

## CLINICAL VIGNETTE

# Case Report: A Case of Cannabis Hyperemesis Syndrome

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### Case

A 29-year-old Hispanic man with a history of anxiety presented to the Emergency Room with nausea and vomiting for the past three days. The patient states he awoke with severe nausea then began vomiting uncontrollably. He has been unable to tolerate anything by mouth, including his pills. As a result, he felt very dehydrated. He has also had some chills but denies any fevers or diarrhea. He had no recent travel or potentially contaminated food exposures. There are no sick contacts at home. Symptoms improved after a hot shower. He has had multiple Emergency Room visits for the same issue with recent workup including normal abdominopelvic CT scan and ultrasounds. Other than his current complaint and anxiety, for which he takes alprazolam, he has no other significant medical history. With regards to his social history, the patient smokes cigarettes, a half pack a day, and drinks alcohol occasionally. He also smokes cannabis on a daily basis for years.

On exam, the patient was well-developed but anxious appearing. His mucous membranes were dry. He was tachycardic, but his heart exam was otherwise unremarkable and lungs were clear. His abdomen was soft and non-tender with active bowel sounds. Vital signs were notable for a temperature of 97.2°F, pulse of 120 bpm, respiratory rate of 20, and blood pressure 153/104mmHg. Pulse oximeter was 100% on room air. Significant laboratory values demonstrated polycythemia to 19.6 g/dL, sodium of 127 mmol/L, potassium of 4 mmol/L, blood urea nitrogen of 48 mg/dL, creatinine 1.46 mg/dL, bicarbonate of 24 mmol/L, lipase 21 U/L. In the Emergency Room, an intravenous line was established and the patient was given 3 liters of normal saline, 4mg IV ondansetron, 10mg IV metoclopramide, 1mg IV lorazepam, as well as potassium chloride repletion. Over the course of several hours, his nausea improved slightly but he was ultimately admitted for oral intolerance and volume depletion. He improved overnight after several rounds of antiemetics. He was eventually discharged with gastroenterology follow-up. Outpatient esophagogastroduodenoscopy demonstrated mild esophagitis but otherwise negative findings. He was ultimately diagnosed with hyperemesis secondary to cannabis use and counseled extensively regarding cannabis cessation.

### Discussion

#### Clinical Features

Cannabis Hyperemesis Syndrome (CHS) is a recently discovered phenomenon due to the increasing use of

recreational cannabis over the last decade. It was first described in 2004 by Allen et al,<sup>1</sup> who published a 9-person case series of patients presenting with recurrent emesis in the setting of long-standing cannabis use. These patients, initially diagnosed with cyclical vomiting syndrome (CVS), were characterized by intractable vomiting with largely negative diagnostic studies. Eight of the nine patients described a recurrent need to take hot showers to alleviate their symptoms, sometimes to the point of waking up in the middle of the night to shower. Of the patients studied, seven patients were weaned off cannabis successfully with relief of their symptoms. This syndrome has been seen in patients who have had as little as 18 months of cannabis use.<sup>2</sup>

Three stages of Cannabis Hyperemesis have been proposed. The prodromal stage, which lasts for months to years, is characterized by early morning nausea and a fear of emesis with nonspecific abdominal discomfort. This leads patient to increase their cannabis use for temporary relief of nausea. The hyperemetic stage is characterized by cyclical and intractable nausea with vomiting, abdominal pain, and autonomic symptoms such as diaphoresis and flushing. Eventually patients will learn that hot showers alleviate their symptoms, leading to this compulsive behavior. This is the period when patients would most likely present to the hospital. The last stage is the recovery stage, in which cannabis cessation leads to resolution of symptoms and usually weight gain. It may take weeks to months for complete resolution.<sup>3</sup>

