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'Ecstasy'-induced subarachnoid haemorrhage: an under-reported neurological complication?

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Summary In the face of escalating recreational use of 'Ecstasy' (3,4-methylenedioxymethamphetamine, MDMA), physicians need to be aware of its possible adverse effects. We report two young patients who suffered subarachnoid haemorrhage following ingestion of 'Ecstasy' tablets. Angiographic studies demonstrated features consistent with vasculitis in both cases. Recognition of this association is important and highlights the significance of eliciting a careful drug history, particularly in cases of 'angiogram negative' subarachnoid haemorrhage.

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INTRODUCTION

It is increasingly well recognised that recreational use of Ecstasy (MDMA) can lead to life threatening consequences. While neurological complications are uncommon, this may represent an under-reported phenomenon. We present two young patients in whom Ecstasy use was associated with non-aneurysmal subarachnoid haemorrhage.

CASE 1

A 29-year-old woman experienced a sudden onset of severe occipital headache which was associated with nausea and vomiting 5 days prior to presentation to the Royal Adelaide Hospital. The patient complained of severe photophobia. On clinical examination, the patient was alert and orientated. There was marked nuchal rigidity. Neurological examination did not reveal any focal deficit. CT head scan was normal. Subsequent lumbar puncture revealed blood stained CSF with photospectrometric evidence of xanthochromia. The patient underwent conventional four vessel-cerebral angiography which demonstrated evidence of 'beading' of vessels within the posterior circulation. The angiographic appearances were most marked on the (L) superior cerebellar artery (Fig. 1). Further investigation with MRI/MRA revealed no significant abnormality. Serum testing revealed an erythrocyte sedimentation rate (ESR) of 11 and C-reactive protein (CRP) of 4. Antinuclear antigen (ANA) was negative.

Following the patient's admission, her friends subsequently volunteered information of illicit drug use by the patient. On repeated questioning, the patient admitted that she had used 'Ecstasy' on the day of ictus. She denied having previously used 'Ecstasy' or any other recreational drugs.

The patient was observed without neurological deterioration. She was discharged at Day 13 of her admission. The delay was due to persistent headaches. Follow-up cerebral angiography 2 months later showed that the abnormalities had completely resolved.

CASE 2

A 24-year-old man smoked marijuana and subsequently consumed one and a half 'Ecstasy' tablets while at a party. Several hours later, he experienced a sudden severe retro-orbital headache and felt unwell. Soon after arriving home, he suffered a witnessed episode of generalised tonic-clonic seizure lasting approximately 1 min. This was followed by a brief period of post-ictal confusion. On arrival at the emergency department, he was alert and orientated. Neurological examination was otherwise unremarkable. He had a further generalised seizure in the emergency department which was aborted by intravenous midazolam.

The patient underwent a CT head scan. This revealed the presence of subarachnoid haemorrhage which was mainly localised to several parasagittal sulci towards the vertex (Fig. 2). Cerebral angiography demonstrated evidence of focal 'beading' of peripheral branches to the (R) anterior cerebral cortex consistent with angiographic arteritis. MRI/MRA head scan confirmed the presence of subarachnoid haemorrhage but no other abnormalities.

The patient remained well subsequently with resolution of his headaches and no further seizures. He was discharged at Day 4 following his admission.

DISCUSSION

MDMA, also known as 'Ecstasy', is a three ring-substituted, methoxylated analogue of methamphetamine. It was first synthesized in Germany in 1914 and used initially as an appetite suppressant.[1,2] During the late 1970s and 1980s, it found a secondary use in the United States as an adjunct to psychotherapy.[1,2] The current widespread recreational use of MDMA by teenagers can primarily be traced back to the British dance hall phenomenon called 'raves'.[3] The use of MDMA was reported by 8% of 15- and 16-year-old British students surveyed in 1994.[4] A more recent survey at three dance events in Edinburgh, Scotland demonstrated that over 80% of participants had previously used Ecstasy and amphetamines. Furthermore, 35% stated that they used Ecstasy on a weekly basis.[5] Its use has since spread across to other continents.[3,6] A random survey of illicit drug use by American undergraduate students revealed that 24% of those surveyed reported use of MDMA, exceeding use of lysergic acid diethylamide (LSD) and cocaine.[3] Furthermore, MDMA has also become a popular choice for University students and attendees at rave parties in major coastal American cities.[3] Studies from Australia [7] and Germany [6] have similarly demonstrated a high rate of MDMA usage. A 1999 survey of drug use in Norwegian adolescents further showed that MDMA was used by adolescents who also used other legal and illegal substances in a polydrug-use pattern.[8]

