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CASE REPORT

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Cardiac arrest after ibogaine intoxication

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Abstract

Ibogaine is a psychoactive herbal medication with alleged antiaddiction properties. We report a case of ibogaine intoxication mimicking Long-QT syndrome resulting in ventricular flutter and nearby cardiac arrest. A 61-year-old man experienced massive QT prolongation and ventricular flutter at a rate of 270 beats per minute requiring defibrillation after ingestion of a large dose of Ibogaine. The ingested dose of 65-70 mg/kg represents the highest survived ibogaine dose reported to date. As a result of the long plasma half-life of ibogaine, it took 7 days for the patient's QT interval to normalize.

KEYWORDS
delayed QT recovery, drug-induced QT prolongation, ibogaine, long-QT, ventricular arrhythmia

1 | INTRODUCTION

Drug-induced QT prolongation can result in life-threatening ventricular arrhythmia and is part of the differential diagnosis of unexplained torsades de point or ventricular fibrillation. We report an uncommon case of life-threatening ventricular arrhythmia caused by massive QT prolongation after ingestion of ibogaine as antiaddiction therapy.

2 | CASE

A 61-year-old male presented to a holistic, naturopathic clinic for alternative treatment to overcome a long-standing opioid dependency related to chronic pain. His past medical history was significant for multiple spine operations resulting in a chronic cervicolumbar pain syndrome. Additional comorbidities included depression, mild hypertension, and dyslipidemia. He had no history of cardiovascular disease, unexplained syncope, presyncope, or sustained palpitations. His family history was negative for unexplained sudden cardiac death or inherited arrhythmia.

The patient was provided with ibogaine capsules (first-time use) that were administered with the intention to blunt opioid addiction symptoms and achieve a sustained anticraving effect. The patient ingested an approximate single dose of 5.6 g of ibogaine corresponding to a total body dose of 65-70 mg/kg. It is important to mention that ibogaine was administered without medical prescription and supervision, as this substance is not approved in North America for medical use. At 6-12 hours postingestion, the patient started to develop severe gastrointestinal symptoms including heavy vomiting and diarrhea. Those symptoms were quickly followed by a significant alteration of his level of consciousness, and the patient was urgently transferred to the ER of the nearest hospital.

On arrival at the ER, the patient was pale, diaphoretic, and barely arousable. His radial pulse was not palpable, and no blood pressure could be measured. The initial 12-lead ECG revealed a monomorphic wide QRS complex tachycardia at a rate of 270 beats per minute—representing almost ventricular flutter (Figure 1A). Emergent defibrillation was performed and converted the patient to sinus rhythm. The ECG postdefibrillation demonstrated massive QT prolongation associated with ventricular bigeminy (Figure 1B). The initial serum potassium concentration was 2.4 mmol/L, and the serum concentrations of Mg^{2+} and Ca^{2+} were normal. After initial stabilization, the patient was transferred to the intensive care unit for further management. His hypokalemia was aggressively treated and corrected within 12 hours. His hemodynamics quickly improved with supportive treatment. Laboratory screening for cointoxication was negative.