#### Diagnosis

Diagnosis is clinical after ruling out more potentially dangerous causes. One needs to be careful to evaluate for acute abdominal crises such as appendicitis, bowel obstruction, or bowel perforation. CHS is often times confused with gastroenteritis, food poisoning, CVS, or psychogenic vomiting. Of these, CVS tends to be the diagnosis most often confused with CHS. However, CVS normally accompanies psychiatric comorbidities such as anxiety and depression, along with a family history of migraine headaches.<sup>4</sup> There are multiple proposals for diagnostic criteria. Sonenti et al<sup>5</sup> first proposed a list of features for the clinical diagnosis of CHS. Major features include severe cyclical nausea and vomiting and resolution of symptoms after stopping cannabis use. Supportive features include compulsive hot baths, abdominal pain, and negative diagnostic studies. Simonetto at the Mayo Clinic modified these criteria in the largest case series of 98 patients. Symptom relief with hot baths and abdominal pain were moved to major criteria

along with the addition of weekly use of cannabis. Other supportive features included: age <50, weight loss >5kg, morning predominance of symptoms, and normal bowel habits. Diagnosis must be made in the setting of long-term cannabis use, although a definitive duration was not mentioned. The authors did note that anyone with habitual use should be considered for this diagnosis even if using for less than a year.<sup>6</sup>

### Pathophysiology

The mechanism of CHS is not well understood. Particularly perplexing is how a drug that is often used to alleviate nausea can also cause vomiting to such a severe degree. Delta-9-tetrahydrocannabinol (THC) is the main active ingredient in the cannabis plant. The large volume of distribution of THC, which is lipophilic and tends to sequester in fat, contributes to its long half-life and thus potential toxicity.<sup>3</sup> THC binds to CB1 receptors that are found in the CNS and gut. Its action in the CNS is what is thought to lead to euphoria and appetite stimulation that is commonly seen in recreational cannabis use.<sup>3</sup> In both rat and human models, THC has been shown to slow gut motility.<sup>7</sup> The prevailing theory involves an “over-riding” of the CNS effects by gastrointestinal dysmotility, leading to nausea and vomiting.<sup>8</sup> However, in the Mayo Clinic case series, not all patients had delayed emptying present.<sup>5</sup> Another theory involves THC effects on the hypothalamic-pituitary-adrenal axis, increasing corticotropin secretion, and mediating autonomic instability effects.<sup>6</sup> Yet, another theory suggests that THC’s inhibitory effects on serotonin receptors can lead to up-regulation and paradoxical sensitivity.<sup>9</sup> Still, it is not clear that THC is the culprit for the paradoxical pro-emetic effects of cannabis since there are a myriad of different chemicals in the cannabis plant that could be implicated, such as cannabidiol and cannabigerol. More studies are needed regarding the pathogenesis and treatment of this disease. However, obstacles include lack of recognition, follow-up, and patient resistance to cannabis cessation.<sup>3</sup>

### Treatment

Treatment of CHS is mainly supportive. Fluid resuscitation may be necessary due to decreased oral intake. While IV antiemetics are typically used, they do not usually produce a longstanding effect.<sup>10</sup> Opioids can be used for abdominal pain in the short term but should be used with caution as they can potentiate nausea. Benzodiazepines have been proposed to assist with autonomic symptoms and anxiety associated with fear of vomiting but chronic use has the potential for addiction.<sup>8,10</sup> The most effective method of temporary relief of vomiting and abdominal symptoms are hot showers. This is usually temperature dependent, sometimes to the point of scalding.<sup>1</sup> The mechanism is thought to involve CB1 receptors’ proximity to the hypothalamic centers of thermoregulation. Cannabis has been shown to cause hypothermia, possibly explaining the need for hot showers.<sup>1,6</sup> Still, others have suggested that increasing peripheral temperatures by hot bathing can shunt blood away from the splanchnic circulation thereby causing a “cutaneous steal syndrome” and thus relief of symptoms.<sup>11</sup> Some have suggested that capsaicin cream, which mimics the effects of hot water, could potentially alleviate symptoms.<sup>12</sup> Regardless, relief from showers tend to be temporary at best, and therapy should

be aimed at patient education, cannabis cessation, and referral to addiction centers, if necessary.<sup>8</sup>

### **Conclusion**

With the push for legalization of cannabis and its widespread use, it has become increasingly important to recognize CHS as it can obviate the need for invasive diagnostic studies. Patients will often receive multiple rounds of imaging and endoscopies before a conclusion can be made. While it is important to consider dangerous diagnoses as in an acute abdomen, cannabis hyperemesis should be considered in a patient who presents with cyclical vomiting in the setting of chronic cannabinoid use.

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