Unusual Presentation of Kratom Overdose With Rhabdomyolysis, Transient Hearing Loss, and Heart Failure

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Abstract
Kratom mainly grows in Southeast Asia. It is widely used for pain management and opioid withdrawal, which is available online for cheaper prices. Alkaloids extracted from kratom such as mitragynine and 7-hydroxy mitragynine exhibit analgesic properties by acting through μ receptors. Commonly reported side effects of kratom include hypertension, tachycardia, agitation, dry mouth, hallucinations, cognitive and behavioral impairment, cardiotoxicity, renal failure, cholestasis, seizures, respiratory depression, coma, and cardiac arrest. Rhabdomyolysis is a less commonly reported lethal effect of kratom. Limited information is available in the literature. In this article, we present a case of a 45-year-old female who is overdosed with kratom and presented with lethargy, confusion, transient hearing loss, and right lower extremity swelling and pain associated with weakness who was found to have elevated creatinine phosphokinase. She was diagnosed with rhabdomyolysis, compartment syndrome, multiorgan dysfunction including acute kidney injury, liver dysfunction, and cardiomyopathy. She underwent emergent fasciotomy and required hemodialysis. Her renal and liver function subsequently improved. We described the case and discussed pharmacology and adverse effects of kratom toxicity with a proposed mechanism and management. We conclude that it is essential for emergency physicians, internists, intensivists, cardiologists, and nephrologists to be aware of these rare manifestations of kratom and consider a multidisciplinary approach.

Keywords
kratom, 7-hydroxy mitragynine, mitragynine, rhabdomyolysis and compartment syndrome

Introduction
Kratom plant (Mitragyna speciosa) is usually grown in Southeast Asia and used as a psychoactive medication. Kratom use in the United States is increasing alarmingly due to its easy availability online, and thus increasing the potential for abuse, which is leading to increased hospital admissions and deaths. The lifetime prevalence of kratom use in the adult US population is 1.3%. It was noted to be used frequently in young male students or preferably health care professionals.1 Thus, the US Drug Enforcement Administration classified kratom as a schedule I controlled substance in 2016.2 Kratom contains mitragynine and 7-hydroxy mitragynine, which exhibit analgesic properties by acting as μ-opioid receptor partial agonists. Mitragynine and 7-hydroxy mitragynine are much more potent than morphine, with 7-hydroxy mitragynine being 4 times more potent than mitragynine. It is widely used for opiate withdrawal and pain management. Adverse effects reported with kratom range from hypertension, tachycardia, agitation, lethargy, nausea, severe emesis, constipation, cognitive and behavioral impairment3 to more lethal effects like cardiotoxicity, renal failure, and hepatic injury.4 Kratom overdose is also associated with seizures,5 respiratory depression, hallucinations, coma, and cardiac arrest.6 There is extensive literature drawing conclusions between heroin and cocaine usage with rhabdomyolysis. But very few case reports reported that rhabdomyolysis is one of the effects of a kratom overdose. We present a case of a 45-year-old lady who used kratom for pain...
management and developed severe rhabdomyolysis leading to compartment syndrome, transient hearing loss, and heart failure. Thorough knowledge of kratom and its toxicities is essential to manage these appropriately especially with its increasing use.

**Case Report**

A 45-year-old Caucasian lady with a medical history of Crohn’s disease, breast cancer status post chemotheraphy, radiation a year ago, and bilateral mastectomy with reconstruction 2 months ago, and chronic pain, was brought in by emergency Medical Service after she had a passing out episode.

The patient had breast reconstruction surgery 2 months ago and suffered a burn injury from a heating pad used for postoperative pain. She started taking kratom 1 month ago for pain associated with burn injury. She was initially taking up to 6 capsules per day. As she was having uncontrolled pain, she increased the dose significantly 2 weeks after starting the drug. She gradually continued to escalate the dose to more than 10 pills per day until a couple of days before admission. The patient was taking extra kratom pills for the last 2 days and was experiencing diffuse body aches particularly right-sided pain, fatigue, and generalized weakness. Eight hours before admission, she took 2 more extra pills. She passed out for 6 hours. On subsequent regaining of consciousness, she was drowsy and noted worsening right lower extremity pain and swelling with difficulty ambulating and called Emergency Medical Service. She also reported an acute decrease in hearing. She denies fever, chills, chest pain, cough, shortness of breath, nausea, vomiting, abdominal pain, seizures, and focal neurological deficit.

