

Subarachnoid Hemorrhage associated with Ecstasy Abuse in a Young Adult: a Case Report

Marwane Bel Haj MD, Camillia Jeddi MD, Mohamed Kilani MD, Hafedh Thabet MD

Corresponding Author:

Camillia Jeddi MD

E: camillia.jeddi@fmt.utm.tn

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ABSTRACT

3,4-Methylenedioxymethamphetamine (MDMA), is a synthetic amphetamine derivative. Its usage can be complicated by in-tracerebral or subarachnoid hemorrhage. Drug-related intracranial hemorrhage (ICH) is a relatively uncommon occurrence, often associated with an underlying vascular anomaly.

We report the case of a 28-year-old male with a history of Ecstasy abuse prior to the onset of a severe holocranial headache. Cerebral computed tomography angiography revealed a right sided sub-arachnoid hemorrhage and blood within all four ventricles, as well as a right sided pontine hematoma and an arteriovenous malformation.

As the drug epidemic continues to worsen, it is important to take a full drug history in patients presenting with a severe head-ache, and to not overlook ICH as a potential complication of recreational drug abuse.

Keywords: MDMA, ecstasy, arteriovenous malformation, intracerebral hemorrhage, case report

Key Messages :

- MDMA abuse complicated with an intracerebral accident is a well-recognized entity, but intracerebral hemorrhage remains relatively uncommon.
- We report the first case of ecstasy abuse complicated with intracerebral hemorrhage, to our knowledge, occurring in a young adult in Tunisia.
- Patients presenting with severe headache and a history of drug abuse might be at risk of developing intracerebral hemorrhage.

Introduction

3,4-Methylenedioxymethamphetamine (MDMA), is a synthetic amphetamine derivative.(1) It was first developed in 1912 and was popularized in the 1980s as a recreational street drug due to its strong empathogen as well as its stimulant and minor psychedelic properties.(1) It is usually taken orally in its tablet form ("Ecstasy") or crystal form ("Molly" or "Mandy").

MDMA abuse is associated with multiple potentially life threatening complications.(1) Intracranial hemorrhage (ICH), including intracerebral and subarachnoid hemorrhage, is a well-known yet relatively uncommon complication. Subsequent brain imaging often reveals an underlying vascular anomaly. (2–7)

After a literature review using MeSH and keywords (MDMA, arteriovenous malformation, intracerebral hemorrhage) in PubMed. We report the first case of ecstasy abuse complicated with intracerebral hemorrhage, to our knowledge, occurring in a young adult in Tunisia.

CASE PRESENTATION

28-year-old male with a past history of infrequent MDMA abuse spanning years presented to the emergency department for an acute onset of a severe headache. At first medical contact he was afebrile and his vital signs were normal. On further history and physical exam, four and half hours prior to his presentation, he had ingested a half of tablet of "Ecstasy". Following this ingestion, he presented with a headache, vomiting, dizziness and dysarthria. There had been no history of hypertension or headache and the patient reported no recent head trauma or loss of consciousness. The patient denied any history of other substance abuse. During his stay at the ED his symptoms progressed and he became sleepy but conscious and orientated. Verbal and motor response, as well as eye opening, were all normal. Pupils were symmetrical and not dilated. Neurologic examination found a nuchal rigidity but Kernig and Brudzinski's signs were both negative. There was no focal deficit and no signs of head trauma. Laboratory tests showed a white blood cell count of 16800 cells per microliter (normal range (NR) : 4.5 to $11.0 \times 10^9/L$), hyperlactatemia of 4.5 mmol/L (NR: 0.5 - 2.2) and hyperglycemia at glucose 11 mmol/L (NR: 4 - 7 mmol/L). The other tests including hemostasis and electrolytes were within NR. Urine sample analysis revealed the presence of MDMA. Tests for other psychoactive substances such as cocaine, heroin and benzodiazepine as well as blood alcohol were all negative. A computed tomography (CT)- head scan was obtained and showed a right-sided sulcal sub-arachnoid hemorrhage and blood within all four ventricles, as well as a right-sided pontine hematoma (figure 1A and B). Within the latter, contrast-enhanced CT showed an arteriovenous malformation (figure 2). The patient was admitted to a neurosurgery unit. The AVM was classified as 4 according to the Spetzler Martin scoring system, thus a conservative treatment was adopted and endovascular embolization of the AVM was scheduled but refused by the patient. He remained stable with resolution of his headaches and no neurological deterioration. He was discharged