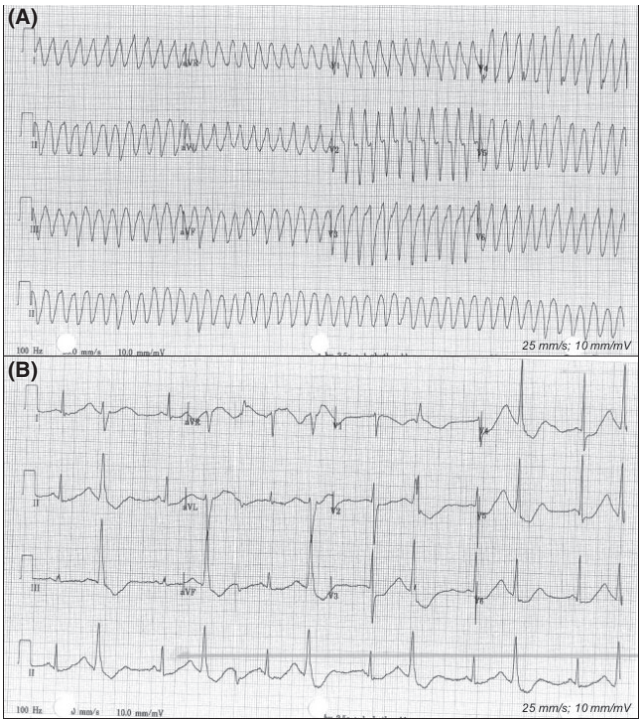

FIGURE 1 Life-threatening ventricular arrhythmia upon ibogaine intoxication. A, The 12-lead ECG after ingestion of an estimated dose of 65-70 mg/kg of ibogaine showed monomorphic ventricular tachycardia/ventricular flutter at a rate of 270 beats per minute requiring emergent defibrillation. B, The ECG postdefibrillation demonstrated massive QT prolongation with prominent U-waves associated with ventricular bigeminy

There was no evidence of any significant heart disease after extensive investigation including coronary CT-angiogram, cardiac magnetic resonance imaging, and echocardiogram.

Serial ECGs demonstrated a delayed recovery for his corrected QT intervals (QTc on admission = 655 ms, QTc 24 hours later = 714 ms) requiring 7 days for complete normalization (Figure 2). No further ventricular arrhythmia occurred during his hospitalization. An exercise treadmill test was performed 12 days after his arrhythmic event to screen for underlying hereditary Long-QT syndrome. The exercise test demonstrated strictly normal QT dynamics during exercise and recovery (Figure S2).

A final diagnosis of ibogaine-induced QT prolongation (cotriggered by secondary hypokalemia) triggering ventricular tachycardia was retained, and the patient was discharged home. Given his normal cardiac test results and the well-known cardiotoxicity of ibogaine, no genetic testing was performed.

3 | DISCUSSION

Ibogaine is a psychoactive indole alkaloid from the root bark of *Tabernanthe iboga*, a West-Central African rainforest shrub (Figure S1).[1] Traditionally, ibogaine has been used by various indigenous nations from Gabon, Cameron, and the Republic of the Congo for spiritual ceremonies because of its neurostimulating and hallucinogen effect.[1]

Ibogaine came into the focus of medical research since the 1960s because of its alleged antiaddiction and anticraving properties.[1] Because of safety concerns, the substance is currently not approved in many Western countries including the United States and Canada.[2] However, increased use of ibogaine by independent, nonmedical addiction clinics has been observed over the last decade. Those clinics often operate in a legal gray zone and typically without any form of cardiac monitoring.

Ibogaine has a complex pharmacology and is metabolized in the liver. The active substance is the metabolite noribogaine, which has a long plasma half-life of 28-40 hours.[1,3] Ibogaine and noribogaine exposition can be detected in serum and urine.[4]

Cardiac effects of ibogaine are characterized by sinus bradycardia and marked QT prolongation, which are the result of complex interaction with various cardiac ion channels.[1] The electrophysiological effect of ibogaine mimics the hereditary Long-QT syndrome type 2 that is caused by a genetic loss-of-function of the I_{Kr} channel (encoded by the KCNH2 gene).[5]

Malignant ventricular arrhythmia and sudden death after ibogaine ingestion have been reported and are thought to be caused by the massive QT prolongation with subsequent torsades de pointes or ventricular fibrillation.[1,6] Mimicking Long-QT syndrome type 2, it is

