CASE REPORT

Late diagnosis of MDMA-related severe hyponatremia

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Abstract

Introduction: 3, 4-methylenedioxymethamphetamine (MDMA) is a popular psychoactive amphetamine derivative with the potential to induce life-threatening hyponatremia. The absence of exposure history and typical toxidromes however make the prompt diagnosis of MDMA-induced hyponatremic coma difficult and easily overlooked.

Case Report: A 24-year-old female presented to the emergency department with an altered mental status. Physical examinations, laboratory workup and brain imaging study were remarkable for severe hyponatremia (serum sodium 116 mmol/L) and diffuse brain edema only. Her family denied that she had used any illicit drugs. The diagnosis of MDMA-related hyponatremic coma was not made until six days later when toxicologic screen confirmed the presence of high concentration of MDMA (7,767 ng/ml) in the patient's urine.

Conclusion: Our case demonstrates the difficulty in the correct diagnosis of MDMA-induced hyponatremic coma in the absence of MDMA exposure history and typical sympathomimetic effects. A high index of suspicion and prompt toxicological screen are thus important in the diagnosis of MDMA-related severe hypontremia.

Keywords

Coma, Ecstasy, Hyponatremia, MDMA

1 Introduction

3, 4-methylenedioxymethamphetamine (MDMA, ecstasy) is a psychoactive amphetamine derivative that is popular among young adults and commonly consumed in night clubs. MDMA is regarded by recreational drug users as harmless with minimal side effects and without habit-forming hazards. However, numerous reports have testified to the direct physical and mental adverse effects, and even mortality associated with MDMA ingestion [1]. MDMA has a chemical structure similar to endogenous catecholamines (i.e. epinephrine and norepinephrine); thus it can stimulate the central nervous system via the release of endogenous catecholamines, resulting in tachycardia, hypertension and dilated pupils [1]. MDMA is known to induce life-threatening hyponatremia [1-3]. Although the diagnosis of MDMA-related hyponatremia is

generally not difficult in the presence of relevant exposure history and/or typical sympathomimetic manifestations, timely diagnosis can be challenging in patients devoid of the above-noted clinical information.

2 Case report

A 24-year-old previously healthy female presented to the emergency department (ED) due to altered mental status. On the night before arrival at the ED, she partied with friends at a karaoke bar. She was found to suffer nausea and vomiting, followed by loss of consciousness in the early morning. She was first dispatched to a local hospital where hyponatremia, coma (Glasgow Coma Scale E2V2M4), and slight mydriasis with bilateral pupil size of 5mm were noted. Initial vital signs were as follows: temperature 36.1℃ and blood pressure of 138/90 mmHg. She was then transferred to our service for further management.

Upon arrival, her vital signs were as follows: blood pressure 93/75mmHg, pulse rate 93/min, respiratory rate 18/min, and body temperature 35.8℃. Glasgow Coma Scale was E1V1M4 and bilateral pupil size was 2 mm with preserved light reflex. Other physical examinations were unremarkable. Pertinent laboratory data were as follows: serum sodium 116 mmol/L (reference range 135-147 mmol/L), potassium 4.3 mmol/L (3.5-4.5 mmol/L), creatinine 0.7 mg/dL (0.5-1.5 mg/dL), free calcium 0.94 mmol/L (1.13-1.31 mmo/L), uric acid 1.2 mg/dL (1.8-6.2 mg/dL), serum osmolality 231 mosm/kg (280-292 mosm/kg), urine osmolality 344 mosm/kg, urine chloride 114 mmol/L and urine sodium 76 mmol/L. Arterial blood gas analysis revealed pH 7.365, pCO_2 30.2mmHg, pO_2 109.2 mmHg, and HCO_3 16.9 mmo/L under 3L/min oxygen supplement. Adrenal and thyroid function tests were both within normal limits.