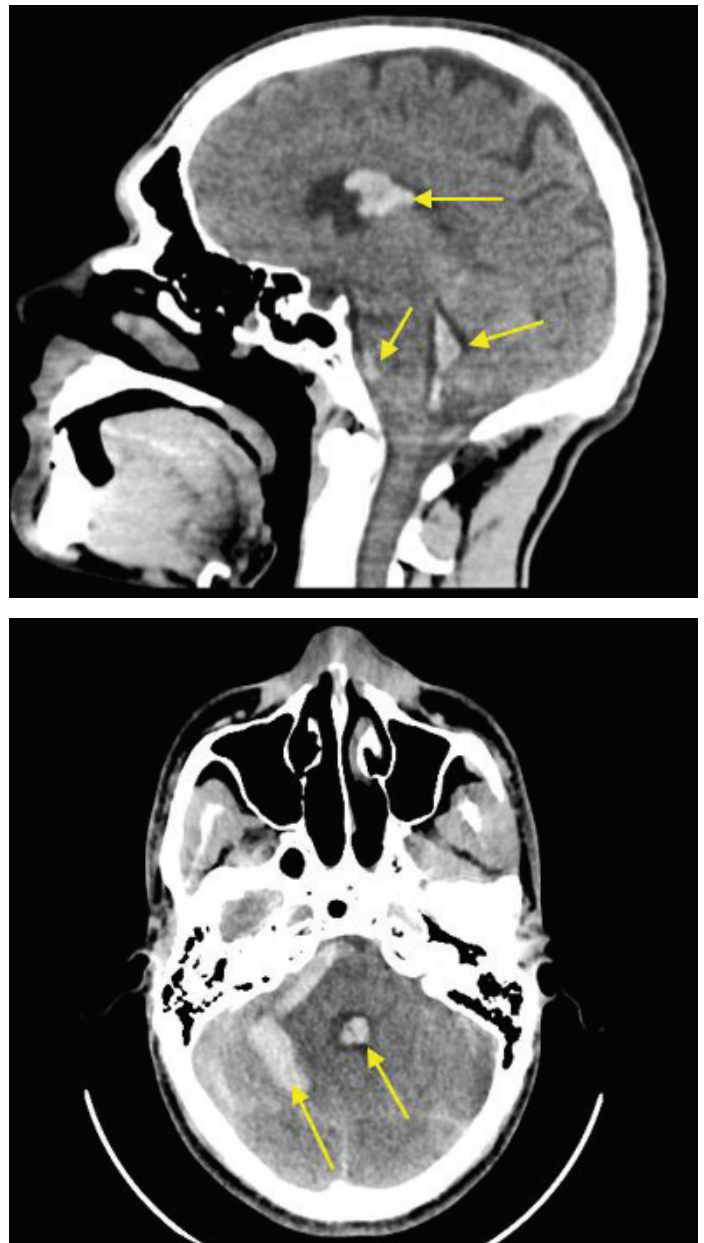


Figure 1: A and B: Noncontrast head CT shows a right-sided cerebellar subarachnoid hemorrhage, blood within all four ventricles and a right-sided parenchymal pontine hematoma.

