Cannabinoid Hyperemesis Syndrome: A Case Report and Discussion Regarding Patients with Concurrent Disorders

Stephen Lee-Cheong, Amrita Grewal, Lukas Hestvik, Reza Rafizadeh, and Christian Schütz

Can J Hosp Pharm. 2020;73(4):290-3

INTRODUCTION

In October 2018, Canada legalized the nonmedical use of cannabis. Usage has traditionally been high in Canada, and after legalization, self-reported use increased from 14% to 18%.[1] Given this increased usage, it is important to understand the adverse effects of cannabis. Here, we focus on a less well-recognized consequence, cannabinoid hyperemesis syndrome (CHS), first described in 2004.[2] It may be seen more often in jurisdictions where cannabis is legalized; for example, from 2009 to 2011, after legalization of cannabis in the state of Colorado, presentations to emergency departments for CHS increased by almost 100%.[3]

CHS presents similarly to cyclic vomiting syndrome, with recurrent nausea and vomiting episodes interspersed with asymptomatic periods.[4] However, several features differentiate CHS from cyclic vomiting syndrome. CHS is associated with a history of chronic cannabis use, cure of the syndrome after cessation of cannabis, and delayed gastric emptying.[4] Cyclic vomiting syndrome is often associated with concurrent migraines and psychiatric conditions, as well as rapid gastric emptying.[4] The prodromal phase lasts up to several years in CHS,[4] but just minutes to hours in cyclic vomiting syndrome.[5]

The following characteristics seem to have the highest sensitivity for diagnosis of CHS: weekly cannabis use for more than 1 year, severe nausea and vomiting with abdominal pain repeating in a cyclic pattern over months, resolution of symptoms after cannabis cessation, and compulsive use of hot baths or showers to provide temporary symptom relief.[6] Normal bowel habits are cited as supportive criteria. However, abnormal bowel habits do not necessarily rule out CHS, as there are a number of recorded cases, including the patient described in this report, with both CHS and abnormal bowel habits.[7] The complications of CHS, which are due to recurrent vomiting, include fluid and electrolyte disorders, nutritional deficiencies, aspiration, pneumonitis, and esophageal wall injury.[8] Unfortunately, given that CHS is poorly recognized, patients often undergo potentially harmful procedures such as radiography, computed tomography (CT), endoscopy, and appendectomy in search of a diagnosis.[4] Here, we describe CHS by means of a clinical case and then discuss the challenges that may be encountered within the subpopulation of patients with concurrent disorders.

CASE REPORT

A 29-year-old man (height 185 cm, weight 84 kg) with a history of schizophrenia, epilepsy, major depressive disorder, cannabis use disorder, and opioid use disorder was admitted in early October 2019 to a treatment centre for concurrent disorders.* After 1 month (starting on October 30), he experienced an 8-day episode of vomiting, diarrhea, and associated nausea. He reported having had 5 hospital admissions during the first half of the year for similar presentations, stating that each of these episodes subsided spontaneously after about 5 days. He further reported about 2 episodes annually for the past 10 years.

The patient described severe cramping abdominal pain lasting throughout the day, rated as 8–10 (on a scale of 1 to 10) during the first several days and then 5–6 near the end of the 8-day period. He denied fever and associated flu-like symptoms, but had been experiencing night sweats for the past 2 months. The patient vomited 3 or 4 times per day during the 8-day episode and experienced nausea only about 15 min before vomiting. During the initial days of the episode, he experienced 3 to 5 episodes of diarrhea associated with vomiting when eating.

The family history was noncontributory for gastrointestinal disease or illness. His father had diagnoses of post-traumatic stress disorder, major depressive disorder, and schizophrenia.

Before admission to the treatment centre, the patient had been living in an apartment with a friend; he was

*The patient provided verbal informed consent for the publication of this case report.

unemployed and was receiving disability support. He was single with no dependants.

The patient denied cannabis use for the past month (i.e., since admission to the treatment centre), although this statement was inconsistent with the results of urine drug screening, which were positive for tetrahydrocannabinol (THC) on the day his symptoms started. However, 1 week earlier, the results of urine drug screening had been negative for THC, amphetamines, methamphetamine, benzodiazepines, cocaine, opiates, fentanyl, methadone, and oxycodone. He reported that his last use of opioids was 2 months prior, which was consistent with staff observations and all prior urine drug screening results; this ruled out opioid withdrawal as the cause of his symptoms. The patient had started smoking cannabis at 12 years of age and smoked heavily (3–4 g/day) around the age of 15. Previous to the onset of his symptoms, he had smoked 1 pack of cigarettes daily for the last 4 years and smoked fentanyl once per month for the last 3 years.

