Chronic kratom use as a precipitant for acquired Brugada syndrome

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Introduction

Mitragyna speciosa (kratom), a medicinal plant native to Southeast Asia, has traditionally been used both as a stimulant to combat fatigue and as a substitute for opium to aid in morphine withdrawal.[1] Recent studies indicate that some of the 40 million Americans experiencing chronic pain purchase kratom online to self-treat opioid withdrawal. It is also gaining popularity as a recreational drug.[2] Kratom toxicity may present with symptoms such as agitation, anxiety, tachycardia, and palpitations. In addition, there have been reports linking kratom use to the onset of seizures and cardiac arrhythmias.[3] In vitro research has demonstrated that mitragynine—kratom's primary alkaloid—inhibits the rapid delayed rectifier potassium current, leading to prolonged action potential duration. These electrophysiological changes suggest a potential for QT interval prolongation and an increased risk of torsades de pointes (TdP).[4] Although corrected QT (QTc) prolongation is the most frequently reported cardiac side effect of kratom, there have been rare instances in which chronic, high-dose kratom use has unmasked or induced Brugada syndrome—a condition that can lead to life-threatening arrhythmias. Unlike previously reported cases that presented with incidental electrocardiogram (ECG) changes, our case uniquely involves a young male who experienced a seizure episode immediately after kratom ingestion, and the temporal relationship to high-dose kratom ingestion, previously normal ECG, and full normalization within 1 week suggests an acquired and reversible etiology.

KEY TEACHING POINTS

- Potential cardiotoxicity: Kratom contains active alkaloids that interact with various receptors and may inhibit myocardial potassium channels, potentially leading to cardiotoxic effects such as corrected QT prolongation and ventricular arrhythmias.
- Association with Brugada syndrome: Documented cases have shown that chronic, high-dose kratom use can unmask type 1 Brugada patterns in individuals without a cardiac history, suggesting a potential link between kratom consumption and the manifestation of this syndrome.
- Clinical implications: Health care providers should remain vigilant for signs of Brugada syndrome in patients using kratom, particularly those presenting with syncope, palpitations, or other cardiac symptoms. Early recognition and appropriate management are essential to prevent potentially fatal outcomes.

Case report

A 27-year-old man with a history of opioid abuse presented to the emergency department after a witnessed generalized tonic-clonic seizure. The seizure occurred approximately 1–2 minutes after the patient ingested 6 tablets of a kratom extract, which he had been taking for chronic back pain for more than a year. Upon arrival by emergency medical services, the patient was postictal, was amnesic to the event, and had bitten his tongue. Initial laboratory evaluation showed potassium, magnesium, and phosphorus levels within normal limits. The comprehensive metabolic panel and complete blood count were also within normal limits. A computed tomography scan of the head was unremarkable. An ECG performed in the emergency department revealed a Brugada pattern, as shown in Figure 1. Review of ECG records from 1 year earlier showed no evidence of a Brugada pattern. The patient denied any family history of sudden cardiac death and reported no previous seizures. Cardiology was consulted, and the patient was placed on telemetry for close observation. A transthoracic echocardiogram and a 24-hour electroencephalogram were performed, both of which showed no abnormalities.

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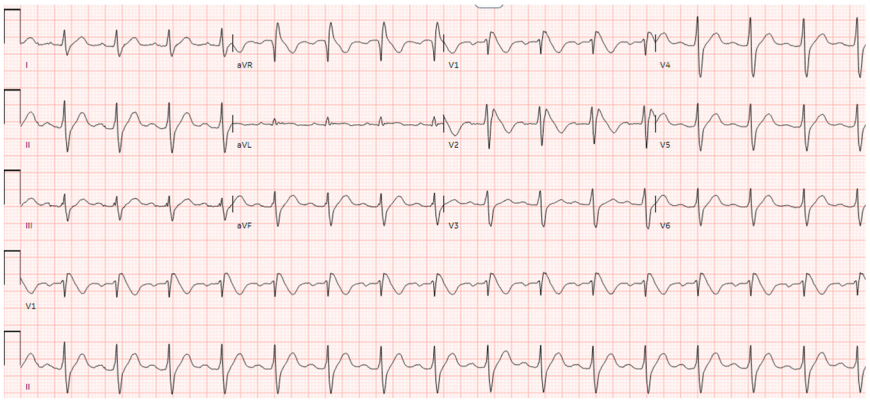

Figure 1 A 12-lead ECG showing sinus rhythm, borderline right bundle branch block with coved ST-segment elevation of >1 mm in V1 and V2, consistent with type 1 Brugada pattern. QTc = 482 ms. ECG = electrocardiogram; QTc = corrected QT.

During admission, the patient described his long-standing use of kratom as a substitute for opioids, stating that it provided pain relief comparable with prescription opioids. He noted that the dose he consumed before the seizure was approximately 3 times his usual intake, although he observed that the effects of kratom often varied.