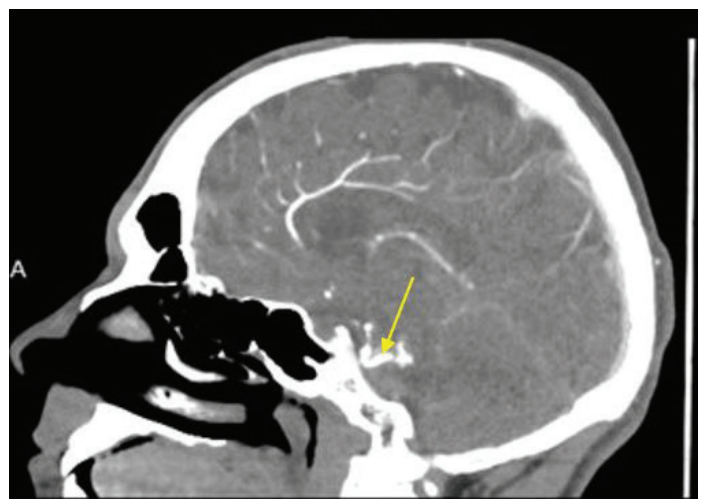


Figure 2: Contrast enhanced CT shows, within the above-mentioned hematoma, an arterial loop communicating with the ipsilateral superior cerebellar artery with probable dilated draining veins communicating with both the transverse and the right inferior petrosal sinuses.

home on day 7 of admission with a spontaneous regression of the hematoma, thus a ventricular shunt was not performed, on follow up, the patient remained asymptomatic and no complications were reported.

DISCUSSION

MDMA is a synthetic amphetamine derivative.(1) It is taken orally to induce pleasurable feelings such as loss of inhibition, euphoria and empathy and is commonly associated with raves, concerts and dance parties .(1) It has a myriad of adverse effects, such as tachycardia, arterial hypertension, nausea, bruxism, headache, blurred vision, insomnia, anxiety and agitation , as well as more serious complications such as rhabdomyolysis, hyperpyrexia, cardiac arrhythmia, hepatic necrosis and disseminated intravascular coagulation.(1) Among its complications, ICH is a well-recognized entity, (2–7) but remains relatively uncommon. To the best of the authors’ knowledge, this represents the first reported case of ICH following ecstasy abuse in Tunisia. Previously reported cases of drug induced ICH have most often revealed an underlying vascular anomaly, mainly cerebral arteriovenous malformations and aneurysms. (2,3,5). However, it is possible that the latter may form either acutely in response to the drug itself, or progressively from repeated abuse(2,5). Furthermore, some case reports of ICH following MDMA abuse have shown no unusual findings in the angiogram,(6) suggesting that a preexisting vascular anomaly is neither necessary nor sufficient to induce it. A summary of cases reported in literature are is provided in table 1. To this date, MDMA’s exact role in precipitating an intracranial hemorrhage is still unclear. Two main mechanisms of action have been postulated in literature: Cerebral vasculitis and transient elevated blood pressure. (2,5)

The proposition of cerebral vasculitis as a possible mechanism stems from MDMA’s resemblance to amphetamine,(5) supported by substantial evidence linking the latter to at least some level of cerebral angiitis. Citron et al.(8) reported 14 cases of necrotizing angiitis in drug abusers, twelve of which had previously used methamphetamine intravenously, and one of which admitted to using it exclusively. Moreover, cerebral angiitis has been experimentally produced in rhesus monkeys following a two week intravenous administration of amphetamine, with the angiographic findings showing an arterial “beading” immediately after its administration.(9)

In the case of MDMA itself, some case reports of MDMA induced ICH reported arterial “beading”.(7) However, to the finest of the authors’ knowledge, there is no direct evidence linking it with cerebral vasculitis.

Transient surge in blood pressure has also been proposed as a causal mechanism.(2) Hypertension is a well-documented adverse effect of MDMA and is related to its sympathomimetic effect.(1) It has been the traditional explanation for drug-induced ICH in the context of a preexisting cerebrovascular anomaly, especially AVMs.(5) This is clearly likely to be the case in our patient.

Another potential mechanism has been suggested through an experimental study on mice,(10) which showed that exposure to methamphetamine elicited an initial five-minute increase of cerebral blood flow, followed by a prolonged decrease over 30 minutes. This study also showed a sustained vasoconstriction of the pial arterioles following the exposure. However, more studies are needed in order to elucidate how much of a role this mechanism plays.

We recognize some limitations in our report. The CT angiography has a lower sensitivity in the detection rate of cerebrovascular anomalies than the gold standard, catheter angiography. With the latter not being performed, it is possible that some vascular anomalies, such as small aneurysms, and especially vasculitis, have evaded detection.

