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CASE REPORT

TOXICOLOGY

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A Drug Fatality Involving Kratom

ABSTRACT: A 17-year-old white man who showed no obvious signs of trauma was found unresponsive in bed and was pronounced dead at the scene. The decedent had a documented history of heroin abuse and chronic back pain and reportedly self-medicated with Kratom (mitragynine). The autopsy was remarkable only for pulmonary congestion and edema and a distended bladder, both of which are consistent with, though not diagnostic of, opiate use. A laboratory work-up revealed therapeutic levels of over-the-counter cold medications and benzodiazepines. However, of interest was a level of mitragynine at 0.60 mg/L. Given the facts of the case, the Medical Examiner certified the cause of death as "possible Kratom toxicity" and the manner of death was classified as "accident."

KEYWORDS: forensic science, mitragynine, Kratom, forensic toxicology, drug fatality, *Mitragyna speciosa*

An inherent plight in forensic toxicology is the infinite emergence of over-the-counter products that serve as "legal highs" or natural remedies. Many of these products induce clinical manifestations that mirror those caused by illicit substances. When antemortem clinical observations are noted, the forensic toxicologist can narrow down what to test for, that is, amphetamines/cocaine if stimulant abuse is suspected versus opiates/benzodiazepines if depressant abuse is suspected. However, with the genesis of designer, over-the-counter products the identification and analysis of such substances remains a challenge for the medical examiner and forensic toxicologist.

The case we are presenting herein involves a possible death resulting from Kratom use. Kratom (*Mitragyna speciosa*) is a leafy tree indigenous to southeast Asia and has been traditionally used for its purported medicinal properties. Kratom, which can be obtained through online sources, is used as a remedy for opioid withdrawal and can also be used recreationally (1–3). The effects of Kratom are attained by the predominant psychoactive substance mitragynine and 7-hydroxymitragynine, which serve as agonists for the opioid mu receptors (1–3). In low doses, mitragynine has a stimulatory effect, while having opioid-like effects following high doses (2).

Case Report

A 17-year-old white man was found unresponsive in bed and was pronounced dead by the EMS unit. The decedent was found supine with no obvious signs of trauma. A small amount of brown vomitus was noted on the decedent's face and on the floor next to him. The decedent had two backpacks that were on a nearby couch and in one of them was found the decedent's medications in a ziplock bag. There was also a box of Bali Kratom. The decedent's girlfriend gave the investigation team an empty bottle of liquid Kratom that the decedent had reportedly taken the night before. These were collected and brought to the Bexar County Medical Examiner's Office (Fig. 1). An empty bottle of promethazine that was prescribed to the decedent's girlfriend was found in the living room where the decedent was found. The decedent had a well-documented history of heroin abuse and chronic back pain, felt to be possibly due to a spinal syrinx. He reportedly self-medicated with Kratom to treat both conditions. There was also a history of depression with a single poorly documented suicide attempt in the past (method and date unknown). The decedent was brought to the Medical Examiner's Office for an autopsy and full toxicology work-up.

Examination of the decedent revealed a slender adolescent male with no remarkable external findings except for some faint transverse linear scars of the ventral left wrist. The autopsy was remarkable only for pulmonary congestion and edema (1100 g combined lung weight) and a distended bladder, both of which are consistent, though not diagnostic, of opiate use. There was no evidence of traumatic injury or anatomic evidence of potentially fatal natural disease, and histologic examination of major organs was either noncontributory or simply confirmed gross autopsy impressions.

Whole blood taken from the femoral vein (peripheral source) and vitreous fluid were analyzed for alcohols, alkaline drugs, acid-neutral drugs, opiates, cocaine, benzodiazepines, cannabinoids, oxycodone/oxymorphone, and fentanyl. Given the circumstances surrounding the case, mitragynine analysis was performed using liquid chromatography–tandem mass spectrometry. Briefly, the system used was an Agilent 1100 Series Liquid Chromatography coupled to an Applied Biosystems/MDS Sciex 3200 QTRAP MS/MS utilizing a C18 analytical column. The analysis was performed in multiple reaction monitoring mode monitoring transitions 399.2/174.2 and 399.2/151.9. No other metabolites of mitragynine were looked for. The blood analysis revealed those analytes and concentrations reported in Table 1. All the levels of therapeutic drugs were within reported "therapeutic limits" with the exception of a slightly elevated diphenhydramine concentration.

