly adrenergic, which have a vasoconstrictor effect at the level of arterial smooth muscle and damage. directly to the vascular endothelium [1]. Likewise, the stimulation of the release of vasopressin is also known, which with the vasoconstrictor effect could generate ischemia at the liver level and therefore cellular damage that, if perpetuated, could cause liver failure [3].

This hepatotoxicity in a few cases has been associated with acute liver failure or also called fulminant hepatitis, which has a high mortality rate, so knowing this type of aspects is of great help in the prevention of addictions and consequences in the short and long term.

2. Clinical Case

Below is a 39-year-old patient. He went to the emergency room due to sudden dyspnea associated with abdominal pain in the region of the right upper quadrant, as well as mixed liver damage (hepatocellular and cholestatic).

As important antecedents, he refers to positive smoking from the age of 15 to the present, social alcoholism, sporadic use of Marijuana and daily use of MDMA for 10 years, negative medical history for blood transfusions, use of allopathic or homeopathic drugs, no risky sexual relations as well as a negative oncological history.

During his clinical evaluation, he presented jaundice in the integuments and skin, as well as pruritus and generalized weakness.

Table 1. Liver biochemical parameters during patient hospitalization.

	Admission	Day 2	Day 3	Day 4	Day 5	Day 6
AST (U/L)	78	144	345	500	810	1409
ALT (U/L)	100	230	370	530	690	787
Total bilirubin (mg/dL)	1.8	2.4	5.9	8.1	13.4	17.5
GGT (U/L)	326	450	530	640	820	910
Alkaline phospfatase (U/L)	200	370	530	660	740	810
INR	1.4	1.7	2.8	4.10	5.20	7.15

AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, GGT: Gammaglutamyl transpeptidase, INR: International normalized index.

Paraclinical on admission: TGO: 78 U/L, TGP: 100 U/L, GGT: 326 U/L, alkaline phosphatase: 200 U/L, direct bilirubin: 0.73 mg/dL, indirect bilirubin: 1.07 mg/dL, leukocytes: $5.83*10^3$/μL, neutrophils: $2.87*10^3$/μL, hemoglobin: 15.6 g/dL, platelets $239*10^3$/μL, prothrombin time: 16.1 seconds, partial thromboplastin time: 26.9 seconds, INR: 1.4 (Table 1).

Imaging studies: Liver ultrasound: Chronic acalculous cholecystitis, mild ascites, grade 1 hepatic steatosis (Figure 1, Figure 2).

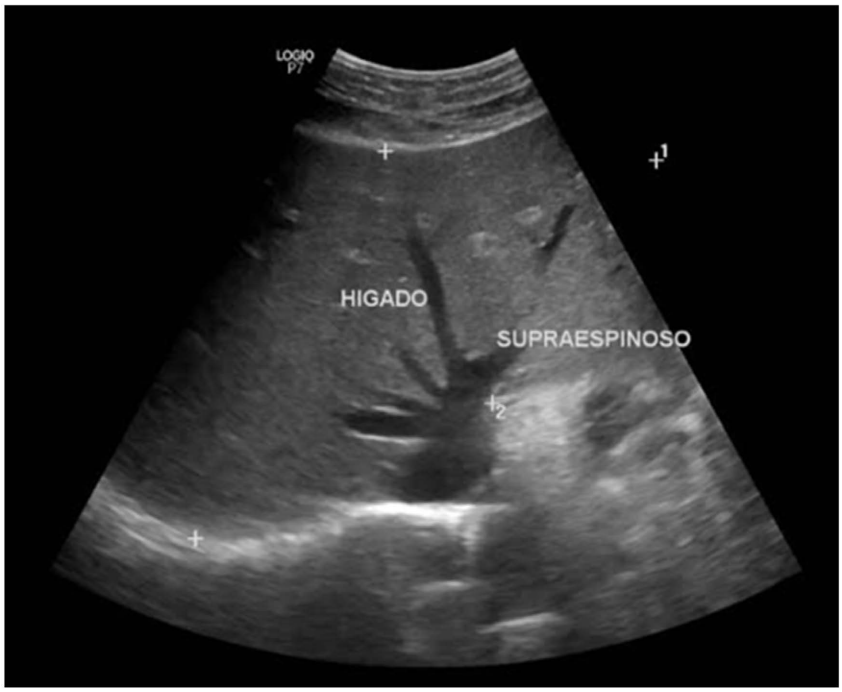

Figure 1. Portal vein at the level of the hepatic hilum. At the intrahepatic level you can see its two branches, a posterior and caudal right one, and an anterior and cranial left one. Grade I hepatic steatosis. Discrete diffuse increase in echogenicity, with normal assessment of the diaphragm and the edges of the intrahepatic vessels.

