

Cannabinoid hyperemesis syndrome from delta-8 tetrahydrocannabinol after discontinuing regular cannabis use

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ABSTRACT

Cannabis is the most frequently used illicit substance in the United States, and its use has only continued to increase as more states legalize or decriminalize its use and an ever-expanding array of cannabinoid products have continued to enter the market. Excessive cannabis use is associated with multiple neuropsychiatric and medical effects. One notable effect of excessive cannabis use is cannabinoid hyperemesis syndrome (CHS), a syndrome of cyclic nausea, vomiting and abdominal pain following prolonged cannabis use. While most existing literature associates CHS with excessive cannabis use, the role of other cannabinoid-related products in the development of CHS is less established. To date, there is only one published case report of CHS developing in a patient exclusively using delta-8 tetrahydrocannabinol (THC). We present the case of a 35-year-old female who was admitted to our hospital for suicidal ideations. During admission, she exhibited classic signs and symptoms of CHS in the setting of a long multiyear history of daily cannabis use. However, she reported that she had discontinued smoking cannabis about 5 months ago after being told about CHS and had been exclusively using delta-8 THC daily with the assumption that this cannabinoid product would not cause the same effect. This case adds to the growing evidence to support delta-8 THC being associated with the development of CHS, thus highlighting the importance of educating patients with CHS on complete abstinence from all forms of cannabinoid products including delta-8 THC.

Keywords: Cannabinoid hyperemesis syndrome; delta-8 tetrahydrocannabinol; cannabis; addiction; tetrahydrocannabinol; substance-related disorders; marijuana abuse

INTRODUCTION

Cannabis is the most frequently used illicit substance in the United States (US), with over a fifth of Americans consuming cannabis in 2022.¹ As cannabis use continues to increase, so does the prevalence of cannabis-related disorders, such as cannabinoid hyperemesis syndrome (CHS), a brain-gut axis disorder associated with chronic cannabis use that causes cyclical nausea, vomiting & abdominal pain. While there is a sizable body of research on CHS in the context of chronic cannabis use, there is only one other

published case, at time of writing, of CHS in the context of chronic exposure to delta-8 tetrahydrocannabinol (THC).² While delta-8 THC is present in small amounts naturally in cannabis, to produce enough of this for commercial products, it is commonly synthesized from cannabidiol (CBD). Since CBD can be extracted from hemp, this allows delta-8 THC to be produced and sold even in states where cannabis remains illegal.³ In this report, we present a case of CHS produced by delta-8 THC after the patient thought she had switched to a healthier alternative from regular cannabis.

CASE REPORT

A 35-year-old woman with a history of major depressive disorder, anxiety, psychogenic nonepileptic seizures, and cyclic vomiting presented to the hospital

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DOI: 10.12746/swjm.v14i59.1623

for suicidal ideations. She also had seizure-like activity lasting about 30 seconds when emergency medical services arrived at her home. She reported worsening depressive and anxiety symptoms along with increasingly intractable nausea and vomiting occurring multiple times a day for 1 week. Home medications were levetiracetam, paroxetine and olanzapine. Initial vital signs were within normal limits and afebrile. She appeared anxious and depressed and her abdomen was soft with mild generalized tenderness to palpation without rebound or guarding. Labs were significant for hypokalemia with potassium of 2.6 mmol/L and urine drug screen positive for cannabinoids and benzodiazepines (administered midazolam on arrival for anxiety prior to urine collection). Lipase was within normal limits. Computed tomography (CT) scan of abdomen/pelvis without contrast revealed no acute abnormality. She was treated with intravenous (IV) fluids and potassium and restarted on levetiracetam, paroxetine and olanzapine, and had no further seizure like episodes. She was medically cleared and admitted involuntarily to the inpatient psychiatric unit.

During her psychiatric hospitalization, she continued with recurrent vomiting multiple times per day. She took numerous long, warm showers daily and reported this helped relieve nausea. She reported having these cyclic and intermittent severe episodes of nausea and vomiting for approximately 10 years and reported smoking cannabis daily for many years prior to development of these symptoms. She reported being previously diagnosed with CHS, so she stopped using cannabis 5 months ago and switched to vaping delta-8 THC daily. While hospitalized, she received ondansetron for nausea but reported no relief with this medication and instead continued with warm showers. She was diagnosed with CHS given her characteristic symptoms, heavy cannabinoid use history, and negative medical workup for alternative etiologies.

Her mood and anxiety symptoms improved during a 5-day psychiatric hospitalization, but she continued with recurrent nausea and vomiting with only mild improvement. On the final day, she had a seizure-like episode and unwitnessed fall. She was sent to the medical emergency department where she was admitted to medicine for repeat hypokalemia.

