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Original Article

Holistic Approach to Ecstasy-induced Atrial Fibrillation in a Young Patient: A Case Report

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Abstract

Stimulants abuse is a global issue. Acute myocardial infarction, heart failure, and arrhythmia have all been linked to stimulants misuse and its synthetic variants but are rather uncommon. Herein, we present a case of a young patient presented with atrial fibrillation that did not respond to digoxin therapy. A suspicion of drug toxicity was later confirmed with a bedside urine screening. Following administration of benzodiazepines, the patient's clinical condition gradually improved, and he was eventually discharged with a prescription of lifelong warfarin. Therefore, patients with a low-to-intermediate risk of coronary artery disease presenting with atypical symptoms may benefit from a full substance use history and urine drug screening to ensure prompt institution of appropriate treatment.

Keywords:- Amphetamine; Atrial Fibrillation; Benzodiazepines; Substance Abuse

Introduction

Drug addiction imposes a major threat to public health and social issue worldwide. Addiction to opioids, methamphetamine, amphetamine-type stimulant (ATS), cocaine, cannabis and other psychoactive substances were commonly reported. Malaysia is facing a serious public health problem associated with drug addiction (Nishida, Ikeda, Kudo, & Esaki, 2003). The actual figures of total drug users may exceed more than half a million as the national database has only reported individuals who have been arrested and convicted for illicit drug use and sent to mandatory (Meng, 2017). Data from the National Anti-Drug Agencies (NADA) Malaysia in 2020 recorded a cumulative total of 128, 325 identified drugs users, a reduction of 9.3% as compared to 2019. Unfortunately, ATS use is steadily rising with the reported figure of 62% among all drug addicts (National Antidrugs Agency Malaysia, 2020).

Amphetamine-type stimulants are derived from phenylethylamines with structural similarities to adrenaline. Stimulants inhibit reuptake of neurotransmitter at the preganglionic neurons involving noradrenaline, dopamine and serotonin which act as neurotransmitter at specific neurological pathways (Fleckenstein *et al.*, 2007; Greene, Kerr, & Braitberg, 2008). The most obvious clinical manifestation is the alpha- and beta-adrenergic receptor-mediated sympathomimetic toxidrome as a result of noradrenaline reuptake failure at preganglionic neuron. On the other hand, mood and cognitive disorder was contributed by the disturbance of dopamine and serotonin reuptake in serotonin and dopaminergic pathway respectively (Katzung, Masters, & Trevor, 2004).

Amphetamine-type stimulants have different eff ects on different systems, resulting in a variety of symptoms or complications involving neurological and cardiovascular system, metabolic disturbances, risking liver toxicity and central hyperthermia (Smets *et al.*, 2005). The most reported symptom was

altered mental status (57%), including agitation, hallucinations, suicidal ideation, delusions, confusion, and despondent affect. However, only 13% of patients presented with cardiovascular complication such as chest pain (9%), palpitation (3%) and dyspnoea (1%) (Schifano *et al.*, 2021). Little is known about the aetiology of sudden death in individuals who had taken ATS but it is likely that sympathomimetic effects of the drug may precipitate dysrhythmic catastrophe (Brinkman, Hunfeld, & Melief, 2014). Herein, we aimed to describe a clinical case of arrhythmia complicated with acute heart failure following amphetamine ingestion in a young patient.

Case Study

A 20-year-old male with no underlying medical illness was referred from a private healthcare facility to our Emergency Department for atrial fibrillation. He complained of acute onset of shortness of breath and palpitation. There was no history of fever, cough, or chest pain. Also, no symptoms suggestive of hyperthyroidism. He is an active smoker and denied history or recent recreational drug use.

He appeared restless and tachypnoeic (Respiratory rate: 32 breaths/min). Pupils were 2 mm reactive bilaterally (actually tak document) There were bilateral lung crepitations up to midzone. Dual heard sounds heard on auscultation, no murmur was appreciated. The documented vital signs on initial arrival include a blood pressure of 130/84 mmHg, a heart rate of 192 beats/min, a temperature of 38.6˚C, and the oxygen saturation of 96% under room air. Chest X-ray showed borderline cardiomegaly with bilateral lower zone haziness (Figure 1).

