

Case Report

Volume 12 Issue 2 - June 2019
DOI: 10.19080/PBSIJ.2019.12.555831

Psychol Behav Sci Int J

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Asystolic Cardiac Arrest and Abrupt Long-Term Use Psychostimulant Suspension: A Case Report



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Submission: May 26, 2019; **Published:** June 20, 2019

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Abstract

Objective: To illustrate a potential serious cardiovascular side effect occurring after abrupt long-term use psychostimulant suspension.

Introduction: Medications for attention deficit disorder with hyperactivity (ADHD): Amphetamine, Atomoxetine and Methylphenidate are widely used among general population. Prescription of psychostimulants should be cautious given reports of serious cardiovascular events in adults.

Case presentation: A 35-year-old female patient with a history of ADHD and Obsessive-compulsive disorder (OCD). Long term levothyroxine, lamotrigine, methylphenidate, modafinil and sertraline user. She presented with two-day history of abdominal pain, vomiting and progressive altered level of consciousness. Lab tests showed a pH 7.01, HCO₃ 5 mEq/L, serum creatinine 1.3 mg/dL blood urea nitrogen 21 mg/dL, K⁺ 5.2 mEq/L, Anion gap 43, osmolar gap 28 and positive ketonemia.

Toxicology results: Blood acetaminophen levels < 1.2 mg/L. Urine drug panel positive for benzodiazepines, sertraline, diphenhydramine, lithium < 0.05 mmol/L, blood salicylate levels < 3.0 µg/mL, B-hCG negative. Head CT and electroencephalography showed no pathological findings. She was admitted with a diagnosis of severe metabolic acidosis possibly secondary to intoxication. During hospitalization, after adequate acid-base and hydro electrolytic correction, patient presented a self-limited episode of *Torsade de pointes* that evolved into asystole, from which she recovered favorably.

Discussion: Abrupt methylphenidate suspension can be potentially deleterious. Future research about cardiovascular security in adults and long-term users is suggested.

Keywords: Psychostimulant; Methylphenidate; Cardiac Arrest; Cardiovascular Safety; Adverse Effects

Abbreviations: ADHD: Attention Deficit and Hyperactivity Disorder; OCD: Obsessive Compulsive Disorder; CV: Cardiovascular; TdP: *Torsade de Pointes*, CAM: *Confusion Assessment Method*; ICU: Intensive Care Unit; ICD: Implantable Cardioverter Defibrillator

Introduction

Among the drugs used for ADHD [1], amphetamine derivatives, atomoxetine and methylphenidate are broadly used by general population. US reports show that 2.7 million children and adolescents and 1.5 million adults are currently methylphenidate users [2]. Population studies regarding CV safety in children and adolescents show this would be a reasonably safe drug [3]. On the other hand, since 1986 it has been suggested an association, although not frequent, with adverse CV effects [4]. There are reports that suggest that its use should be cautious in adults given that, although adverse effects be rare, they might be potentially fatal [3,5].

B-agonists' adrenergic effect in heart rate and blood pressure have been thoroughly described [6]. Recent reports have shown association between methylphenidate and syncope, arrhythmias and sudden death, mainly on the first days of treatment and among patients with congenital heart disease [3,7,8]. This association is stronger at lower doses of methylphenidate, therefore suggesting a non-causal association [9]. There are several reports of cardiovascular side effects of methylphenidate in children and adolescents. In adults, however, it remains yet unclear mainly due to lack of research. Nonetheless, there is a study showing similar results to those in children [9], as well as possible side effects at withdrawal. One study carried out in children and adolescents

in which the drug *washout period* was followed up found an increased rate of arrhythmias after seven days of discontinuation of methylphenidate [3]. This article's purpose is to illustrate, by a clinical case, a potential serious cardiovascular side effect of abrupt long-term use psychostimulant suspension.

Case Presentation

A 35-year-old female patient, single, kinesiologist. She lived with her parents and didn't have children. She first attended mental health services at age 15, when she was diagnosed with OCD [1] and ADHD [1]. During college she presented with a mood disorder for which she started proper treatment. Two years ago, after a work conflict and subsequent worsening of her OCD, she restarted follow-up. She also had a medical record of hypothyroidism. She was regularly using levothyroxine, lamotrigine, methylphenidate, modafinil and sertraline (Table 1).

Table 1: Previous regular use medications and dose.

Medication	Dose
Levothyroxine	200 mcg qd
Aripiprazole	5 mg qd
Lamotrigine	125 mg qd
Methylphenidate Retard	40 mg qd
Modafinil	200 mg qd
Sertraline	225 mg qd

Patient was brought to the emergency service with a two-day history of abdominal pain and vomiting, which evolved to progressive alteration of mental status. Patients and relatives denied any recent change in medication doses or any substance abuse. At presentation patient was agitated, hemodynamically stable, slightly tachycardic, afebrile. Lab tests showed a pH 7.01, HCO₃ 5 mEq/L, serum creatinine 1.3 mg/dL blood urea nitrogen 21 mg/dL, K⁺ 5.2 mEq/L, anion gap 43, osmolar gap 28 and positive ketonemia. Toxi-lab drug screening results: blood acetaminophen levels < 1.2 mg/L. Urine drug panel positive for benzodiazepines, sertraline, diphenhydramine, lithium < 0.05 mmol/L, blood salicylate levels < 3.0 µg/mL, β-hCG negative. Head CT and electroencephalography didn't show pathological findings nor epileptiform activity.