Despite the lack of documented head trauma or seizures, computed tomography of brain was performed to rule out possible intracranial lesions leading to the patient's comatose status (e.g. subarachnoid or intracerebral hemorrhage), which revealed the presence of diffuse brain swelling (see Figure 1). She was then admitted to the intensive care unit where intravenous 3% saline was administered for the treatment of severe euvolemic hyponatremia. Urine sodium concentration and urine osmolality after saline therapy were 160 mmol/L and 379 mosm/kg, respectively.

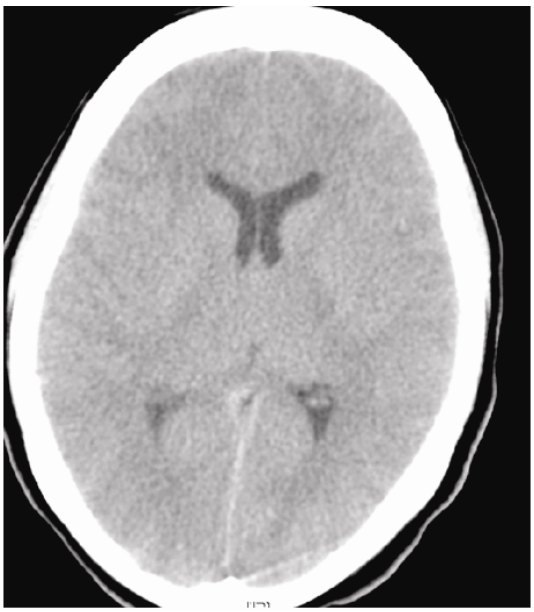

Figure 1. Brain computed tomography in a 24-year-old female with MDMA-induced hyponatremic coma revealed diffuse swelling of brain parenchyma.

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Although her serum sodium level was once as low as 110 mmol/L, it gradually increased to 133 mmol/L by the end of day 2. The patient was fully awake on day 3 with serum sodium levels ranging between 133 and 137 mmol/L. Drug/toxicant related syndrome of inappropriate antidiuretic hormone secretion (SIADH) was suspected; however the patient denied taking any recreational drugs or toxicants.

Urine toxicologic screen performed upon arrival at the ED by employing gas chromatography/mass spectrometry analysis was positive for MDMA (7,767 ng/ml) and its metabolite MDA (375 ng/ml) on day 6. It was with much reluctance that the patient finally admitted to having ingested one tablet of MDMA at the party where she also drank 1,200ml of bottled water prior to loss of consciousness. The patient was discharged uneventfully.

3 Discussion

Hyponatremia, defined as a serum sodium concentration less than 135 mmol/L, is multi-factorial, thus rendering differential diagnosis difficult. Hyponatremia may be a result of depletion in effective circulating volume such as true volume depletion, heart failure and cirrhosis. Moreover, hormonal diseases such as adrenal insufficiency and hypothyroidism can be associated with low serum sodium. Athletes participating in competitive sports are also at high risk for hyponatremia, as a result of excess free water drinking and sweating [4]. SIADH is a disorder of impaired water excretion caused by an inability to suppress the secretion of antidiuretic hormone (ADH), and may be a result of CNS disturbances, malignancies, drugs, HIV infection or surgery [5]. All of the above-mentioned potential causes of hyponatremia deserve attention in the differential diagnosis.

In our patient, history-taking and detailed physical examinations revealed neither history of fluid loss (e.g. vomiting, diarrhea, diuretic therapy and strenuous exercise) nor signs of fluid overload that indicates the diagnosis of heart failure, cirrhosis and renal failure. Moreover, a measured serum osmolality of 231 mosm/kg ruled out the possibility of non-hypotonic hyponatremia [6], such as hyperglycemia, azotemia and alcohol poisoning related hyponatremia. The presence of high urine osmolality (344 mosm/kg) further excluded the diagnosis of primary polydipsia and low solute intake that were commonly associated with a urine osmolality of less than 100 mosm/kg [7]. The finding of high urine sodium (75 mmol/L) also suggested that effective volume depletion (e.g. hypovolemia, heart failure, and cirrhosis) was unlikely to be present in the patient [8]. Drug-induced SIADH was finally diagnosed by taking into account the patient's overall clinical features and excluding all of the above-mentioned alternative diagnoses [5, 6, 8, 9].