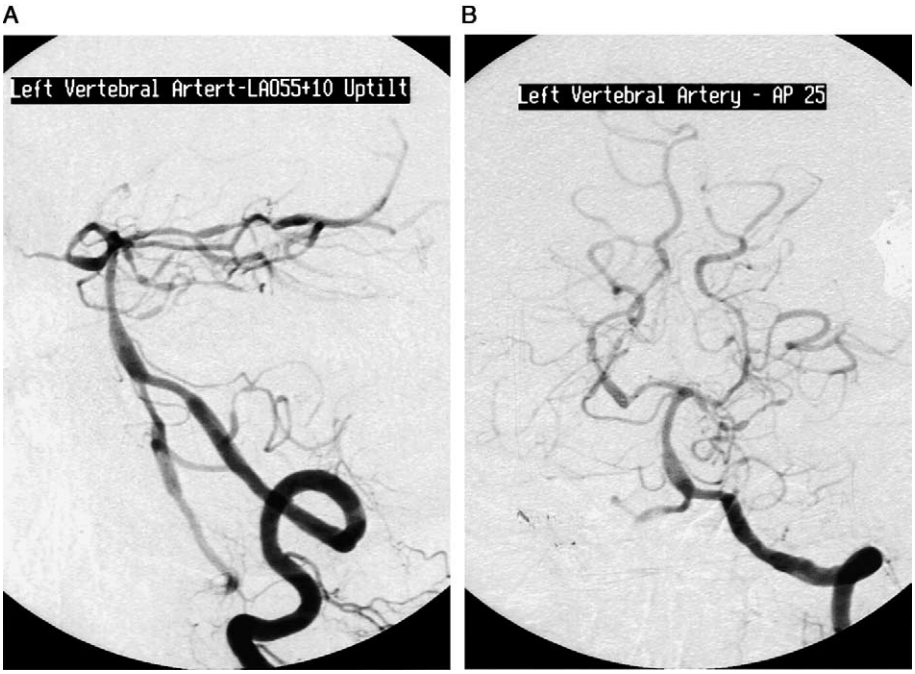

Fig. 1 (A,B) Conventional cerebral angiogram demonstrating focal narrowings ('beading') in multiple vessels within the posterior circulation.

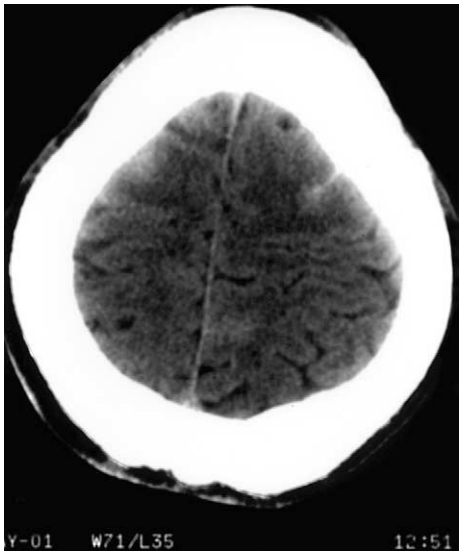

Fig. 2 Non-contrast enhanced CT head scan demonstrating subtle subarachnoid haemorrhage within several parasagittal sulci on the left.

MDMA induces a feeling of euphoria and ecstasy.[1] This is said to contribute to the pleasure of dancing at raves and discos.[9] The drug can also lead to transcendental experiences and other 'desired' perceptual changes.[1] Its use, however, has been associated with a number of adverse effects. These may include anorexia, trismus, bruxism, nausea, muscle aches, stiffness, gait ataxia, sweating, restlessness, brooding, insomnia and fatigue.[3,10,11] More serious adverse effects include hyperthermia, convulsions, cardiac tachyarrthymias, aortic dissection, rhabdomyolysis, disseminated intravascular coagulation, renal failure, hyponatraemia, hepatotoxicity and aplastic anaemia. Reported neurological complications include cerebral infarction, cerebral haemorrhage, cerebral venous sinus thrombosis and seizures.[1,9,12–16]