Concerning management, according to Expert Consensus on the Management of Brain Arteriovenous Malformations in 2019, brain arteriovenous malformations (bAVMs) can be treated by one or a combination of the following treatment modalities, namely embolization, radiosurgery, or microsurgical resection. The committee made recommendations based on age, eloquence of adjacent cortex, feeders’ example superficial versus deep. These items were gathered to create the Spetzler Martin scoring system, which is an easy and successful scoring tool. In fact, Grade 4 and 5 arteriovenous malformations (AVMs), conservative management may be the best option, which is the case in our patient. (11)

TABLE 1: Summary of case reports

	Reference Title	Author(s)	Date	Age/Sex (years)	Drug abused	Presentation	Imaging findings	Surgery	Outcome
1.	Subarachnoid haemorrhage associated with MDMA abuse.(2)	Gledhill et al.	Sep. 1993	25/F	Ecstasy	H, V, Meningism	SAH, L. PCOM aneurysm	Craniotomy +Clipping	Complete recovery
2.	Subarachnoid haemorrhage with "Ecstasy" abuse in a	Auer et al.	Oct. 2001	18/M	Ecstasy	H, Seizure, Meningism	SAH, R. MCA aneurysm	Craniotomy +Clipping	Complete recovery
3.	'Ecstasy' and intracerebral haemorrhage.(4)	Harries, De Silva	Oct. 1992	30/F	Ecstasy+ Amphetamine	H, Dysphasia, R Hemiparesis	ICH	Nil	Complete recovery
				22/F	Amphetamine	H, Urinary incontinence, Agitation, Seizure, Dysphasia, R.	ICH	Nil	Complete recovery
				20/M	Ecstasy	Seizure, Coma, Pupils fixed +dilated	ICH, AVM	Emergency Craniotomy	Died
				16/M	Ecstasy	R. Hemiparesis, Dysphagia	ICH.	Nil	Complete recovery
4.	Intracerebral haemorrhage and drug abuse in young adults.(5)	McEvoy et al.	Oct. 2000	30/M	Crack	H, Confusion	SAH, ACOM aneurysm	Craniotomy +Clipping	Complete recovery
				22/F	Amphetamine	H, V, Neck stiffness	SAH	Nil	Complete recovery
				39/M	Cocaine	H, P, Neck stiffness	SAH, R. Ant. Chor. Art. aneurysm	Craniotomy +Clipping	L. Hemiplegia
				19/M	Ecstasy +Amphetamine	H, V, Neck stiffness	SAH +ICH, L. Occipital AVM	Embolization	Complete recovery
				29/M	Cocaine	H, P, V	ICH, R. Parietal AVM	Craniotomy +Removal	Complete recovery
				28/M	Ecstasy +Amphetamine	H, P, V, Neck stiffness	SAH, ACOM aneurysm	Craniotomy +Clipping	Complete recovery
5.	3 cases of primary intracranial hemorrhage associated with "Molly", a purified form of 3,4-methylenedioxymethamphetamine (MDMA).(6)	Kahn et al.	Dec. 2012	23/M	Molly +Cannabis	H, P, V, Seizure	SAH	Nil	Complete recovery
				25/M	Molly	Seizure, L. Hemiparesis	ICH	Emergency Craniotomy	Complete recovery
				23/M	Molly	H, P, V	SAH	Nil	Complete recovery
6.	'Ecstasy'-induced subarachnoid haemorrhage: an under-reported neurological complication?(7)	Lee et al.	Nov. 2003	29/F	Ecstasy	H, P, V, Neck stiffness	"Beading" within the posterior circulation	Nil	Complete recovery
				24/M	Ecstasy +Cannabis	H, Seizure, Confusion	SAH, Focal "beading"	Nil	Complete recovery

Abbreviations: H, headache; V, vomiting; P, photophobia; R., right; L., left; SAH, subarachnoid hemorrhage; ICH, intracerebral hemorrhage; MCA, middle cerebral artery; ACOM, anterior communicating artery; PCOM, posterior communicating artery; Ant. Chor. Art., anterior choroidal artery; ICA, internal carotid artery; AVM, arteriovenous malformation; Rehab., rehabilitation.

Conclusion

We describe a case of ICH complicating MDMA abuse in a young adult. Cerebral accidents are a well-recognized entity in these patients, but ICH remains relatively uncommon. Patients with MDMA abuse are at risk for intracerebral accidents including intracerebral hemorrhage. A full medical history including illicit drug abuse must be taken in patients presenting with the onset of a severe headache.

