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Ecstasy Intake Related Coagulopathy

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Abstract. 3,4-methylenedioxymethamphetamine (MDMA), substance known as "Ecstasy" among the people and used due to entertainment, euphoric and energy booster effect, is one of the famous synthetic stimulants. 22-year-old man was found as unconscious in the early morning. According to the expressions of his family and friends, it was learned that he drank alcohol until late in the previous evening and took ecstasy besides this before he died. It was reported that he was taken to intensive care unit with temperature of 41°C and death occurred 12 hours later. At autopsy in external examination, petechial and purpuric hemorrhages in purple and red color were detected on body. In internal examination, petechial hemorrhages on the surface of the heart and lungs, subendocardial hemorrhage in the heart, hemorrhage on the mucosal surface of the stomach were seen. In the toxicological analyses of the blood, Paracetamol (4870 ng/ml), MDMA (847 ng/ml), MDA (94,2 ng/ml), Lidocaine (23 ng/ml), Pantoprazole (10,5 ng/ml), Midazolam (1,83 ng/ml) were detected. The death occurred due to coagulopathy related MDMA intoxication. Here, we present a case of autopsy, clinical findings and histopathologic findings, laboratory results in medicolegal literature.

Key words: MDMA intoxication, coagulopathy, death.

Introduction

3,4-methylenedioxymethamphetamine (MDMA), which is also known as "Ecstasy" among the people and used due to entertainment, euphoric and energy booster effect, is one of the popular synthetic stimulants. After ingestion of an overdose, it is known that tachycardia, hypertension, hyperthermia, rhabdomyolysis, brain edema and renal failure are caused by the excessive sympathetic stimulation [1]. Death cases related to hyperthermia and coagulation were reported to taken of MDMA [2, 3]. Here, we report a case of the death occurred due to coagulopathy related MDMA intoxication with autopsy, clinical findings and histopathologic findings, laboratory results in medico legal literature.

Case report

In our case, 22-year-old man was found as unconscious in the early morning. According to the expressions of his family and friends, it was learned that he drank alcohol until late in the previous evening and took ecstasy besides this before he died. It was reported that he was taken to intensive care unit with temperature of 41°C and death occurred 12 hours later. INR: 5.65 (0.85-1.15), APTT: 116.1 sec (22.7-31.8), PT: 41.2 sec (10.8-15) HGB: 6.73 g/dL(12.20-18.10), PLT: 15.1 K/ μ L(142-10.8-15) HGB: 6.73 g/dL(12.20-18.10), PLT: 15.1 K/ μ L(142-10.8-15)424), Ethanol: 13.6 mg/dL (0.00 - 10.60), Creatinine: 3.88 mg/ dL (0.65 - 1.01), AST: 1664 IU/L (13 – 28), ALT: 1585 IU/L (8 -45), CK > 42670 IU/L (47 – 240), Glucose: 21 mg/dL (70 – 100), Sodium (Na): 155 mmol/L (136 – 145), LDH: > 4500 IU/ L (125 - 243) were detected as laboratory findings. At autopsy in external gross examination, petechial and purpuric hemorrhages in purple and red color were detected on the whole body. Bilateral periorbital ecchymosis especially prominent in

left, petechial and purpuric hemorrhages in dark purple and red color on the back and both sides of the gluteal region, purpuric hemorrhages 4x1 cm in length on right sides of both upper and lower lips, 2.5x1 cm in length on left sides of both upper and lower lips, 1.5x1 cm in length on left side of lower lip, 1 cm in length on right side of lower lip, large purpuric hemorrhages making invasion subcutaneous tissue on medial upper sides of both arms, bleeding 6x5 cm in length on right iliac and purpuric hemorrhage 25x14 cm in length on the right upper front of thigh were detected. In internal examination, purpuric hemorrhage under the scalp, petechial hemorrhages on the surface of the heart and lungs, subendocardial hemorrhage in the heart, hemorrhage on the mucosal surface of the stomach were seen. In the toxicological analyses of the blood, Paracetamol (4870) ng/ml), MDMA (847 ng/ml), MDA (94.2 ng/ml), Lidocaine (23 ng/ml), Pantoprazole (10.5 ng/ml), Midazolam (1.83 ng/ml) were detected. It was recorded that death occurred due to coagulopathy related MDMA intoxication.

Discussion

3,4-Methylenedioxymethamphetamine (MDMA) is ringsubstituted amphetamine derivative that is potent CNS (Central Nervous System) stimulants and structurally related to the hallucinogen mescaline [4]. Its amphetamine-like characteristics produce effects such as tachycardia, hyperthermia, emotional warmth, distortions in sensory and time perception and sweating, whereas its quasi-hallucinogenic effects are euphoria and a psychological "high" [1, 4]. MDMA has a plasma half-life of 7.6 hour. Typically, after oral ingestion (75–150 mg), effects begin within 1 hour and last 4–6 hour [5]. Many fatalities have been reported with blood levels of MDMA 0.1–2.1 mg liter [6]. However, a case of an overdose of MDMA in which the blood level reached 4.3 mg liter with mild sinus tachycardia, somnolence degree and no other clinical findings [7]. Henry et al. reported that another overdose case which blood level of MDMA was 7.72 mg liter, was the highest recorded in a surviving patient, with just a 'hangover', tachycardia and hypertension [6]. This case shows a rare constellation of severe adverse effects that can occur from MDMA: the 'syndrome' of hyperpyrexia, multi-organ failure, and DIC (Disseminated Intravascular Coagulation). A review of literature showed only one other reported survival from MDMA associated serotonin syndrome with a temperature above 42.9°C [8]. Hunter criteria, serotonin syndrome is suggested if the patient has taken a serotonergic agent and has one of the four following cluster of symptoms/ signs: a) spontaneous clonus, b) inducible clonus and agitation or diaphoresis, c) ocular clonus and agitation or diaphoresis, d) tremor and hyperreflexia, e) hypertonia, hyperthermia (>38°C or >100.4°F) and ocular or inducible clonus [9]. Our patient fit into cluster 'e' above and also had coagulation.



