Int J Legal Med (1996) 108:272–275

CASE REPORT

Vittorio Fineschi · Alessandra Masti

Fatal poisoning by MDMA (ecstasy) and MDEA: a case report

Received: 17 July 1995 / Received in revised form: 13 December 1995

Abstract The first observation of lethal recreational use of MDMA (ecstasy) and MDEA in Italy is reported, together with extensive toxicological and histopathological documentation. Findings such as disseminated intravascular coagulation, rarely reported before, are colocated in the framework of the toxic syndrome for a better definition of criteria for forensic diagnosis.

Key words MDMA · MDEA · Fatal intoxication · Drug addiction

Introduction

MDMA (3,4-methylenedioxymethamphetamine, also known as ecstasy, Adam, XTC) was first synthesized in 1914 in the laboratories of the Merck Company [1] but was never used in therapy because of its anorexic side effects. In the 1970s it was proposed as a stimulant in the treatment of depression and alcoholism [2], since the sense of wellbeing and ease of communication that it produced did not seem to have any side effects at therapeutic doses (75–100 mg, orally; G Greer, unpublished results). Renewed interest in this phenylisopropylamine derivative led to a series of studies with volunteers to determine the exact mechanism of action [3]. The only effects documented were marked cardiovascular stimulation with an increase in blood pressure and heart rate, associated in rare cases with nausea and vomiting. Since a single dose of MDMA did not cause any significant immediate physical or psychic damage in normal subjects, it was regarded in psychiatry as a safe, non-addictive drug [3]. Subsequent studies showed many side effects, such as loss of appetite, gnashing of the teeth, nausea, muscle pain and/or cramps, ataxia [4] and a build-up of tolerance [5]. When administered orally, MDMA and MDA are rapidly absorbed, reaching peak plasma levels in about 2 h [6], and are metabolized in the liver and excreted in the urine. When a single dose is taken, the psychotropic effects appear within 30 min and last for a few hours, with manifestations that vary from subject to subject [7]. Although the effects disappear within 4–6 h, mental confusion, depression and anxiety have been reported up to several weeks after a single dose [8]. About the time of these studies, the use of ecstasy became widespread among young people, finally providing clear evidence that the drug is not harmless. Like MDA, MDMA is now listed in Schedule I of the US Drug Enforcement Administration as a highly addictive and therapeutically risky drug [9]. As a result, other molecules of similar structure with similar psychoactive and weakly hallucinogenic properties (but not yet listed as legally controlled drugs) were the subject of drug traffic, among them, MDEA (3,4-methylenedioxyethylamphetamine) which was only occasionally detected by toxicological analysis in cases of drug-related deaths. The increasing recreational use of MDMA and MDEA led to a number of cases of intoxication, but these were still insufficient (partly due to the superficiality of case reports) to draw a clear picture of the forensic effects. Here we report the first case of a MDMA/MDEA-related death in Italy, in which we were able to carry out exhaustive histological and toxicological studies on autopsy specimens.

V. Fineschi (✉) · A. Masti
Department of Forensic Science, University of Siena,
Policlinico Le Scotte, I-53100 Siena, Italy

Case report

On the evening of 25 December 1994, C. C. (aged 20 years), went with friends to a discotheque where he stayed until after midnight and was seen to take many ecstasy tablets. When he returned home at about 2 a.m. he told his mother that he felt feverish. The armpit temperature was 40° C and he went to bed at once. At midday he was found dead with his pillow soaked in blood.

At autopsy, nothing was visible externally but when the body was dissected, subserous petecchiae and extreme pluriparenchymal congestion were observed. Histological examination revealed generalized stasis and subpleural haemorrhaging together with microthrombotic formations partially obstructing the lumina of cardiac vessels and septal capillaries of the lung (Fig. 1). The renal tubules contained eosinophilic material identified as myoglobin by immunohistochemistry (Fig. 2).