Despite the presence of a Brugada pattern on ECG, the patient remained hemodynamically stable, and no urgent invasive interventions were deemed necessary at the time. He was observed for 2 days under continuous telemetry monitoring. The telemetry strip recorded before discharge is shown in Figure 2. A plan was made for outpatient cardiology follow-up and continued telemetry monitoring.

Psychiatry was also consulted, and the patient was educated on the risks associated with chronic kratom use and informed about detox programs and available support resources. Collaborative management included the initiation of gabapentin to address both chronic pain and potential antiseizure benefits. The patient expressed understanding and agreement with the proposed treatment plan.

At a 1-week follow-up with his primary care provider, the patient's ECG was completely normal as shown in Figure 3, but an early repolarization pattern observed in the inferior and lateral leads may represent a benign variant, commonly seen in healthy young adults. However, in the context of the Brugada pattern, some studies suggest this coexistence could imply a higher arrhythmic risk. This underscores the importance of continued follow-up in such patients.

Discussion

Mitragyna speciosa, commonly known as kratom, is a plant native to Southeast Asia, particularly Thailand and Malaysia. Traditionally, its leaves have been used for their stimulant properties to combat fatigue and enhance work endurance and their analgesic and sedative effects. Historically, kratom has also been used as a substitute for opium and to aid in morphine withdrawal. However, owing to its narcotic effects, the use of kratom has been banned in several Southeast Asian countries.[1] A survey of 644 current kratom users revealed that, despite reporting distinct subjective experiences associated with red, green, and white kratom strains—aligning with common marketing descriptions—laboratory analyses showed no significant differences in alkaloid content among these strains.[5] This suggests that the perceived differences in effects may be more influenced by marketing narratives and anecdotal reports than by actual chemical variations.

Kratom offers consumers various consumption methods. Traditionally, fresh leaves are chewed or brewed into tea. In modern contexts, kratom is commonly found in powdered form, which can be swallowed directly or encapsulated for convenience. In addition, some users opt to smoke dried leaves. These diverse methods provide flexibility for individuals seeking its effects.

Mitragyna speciosa, commonly known as kratom, contains more than 40 alkaloids, with mitragynine and 7-hydroxymitragynine (7-OH-mitragynine) being the most pharmacologically active. The interaction of these alkaloids with opioid receptors is complex and not yet fully understood. Some studies suggest that mitragynine and 7-OH-mitragynine act as partial agonists at μ-opioid receptors and competitive antagonists at δ-opioid receptors, with minimal activity at κ-opioid receptors. Kratom's active compounds interact with multiple receptors in the body, producing a combination of stimulant and analgesic effects. Mitragynine and 7-OH-mitragynine contribute to pain relief through partial agonism at μ-opioid receptors. In addition, mitragynine stimulates α2-adrenergic receptors, which may contribute to its stimulant properties. Furthermore, mitragynine interacts with 5-HT2A serotonin receptors, potentially influencing mood and cognition.[6,7]

Mitragynine, the primary active alkaloid in kratom, has been implicated in cardiac electrophysiological disturbances. Studies have demonstrated that mitragynine inhibits the human ether-à-go-go-related gene (hERG) potassium channels, leading to suppression of the rapidly activating delayed rectifier potassium current in human cardiomyocytes. This inhibition can prolong the action potential duration, thereby increasing the risk of developing TdP, a potentially

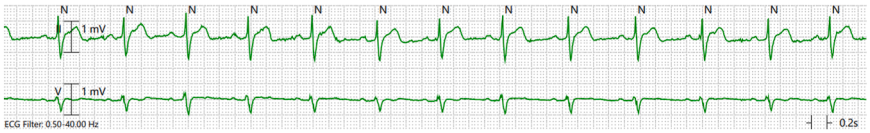

Figure 2 Telemetry strip after 2 days showing no evidence of Brugada pattern.

fatal ventricular arrhythmia. In addition, mitragynine has been shown to cause a significant reduction in the fully glycosylated hERG1a protein expression, suggesting possible impaired hERG1a trafficking, which may further contribute to its cardiotoxic effects.[4] Although kratom's association with QTc prolongation and TdP is documented, its interaction with sodium channels and potential to induce Brugada syndrome remain less well understood, warranting further investigation.

Kratom (*Mitragyna speciosa*) consumption can lead to various adverse effects, including nausea, vomiting, tremors, excessive sweating, tachycardia, palpitations, hypertension, and elevated creatine phosphokinase levels. Management of kratom toxicity primarily involves supportive care, such as the administration of intravenous fluids, sedatives, antiemetics, and, in certain cases, antihypertensive medications and supplemental oxygen.

Chronic kratom use may result in both psychological and physical dependence, with withdrawal symptoms emerging upon cessation. Psychological manifestations of withdrawal include depressed mood, anxiety, restlessness, and irritability. Physical symptoms often resemble those of opioid withdrawal and may include lacrimation, rhinorrhea, piloerection, myalgia, arthralgia, diarrhea, nausea, vomiting, insomnia, autonomic hyperactivity, and yawning. Treatment for kratom withdrawal is mainly supportive and may include the use of medications such as buprenorphine, naloxone, and clonidine.[3] A case-control study involving Malaysian males indicated that an average daily intake of 434 mg of mitragynine—kratom's primary alkaloid—was associated with higher odds of sinus tachycardia and borderline QTc intervals.[8] Notably, this daily consumption is substantially lower than the estimated 120–140 g per day reported in our patient, underscoring the potential cardiotoxic risks associated with high-dose kratom use.

