Brodifacoum Poisoning Linked to Synthetic Marijuana Use in Wisconsin

Madison Kircher, Jude Perez, MD

ABSTRACT

Introduction: Recent outbreaks of brodifacoum-induced coagulopathy resulting from the use of synthetic cannabinoids represents a growing public health concern. Brodifacoum is a commonly used and commercially available rodenticide that has anticoagulant properties. As new, unregulated synthetic cannabinoids enter the market, the potential for further outbreaks continues to rise.

Case Presentation: We report a case of severe bleeding secondary to inhalation of synthetic cannabinoids contaminated with brodifacoum. The patient had been evaluated for several months of ongoing, unexplained vaginal bleeding and developed hematemesis and rectal bleeding 2 weeks after her last reported use.

Discussion: There have been previous reports of hemorrhage after exposure to synthetic marijuana in rare cases, including an outbreak of severe bleeding and reported synthetic marijuana use in the Midwestern region of the United States in 2018.

Conclusion: While hemorrhaging after exposure to synthetic cannabinoids has been reported previously, we use this case to increase awareness of the potentially deadly exposures to brodifacoum from synthetic cannabinoids use in Wisconsin. By increasing awareness, emergency department physicians and state agencies can collaborate more effectively when responding in these cases.

INTRODUCTION

Brodifacoum is a highly lethal vitamin K antagonist anticoagulant poison.[1] Vitamin K is an essential cofactor for the synthesis of blood-clotting factors.[1] Brodifacoum acts as a blood thinner by inhibiting vitamin K epoxide reductase, an enzyme required for the recycling of Vitamin K.[1] It has been called "superwarfarin" because it acts similarly to warfarin, the leading anticoagulation therapy. However, at the same molecular dose, brodifacoum is 100 times more potent than warfarin.[1] Developed in 1975 to combat warfarin-resistant rodents, brodifacoum has become one of the most widely used, commercially available rodenticides in the world. While the half-life of warfarin is between 20 to 60 hours, the half-life of brodifacoum is estimated to be between 20 and 130 days,[2] and it can remain active in the body for 2 to 9 months after exposure.[3] Recently, brodifacoum poisoning has been linked to synthetic cannabinoid use.

Synthetic cannabinoids are a class of manufactured chemicals that act on the same receptors as tetrahydrocannabinol (THC), the main active ingredient in marijuana.[2] Synthetic cannabinoids are typically manufactured abroad and were first reported in the United States in 2008.[2] There are hundreds of synthetic cannabinoids that have been widely available at convenience stores and through the internet under names such as "K2" and "Spice." However, there are no standards for manufacturing, packaging, or selling of synthetic cannabinoids. In recent years, many of these chemicals have been banned by federal and state governments.[4]

CASE DESCRIPTION

In 2019, a 29-year-old woman presented to the emergency department (ED) at a community hospital with vaginal bleeding, rectal bleeding, and hematemesis. She had been seen at an outside facility 2 months prior for vaginal bleeding and was diagnosed

• • •

Author Affiliations: University of Wisconsin School of Medicine and Public Health, Madison, Wis (Kircher, Perez).

Corresponding Author: Madison Kircher, MPH Candidate, University of Wisconsin School of Medicine and Public Health, 4600 University Ave #305-D, Madison, WI 53705; phone 507.250.5462; email mrkircher@wisc.edu.

Published online April 27, 2020.

with dysfunctional uterine bleeding and started on oral birth control. She also was seen in the same ED 2 days prior for continued vaginal bleeding. During this visit, she had an abdominal x-ray and lab work that were unremarkable, including a normal platelet count and negative pregnancy test. Her hemoglobin was 10.8 g/dL at that visit, so follow-up with her gynecologist was recommended and she was discharged home. She denied illicit drug use at this time.

The patient returned to the ED 2 days later reporting worsening vaginal bleeding in addition to new rectal bleeding and 1 episode of hematemesis during the previous night. She also had developed bruising to her bilateral lower extremities. She was confirmed to be previously healthy with no prior episodes of unexplained bleeding. During this visit, she reported recent use of synthetic marijuana. She stated that she initially withheld information about the drug use because she had been using synthetic marijuana intermittently since she was released from jail and was concerned it would be a violation of her probation.

During evaluation, the patient's hemoglobin was 5.6 g/dL, a marked decrease from 2 days prior. Her international normalized ratio (INR) resulted as "no clot detected," meaning it was above the highest detectable value. Her partial thromboplastin time was approximately 130 seconds, and her platelet count was slightly elevated at 477. Her basic metabolic panel was normal, with the exception of glucose of 159, bicarbonate of 21, and calcium of 7.8. Her liver function test was normal, and her fibrin split products level was negative. She was unable to provide a urine sample for a urine drug screen test and refused catheterization. Synthetic marijuana is not part of the typical urine drug screen testing. The medical team also contacted poison control, who advised that a blood sample be collected and sent to the Wisconsin State Lab of Hygiene for brodifacoum testing. She tested positive for brodifacoum with a level of 127. Expected concentrations in the population fall below the limit of quantification.