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FIG. 1—*The bag of Kratom and bottle of liquid Kratom found at the scene.*

TABLE 1—*All of the remarkable analytes found in whole blood analysis. All other drugs screened for were none detected.*

Dextromethorphan	0.28 mg/L
Diphenhydramine	0.33 mg/L
Temazepam	0.21 mg/L
7-amino-clonazepam	0.21 mg/L
Mitragynine	0.60 mg/L

Literature Review

Of interest was a mitragynine level of 0.60 mg/L. Unfortunately, there is a paucity of published case reports giving blood drug concentrations in Kratom/mitragynine fatalities. As such, no toxic or lethal ranges have been established. Nelsen et al. (4) reported a case involving a 64-year-old man who suffered a seizure following Kratom use. The authors reported that the individual suffered from a second seizure, while at the hospital and fell into a coma. A urine analysis by high-performance liquid chromatography confirmed the presence of mitragynine at a level of 167 ng/mL. Urine, however, can only be used as a qualitative assessment indicating use and concentrations are not correlated with impairment or level of toxic manifestations. Another report by Holler et al. (5) indicated a drug toxicity death involving the coadministration of both mitragynine and propylhexedrine. Liquid chromatography–tandem mass spectrometry revealed a mitragynine level in the blood of 0.39 mg/L. The ultimate cause of death was determined to be propylhexedrine toxicity and the manner of death was ruled as accidental. The authors concluded that mitragynine could have contributed to the demise, but because there was no data relating to mitragynine blood concentrations, the drug was not listed as contributing to death. Finally, Kronstrand et al. (6) looked at nine different fatality cases, all presenting within a year, in which both mitragynine and O-desmethyltramadol were found in the postmortem blood samples. Their analyses showed concentrations of mitragynine, as determined by ultra-performance liquid chromatography–tandem mass spectrometry, ranging from 0.02 to 0.18 μg/g blood. The authors concluded that mitragynine could have contributed to the deaths, but again because of the dearth of information regarding mitragynine blood concentrations, nothing definitive could be established.

Conclusion

The cause and manner of death determination in the current case rested largely on the interpretation of the role mitragynine played in the subject's demise. In this case, no other compelling cause of death was evident on investigation and examination of the decedent. A well-established history of opioid abuse, including Kratom abuse, was present and the active compound of this substance was identified in the decedent's blood. Other drugs found were not felt to be significantly related to death. Autopsy findings, while nonspecific, were consistent with deaths seen with opiates or similar compounds (pulmonary congestion and edema, urinary bladder distention). The mitragynine concentration in our case appears high in comparison with other reported fatal cases of Kratom intoxication, although each of the comparison cases did have other drugs present that were felt to have caused or contributed to death. With these considerations, the Medical Examiner certified the cause of death as "possible Kratom toxicity," with commentary in the autopsy protocol about the rationale for this decision and the somewhat speculative nature of the conclusion, given the paucity of data on the compound. In spite of a history of a previous suicide attempt and wrist scars consistent with possible remote incised wounds, there was no evidence in the current case to suggest that the compound was taken to intentionally cause death. For that reason, the manner of death was classified as "accident."

Because of the relatively sparse data on blood concentrations of mitragynine, particularly in fatal intoxication cases, interpretation of the demonstrated drug concentrations is particularly difficult. However, in any drug intoxication-related death case, the absolute concentration of the drug in blood or other tissues is of secondary importance to the correlation of that concentration with the scene investigation, medical history, autopsy findings, and other data. All of these data points must be established and considered in the formation of the most plausible and defensible opinion on the cause of death in an individual case, regardless of the absolute drug concentrations present.

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