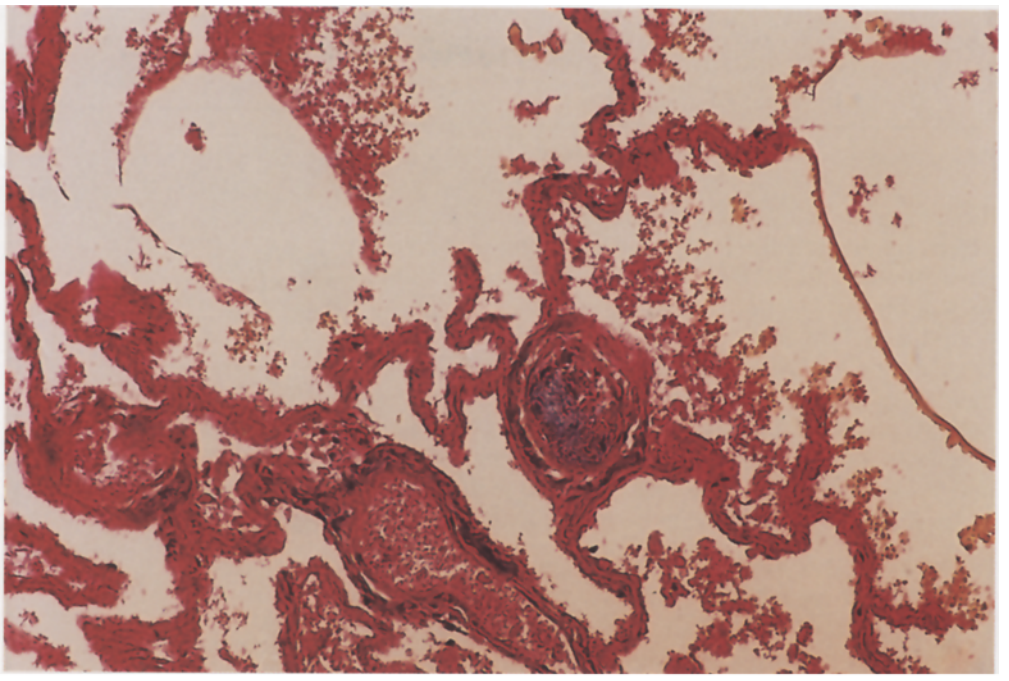

Fig. 1 Lung septum capillaries showing microthrombosis (PTAH, 128 ×)

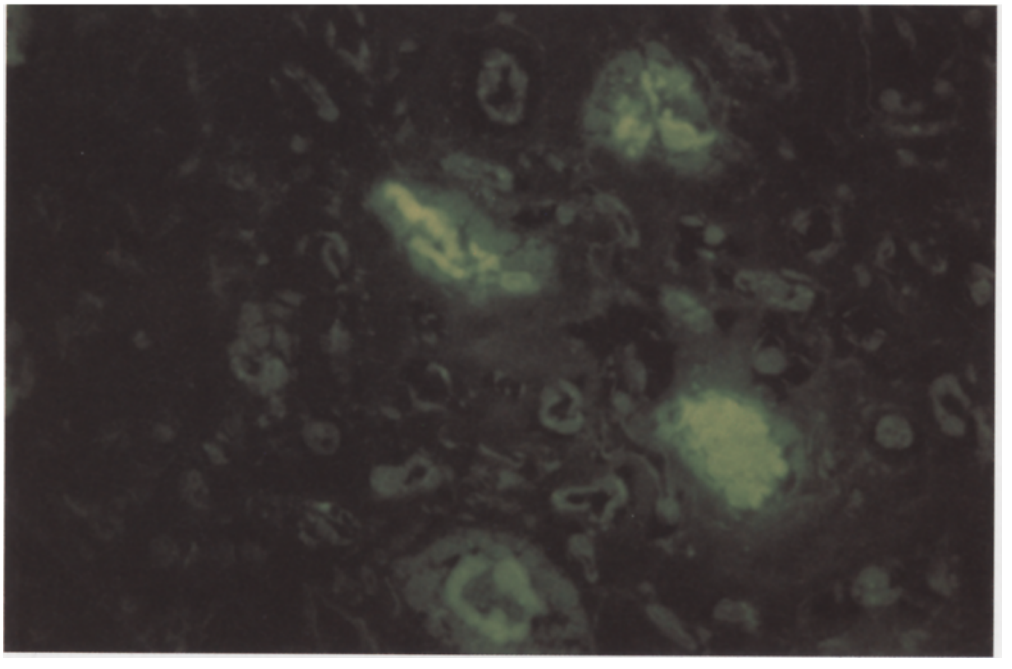

Fig. 2 Myoglobin in renal tubules (immunofluorescence polyclonal antibody against myoglobin, 274 ×)

Amphetamines were detected in the urine of the subject by immunoenzymatic screening. Toxicological analysis by solid-liquid extraction and gas chromatography – mass spectrometry (GC-MS) analysis was therefore carried out to identify and quantify the individual substances present in the biological fluids and organs.