Conflict of interests

The authors declare no conflicts of interest.

References

1. Kalant H. The pharmacology and toxicology of “ecstasy” (MDMA) and related drugs. *CMAJ Can Med Assoc J*. 2001;165:917–928. PMID: 11599334. url: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC81503/>
2. Gledhill JA, Moore DF, Bell D, Henry JA. Subarachnoid haemorrhage associated with MDMA abuse. *J Neurol Neurosurg Psychiatry*. 1993;56:1036–1037. doi: 10.1136/jnnp.56.9.1036. PMID: 8105032. url: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC489748/>
3. Auer J, Berent R, Weber T, Lassnig E, Eber B. Subarachnoid haemorrhage with “Ecstasy” abuse in a young adult. *Neurol Sci Off J Ital Neurol Soc Ital Soc Clin Neurophysiol*. 2002;23:199–201. doi: 10.1007/s100720200062. PMID: 12536290. url: <https://pubmed.ncbi.nlm.nih.gov/12536290/>
4. Harries DP, De Silva R. ‘Ecstasy’ and Intracerebral Haemorrhage. *Scott Med J*. 1992;37:150–152. doi: 10.1177/003693309203700508. PMID: 1492208. url: <https://pubmed.ncbi.nlm.nih.gov/1492208/>
5. McEvoy AW, Kitchen ND, Thomas DG. Intracerebral haemorrhage and drug abuse in young adults. *Br J Neurosurg*. 2000;14:449–454. doi: 10.1080/02688690050175247. PMID: 11198766. url: <https://pubmed.ncbi.nlm.nih.gov/11198766/>
6. Kahn DE, Ferraro N, Benveniste RJ. 3 cases of primary intracranial hemorrhage associated with “Molly”, a purified form of 3,4-methylenedioxymethamphetamine (MDMA). *J Neurol Sci*. 2012;323:257–260. doi: 10.1016/j.jns.2012.08.031. PMID: 22998806. url: <https://pubmed.ncbi.nlm.nih.gov/22998806/>
7. Lee GYF, Gong GWK, Vrodos N, Brophy BP. ‘Ecstasy’-induced subarachnoid haemorrhage: an under-reported neurological complication? *J Clin Neurosci Off J Neurosurg Soc Australas*. 2003;10:705–707. doi: 10.1016/s0967-5868(03)00151-6. PMID: 14592627. url: <https://pubmed.ncbi.nlm.nih.gov/14592627/>
8. Citron BP, Halpern M, McCarron M, Lundberg GD, McCormick R, Pincus IJ, Tatter D, Haverback BJ. Necrotizing angiitis associated with drug abuse. *N Engl J Med*. 1970;283:1003–1011. doi: 10.1056/NEJM197011052831901. PMID: 4394271. url: <https://pubmed.ncbi.nlm.nih.gov/4394271/>
9. Rumbaugh CL, Bergeron RT, Scanlan RL, Teal JS, Segall HD, Fang HC, McCormick R. Cerebral vascular changes secondary to amphetamine abuse in the experimental animal. *Radiology*. 1971;101:345–351. doi: 10.1148/101.2.345. PMID: 5000427. url: <https://pubmed.ncbi.nlm.nih.gov/5000427/>
10. Polesskaya O, Silva J, Sanfilippo C, Desrosiers T, Sun A, Shen J, Feng C, Polesskiy A, Deane R, Zlokovic B, et al. Methamphetamine causes sustained depression in cerebral blood flow. *Brain Res*. 2011;1373:91–100. doi: 10.1016/j.brainres.2010.12.017. PMID: 21156163. url: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3026925/>
11. Samaniego EA, Dabus G, Meyers PM, Kan PT, Frösen J, Lanzino G, Welch BG, Volovici V, Gonzalez F, Fifi J, et al. Most Promising Approaches to Improve Brain AVM Management: ARISE I Consensus Recommendations. *Stroke*. 2024;55:1449–1463. doi: 10.1161/STROKEAHA.124.046725. PMID: 38648282. url: <https://pubmed.ncbi.nlm.nih.gov/38648282/>