Many drugs can induce hyponatremia via various mechanisms, such as the alteration of sodium and water homeostasis, increased production of ADH, potentiation of the effect of ADH and reset osmostat [3]. Among drug-induced hyponatremia, SIADH is not uncommonly seen and has been linked to numerous drugs such as antidepressants, antipsychotic, antiepileptics, anticancer agents, and narcotics [3, 5]. Notably, MDMA has also been associated with the development of SIADH [1, 2, 5, 10].

MDMA, a psychoactive amphetamine with structural similarity to serotonin, possesses more potent serotonergic properties and generates positive feelings and mood elevation to recreational users [11]. Side effects of MDMA include dry mouth, increased thirst, restlessness, palpitation, dizziness, drowsiness, confusion and anxiety.[10] MDMA-induced hyperthermia in the acutely poisoned patients was also well-documented [12, 13] along with rhabdomyolysis [14], hepatic failure [15], disseminated intravascular coagulation (DIC) [14], and death [2]. Users of MDMA learn to increase their oral water intake as a preventive measure for hyperthermia, resulting in potentially severe cases of MDMA-associated hyponatremia [1].

Symptoms related to hyponatremia generally occur within hours after MDMA ingestion. Patients might present with altered mental status and cerebral edema [1, 14]. Symptomatic hyponatremia with a serum sodium level less than 130 mmol/L is one of the serious complications associated with MDMA [5]. MDMA-induced dipsogenic effect [16], ready

availability of drinks and excessive intake of free water all directly contribute to the development of hyponatremia. Moreover, the parent compound of MDMA and its major and more potent metabolite, 4-hydroxy-3-methoxymethamphetamine (HMMA), both can lead to the release of arginine vasopressin (AVP), which further aggravates symptomatic hyponatremia [17]. Animal studies showed that MDMA and its metabolites led to serotonin secretion in the central nervous system [18], resulting in the release of AVP from the neurohypophysis [19]. A rapid decrease in serum sodium levels then results in an osmotic shift of free water from plasma into the cells, predisposing MDMA poisoned patients to pulmonary edema, cerebral edema, seizures, coma, brain stem herniation, and even death [20]. Among previous case reports of MDMA-induced hyponatremia, many were women aged between 15 and 30 years who ingested a single dose of ecstasy [21]. Moreover, the incidence of hyponatremia was markedly higher in women (27.3%) as compared to that in men (3.0%) [22].

Although the diagnosis of MDMA-related hyponatremia is generally not difficult, timely diagnosis can be challenging in patients without relevant exposure history and/or typical sympathomimetic manifestations, as evidenced in this case report. Patients with MDMA-related hyponatremia may present in a state of profound coma rendering history-taking impossible. Moreover, most MDMA abusers are reluctant in revealing their habit of illicit drug use, making it difficult in acquiring accurate exposure information even among those who are awake. The diagnosis is further complicated when patients suffering from MDMA-induced coma do not present with typical features of sympathomimetic toxidrome.

Our patient presented to the ED in a comatose status without manifesting mydriasis, diaphoresis, elevated blood pressure, tachycardia, or tachypnea. The only telltale sign was transient mydriasis that was documented at a local hospital. If prompt toxicologic screen had not been performed in this patient, the diagnosis of MDMA-related hyponatremic coma would have been overlooked. Therefore, emergency physicians should harbor a high index of suspicion of MDMA abuse among young patients who present to the ED with undetermined cause of hyponatremia. Appropriate toxicologic screen should then be conducted to confirm the diagnosis.

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