Potashev Aleksandr/shutterstock.com

Abstract

Currently, cannabis is legal in 38 U.S. states in some form. Tetrahydrocannabinol (THC) intoxication from marijuana consumption has become a common presentation in all types of veterinary practices across the country. This case report reviews THC intoxication and its treatment with a focus on an unusual route of exposure in a patient with a complex medical history.

CASE REPORT: EMERGENCY MEDICINE/CRITICAL CARE

A New High and a New Low: An Unusual Case of THC Intoxication

***Alice Murtas**, BS, CVT, VTS (ECC)*
Veterinary Emergency Group, Chicago, Illinois

Tetrahydrocannabinol (THC) intoxication is becoming a common presentation in veterinary emergency rooms across the country. Emergency management of THC intoxication can be simple and does not always involve advanced interventions beyond general supportive care and intravenous lipid emulsion (ILE) therapy. Patients that present with this common exposure often experience an uncomplicated recovery. When a patient presents with severe intoxication, careful consideration must be taken to weigh the risk versus benefit of available therapies for that individual patient, based on history as well as signs at presentation.

HISTORY AND PRESENTATION

Mahi, a 4-year-old, 25-kg, spayed female golden

Take-Home Points

- Tetrahydrocannabinol (THC) intoxication has become a common reason for animals to present to veterinary emergency rooms across the United States.
- Identifying potential exposure and having candid, nonjudgmental conversations with clients can help direct treatment and rule out other, more serious presentations.
- Signs of THC intoxication include bradycardia, ataxia, hyperesthesia, respiratory depression, nausea, mydriasis, urinary incontinence, hypothermia, and seizure. These signs can also be attributed to several other neurologic pathologies.
- More than 65% of THC is excreted in feces in various forms, including the predominant metabolite (11-hydroxy-Δ9-THC), which is psychoactive.
- Ingestion of human feces containing THC and its metabolites is a potential route for intoxication in dogs.
- Common over-the-counter drugs-of-abuse home-use tests can be used in veterinary practices to evaluate for THC in the urine; however, dogs often have significant clinical signs of THC intoxication before these tests show a positive result.
- Treatment of THC intoxication can include observation, hospitalization, supportive care, intravenous lipid emulsion (ILE) therapy, and/or extracorporeal therapy.
- ILE can be used to "shuttle" lipophilic intoxicants like THC to the liver and digestive system for excretion.
- ILE should be used with caution in patients with preexisting liver or pancreatic disease.

retriever mix, presented to the emergency department for evaluation of suspected THC ingestion. That afternoon, Mahi had ingested feces from a person who had consumed an unknown number of marijuana edibles the previous day. Subsequently, over the course of a few hours, Mahi became ataxic, exhibited urinary incontinence, and became progressively more sedate. The owner did an internet search, realized Mahi was showing signs of THC ingestion from the feces, and brought her to the emergency room.

Mahi had a history of immune-mediated meningitis and elevated liver enzymes. At presentation, she was being treated with prednisolone and was on a tapering oral dose of 0.2 mg/kg once a week. Her last dose was given 24 hours prior to presentation. In her history, it was noted that a suspected intolerance of the drug mycophenolate, an immunosuppressant, was possibly responsible for her historical liver enzyme elevations. That drug had been discontinued 11 months prior to this encounter.

Four hours after completion of the first ILE CRI, Mahi was still unable to stand and minimally responsive. The ILE CRI was then repeated at the same dose of 380 mL/h for 1 hour.

INITIAL ASSESSMENT, DIAGNOSTIC TESTING, AND DIAGNOSIS

On presentation to the emergency service, Mahi was laterally recumbent and obtunded. Her heart rate was 100 beats per minute (bpm; normal, 80 to 120 bpm) and her pulses were strong and synchronous. Her temperature was 36.3 °C (97.3 °F; normal, 38 °C to 39.2 °C [100.5 °F to 102.5 °F]), respiration rate was 32 breaths per minute (normal, 20 to 40 breaths/min), and mucous membranes were pink (normal) with a capillary refill time (CRT) of 1 to 2 seconds (normal, <2 sec). While the physical examination was being performed, Mahi began to retch and was held in sternal recumbency as she began to vomit. Mahi was dribbling urine and remained obtunded.