The patient was started on blood transfusions and intravenous vitamin K. She also was given 4-factor prothrombin concentrate complex (Kcentra). She was subsequently transferred to a trauma center that had hematologists and intensivists available. She was admitted to the intensive care unit for monitoring and management of blood loss in the setting of acute chemical induced coagulopathy. She remained in the hospital for 4 days until her INR stabilized. When she was discharged, she was started on 50 mg of vitamin K 3 times per day. She also was scheduled to have her INR checked weekly. Once her INR normalized about 3 to 6 months later, she was weaned off vitamin K. During her most recent visit, her INR was 1.02. At this point, she was lost to follow-up.

DISCUSSION

Many recent outbreaks of brodifacoum-induced coagulopathy have been linked to synthetic cannabinoid use, including a multistate outbreak in the Midwest in 2018 of individuals suffering from severe bleeding and reported synthetic cannabinoid use. At least 324 individuals presented to health care facilities with serious bleeding from possible exposures, with the largest number of cases in Illinois (164) and Wisconsin (86).[5] Laboratory investigation confirmed brodifacoum exposure in at least 150 patients, and there were at least 8 fatalities associated with the outbreak.[5] At this time, no information is available about the factors contributing to differences in survival among these patients. The rationale for combining brodifacoum with synthetic cannabinoids also remains unknown.

There are 12 manufacturing sites for brodifacoum in the world, including 1 site in Madison, Wisconsin.[6] Thus, physicians in the area need to be aware of this potentially deadly condition to begin aggressive treatment as soon as possible. The prolonged half-life of this chemical requires extensive treatment with high-dose vitamin K supplements over long periods of time. Vitamin K supplements are currently the only available treatment option. However, this treatment is expensive, costing $24,000 to $34,000 for a 1-month supply, which can result in medication noncompliance and additional hospital visits.[3]

In response to the recent outbreaks, a laboratory test was developed at the Wisconsin State Lab of Hygiene to quantify the amount of brodifacoum in the blood.[7] By quantifying the amount of this chemical in the blood, patients with brodifacoum poisoning can be treated with a precisely calibrated dose of vitamin K, and treatment can be ended when it is no longer medically necessary. Additionally, this test provides better information on the threshold of brodifacoum that leads to excessive bleeding.[7] However, for this test to be useful and beneficial to patients, physicians must send blood samples to the State Lab of Hygiene.

Research has shown that social factors affect health, but physicians are not always made aware of social issues affecting their patient's lives. Physicians often face challenges obtaining accurate histories from patients who withhold relevant information, such as drug use. By reassuring patients that this information will not be used against them and may be vital to their health and safety, physicians may be able to obtain a more accurate history. This case demonstrates the importance of asking questions about social history when patients present to the ED, particularly if their chief complaint involves abnormal bleeding. It also highlights the difficulty of maintaining contact and providing appropriate care for patients with complex social histories.

CONCLUSION

This case report seeks to increase awareness of brodifacoum exposure from synthetic marijuana use in Wisconsin. The number

Published online April 27, 2020.

of cases has increased in recent years, and it will continue to be important for physicians to recognize these cases and respond efficiently and effectively. By increasing awareness of this condition and increasing collaboration between local hospitals and state agencies, health care professionals in the region can be better prepared to address outbreaks and protect public health.

Funding/Support: None declared.

Financial Disclosure: None declared.

REFERENCES

1. Shahid Z, Kalayanamitra R, Hanafi M, Anwar K, Jain R. Sugar, spice, and bleeding. *Cureus*. 2019;11(4):e4437. doi:10.7759/cureus.4437

2. Ross CH, Singh P, Simon EL. Hemorrhagic soft tissue upper airway obstruction from brodifacoum-contaminated synthetic cannabinoid. *J Emerg Med*. 2019;57(1):47-50. doi:10.1016/j.jemermed.2019.03.007

3. Kelkar AH, Smith NA, Martial A, Moole H, Tarantino MD, Roberts JC. An outbreak of synthetic cannabinoid–associated coagulopathy in Illinois. *N Engl J Med*. 2018;379(13):1216-1223. doi:10.1056/NEJMoa1807652

4. Alipour A, Patel PB, Shabbir Z, Gabrielson S. Review of the many faces of synthetic cannabinoid toxicities. *Ment Health Clin*. 2019;9(2):93-99. doi:10.9740/mhc.2019.03.093

5. Centers for Disease Control and Prevention. Update—outbreak of life-threatening coagulopathy associated with synthetic cannabinoids use. Health Alert Network CDCHAN-00416. December 10, 2018. Accessed July 24, 2019. https://emergency.cdc.gov/han/han00416.asp

6. Brodifacoum, CID=54680676. PubChem Database. National Center for Biotechnology Information. Accessed July 24, 2019. https://pubchem.ncbi.nlm.nih.gov/compound/brodifacoum

7. Klawitter J. Lab culture extra: how the Wisconsin state lab developed a test for brodifacoum and why it matters. Association of Public Health Laboratories Lab Blo. April 3, 2019. Accessed July 28, 2019. http://www.aphlblog.org/lab-culture-extra-wisconsin-state-lab-developed-test-brodifacoum-matters/

Published online April 27, 2020.