The patient's regular medications were suboxone 16 mg SL daily, escitalopram 20 mg PO daily, carbamazepine extended-release 600 mg PO at bedtime, paliperidone 263 mg IM q12weeks, and pantoprazole 40 mg PO at bedtime.

The patient was admitted to the internal medicine service at a separate facility 4 days after symptom onset. On admission to that facility, he was alert and oriented; the mucous membranes were slightly dry, the chest was clear to auscultation, and heart sounds were normal. Jugular venous pressure was also normal. Rectal examination results were negative for occult blood and rectal masses. The white blood cell count was 14.9 (normal range 4.0–11.0) $\times 10^9$/L with left shift, hemoglobin was 152 g/L, and the platelet count was 306×10^9/L. Blood pressure was 129/84 mm Hg, heart rate 107/min, respiratory rate 22/min, temperature 37.5 °C, and oxygen saturation by pulse oximetry 98% on room air. Electrolyte results were unremarkable.

The patient was given IV fluids, ondansetron, and dimenhydrinate, which helped to reduce the symptoms slightly. More specifically, ondansetron 4 mg SL tid PRN was given initially, and the dosage was then switched to 8 mg PO bid after slight symptom improvement. Dimenhydrinate 50 mg IM stat was given twice, which controlled vomiting episodes effectively; loperamide 2 mg PO PRN provided diarrhea control. CT of the abdomen and pelvis showed that the appendix appeared normal. He had a history of intestinal parasites at 10 years of age, and there were current self-reports of poor hand hygiene. This information prompted collection of stool samples for culture; the results were negative for all parasites and *Helicobacter pylori*. No other significant abnormality could be found, and the patient was discharged back to the treatment centre (after a 6-h stay) without full resolution of his symptoms.

Upon return to the treatment centre, ginger (20-mg tablets; 1 or 2 tablets PO q4h PRN) was trialled for several days for treatment of nausea, without effect. Acetaminophen 1000 mg PO q6h PRN for pain did not relieve the patient's stomach cramps. He achieved symptomatic relief by using a heating pad on his abdomen throughout the day and experienced about 20 min of relief by showering with hot water, which he did 3 to 12 times daily. At this point, staff in the treatment centre diagnosed CHS, on the basis of presentation and the exclusion of other diagnoses. The patient's observed "excessive" showering was related to "self-treatment" and not to any psychotic disorder or symptoms of obsessive-compulsive disorder.[2] He had full resolution of symptoms after about 10 days.

DISCUSSION

The patient described here was an inpatient at a treatment and recovery centre for patients with concurrent disorders, which provided comprehensive integrated care for severe mental health and substance use disorders. Patients at this centre often present with the complex chief concern of vague nausea and vomiting of a chronic, intermittent nature. Many of the patients are marginalized and have a detrimental "lifestyle" arising from a lack of daily structures and unhealthy nutrition.[9] As staff in the centre, we have proposed that lifestyle choices (excessive use of coffee, tobacco, and/or alcohol) may contribute to perpetuation of these symptoms and potential diagnostic delay.

For CHS, as with any medical syndrome, it is important to carefully seek out the cause of the symptoms and to conduct diagnostic screening to exclude effects of other substances, such as opioid withdrawal; adverse effects of medication abuse, such as intermittent gastroenteritis or gastroesophageal reflux disease (GERD); neurological disorders, such as migraine; or pregnancy. According to the guidelines on the management of cyclic vomiting syndrome in adults, rigorous and repetitive diagnostic testing is often required before this particular diagnosis is even included in the differential diagnosis.[10] Careful exclusion of other diagnoses is necessary, as was done here for intestinal parasites and *H. pylori*. Testing to exclude gallbladder and pancreatic abnormalities is also suggested as part of the workup.[2]