Fig. 1. The purpuric hemorrhages under the scalp

The hyperthermia in serotonin syndrome is caused by increased muscle activity and not from an alteration in temperature regulation by the hypothalamus; antipyretic such as acetaminophen is not effective in the treatment [10]. Hyperthermia could cause further side effects, such as rhabdomyolysis, myoglobinuria, renal failure, liver damage, and DIC [11]. The side effects were seen in our case. Death is possible these adverse effects.

MDMA act on at least three neurotransmitter pathways: the serotonergic (5-hydroxytryptamine) pathway, the dopaminergic system, and the noradrenergic system. The serotonergic pathway is mainly affected, which would account for the more pronounced effect on mood. Serotonin plays a major role in thermoregulation, and interference with this mechanism is believed to be the cause of the hyperthermia that arises as a complication of ring-substituted amphetamine abuse. In addition, stimulation of the noradrenergic system also probably contributes to hyperthermia. Thus, hyperthermia may account for many of the changes seen in deaths from ring-substituted amphetamine abuse [12].

MDMA (also known as ecstasy) and ethanol (alcohol) are two of the most commonly co-abused substances [13]. According to the statement of friends he abused alcohol, and MDMA. Blood level of alcohol was 13.6 mg/dL. We think that blood alcohol level may decrease because of testing 6 hours later after intake of alcohol. Alcohol use in rats alters neurotransmission in the dopamine system [14], and long-term MDMA use affects serotonergic neurotransmission [15]. Drug-induced alterations in monoaminergic neurotransmission systems that received previously might have interacted with the acute effects of the drugs [16].

Sano R et al. reported that myocardial fibrosis and calcification might have been caused by repeated use of MDMA [11].

Here, we presented a case of autopsy, clinical findings and histopathologic findings, laboratory results in medicolegal literature.

References

- 1. S. Ramcharam, P.L. Meenhorst, J.M.M.B. Otten et al. Survival after massive Ecstasy overdose, Clin. Toxicol. 1998;727-731.
- 2. Chadwick IS, Curry PD, Linsley A, Freemont AJ, Doran B. Ecstasy, 3-4 methylenedioxymethamphetamine (MDMA), a fatality associated with coagulopathy and hyperthermia. J R Soc Med. 1991;84(6):371.
- 3. Garcha-Repetto R, Moreno E, Soriano T, Jurado C, Gimňnez MP, Menňndez M. Tissue concentrations of MDMA and its metabolite MDA in three fatal cases of overdose. Forensic Sci Int. 2003;135(2):110-114.
- 4. Kalant H. The pharmacology and toxicology of "ecstasy" (MDMA) and related drugs. CMAJ 2001;165: 917-928.
- 5. de la Torre R, Farre M, Roset PN, et al. Human pharmacology of MDMA: pharmacokinetics, metabolism and disposition. Ther Drug Monit 2004; 26: 137-144.
- 6. Henry JA, Jeffreys KJ, Dawling S. Toxicity and deaths from 3,4-methylenedioxymethamphetamine ('Ecstasy'). Lancet 1992;340: 384-387.
- 7. Regenthal R, Kruger M, Rudolph K, Trauer H, Preiss R. Survival after massive 'ecstasy' (MDMA) ingestion. Intensive Care Med 1999; 25: 640–641.
- 8. Mallick A, Bodenham AR. MDMA induced hyperthermia: a survivor with an initial body temperature of 42.9 degrees C. J Accid Emerg Med. 1997;14(5):336-338.
- 9. Dunkley EJ, Isbister GK, Sibbritt D, et al. The Hunter serotonin toxicity criteria:simple and accurate diagnostic decision rules for serotonin toxicity. QJM. 2003;96:635.
- 10. Boyer EW, Shannon M. The serotonin syndrome. N Engl J Med. 2005; 352:1112-1120.
- 11. Sano R, Hasuike T, Nakano M, Kominato Y, Itoh H. A fatal case of myocardial damage due to misuse of the "designer drug" MDMA. Leg Med (Tokyo). 2009;11(6):294-297.
- 12. Milroy CM, Clark JC, Forrest ARW. Pathology of deaths associated with "ecstasy" and "eve". J Clin Pathol 1996;49:149-153.
- 13. Gouzoulis-Mayfrank E, Daumann J (2006) The confounding problem of polydrug use in recreational ecstasy/MDMA users: a brief overview.J Psychopharmacol 20:188-193.
- 14. Kashem MA, Ahmed S, Sarker R, Ahmed EU, Hargreaves GA,McGregor IS (2012) Long-term daily access to alcohol alters dopamine-related synthesis and signaling proteins in the rat striatum. Neurochem Int 61:1280-1288.
- 15. Urban NB, Girgis RR, Talbot PS et al. Sustained recreational use of ecstasy is associated with altered pre and postsynaptic markers of serotonin transmission in neocortical areas: a PET study with [(1)(1)C]DASB and [(1)(1)C]MDL 100907.Neuropsychopharmacology 2012;1465-1473.
- 16. Spronk DB, Dumont GJ, Verkes RJ, De Bruijn ER. The acute effects of MDMA and ethanol administration on electrophysiological correlates of performance monitoring in healthy volunteers. Psychopharmacology (Berl). 2014;231(14):2877-2888.

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