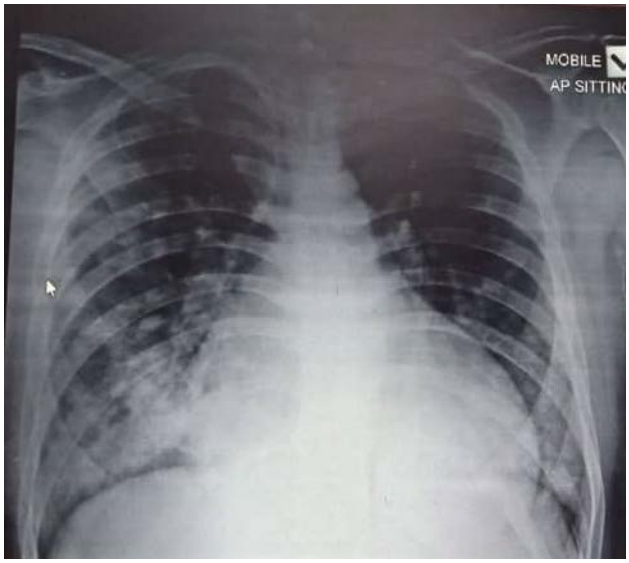

Figure 1: CXR showing cardiomegaly with bilateral lower zone heterogenous opacity and upper lobe diversion.

Electrocardiogram (12-lead) showed atrial fibrillation with the rate of 160 to 180 beats/min (Figure 2).

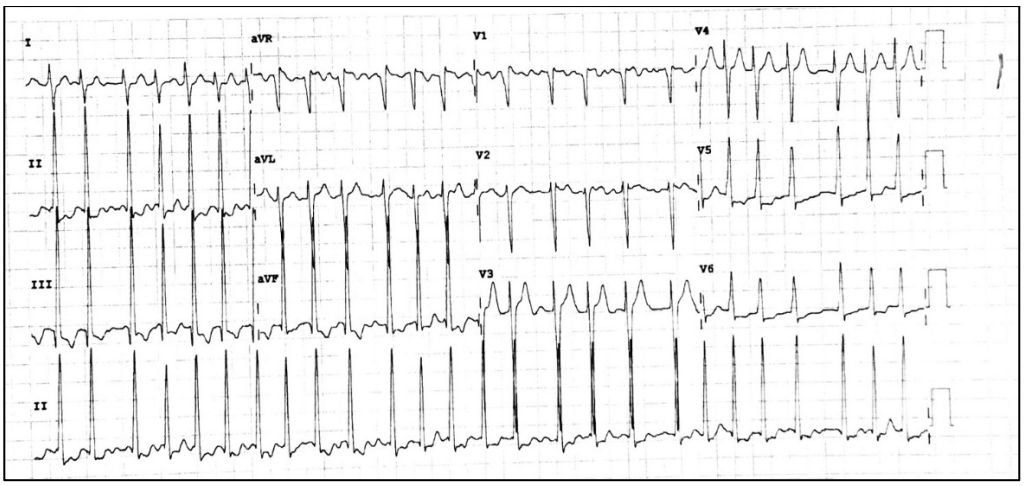

Figure 2: Electrocardiogram showing atrial fibrillation with rate 160 beats/min.

His creatine kinase (182 U/L) and creatine kinase-MB (40 U/L) were elevated. Arterial blood gas (ABG) showed evidence of type 1 respiratory failure (pH: 7.43, pCO2: 28.4 mmHg, pO2: 84.9 mmHg, HCO3-: 18.8 mEq/L, BE: -5.5, oxygen saturation 97% under high flow mask oxygen 15L/min). Routine haematological and biochemical tests showed were within normal limits: Total white cell count: 19.93 x 10^9/L, Hb: 15 g/dl, Hct: 44%, Platelet: 186 x 10^3/uL, sodium: 138 mmol/L, potassium: 3.6 mmol/L, urea 5.9 mmol/L and creatinine 99 umol/L.

At the point, he was treated for fast atrial fibrillation. He was given oral paracetamol 1g, crushed aspirin 300 mg, oral clopidogrel 300 mg and intravenous digoxin infusion 0.5 mg. However, despite completion of digoxin, his heart rate was still well above 150 beats/min with no clinical improvement. A high index suspicion of substance toxicity prompted a bedside urine drug test that came back positive for amphetamine.

He remained agitated and restless, hence an intravenous midazolam 2 mg was given with notable clinical improvement. His heart rate began to stabilise with improved arterial oxygenation (pH: 7.48, pCO2: 28.3 mmHg, pO2: 254 mmHg, HCO3-: 21 mEq/L, BE: 2.4, oxygen saturation 100% under HFM oxygen 15L/min).

In the ward, he was started on oral warfarin 5 mg daily and was discharged once his INR was stable above 1.5. In view of the chest x-ray findings, raised white cell count and minimal crepitations on lungs auscultation, he was also covered for community acquired pneumonia. Later echocardiogram revealed an ejection fraction of 59%, severe mitral regurgitation, mild-to-moderate tricuspid regurgitation, with dilated left ventricular and left atrium. Otherwise, there was no pericardial effusion, no clot, or thrombi.