Surgical history includes appendectomy, hysterectomy, Koch ileostomy, proctocolectomy, carpal tunnel, ureteral stents, surgery for bowel obstruction, breast reconstruction surgery, and burn wound status post debridement. She describes known medical allergies to penicillins, cephalosporins, vancomycin, and sulfa drugs. Family history was reviewed and was not contributory. She denied smoking, alcohol, or the use of other illicit drugs.

In the emergency room, vitals revealed 37.2 °C oral temperature, respiratory rate 20 breaths per minute, blood pressure 124/92 mm Hg, heart rate 99 beats per minute, saturation oxygen 95% on room air, and body mass index 22 kg/m². On examination, she had decreased right-sided hearing, she was noted to have significant swelling of the right lower extremity with tenderness to palpation and also has weakness on the right side. Pulse on the extremity was felt to be decreased but was noted on Doppler ultrasound. The rest of the examination is unremarkable.

While in emergency room, the patient underwent an initial workup for altered mental status with computed tomography (CT) brain, showing no acute finding. She underwent a CT neck for neck pain and swelling, which showed a nonspecific inflammatory change in the sternocleidomastoid muscle. CT thorax, abdomen, and pelvis showed pneumonia and probable colitis. Admission laboratory results and imaging are summarized in Tables 1 and 2.

**Clinical Course**

On admission, due to significant right lower extremity pain and swelling, an ultrasound lower extremity was done, which was negative for deep vein thrombosis. Surgery was consulted, who diagnosed the patient with compartment syndrome of the right lower extremity and planned emergent 4-compartment fasciotomy with wound vacuum-assisted closure placement. Postoperatively, the patient developed hypoxia with gross cyanosis of the upper body requiring intubation and mechanical ventilation. She noted to have worsening abnormal liver and renal function tests. Echo was done, which revealed ejection fraction (EF) <15%, a significant drop from the previous echocardiogram. She developed severe rhabdomyolysis causing acute kidney injury from acute tubular necrosis complicated with severe hyperkalemia prompting the initiation of hemodialysis emergently. She was aggressively hydrated on the presentation. Cardiology was consulted for low EF who recommended ischemic workup once more stable. After dialysis, the patient’s mental status improved, hearing loss resolved, and eventually extubated with improvement in liver function test and creatinine phosphokinase as summarized in Table 3. The patient underwent

| Table 1. Admission Laboratory Results. |
|---------------------------------------|
| Laboratory findings | Result | Normal range |
|----------------------|--------|-------------|
| WBC | 28.6 H | 4.10 × 10⁳/µL |
| Hemoglobin | 13.3 | 11.2-15.7 g/dL |
| Platelets | 664 | 163-369 × 10⁴/µL |
| Sodium | 140 | 136-144 mEq/L |
| Potassium | 6.5 H | 3.5-5.1 mEq/L |
| Chloride | 100 | 98-110 mEq/L |
| Bicarbonate | 22 | 20-30 mEq/L |
| BUN | 12 | 7-23 mg/dL |
| Creatinine | 1.72 H | 0.57-1.11 mg/dL |
| Glucose | 67 | 70-99 mg/dL |
| Calcium | 9.3 | 8.5-10.3 mg/dL |
| AST | 509 H | 5-42 units/L |
| ALT | 155 H | 5-49 units/L |
| Total bilirubin | 0.4 | 0.1-1.2 mg/dL |
| Alkaline phosphatase | 345 H | 35-141 units/L |
| Phosphorus | 6.5 H | 2.3-4.7 mg/dL |
| Total protein | 7.8 | 6.1-8.3 g/dL |
| CPK | >24 165 H | 43-237 units/L |
| Troponin | 5.6 H | 0.0-0.028 ng/mL |
| Urine drug screen | Negative |

Abbreviations: WBC, white blood cell; BUN, blood urea nitrogen; AST, aspartate aminotransferase; ALT, alanine aminotransferase; CPK, creatinine phosphokinase.
multiple debridements of the right lower extremity followed by final wound closure with a skin graft. Echocardiogram was repeated with a return to normal EF of 55%. She was eventually discharged home with home health care.