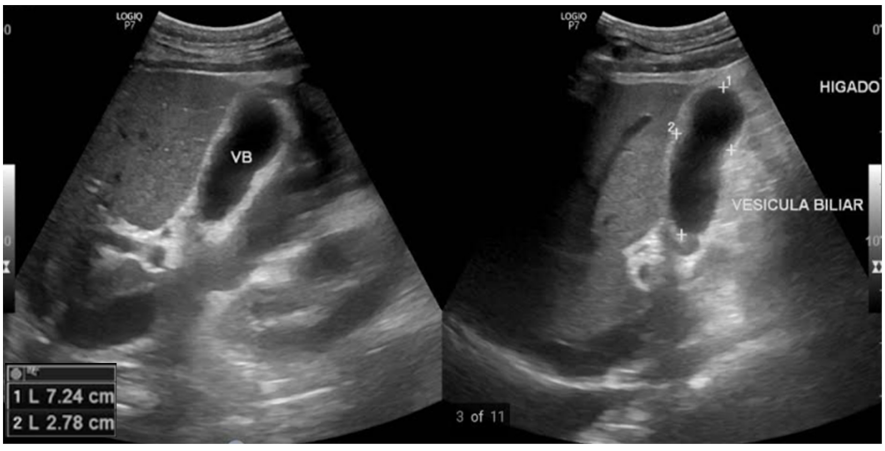

Figure 2. Upper abdominal ultrasound. Chronic acalculous cholecystitis, thickening of the wall, with echogenic material inside, without posterior acoustic shadow, compatible with biliary sludge.

A few days after admission, there was an acute increase in bilirubin and transaminases, as well as an INR greater than 1.5, as well as grade IV hepatic encephalopathy, which is why it is classified as acute liver failure. Due to the above and to clarify the etiology of the condition, the following laboratories are performed: Viral serologies (HBV, HAV, HCV, Epstein-Barr virus, cytomegalovirus and HIV), as well as screening for autoantibodies (AMA, ANA, AAML, LKM), were negative. Due to the above and the only history of MDMA consumption, we made the diagnosis of acute toxic hepatitis.

Later, during his evolution, the patient presents hypotension, tachypnea, as well as severe desaturation, which is why intubation and the start of assisted mechanical ventilation are continued. Renal replacement therapy (hemodialysis) is performed due to acute kidney injury as well as initiation of dobutamine and norepinephrine due to association with a mixed state of shock (cardiogenic and hypovolemic). General measures and support are initiated to continue the evolution and possibility of a liver transplant. However, due to his serious condition, the patient died 48 hours after the start of assisted mechanical ventilation.

3. Discussion

Recreational use of 3,4-methylenedioxymethamphetamine (MDMA) among young people is very popular as it increases psychomotor activity, ease of communication, as well as increasing alertness, etc. [4]. In relation to chronic diseases, damage to the nervous and cardiac systems, rhabdomyolysis and hyperthermia are known [5]. In the case of hepatotoxicity due to MDMA, this is multifactorial, although it has been described that the metabolism of MDMA is metabolized by two main pathways: the first is N-desakilation, deamination and oxidation and the second is demethylation followed by methylation catalyzed with catechol-O-methyltransferase, the latter involves a CYP2D6 isoenzyme of the cytochrome P450 system, which can form inhibitory complexes with MDMA molecules and thus potential toxicity [3].

Hypersensitivity reactions, direct hepatocellular damage or its adulterants, ischemia have also been described, the latter being very important due to its effect on monoaminergic receptors, mainly the adrenergic receptor, which has a vasoconstrictive effect at the level of arterial smooth muscle, and direct damage to the hepatic endothelium, as well as by secretion of vasopressin, which will have a similar effect [6].

In the case of our patient, a diagnosis of acute liver failure or also called fulminant type was made since he completed a period of less than 26 weeks, he was not known to have previous liver disease, he had elevated liver enzymes associated with coagulopathy (INR > 1.5) and alterations in mental status (encephalopathy) [7].With the description of the time elapsed between the appearance of jaundice and the development of encephalopathy, as acute according to the O'Grady Classification [8]. The role of liver biopsy is limited by hemodynamic instability and as-

sociated coagulopathy, in addition to not having pathognomonic signs that could suggest the origin of 3,4-methylenedioxymethamphetamine (MDMA) consumption.

Due to the multiple causes of acute liver failure, which is associated with 3,4-methylenedioxymethamphetamine (MDMA) toxicity, other causes of hepatotoxicity such as medications, foods, infectious diseases, thrombotic events, as well as alcohol, will have to be ruled out. In the case of our patient, they were discarded [6].