Table 1: Rome IV Criteria for Cannabinoid Hyperemesis Syndrome

Must include:
1) Stereotypical episodic vomiting resembling cyclic vomiting syndrome in terms of onset, duration, and frequency
2) Presentation after prolonged excessive cannabis use
3) Relief of vomiting episodes by sustained cessation of cannabis use
Criteria fulfilled for the last 3 months with symptom onset at least 6 months before diagnosis
Supportive remarks: May be associated with pathologic bathing behavior (prolonged hot baths or showers)

She was again medically cleared after 1 day and was discharged home on levetiracetam, paroxetine, and olanzapine, and counseled on complete cannabinoid cessation including delta-8 THC.

DISCUSSION

Cannabinoid hyperemesis syndrome is a disorder of the brain-gut axis that is characterized with episodic and cyclic vomiting associated with chronic excessive cannabis use, as defined by Rome IV criteria (See Table 1).⁴ The syndrome was first described though a case series of 9 patients in 2004, and since then there has been an explosion of case reports and series; one systemic report identified 271 published cases.⁵ Despite the growth of literature on CHS with cannabis use, the role of other cannabinoid products such as delta-8 THC vapes, like in this case, remains less understood. There is only one previously published report of CHS secondary to delta-8 THC.² Other literature have reported cases of CHS secondary to excessive use of CBD products such as oils^{6,7} and synthetic designer cannabinoids, such as K2 and spice.^{8,9}

In this case, the patient had classic symptoms of cyclic episodic vomiting in the setting of 5 months of excessive delta-8 THC vape use after she switched from using regular cannabis. Other medical causes of vomiting were excluded by negative laboratory and imaging findings. Her classic symptoms met two out of the three Rome IV criteria for CHS and her

pathologic bathing behavior was a supportive finding in favor of CHS. However, the third criteria requires “relief of vomiting episodes by sustained cessation of cannabis use,” which could not be established as the patient remained symptomatic during the hospital course and did not attend scheduled follow-up appointments. Although this is a limitation, we do believe that the consistent history, exam findings, and classic signs and symptoms were sufficient to make a presumptive CHS diagnosis.

The mechanism behind the development of CHS is not well understood but the leading theory asserts that down-regulation of the CB1 receptor is involved. The CB1 receptor is involved in the endocannabinoid system that normally exhibits negative feedback on the hypothalamic-pituitary-adrenal axis and impairs emesis when activated by endocannabinoids or the active ingredients in cannabis such as THC. However, when exposed to chronic overstimulation of CB1 by excessive cannabis use, the CB1 receptor may be down-regulated, which may lead to loss of this negative feedback and the resultant emesis that occurs in CHS.^{10,11} Another postulated mechanism for CHS involves the transient receptor potential vanilloid 1 (TRPV1) receptor. The TRPV1 receptor is activated by CBD and normally produces an antiemetic effect. It is similarly postulated that excessive activation of the receptor may contribute to its downregulation and the development of CHS.¹²

This case remains consistent with these current theories as delta-8 THC is a CB1 agonist and the CBD often present in delta-8 THC vapes is also a potent activator of TRPV1. More research is needed to understand the mechanisms behind CHS. In addition, given the growth of cannabinoid products such as delta-8 THC, more research is needed to establish both the short term and long-term effects of use of these products.

The definitive treatment of CHS remains cessation of cannabis. However, there can be some symptomatic relief from using antipsychotics such as haloperidol which may exert their efficacy from dopamine antagonism, and capsaicin cream to the abdomen which may be effective due to its TRPV1 activation.¹¹ In this case, the antipsychotic olanzapine was not effective, and we did not have access to capsaicin cream. Further research is needed to establish high

evidence standards for treatment as current symptomatic approaches remain relatively low evidence.

Overall, this case adds to growing evidence that cannabinoid products other than regular cannabis may also produce CHS. We describe only the second published case of CHS development due to delta-8 THC use. Given that this patient switched to vaping delta-8 THC from regular cannabis use because she believed it was a safer alternative for her CHS, and given the growth of these products, clinicians should take particular attention to counseling complete cannabinoid product cessation including delta-8 THC in patients with CHS.

Article citation: Carswell N, Ballesteros A, Huffhines S. Cannabinoid hyperemesis syndrome from delta-8 tetrahydrocannabinol after discontinuing regular cannabis use. *The Southwest Journal of Medicine*. 2026;14(59):79–82

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Conflicts of interest: none

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