**Discussion**

Rhabdomyolysis is a breakdown of skeletal muscle leading to the release of intracellular contents into the plasma. It is predominantly caused by a crush injury, trauma, immobilization, alcohol abuse, illicit drugs including cocaine and heroin, electrolyte disturbances, heart stroke, and exertion. Rhabdomyolysis can be diagnosed early with serum and urine myoglobin and elevated creatinine phosphokinase. Prompt diagnosis and early treatment prevent life-threatening complications of rhabdomyolysis, which includes severe organ damage such as acute renal failure, hepatic injury, compartment syndrome, metabolic acidosis, disseminated intravascular coagulation, electrolyte disturbances including severe hyperkalemia, hyperphosphatemia, hypocalcemia, and hyperuricemia. Few case reports are available in the literature on kratom overdose causing rhabdomyolysis.4,7

Studies show that the adverse effects of kratom are heavily dose-dependent. It has been observed that excessively high doses of kratom, 15 g or more, can lead to severe toxic effects that deviate from the expected effects of kratom use.8 Given that high doses of kratom can cause unexpected severe effects, it is not highly unlikely that excessive kratom use could lead to rhabdomyolysis. The patient’s report of taking 10 pills of kratom per day could potentially be a significantly high dose to cause the unexpected toxic effect of rhabdomyolysis.

Given the similarities in the pharmacokinetics of scheduled stimulants and kratom, they differ in how they are available to the public. Since kratom is listed as a herbal supplement, the measures for regulation are not as extensive as seen with heroin, causing a rise in cases associated with kratom overdose. With the increasing concern with the safety of the drug and its high abuse potential, the Food and Drug Administration is advising consumers to be aware of the psychoactive compounds found in kratom, such as mitragynine and 7-hydroxy mitragynine, which is responsible for the high abuse potential.10 Treatment of kratom toxicity is mainly supportive, and benzodiazepines should be considered for seizures and naloxone for respiratory depression. Most of the deaths with kratom toxicity occur only when it is taken with a combination of other sedative drugs.11

**Conclusion**

Kratom is an emerging drug in the West and its use is increasing since the past decade especially due to its easy availability

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**Table 2. Imaging Studies.**

| CT brain | No acute findings |
| CT neck | CT neck nonspecific inflammatory change of the right sternocleidomastoid muscle |
| CT thorax, abdomen, and pelvis | Probable bilateral pneumonia of the upper lobes and right middle lobe versus post-radiation changes |
| | Mild edema of the sigmoid and descending colon suggestive of mild colitis |
| | No metastasis was identified |

Abbreviation: CT, computed tomography.

**Table 3. Trend of labs from day 1 to day 14.**

| Lab (normal value) | Day 1 | Day 2 | Day 3 | Day 7 | Day 14 |
|--------------------|-------|-------|-------|-------|-------|
| Potassium (3.5-5.1 mEq/L) | 6.5 | 7.6 | 5.4 | 3.8 | 3.6 |
| Creatinine (0.57-1.11 mg/dL) | 1.72 | 2.39 | 3.80 | 5.71 | 4.19 |
| AST (5-42 U/L) | 509 | 3113 | 2049 | 331 | 65 |
| ALT (5-49 U/L) | 155 | 573 | 503 | 184 | 52 |
| Phosphorus (2.3-4.7 mg/dL) | 6.5 | 7.9 | 7.0 | 6.0 | 5.4 |
| CPK (43-237 U/L) | 24165 | 42670 | 29286 | 6166 | 736 |
| Myoglobin (0-80 ng/mL) | >1200 | >1200 | >1200 | 979 | 330 |

Abbreviations: AST, aspartate aminotransferase; ALT, alanine aminotransferase; CPK, creatinine phosphokinase.
and potential use in managing pain. There is limited information available in the literature regarding its effects. Kratom overdose causing rhabdomyolysis, stress cardiomyopathy, and hearing loss have not been described. The mechanism of these effects is uncertain and more research is needed in this regard. It is essential for physicians to recognize the effects of kratom overdose and be familiar with treatment options. There is no antidote for kratom. Treatment of kratom overdose is mainly supportive care.

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VS, NS, KG, and MP conducted the chart review. VK, NS, KG, AR, AM, and MP contributed to writing the introduction, discussion, and conclusion. VS drafted the manuscript, and all authors contributed substantially to its revision.

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