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EDITORIAL COMMENT

A Kratomic Bomb

Cardiotoxicities From *Mitragyna speciosa* Extract

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"I made one great mistake in my life, when I signed a letter to President Roosevelt recommending that atom bombs be made."
—Albert Einstein

Kratom (*Mitragyna speciosa*), a plant native to Southeast Asia, has been traditionally used for centuries to alleviate muscle pain and fatigue. Typically ingested as a tea or powder, kratom exhibits both opioid-like effects (anxiolytic and sedative) and stimulant properties, contributing to its increasing popularity in Western countries in recent years.[1]

In this issue of *JACC: Case Reports*, Miller et al[2] present a case of type I Brugada pattern associated with kratom use in an asymptomatic individual. Gas chromatography mass spectrometry proved the presence of the active metabolites of kratom in serum samples obtained during presentation and, importantly, the absence of other confounding substances. The case is illustrative of the different physiologic manifestations unregulated substances may have on our patients, and the importance of careful history-taking, as these substances will not be evident with routine toxicology testing.

Brugada syndrome (BrS) was initially described as an autosomal-dominant arrhythmic disorder marked by ST-segment elevation followed by negative T waves in the right precordial leads, occurring in the absence of structural cardiac abnormalities, predisposing affected individuals to ventricular tachyarrhythmias and sudden cardiac death.[3] Although a type 1 electrocardiogram (ECG) pattern (coved ST-segment elevation) is diagnostic for BrS and the highest risk for subsequent arrhythmia, less definitive type 2 and type 3 patterns (saddle-back ST-segment elevation) typically require a provocative challenge with class I antiarrhythmic agents, such as procainamide or flecainide, for confirmation. Several clinical factors, including fever, tricyclic antidepressants, lithium, antihistamines, cocaine, calcium channel blockers, and anesthetics like propofol and bupivacaine, can precipitate spontaneous type 1 BrS ECG changes in individuals with normal baseline ECG.[4] The case report by Miller et al[2] compels us to add another agent, kratom, to the list. Because these substances accentuate or unmask the Brugada pattern, it is plausible that these drugs further disrupt the balance of inward and transient outward currents in the right ventricular outflow tract, which trigger the characteristic surface ECG pattern of BrS, and in the worst case, result in phase 2 reentry and sudden death. Indeed, instances of sudden death with kratom and other agents are abundant. Although causality is not proven, it is likely cases such as these require a genetic predisposition or a subclinical BrS genotype that results in the drug-induced phenotype.

The active metabolites of kratom, mitragynine and 7-hydroxymitragynine, have been shown to inhibit potassium channels in a concentration-dependent manner, but the electrophysiologic reason for resulting in a Brugada pattern, such as sodium channel blockade or transient outward current potentiation, is not known.[5] A large host of other alkaloids present in kratom may be equally culpable for these effects.[6] It is worth noting that the authors tested the sample of kratom used by the patient for other contaminants to rule out alternate causes of drug-related BrS, which distinguishes it from other prior cases of kratom-related Brugada.

Miller et al[2] are to be congratulated on a case that highlights a potentially lethal ECG pattern related to kratom use. This is one of just a few emerging cases of

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this ECG pattern related to kratom. The case highlights the particularly dangerous aspects of this substance: 1) kratom is widely known to have some psychotropic properties, that is, it is not just a gimmick or placebo; 2) it is relatively mild in potency, which encourages larger doses, thereby increasing the risk of nontarget organ effects; 3) it contains up to 40 alkaloids whose effects on other organ systems are essentially unstudied; and 4) kratom is either loosely regulated or completely unregulated in terms of ingredient standards and commercial availability. Only case reports like these and larger published clinical experience will determine whether kratom will be the next atomic threat in the substance abuse war.

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