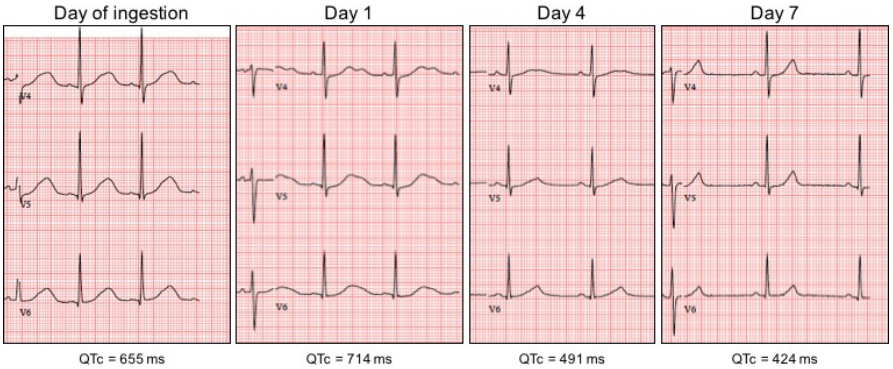

FIGURE 2 Delayed QTc recovery after ibogaine intoxication. Serial ECGs demonstrating delayed recovery of the corrected QT (QTc) interval due to long plasma half-life of the active metabolite noribogaine. Complete QTc normalization required 7 d. The absolute QT interval was measured using maximal slope technique that has been described previously.[7] The QTc interval was then calculated using Bazett's formula

thought that ventricular arrhythmia is caused by triggered activity and initiated by late-coupled ventricular ectopy as demonstrated in the postarrest ECG of our patient (Figure 1B).

The present case extends our knowledge about the clinical manifestation of ibogaine-related cardiotoxicity. As previously reported, our patient presented with significant hypokalemia, which served as a proarrhythmic cotrigger and was related to the heavy gastrointestinal symptoms.[1] Those symptoms are predominantly caused by activation of central dopaminergic and serotonergic receptors.[3] The onset of symptoms in our case was consistent with the literature. Symptoms of cardiotoxicity can manifest within 1.5-76 hours postingestion.[1,6] The massive QT prolongation up to 714 ms in our patient is among the highest reported so far.[1] The estimated ingested dose of 65-70 mg/kg would represent the highest survived ibogaine dose reported to date.[1] However, this has to be interpreted with caution, as nonstandardized preparation of ibogaine capsules makes dose estimations challenging, and we did not perform a direct measure of the serum ibogaine concentration. Depending on the type of preparation, the total content of ibogaine alkaloid may vary from 15% to 50%.[6] It becomes obvious that those uncontrolled and nonstandardized preparations result in unpredictable dosing putting potential customers at risk.

The long half-life of the active metabolite noribogaine is well illustrated by the delayed QT recovery of our patient. As illustrated in Figure 2, it took 7 days for our patient to normalize his corrected QT interval despite normal electrolytes and in the absence of any competing QT-affecting medication. None of the previous reports on ibogaine intoxication provided a detailed documentation of the QT recovery. Our findings illustrate the potential risk for late recurrence of ventricular arrhythmia and emphasize the need for prolonged cardiac monitoring in those patients.

In conclusion: Ibogaine intoxication is an uncommon, but potentially life-threatening scenario due to the high cardiotoxicity of this substance and urgent admission to a critical care unit is required. Cardiotoxicity is characterized by massive QT prolongation with risk of ventricular arrhythmia that may develop early or late after ingestion. Delayed QT recovery is related to the long plasma half-life of the active metabolite and prolonged cardiac monitoring until entire QT normalization is recommended.

CONFLICT OF INTEREST

Authors declare no conflict of interests for this article.

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REFERENCES

1. Koenig X, Hilber K. The anti-addiction drug ibogaine and the heart: a delicate relation. Molecules. 2015;20:2208–28.
2. Brown TK. Ibogaine in the treatment of substance dependence. Curr Drug Abuse Rev. 2013;6:3–16.
3. Litjens RP, Brunt TM. How toxic is ibogaine? Clin Toxicol (Phila). 2016;54:297–302.
4. O'Connell CW, Gerona RR, Friesen MW, Ly BT. Internet-purchased ibogaine toxicity confirmed with serum, urine, and product content levels. Am J Emerg Med. 2015;33:985.e5–6.
5. Giudicessi JR, Ackerman MJ. Genotype- and phenotype-guided management of congenital long QT syndrome. Curr Probl Cardiol. 2013;38:417–55.
6. Alper KR, Stajic M, Gill JR. Fatalities temporally associated with the ingestion of ibogaine. J Forensic Sci. 2012;57:398–412.
7. Postema PG, Wilde AA. The measurement of the QT interval. Curr Cardiol Rev. 2014;10:287–94.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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