A free-catch urine sample was submitted for a urine drug screen (UDS) test (One Step Drugs-of-Abuse Screening Test; InTec Products, **intecasi.com**) and blood was collected for i-STAT Chem8+ (Zoetis, **zoetisus.com**) and packed cell volume with total solids (PCV/TS) analysis. The UDS test results were positive for THC, and the serum biochemical profile and PCV/TS (40%/7.4 mg/dL; reference range, 35% to 50%/5.4 to 8.2 mg/dL) were within normal limits relative to analyzer reference ranges with the exception of 1+ plasma lipemia (normal, clear). The diagnosis was suspected THC intoxication.

TREATMENT

Mahi was held in sternal recumbency and an 18-gauge IV catheter was aseptically placed in her right cephalic vein. She was started on a constant-rate infusion (CRI) of Normosol-R, a crystalloid, at 90 mL/kg/day. She was also given 10 mg IV of ondansetron, a serotonin receptor antagonist (antiemetic), and 24 mg IV of pantoprazole, a proton pump inhibitor; these doses were subsequently scheduled to repeat every 8 hours and every 12 hours, respectively.

After medication administration was complete, the IV catheter was flushed with 0.9% saline and 38 mL (1.5 mL/kg) of ILE 20% was administered intravenously as a bolus over 5 minutes. This was followed by an ILE CRI of 380 mL/h (15 mL/kg) for 1 hour. Mahi's vitals were monitored and were stable throughout the ILE infusion. Normosol-R was restarted at a CRI of 90 mL/kg/day.

Mahi's intensive care veterinary nurse was responsible for monitoring her vitals, administering her medications, conducting recumbent patient care and passive range of motion exercises, and reporting any changes in her neurologic status. Mahi was scheduled for a CRI of the same dose of ILE 4 hours later if neurologic signs persisted. Mechanical ventilation and extracorporeal therapies (ECTs) were discussed but were not available on site.

Four hours after completion of the first ILE CRI, Mahi was still unable to stand and minimally responsive. The ILE CRI was then repeated at the same dose of 380 mL/h for 1 hour. Her vitals were as follows: heart rate, 72 bpm; respiration rate, 24 breaths/min; mucous membranes, pink; CRT, <2 sec; temperature, 37 °C (98.6 °F). Six hours later, she was much more alert but still unable to stand on her own.

The following morning, Mahi was still very sedate, but brighter and more alert than the night before. She had a persistent low heart rate (68 bpm) and would not walk or stand. Her temperature was 39.7 °C (103.5 °F). She was given another 380 mL of ILE over 1 hour at 10 AM. At 1 PM she went out on a walk and was slightly more alert. She vomited bile around 2 PM and was given a 1 mg/kg IV dose of maropitant for nausea. She did not have any interest in food. At this time, her temperature had come down to 39.4 °C (102.9 °F).

Mahi was discharged to her owner around 3 PM with hopes that her recovery would continue in the comfort of her own home without the need for further medication, like most THC intoxication patients. Her owners were instructed to offer her normal diet and to return for continued care if there was no improvement or if additional signs or concerns were noted.

RECOVERY

Four days after the initial exposure, Mahi returned to the emergency room with vomiting and diarrhea. She was described as still being "spacey and aloof." She was again hospitalized. The suspicion was severe pancreatitis. The relationship between ILE therapy and pancreatitis, as well as the necessity of that therapy at the time, were discussed, and a plan was formulated that included rehydration, pain management, abdominal ultrasonography, a neurology consultation, and possible nasogastric tube placement. Parameters for potential future discharge were also discussed and included being afebrile, eating well enough to sustain her resting energy requirement, and a transition to oral medications with a continued appetite.