Discussion

We presented a case of a young gentleman presenting with cardiotoxic manifestation of ecstasy abuse. Ecstasy (a modified synthetic 3, 4-methylenedioxymethamphetamine (MDMA)) ia a type of ATS, belonging to a class of noncatechol-sympathomimetic amines that produce central nervous stimulation. In excessive doses, it causes anxiety, hallucinations, coma, seizures, cardiotoxicity, and agitation (Fleckenstein *et al*., 2007; Greene, Kerr, & Braitberg, 2008; Schifano *et al*., 2021). ATS is typically abused orally, via inhalation, or intravenously, however a strong and direct effect was observed following inhalation (Brinkman *et al*., 2014). Twenty to 65% of ATS are eliminated through the kidneys in unchanged form, and the remaining percentage is excreted as metabolite (Carvalho *et al*., 2012).

ATS and its synthetic derivates' cardiotoxicity can manifest itself as acute myocardial infarction or necrosis, arrhythmias, cardiomyopathy, and acute heart failure (Bonsignore *et al*, 2019; Frishman *et al*., 2003; Nishida *et al*., 2003; Radaelli *et al*., 2021) as its sympathomimetic can stimulate the release of noradrenaline from sympathetic nerves. This release of noradrenaline has a pressor effect on the coronary circulation and may precipitate vascular spasm, therefore causing ischemic infarction, which in turn leads to a massive efflux of potassium. This efflux of potassium can then lead to cardiac

arrhythmias (Brinkman *et al*., 2014; Won *et al*,. 2013) as evident in our case who presented with atrial fibrillation.

Secondly, ATS can also induce myocardial necrosis. It has been demonstrated in rats that administration of methamphetamine results in the loss of myoglobin in the ventricular myocardium, causing swelling and degeneration of mitochondria in affected myocytes, resulting in sarcolemma damage, myocytolysis and fibrosis (Brinkman *et al*., 2014; Yeo *et al*., 2007). We have observed significant echocardiographic changes of dilated left-sided chambers and moderate-to-severe valvular insufficiencies in our patient following his first episode of fast AF following ecstasy ingestion.

Thirdly, it has been described that ATS can also induce acute as well as chronic cardiomyopathy depending on dosage and route taken besides leading to secondary pulmonary hypertension (Won *et al*., 2013). Previous study was conducted among 3,870 patients referred to the Toxicology Emergency Department of Baharlou Hospital, Tehran University of Medical Sciences, Tehran, Iran to evaluate cardiovascular complications among patients who abused amphetamines. They found that the ECG results were normal for the majority of their patients (45.2%), while others include sinus tachycardia and sinus tachycardia with prolonged QT interval. Other cardiovascular findings included arrhythmias with first-degree atrioventricular block (2.6%), tall T-waves (1.7%), ST segment elevation plus anterior myocardial infarctions (1.7%), arrhythmias plus ST segment elevation (1.3%), anterior myocardial infarctions (0.4%) and ST segment elevation (0.4%) (Bazmi *et al*., 2017). Therefore, the finding of atrial fibrillation from ecstasy toxicity is relatively uncommon in the clinical setting.

It is also important to highlight the permanent structural cardiac sequelae following acute cardiotoxicity from ecstasy abuse in our case. The patient accordingly required lifelong warfarin as a prophylaxis against future cardiac-related events.

We would also suggest the management of similar cases related to complications from substance use and misuse be dealt meticulously beyond acute emergency care. Addiction is a complex disorder, affecting brain function and human behaviour (Liu & Li, 2018). There is no single treatment that is right for everyone and an effective management should address all of the patients' needs, not just the drug use. Hence, beyond emergency medical care, other management that should be planned ahead include counselling with behavioral and psychotherapy, treatment to address other possible mental disorder, and a medically-assisted detoxification. Testing for high-risk infectious diseases such as HIV/AIDS, hepatitis B and C, and tuberculosis should also be communicated to the patients.

Conclusion

The recent trend of increase in amphetamine abuse should prompt clinicians to watch out for potentially dire cardiac complication. Patients with low-to-intermediate risk for coronary artery disease with atypical presentation may benefit from detailed substance abuse history and urine drug screen. Meticulous supportive care aided by judicial use of benzodiazepines forms the cornerstone of management in such cases.

Conflicts of Interest

The authors declare that they have no conflict of interests.

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