Although there are international guidelines for treatment of acute liver failure, treatment usually consists of supportive measures as well as treatment of the condition that is causing the liver failure. In relation to 3,4-methylenedioxymethamphetamine (MDMA) poisoning, there is no standardized treatment, only liver transplantation, and recently research has been done on molecular sorbent recirculation (MARS) or liver dialysis, which consists of two circuits of recirculation one with albumin with high affinity to toxins and the second circuit to clean the albumin solution and therefore the toxins [9].

MDMA consumption has grown worldwide and is associated with low economic status, dysfunctional families, psychiatric disorders, etc. Therefore, it is very important for health ministries to have social programs for addictions, as well as reintegration programs in educational, cultural, as well as social activities.

4. Conclusions

3,4-methylenedioxymethamphetamine (MDMA) is a currently fashionable drug of abuse with a high incidence in young people, therefore, knowing about acute and chronic complications is of utmost importance to raise awareness in society so that they know the risks of its consumption and programs are made for its prevention.

Early attention to this type of pathology in intensive care units, as well as centers specialized in liver transplantation, could increase survival. In recent years, liver support devices such as MARS have been of great help as a bridging therapy for liver transplantation or as an opportunity to recover liver function and thus avoid transplantation. Although these types of therapies are still under investigation and their use is limited even in several countries.

5. Ethical Considerations

The authors declare that they have met all ethical responsibilities regarding data protection, right to privacy and informed consent.

Authorization from the institution's ethics committee is not necessary since at no time do they fail to comply or violate patient anonymity rules, nor is any experimental procedure performed that puts the patient's integrity at risk.

The authors declare that this article does not contain personal information that would allow the patient described to be identified, which makes the patient's informed consent unnecessary for the publication of the article.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Luethi, D. and Liechti, M.E. (2020) Designer Drugs: Mechanism of Action and Adverse Effects. *Archives of Toxicology*, **94**, 1085-1133. https://doi.org/10.1007/s00204-020-02693-7

[2] Christophersen, A.S. (2000) Amphetamine Designer Drugs—An Overview and Epidemiology. *Toxicology Letters*, **112-113**, 127-131. https://doi.org/10.1016/S0378-4274(99)00205-2

[3] Campbell, G.A. and Rosner, M.H. (2008) The Agony of Ecstasy. *Clinical Journal of the American Society of Nephrology*, **3**, 1852-1860. https://doi.org/10.2215/CJN.02080508

[4] Colado, M.I. (2008) Éxtasis (MDMA) y drogas de diseño: estructura, farmacología, mecanismos de acción y efectos en el ser humano. *Trastornos Adictivos*, **10**, 175-182. https://doi.org/10.1016/S1575-0973(08)76364-5

[5] Montiel-Duarte, C., Varela–Rey, M., Oses-Prieto, J., López-Zabalza, M.J., Beitia, G., Cenarruzabeitia, E. and Iraburu, M.J. (2002) 3,4-Methylenedioxymethamphetamine ("Ecstasy") Induces Apoptosis of Cultured Rat Liver Cells. *Biochimica et Biophysica Acta* (*BBA*)—*Molecular Basis of Disease*, **1588**, 26-32. https://doi.org/10.1016/S0925-4439(02)00112-6

[6] Jones, A.L. and Simpson, K.J. (1999) Review Article: Mechanisms and Management of Hepatotoxicity in Ecstasy (MDMA) and Amphetamine Intoxications. *Alimentary Pharmacology & Therapeutics*, **13**, 129-133. https://doi.org/10.1046/j.1365-2036.1999.00454.x

[7] Shingina, A., Mukhtar, N.A., Wakim-Fleming, J., Alqahtani, S.A., Wong, R.J., Limketkai, B.N., Larson, A.M. and Grant, L. (2023) Acute Liver Failure Guidelines. *The American Journal of Gastroenterology*, **118**, 1128-1153. https://doi.org/10.14309/ajg.0000000000002340

[8] O'Grady, J., Schalm, S.W. and Williams, R. (1993) Acute Liver Failure: Redefining the Syndromes. *The Lancet*, **342**, 273-275. https://doi.org/10.1016/0140-6736(93)91818-7

[9] Peck, J., Replete, N., Melquist, S.J., Flores, F. and Wilsey, M. (2020) Adolescent with Acute Liver Failure in the Setting of Ethanol, Cocaine, and Ecstasy Ingestion Treated with a Molecular Adsorbent Recirculating System. Cureus. https://doi.org/10.7759/cureus.9699