Ultrasonography supported the diagnoses of pancreatitis and hepatopathy. She was treated supportively and began to eat after 24 hours. She was discharged with the addition of oral metronidazole, tramadol, gabapentin, omeprazole, and maropitant to her original once-weekly dose of prednisolone. Mahi went home with a supply of a low-fat digestive care diet and instructions to monitor her appetite closely.

Nine days after the initial exposure, Mahi visited her primary veterinarian for continued inappetence and lethargy and was subsequently transferred to an internist for further hospitalization. She was discharged 48 hours later with the addition of enrofloxacin and a nutraceutical liver supplement. Under the internist's close supervision, she avoided further hospitalization. However, her liver enzymes did not normalize until nearly 2 months after her dietary indiscretion (**TABLE 1**).

DISCUSSION

Currently, 38 U.S. states have legalized the use of cannabis in some form.[1] The legalization of marijuana can be correlated to an increase in the number of pets presenting for THC intoxication.[2]

Symptoms of THC intoxication include bradycardia, ataxia, hyperesthesia, respiratory depression, nausea, mydriasis, urinary incontinence, hypothermia, and seizures. For dogs, the minimum lethal oral dose of THC is more than 3 g/kg,[3] making THC a drug with a relatively high margin of safety. Deaths have been reported but are considered rare.

TABLE 1 Timeline of Liver Function Results

ANALYTE (REFERNCE RANGE)	2/6	2/9	2/11	2/15	2/17	2/19	3/2	4/4
Glucose (63–114 mg/dL)	101	113	n/a	n/a	108	83	97	89
Blood urea nitrogen (9–31 mg/dL)	13	31	7	7	5	15	13	13
Creatinine (0.5–1.5 mg/dL)	0.6	1.3	n/a	n/a	n/a	0.6	0.6	0.8
Alanine transaminase (18–121 U/L)	n/a	100	80	759	1373	943	136	58
Alkaline phosphatase (5–160 U/L)	n/a	206	242	>2400	5149	5962	1459	74
Total bilirubin (0–0.3 mg/dL)	n/a	0.6	0.5	5.6	6.8	4.9	0.7	0.2

n/a = not available

The most abundant psychoactive compound in marijuana is Δ-9-tetrahydrocannabinol (Δ-9-THC), generally referred to as simply THC. THC is highly lipid soluble[4] and is distributed in fat, liver, brain, and renal tissue (**FIGURE 1**). Only 20% of THC is excreted in urine; most of the rest is eliminated in feces through biliary excretion.[4]

Commonly, over-the-counter drugs-of-abuse tests are used in veterinary practice to evaluate for THC in the urine. This is an imperfect method,[5] as it typically relies on the concentration of the measured metabolite—an inactive compound—to exceed 5 ng/dL to generate a positive result. Canine patients often have significant clinical signs before that concentration is reached. Treatment of THC intoxication can include as little as observation and as much as hospitalization, supportive care, ILE therapy, and even ECT.[6]

What distinguished Mahi's case was the unusual type of exposure, the duration of clinical signs, and the protracted path to recovery.

Route of Exposure

Mahi ate human feces. A retrospective study published in 2022 highlighted this route of exposure in 15 dogs.[7] Feces is composed of bacterial biomass, undigested carbohydrate, fiber, fats, and protein. Depending on the dietary choices of the person responsible for producing the stool, the fat content could have exceeded that of Mahi's normal diet. Her plasma was lipemic before lipid administration, making this a dietary indiscretion with potential complications independent of the THC component.

More than 65% of Δ-9-THC is excreted in the stool in various forms,[4] including the predominant metabolite, 11-hydroxy-Δ9-THC (11-OH-Δ9-THC). This psychoactive compound is responsible for the psychological "high" experienced by cannabis users.[8] Mahi potentially directly ingested this potent metabolite, which may explain how she was so profoundly affected. A less abundant metabolite of cannabis, Δ-8-THC, is known to cause central nervous system depression in humans.[9]