Within the field of addiction recovery, staff regularly view nausea and vomiting as consequences of problematic lifestyle choices, including excessive intake of coffee, tobacco, and/or alcohol, which may cause GERD.[11] Excessive caffeine intake is common among patients with mental health disorders, particularly schizophrenia.[12] Studies of patients with schizophrenia have reported consumption of more than 750 mg of caffeine daily.[13] Alcohol may also lead to alcoholic gastritis,[14] and poor hygiene may lead to *H. pylori* infection.[15] However, the patient described here did not drink caffeine or alcohol. These factors, which cause symptoms similar to those of CHS, may act as distractors in the development of a differential diagnosis, because they may cause symptom prolongation and overlap. For example,

the prodromal phase described by Allen and others[2] may be misinterpreted in the presence of any of these factors. Diagnosis of CHS may also be delayed by a lack of awareness about the syndrome, as has been suggested throughout the current literature.[4,7,16,17] Aside from taking the appropriate diagnostic approach, it is important that the consequences or complications of nausea and vomiting (e.g., fluid depletion, hypokalemia, and metabolic alkalosis) are identified and corrected.

There are several hypotheses for the pathophysiological mechanisms for CHS. One is the desensitization and downregulation of the CB1 cannabinoid receptors, which ordinarily have antiemetic effects (GRADE [Grading of Recommendations Assessment, Development and Evaluation] rating very low).[16] Cannabis is used as an antiemetic,[18] which has been discussed as another factor that may cause perpetuation of the syndrome.[2] At the time of symptom onset, people with CHS may increase their cannabis usage in an attempt to self-medicate, thereby inadvertently perpetuating and worsening their symptoms. Allen and others[2] found a dose-related response in their study.

High-quality evidence for pharmacologic treatment of CHS is limited.[2] The only definitive treatment identified to date is abstinence from cannabis (GRADE rating low),[16] with full resolution typically taking 7 to 10 days.[2] Benzodiazepines are the most commonly reported treatment option, followed by haloperidol and topical capsaicin[2]; first-line antiemetics have been found to be ineffective, although did have some efficacy in this case.[16] A challenging caveat is that benzodiazepines are drugs of abuse and therefore contraindicated for these patients. Tricyclic antidepressants also have some efficacy,[2] although were not given in this case because of the potential for interaction with escitalopram. Short-term relief of symptoms by means of hot showers or topical capsaicin may be due to activation of transient receptor potential vanilloid 1 ($TRPV_1$) through interaction with the endocannabinoid system.[16,17]

With the recent legalization of cannabis in Canada, it is important that conditions like CHS receive appropriate attention. This can be achieved, as suggested by previous authors,[4,7,16] by increasing the amount of research on the subject that is conducted and published, as we have done here. In addition, it would be prudent for the government to increase awareness of cannabis complications through warnings on packages, as is done for tobacco products. Given that hospital admissions due to CHS are likely to increase, we propose building CHS screening protocols or tools to be used at the hospital level for patients who present with nausea, diarrhea, and/or stomach pain. Being more readily able to discuss cannabis use with patients may help direct physicians toward a more accurate diagnosis.

This case has highlighted the difficulty of diagnosis and treatment of CHS in a population of patients with concurrent disorders, including unnecessary exposure to potentially harmful procedures such as CT. One challenge that can arise in any population, but particularly this one, is dealing with poor reporting of the history by the patient. In this case, it was not possible to confirm the amount of cannabis that was being used, because the patient denied any use at all; this forced the team to use clinical judgment. The patient expressed much frustration with the situation, and although he admitted to being aware that cannabis was the source of his symptoms, he continued to deny any recent usage.