Materials and methods

Homogenates of each organ (1 g) and 1 ml of blood, urine and bile were hydrolysed with 100 µl of enzyme (β-glucuronidase-arylsulphatase) and incubated overnight at room temperature. The samples were supplemented with known quantities of internal standard (phenmetrazine) and extracted by the solid-liquid technique using Bond Elut Certify columns previously activated by elution with 2 ml methanol and 2 ml 0.1 *M* phosphate buffer at pH 6. After adsorption of the sample, the column was washed with 1 ml 1.0 *M* acetic acid and 6 ml methanol. The solid phase was dried and eluted with 4 ml ethyl acetate containing 2% ammonium hydroxide. Dimethylformamide (50 µl) was added to the eluate, which was dried under a nitrogen stream to a volume of 50 µl. For each biological sample, 1 µl of this solution was injected into a GC-MS apparatus to analyse for amphetamines.

The gas chromatograph was a Varian model 3300/3400 with an Alltech OVI fused silica capillary column (length 15 m, i.d. 0.25 mm, film thickness 0.25 µm). The chromatograph was in line with a Finnigan Mat model ITS 40 mass spectrometer with ion trap detector operating in full scan (40–500 amu). Operating conditions were as follows: splitless injection, 1 min initial isotherm, 30 min

final isotherm, injector temperature 280° C, transfer line 290° C, ignition filament after 150 s, column temperature programmed between 100 and 280° C.

Discussion

Toxicological analysis revealed that C. C. died of acute poisoning due to MDMA and MDEA. Table 1 shows the concentrations of MDMA and MDEA in organs and biological fluids.

In the present case death could be ascribed to an overdose of the amphetamines MDMA and MDEA. There have only been a few reports of similar deaths [10–16], and this is the first in Italy. According to Ferrara et al. [17] amphetamine-related deaths show a wide range of causal and associated factors. The cases reported in the literature suggest the following general considerations:

1. Acute intoxication by amphetamines (overdose) is characterized by acute irreversible cardiovascular failure that rapidly leads to death.

2. Chemical and toxicological analysis of postmortem biological material shows variable concentrations of amphetamines, suggesting hypersensitivity in the case of low doses.

3. The conditions under which ecstasy is taken play a role in determining the pathological effects (e.g. malignant hyperthermia) it provokes. For example, increased physical activity, such as dancing, and overheated environments, as in discotheques, may combine with pharmacodynamic effects, such as dehydration due to profuse sweating and suppression of thirst, to upset thermoregulation. The same effect may be due to direct toxicity.

4. Pre-existing pathological conditions, manifest or silent, such as cardiomyopathy, coronary disease, functional arrhythmia and asthma, all characterized by a basal deficit of heart muscle oxygenation, can be aggravated by amphetamines due to an arrhythmogenic cardiotoxic effect [17].

In the present case, the morphological picture is in accordance with a well-described and studied clinical entity, i.e. hyperthermia and disseminated intravascular coagulation (DIC), but the macro- and microscopic findings have not yet been classified or defined in a satisfactory manner. Plurivascular stasis with intravascular coagulation and massive edema of the lungs are succinctly described only in older reports of cases of MDA intoxication [18–22], and only Dowling et al. [10], and recently Forrest et al. [23], give macroscopic descriptions based on a substantial case series. The clotting observed in the present case is well demonstrated and documented in the heart and lungs by evidence of DIC, which presumably arises as a result of hyperpyrexia and rhabdomyolysis [15–24], confirmed in our case by the immunohistochemical finding of myoglobin in the renal tubules.

The clear toxicological results and incisive autopsy and microscopical findings in the present case contribute to the forensic definition of acute poisoning due to MDMA and MDEA with striking elements such as DIC [16]. The increasing use of ecstasy [25] makes a thorough knowledge of its toxic effects important from the forensic and emergency therapy points of view [12, 14, 15, 26].

Table 1 Concentrations of MDMA and MDEA

Organ or biological fluid	MDMA (μg/ml or μg/g)	MDEA (μg/ml or μg/g)
Blood	0.185	1.596
Bile	27.34	21.934
Urine	263.132	183.737
Brain	12.794	8.430
Lung	10.705	8.031
Liver	13.231	10.688
Spleen	9.178	7.059
Kidney	9.818	8.048

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