Patient was admitted to a monitored unit with the diagnoses of severe metabolic acidosis of undetermined cause and acute kidney injury. Early fluid replacement was started along with bicarbonate solution, thiamine, folic acid and B6 vitamin administration. Lorazepam was given for agitation control. Adequate acid-base and hydro electrolytic balance was achieved, along with proper kidney function recovery, without need for renal replacement therapy. Chronic use drugs were held suspended.

She was evaluated by the hospital's consultation-liaison psychiatry unit due to suspected intoxication. At first, a formal interview was impossible due to consciousness impairment (she tested positive on CAM evaluation) [10]. None of the previously

used psychotropic medication was reintroduced. Lorazepam was prescribed in cases of anxiety, insomnia or psychomotor agitation. Reevaluated twenty-four hours later patient was vigilant and orientated in time and space. She denied any recent alcohol, tobacco or other substance use. She denied self-injurious behavior or any suicide attempts. During interview she impressed exhausted. On mental examination patient was described drowsy, uncooperative, querulous and childish. She had a fluid and coherent speech, although poorly spontaneous and bradypsychic. Mood was euthymic, with emotional lability and crying at remembrance of romantic relationships, and spontaneous smiling. She had poor insight. Didn't show psychotic symptoms.

Afterwards, she evolved with persistent symptomatic sinus bradycardia down to 37 bpm. A rhythm Holter monitoring was performed. On the fifth day of stay she presented an episode of Torsade de Pointes which manifested as syncope, evolving into ventricular fibrillation and a subsequent 47-second-long asystole. The entire episode lasted three minutes. Earlier that day blood lab tests showed pH 7.4, HCO₃ 21 mEq/L, K⁺ 3.6 mEq/L, mEq/L Mg 1.6 mg/dL. Magnesium sulphate was appointed, with recovery of sinus rhythm. She was then transferred to the hospital ICU, where isoproterenol was started along with clobazam due to initial suspicion of a convulsive episode, which was discarded later by neurology consultants. Rest electrocardiography performed previous to TdP episode showed a corrected QT (QTc) of 470 ms. Following electrocardiographic study showed a QTc of 520 ms. Echocardiography didn't reveal structural heart lesions.

Patient was started on low dose bisoprolol. She did not meet indications for neither ICD nor pacemaker. Ventricular fibrillation was attributed to toxic-metabolic derangement. She was kept on oral magnesium and potassium supplementation. Electrophysiology consultants approved restart of psychotropic medication under close electrocardiographic monitoring. Olanzapine was started for impulsivity symptoms management, slowly titrated up to a 10 mg once-daily dose. Patient didn't present any new arrhythmias afterwards, being re-transferred to a non-ICU monitored unit.

Among other studies performed during her stay, a lumbar puncture was performed, with a cerebrospinal fluid study that showed hyperproteinorrachy, slightly elevated IgG index, negative for oligoclonal bands, negative autoimmune encephalitis panel and negative Gram stain and culture. Given following favourable clinical evolution, with stabilization of behavioral symptoms and satisfactory acid-base and electrolyte balance, patient was discharged with an ambulatory follow-up plan.

Discharge diagnosis

- i. Solved, Anion gap metabolic acidosis (5C73.2) [11]
- ii. Solved, Polymorphic ventricular tachycardia (TdP), Ventricular fibrillation, Asystolic cardiac arrest (BC71.01, BC71.1, MC82.2) [11]

- iii. Attention deficit hyperactivity disorder (314.01) [1]
- iv. Hypothyroidism (5A00) [11]

Discussion

The presented case shows a patient with prolonged psychostimulants use, methylphenidate and modafinil, both having a synergic effect. Five days after abrupt suspension, patient presents an ominous event: TdP and a 47 second asystole. Former potentially QT prolonging medication had been suspended, with minimal attributable role to current event. And although a major acid-base disorder existed at presentation, at the time of the arrhythmia it had already been corrected. Given there was no evident cause to this event, we might consider - as has been proposed in literature [3] - the effect of psychostimulant suspension as a possible trigger.

It seems reasonable to suggest more extensive research regarding psychostimulant cardiovascular safety adults. Besides, its medical indication should be regarded cautious and always supervised. Informal and irregular use is otherwise frequent with these medications, which is not free from hazard and might bring even fatal consequences. Lastly, it is important to keep in mind the effects of medication suspension - commonly at admission - when facing interurrences like the one described in this case.

Conflict of Interest

The authors declare that there is no conflict of interest.

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DOI: [10.19080/PBSIJ.2019.12.555831](https://doi.org/10.19080/PBSIJ.2019.12.555831)

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