References

1. Rotermann M. Analysis of trends in the prevalence of cannabis use and related metrics in Canada. *Health Rep*. 2019;30(6):3.
2. Allen JH, De Moore GM, Heddle R, Twartz J. Cannabinoid hyperemesis: cyclical hyperemesis in association with chronic cannabis abuse. *Gut*. 2004;53(11):1566-70.
3. Kim HS, Anderson JD, Saghafi O, Heard KJ, Monte AA. Cyclic vomiting presentations following marijuana liberalization in Colorado. *Acad Emerg Med*. 2015;22(6):694-9.
4. Blumentrath CG, Dohrmann B, Ewald N. Cannabinoid hyperemesis and the cyclic vomiting syndrome in adults: recognition, diagnosis, acute and long-term treatment. *Ger Med Sci*. 2017;15:Doc06.
5. Hayes WJ, VanGilder D, Berendse J, Lemon MD, Kappes JA. Cyclic vomiting syndrome: diagnostic approach and current management strategies. *Clin Exp Gastroenterol*. 2018;11:77-84.
6. Richards JR, Gordon BK, Danielson AR, Moulin AK. Pharmacologic treatment of cannabinoid hyperemesis syndrome: a systematic review. *Pharmacotherapy*. 2017;37(6):725-34.
7. Simonetto DA, Oxentenko AS, Herman ML, Szostek JH. Cannabinoid hyperemesis: a case series of 98 patients. *Mayo Clin Proc*. 2012;87(2):114-9.
8. Chu F, Cascella M. Cannabinoid hyperemesis syndrome. In: *StatPearls*. StatPearls Publishing; 2019 Nov 6.
9. Heald A, Pendlebury J, Anderson S, Narayan V, Guy M, Gibson M, et al. Lifestyle factors and the metabolic syndrome in schizophrenia: a cross-sectional study. *Ann Gen Psychiatry*. 2017;16(1):Article 12.
10. Venkatesan T, Levinthal DJ, Tarbell SE, Jaradeh SS, Hasler WL, Issenman RM, et al. Guidelines on management of cyclic vomiting syndrome in adults by the American Neurogastroenterology and Motility Society and the Cyclic Vomiting Syndrome Association. *Neurogastroenterol Motil*. 2019;31 Suppl 2:e13604.
11. Yuan LZ, Yi P, Wang GS, Tan SY, Huang GM, Qi LZ, et al. Lifestyle intervention for gastroesophageal reflux disease: a national multicenter survey of lifestyle factor effects on gastroesophageal reflux disease in China. *Ther Adv Gastroenterol*. 2019;12:1756284819877788.
12. Meredith SE, Juliano LM, Hughes JR, Griffiths RR. Caffeine use disorder: a comprehensive review and research agenda. *J Caffeine Res*. 2013;3(3):114-30.
13. Greden JF, Fontaine P, Lubetsky M, Chamberlin K. Anxiety and depression associated with caffeinism among psychiatric inpatients. *Am J Psychiatry*. 1978;135(8):963-6.
14. Roberts DM. Chronic gastritis, alcohol, and non-ulcer dyspepsia. *Gut*. 1972;13(10):768-74.
15. Amaral O, Fernandes I, Veiga N, Pereira C, Chaves C, Nelas P, et al. Living conditions and *Helicobacter pylori* in adults. *BioMed Res Int*. 2017;2017:9082716.
16. Sorensen CJ, DeSanto K, Borgelt L, Phillips KT, Monte AA. Cannabinoid hyperemesis syndrome: diagnosis, pathophysiology, and treatment—a systematic review. *J Med Toxicol*. 2017;13(1):71-87.
17. Lapoint J, Meyer S, Charles KY, Koenig KL, Lev R, Thihalolipavan S, et al. Cannabinoid hyperemesis syndrome: public health implications and a novel model treatment guideline. *West J Emerg Med*. 2018;19(2):380-6.
18. Abrams DI. Should oncologists recommend cannabis? *Curr Treat Options Oncol*. 2019;20(7):Article 59.

Stephen Lee-Cheong, MB, BCh, BAO, is a student in the Post-Graduate Certificate in Pain Management program of the Faculty of Rehabilitation Medicine, University of Alberta, Edmonton, Alberta.

Amrita Grewal, BSc, PharmD, was, at the time of this study, a student in the PharmD program of the Faculty of Pharmaceutical Sciences, The University of British Columbia, Vancouver, British Columbia. She has since graduated from the program.

Lukas Hestvik, MN-NP(F), BSN, is with the Burnaby Centre for Mental Health and Addiction, Burnaby, British Columbia.

Reza Rafizadeh, BSPharm, ACPR, BCPP, RPh, is with The University of British Columbia and the BC Psychosis Program, Vancouver, British Columbia, and is also with the Burnaby Centre for Mental Health and Addiction, Burnaby, British Columbia.

Christian Schütz, MD, PhD, MPH, FRCPC, is with the University of British Columbia, Vancouver, British Columbia, and the Burnaby Centre for Mental Health and Addiction, Burnaby, British Columbia.

Competing interests: None declared.

Address correspondence to:
Dr Stephen Lee-Cheong
Noel Lee-Cheong Medical Professional Corporation
2155 Lawrence Avenue East, Unit 109
Scarborough ON M1R 5G9

e-mail: stephenleecheong@gmail.com

Funding: None received.