Brugada syndrome is diagnosed by identifying characteristic patterns on an ECG, particularly ST-segment elevation in leads V1–V3 with a right bundle branch block appearance. There are 3 recognized ECG patterns: types 1, 2, and 3. A definitive diagnosis requires the presence of a spontaneous type 1 ECG pattern or its unmasking via a sodium channel blocker challenge in individuals with clinical symptoms such as syncope, seizures, or sudden cardiac arrest.[9] A sodium channel blocker provocation test was not performed because the patient was hemodynamically stable and asymptomatic after the seizure and demonstrated complete ECG normalization on follow-up. This clinical course favored an acquired pattern rather than concealed Brugada syndrome. Although Brugada patterns can show day-to-day variability, the temporal relationship to high-dose kratom ingestion, previously normal ECG, and full normalization within 1 week suggests an acquired and reversible etiology rather than an idiopathic Brugada syndrome. Although ECGs from higher intercostal spaces were not obtained, which may have enhanced diagnostic sensitivity for latent Brugada syndrome, the normalization of the type 1 pattern after kratom abstinence without recurrence supports a reversible, substance-related phenomenon.

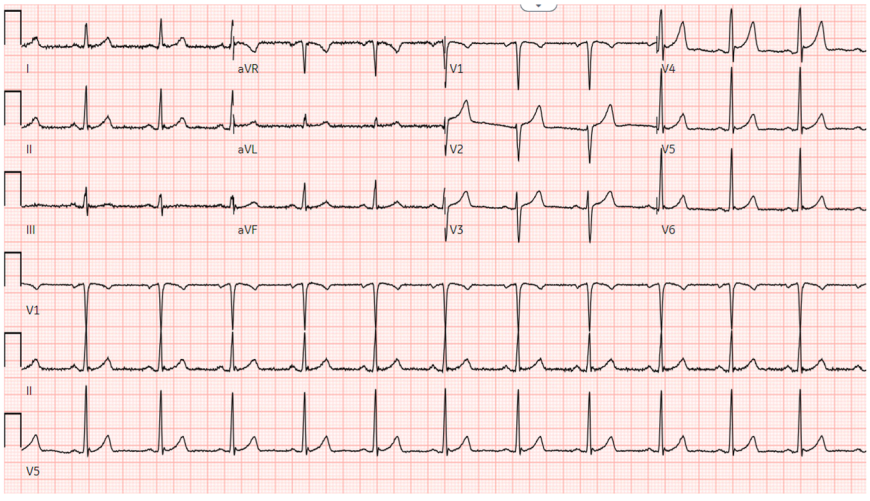

Figure 3 A 12-lead ECG after 7 days showing sinus rhythm, normal ECG with no Brugada pattern. QTc = 395 ms. ECG = electrocardiogram; QTc = corrected QT.

A comprehensive review published in 2021 highlighted kratom's potential cardiovascular risks, including QTc prolongation, TdP, and cardiopulmonary arrest. However, the review did not address any association between kratom use and Brugada syndrome.[7] As stated earlier, only 3 cases of Brugada syndrome linked to kratom use have been documented in the literature, all sharing notable similarities. Each patient had been consuming kratom in high doses or for an extended period and presented with dizziness, syncope, or new-onset seizure. None had a personal or family history of Brugada syndrome or sudden cardiac death. Their ECGs revealed a type 1 Brugada pattern, yet laboratory tests and imaging—including echocardiograms—were unremarkable. In 1 case, electrophysiological studies were performed but did not provoke ventricular arrhythmias. Within 24–48 hours, follow-up ECGs normalized to sinus rhythm. All patients were counseled to avoid kratom and were discharged without complications. These cases suggest a credible association between frequent, high-dose kratom use and the development of Brugada syndrome.[10–12]

Although Brugada patterns can show day-to-day variability, the temporal relationship to high-dose kratom ingestion, previously normal ECG, and full normalization within 1 week suggests an acquired and reversible etiology.

Conclusion

Chronic, high-dose kratom consumption has been linked to the development of acquired type 1 Brugada syndrome—a condition that increases the risk of life-threatening ventricular arrhythmias and sudden cardiac death. Although kratom's association with QTc prolongation and TdP is documented, its interaction with sodium channels and potential to induce Brugada syndrome remain less well understood, warranting further investigation.

Given kratom's increasing popularity, ease of access, and lack of regulatory oversight, it is imperative for health care professionals to recognize these serious cardiac risks. Patients should be thoroughly educated about these potential dangers, and the use of kratom should be strongly discouraged to prevent fatal cardiac events.

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