MDMA is believed to principally affect the serotonergic system. It selectively destroys serotonin nerve terminals in rats and primates.[17,18] Serotonin plays a major role in thermoregulation and interference with this mechanism is believed to be the cause of the hyperthermia which arises as a complication of MDMA misuse. It also acts on the noradrenergic pathway which probably contributes to hyperthermia.[9] Hyperthermia was postulated to account for many of the changes seen in deaths associated with the misuse of amphetamine derivatives. Postmortem examination typically reveals pathological changes in the liver, brain and heart which are similar to those found in heat stroke.[9] Milroy et al.[9] concluded that that the deaths associated with MDMA use in their study resulted from hyperthermia, disseminated intravascular coagulopathy and shock.

Cocaine and amphetamine misuse are both well recognized causes of intracerebral and subarachnoid haemorrhage.[1,19–23] Administration of either drug can lead to a hypertensive crisis. This may trigger a haemorrhage from a pre-existing vascular abnormality.[1] Cocaine can further induce vasospasm by a direct smooth muscle effect as well as augmenting the physiological effects of catecholamines.[1] This leads to cerebral ischaemia which may be further aggravated by increased thromboxane production and enhanced platelet aggregation.[1,24] In contrast, cerebral angiitis has been reported to occur more frequently with amphetamine misuse.[1,25] In these cases, angiography has demonstrated pronounced irregularity and 'beading' in the middle and anterior cerebral arterial branches.

In contrast, the effect of MDMA on cerebral vasculature is not known. To date, there has only been one publication alluding to the possible association of subarachnoid haemorrhage with MDMA abuse. Gledhill et al.[26] described a 25-year-old patient who presented with a ruptured posterior communicating artery aneurysm 6 h following Ecstasy ingestion. The authors suggest that an 'acute sympathetically mediated surge in blood pressure' may have triggered aneurysmal rupture. They further hypothesized that repeated use causes recurrent surges in systemic blood pressure which may also lead to a progressive weakening of the vessel wall, thus predisposing to aneurysmal formation.[22,26] On the other hand, McEvoy et al.[22] reason that MDMA 'probably causes a degree of vasculitis' on the basis of its chemical derivation from amphetamines. The current report provides circumstantial

evidence that MDMA can lead to subarachnoid haemorrhage in the absence of a vascular malformation. In both cases, there were angiographic features typical of vasculitis.

The current report highlights several points. Firstly, an accurate and truthful history of drug intake is required from any young patient who presents with spontaneous subarachnoid haemorrhage, particularly in 'angiogram negative' cases. Secondly, it is difficult to 'prove' that an adverse neurological event is related to a drug particularly when there are no previous reports of such an association.[22] Causation can only be established as clinicians and researchers begin to recognise such a possibility. Thirdly, the precise incidence of MDMA-induced non-aneurysmal subarachnoid haemorrhage is unknown. To the best of our knowledge, there are no previous case reports of such a neurological complication. Whether this represents a rare phenomenon or significant under-reporting from lack of awareness remains to be determined.

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Management of massive calcified transdural thoracic disk herniation

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Summary Thoracic disc herniation is a not uncommon pathology faced by the spinal surgeon. The management of massive intradural thoracic disc herniation with ventral cord compression is problematic both in terms of obtaining adequate decompression and ensuring no subsequent leakage of cerebrospinal fluid. A 54-year-old woman presented with a 10 year history of back pain and left leg pain. Over the past 6 months she experienced a progressive spastic paraparesis in both legs with recent urinary incontinence. A left anterolateral thoracotomy for excision of T8/9 thoracic disc protrusion was affected. A transdural decompression was performed with resection of the calcified dura and performance of a Gore-Tex duraplasty and pleuroplasty. A free muscle graft was placed in the intervening space and the chest drains were placed on non-suction. A spinal drain was maintained for 5 days. She made an excellent neurological recovery. Avoidance of cerebrospinal leakage is paramount when performing transthoracic approaches as negative intrapleural pressure can lead to persistence of leakage. This report documents a safe and reliable way to deal with massive intradural thoracic disc rupture with avoidance of subsequent spinal fluid leak.

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INTRODUCTION

Thoracic disc herniation (TDH) is a common MR imaging finding, but clinically significant TDH is rare, occurring with an