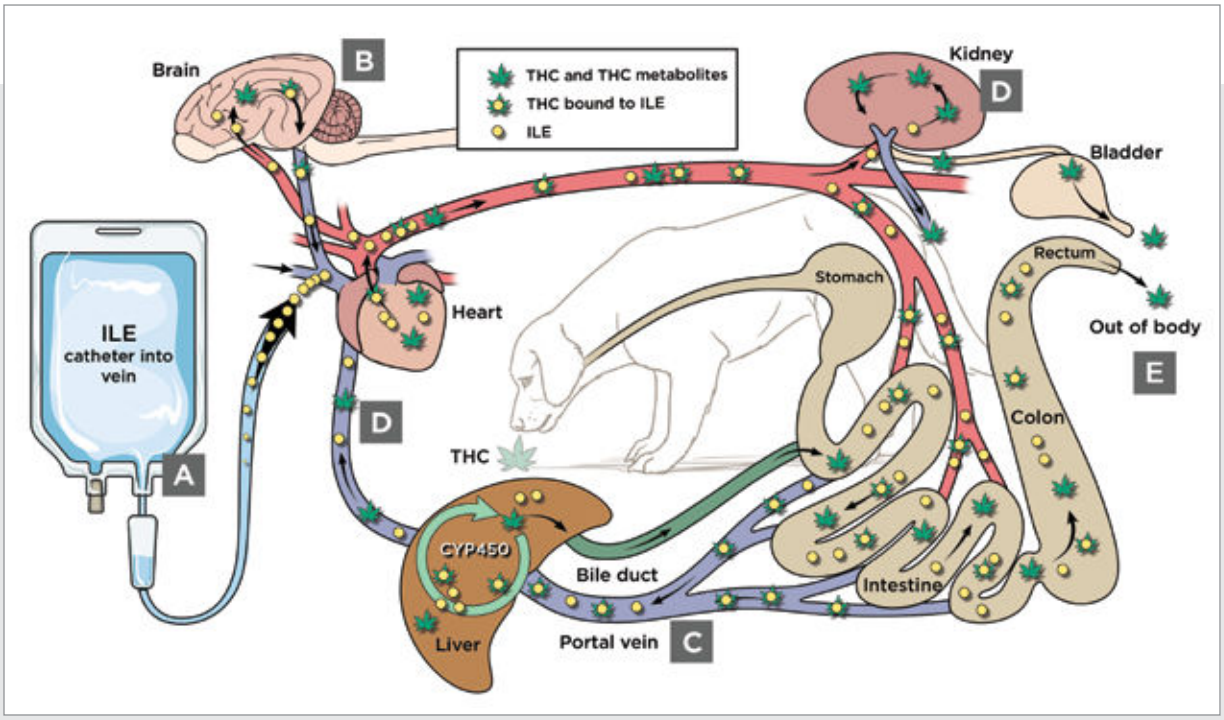

FIGURE 1. The "lipid shuttle" is a theoretical explanation for the effect of ILE on lipophilic intoxicants like THC. In this model, ILE scavenges THC and its metabolites from affected organs. After ingestion, THC is metabolized by CYP450 enzymes in the liver and is then deposited in the brain, heart, kidney, liver, and adipose tissue. **(A)** ILE is infused intravenously and carried to the organs. **(B)** THC that has been deposited in the organs binds to ILE. **(C)** THC bound to ILE is carried through the circulation to the liver for further metabolism. **(D)** Some THC metabolites (about 20%) are excreted in the urine.[4] **(E)** Most (65%–80%) of THC metabolites are excreted in feces.[4]
CYP 450 = cytochrome P450, ILE = intravenous lipid emulsion, THC = tetrahydrocannabinol

Figure 1: Kip Carter

The use of ILE in veterinary patients has been established for many lipophilic intoxicants.[10] It is postulated that ILE shuttles these toxins (such as THC) from other organs to the liver for metabolism (**FIGURE 1**). It is known that THC undergoes hepatic metabolism, with 10% to 15% of metabolites undergoing enterohepatic recirculation.[11] In humans, metabolites of THC have been found to inhibit major hepatic cytochrome P450 (CYP450) enzymes.[12] Canine patients also rely on this family of enzymes to metabolize all kinds of drugs, including THC. It is unknown in Mahi's case if she had any liver dysfunction at the time of her dietary indiscretion, as those values were not evaluated on presentation. She did, however, have a history of previously elevated liver enzymes and had lipemic plasma prior to ILE therapy. In cases of liver disease, CYP450 enzyme activity has been shown to be affected.[13] This may account for her profound clinical signs at presentation, as THC relies on these enzymes for metabolism. Her subsequent escalating hepatic injury may have been the result of hyperlipidemia, pancreatitis, and associated inflammation.

The use of ILE in veterinary patients has been established for many lipophilic intoxicants.[10] It is postulated that ILE shuttles these toxins (such as THC) from other organs to the liver for metabolism.

Prolonged Recovery

One factor in Mahi's case was her protracted neurologic symptoms. Her history of immune-mediated meningitis was a consideration, and her neurologic status was monitored by her intensive care veterinary nurse at regular intervals. One tool that can be used to assess changes in neurologic status for comatose or obtunded patients is the Modified Glasgow Coma Scale (MGCS). The MGCS is an objective assessment tool for evaluating neurologic status. Mahi was not assigned an MGCS score. Use of this tool at presentation may have been beneficial for her subsequent assessments.

Mahi also experienced severe acute pancreatitis (SAP). This led to hyperlipidemia and likely hypertriglyceridemia. In patients with SAP, activated digestive enzymes attack the pancreatic acinar cells and hepatocytes, simultaneously inducing neutrophils to release a large number of inflammatory factors such as tumor necrosis factor and interleukins 1, 6, and 8, which can lead to a systemic inflammatory response causing damage to multiple organs, ultimately leading to multiple organ dysfunction.

Mahi was obtunded at presentation, and concerns included potential aspiration pneumonia, coma, and respiratory arrest without emergent intervention. ILE therapy is generally chosen when standard resuscitation measures are insufficient. The relationship between ILE, hyperlipidemia, and pancreatitis is multifactorial and poorly understood. It has been found that dogs with pancreatitis can have increased serum concentrations of triglycerides and/or cholesterol. Specific lipoproteins have been correlated with pancreatitis.[14] Increased serum triglyceride levels have been associated with canine lipase immunoreactivity concentrations in dogs.[15] Typically, ILE administration is contraindicated in patients with abnormal lipid metabolism, hyperlipidemia, or severe liver damage.[16] In Mahi's case, it was a calculated risk.

SUMMARY

Emergency management of THC intoxication can be simple and does not always involve advanced interventions beyond general supportive care and ILE therapy. Patients that present with this exposure often experience an uncomplicated recovery. Mahi was not that patient. Her severe level of intoxication and preexisting conditions made her unique, and although alternatives to repeated ILE treatments such as mechanical ventilation and ECT were not an option, in retrospect, more conservative use of ILE therapy and the addition of early aggressive supportive care—such as nasogastric feeding, early antibiotic therapy, and close monitoring of gastrointestinal and liver function based on her history—might have been warranted. However, it is unknown whether these measures would have been enough to dampen the impact of this unique intoxication.

Little is known about the impact of 11-OH-Δ9-THC ingestion and the ingestion of other metabolites of Δ-9-THC. It is impossible to say what benefit any of

these unexplored treatment avenues may have had. The relationship between the ingestion of commonly known metabolites of THC such as 11-OH-Δ9-THC and Δ-8-THC and increased or prolonged clinical signs warrants further research. TVN

References

1. National Conference of State Legislatures. State medical cannabis laws. Updated June 22, 2023. Accessed July 17, 2023. https://www.ncsl.org/research/health/state-medical-marijuana-laws.aspx
2. Meola SD, Tearney CC, Haas SA, Hackett TB, Mazzaferro EM. Evaluation of trends in marijuana toxicosis in dogs living in a state with legalized medical marijuana: 125 dogs (2005–2010). *J Vet Emerg Crit Care*. 2012;22(6):690-696. doi:10.1111/j.1476-4431.2012.00818.x
3. Fitzgerald KT, Bronstein AC, Newquist KL. Marijuana poisoning. *Top Companion Anim Med*. 2013;28(1):8-12. doi:10.1053/j.tcam.2013.03.004
4. Sharma P, Murthy P, Bharath MS. Chemistry, metabolism, and toxicology of cannabis: clinical implications. *Iran J Psychiatr*. 2012;7(4):149-156.
5. Teitler JB. Evaluation of a human on-site urine multidrug test for emergency use with dogs. *JAAHA*. 2009;45(2):59-66. doi:10.5326/0450059
6. Culler CA, Vigani A. Successful treatment of a severe cannabinoid toxicity using extracorporeal therapy in a dog. *J Vet Emerg Crit Care*. 2019;29(6):674-679. doi:10.1111/vec.12899
7. Lauinger CA, Peacock R. Marijuana toxicosis in dogs in Melbourne, Australia, following suspected ingestion of human faeces: 15 cases (2011-2020). *Aust Vet J*. 2022;100(3):90-97. doi:10.1111/avj.13134
8. Lemberger L, Martz R, Rodda B, Forney R, Rowe H. Comparative pharmacology of Δ 9-tetrahydrocannabinol and its metabolite, 11-OH-Δ 9-tetrahydrocannabinol. *J Clin Invest*. 1973;52(10):2411-2417.
9. Tagen M, Klumpers L. Review of Delta-8-tetrahydrocannabinol (Δ8-THC): comparative pharmacology with Δ9-THC. *Br J Pharmacol*. 2022;179(15):3915-3933. doi:10.1111/bph.15865
10. Fernandez AL, Lee JA, Rahilly L, Hovda L, Brutlag AG, Engebretsen K. The use of intravenous lipid emulsion as an antidote in veterinary toxicology. *J Vet Emerg Crit Care*. 2011;21(4):309-320. doi:10.1111/j.1476-4431.2011.00657.x
11. Garrett ER, Hunt CA. Pharmacokinetics of Δ9-tetrahydrocannabinol in dogs. *J Pharma Sci*. 1977;66(3):395-407. doi:10.1002/jps.2600660322
12. Nasrin S, Watson CJ, Perez-Paramo YX, Lazarus P. Cannabinoid metabolites as inhibitors of major hepatic CYP450 enzymes, with implications for cannabis-drug interactions. *Drug Metab Dispos*. 2021;49(12):1070-1080. doi:10.1124/dmd.121.000442
13. Frye RF, Zgheib NK, Matzke GR, et al. Liver disease selectively modulates cytochrome P450–mediated metabolism. *Clin Pharmacol Ther*. 2006;80(3):235-245. doi:10.1016/j.clpt.2006.05.006
14. Xenoulis PG, Cammarata PJ, Walzem RL, Suchodolski JS, Steiner JM. Serum triglyceride and cholesterol concentrations and lipoprotein profiles in dogs with naturally occurring pancreatitis and healthy control dogs. *J Vet Intern Med*. 2020;34(2):644-652. doi:10.1111/jvim.15715
15. Xenoulis PG, Suchodolski JS, Ruaux CG, Steiner JM. Association between serum triglyceride and canine pancreatic lipase immunoreactivity concentrations in miniature schnauzers. *JAAHA*. 2010;46(4):229-234. doi:10.5326/0460229
16. Plumb DC. *Plumb's Veterinary Drug Handbook: Desk*. 9th ed. Wiley-Blackwell; 2018.

Alice Murtas
Alice is a nursing trainer at Veterinary Emergency Group in South Loop, Chicago. She began her career in emergency and critical care medicine in 1993, earned her CVT credential in 2012 and her VTS (ECC) credential in 2020, and most recently became a RECOVER certified instructor. In addition to a 30-year career in emergency and critical care, her professional experiences include ophthalmology, shelter medicine, primary care practice, veterinary home health care, leadership, and teaching. When she is not working, she may be found cooking, gardening, hiking, traveling, mushroom hunting, or constructing work-related haikus. She shares a home in Chicago's Edgewater neighborhood with her husband and his cat.