

## CASE REPORT

## Cannabinoid hyperemesis syndrome and the onset of a manic episode

Phillip Gregoire, Michael Tau, David Robertson

University of Toronto Faculty of Medicine, Toronto, Ontario, Canada

**Correspondence to**  
Phillip Gregoire,  
phillip.gregoire@mail.utoronto.ca

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**SUMMARY**

Cannabinoid hyperemesis syndrome is a rare, recently described, clinically diagnosed condition that is characterised by a chronic history of cannabis use, cyclic nausea and vomiting, symptomatic relief with hot water bathing, and resolution with cessation of use. We present a case of this syndrome concurrent in a patient with bipolar mania. We suggest that a 3-week period of vomiting in the context of this syndrome contributed to the precipitation of a manic episode by lowering mood stabiliser serum levels, and that this syndrome will have significant consequences for the patient's mental health.

**BACKGROUND**

Cannabis is the most widely used illicit drug in Canada and worldwide.<sup>1</sup> In 2012, the incidence of lifetime cannabis use in Canada was estimated at 41%.<sup>1</sup> Cannabinoid hyperemesis syndrome (CH) was first described in 2004, and it is an uncommon condition that can affect chronic cannabis users.<sup>2</sup> Despite the more widely acknowledged antiemetic effects of cannabis, this paradoxical condition can result in cyclic nausea and vomiting that typically resolve with cessation of use.<sup>3 4</sup> Other major diagnostic criteria include symptomatic relief with hot water bathing, abdominal pain and frequent current use of cannabis.<sup>3 4</sup> The syndrome can recur with resumed cannabis use.<sup>5</sup> Supportive typical features of the diagnosis include age <50 years, worsening of symptoms in the morning, weight loss, normal bowel habits and negative results on investigation.<sup>3</sup> According to a 2012 case series of 98 patients with CH, 23% of patients experienced diarrhoea associated with the syndrome.<sup>3</sup>

Patients who are actively managed for bipolar I disorder often require tight control of serum levels of mood stabilising medications in order to prevent deterioration of mental state.<sup>6</sup> Since substance abuse is often comorbid in patients with bipolar I disorder, these patients may be at higher risk of subtherapeutic levels of medication as a result of vomiting if they have comorbid CH.<sup>7</sup>

**CASE PRESENTATION**

A 27-year-old man with a history of cannabis use disorder and bipolar I disorder, treated with lithium, presented to the emergency department after being sent there involuntarily by his community psychiatrist. His illness was previously well controlled, following an index manic episode 7 years before.

The patient had been slowly tapering his daily lithium under supervision of his community

psychiatrist in order to mitigate side effects. Most recently, his lithium was decreased from 900 to 600 mg daily. Two months later, at a routine visit, the psychiatrist had found the patient significantly off his baseline (decreased sleep, increased activity and talkativeness, and aggression) and ordered a 72 h assessment at an academic hospital. The patient presented to the emergency department with a 3-week history of daily vomiting and fluctuating periumbilical abdominal pain. He denied fever, haematemesis, bilious emesis, haematochezia, melena or abnormal bowel movements; however, the week prior to admission, he had experienced diarrhoea. He had felt nauseated for ~4 weeks before the vomiting started and had not previously experienced an extended period of vomiting. He had used 'every over-the-counter antiemetic medication', particularly dimenhydrinate, to no effect, in treating his nausea. In the weeks preceding admission, he took 2–3 h hot baths and showers daily, as he found this to be the only intervention that provided symptomatic relief. His vomiting ceased on admission to the hospital, although the nausea persisted.

The patient had begun using cannabis at 13 years of age, which persisted as chronic, daily use that had increased in frequency and quantity in the weeks leading up to his admission. While he was in hospital, he denied alcohol or recreational drug use during the period leading up to his admission, but after discharge, he endorsed some alcohol use during that period. On admission, the patient denied continuing consumption of cannabis, despite significant cravings.

**INVESTIGATIONS**

The patient was assessed several times by emergency physicians; his abdomen was tender on palpation of the periumbilicus. Complete blood count revealed mild neutrophilia; a metabolic panel and vital signs were within normal limits. Lithium level at presentation was <0.20 mmol/L (therapeutic range of 0.50–1.50 mmol/L). The patient denied missing medication doses, and this claim was endorsed by his wife. However, his community psychiatrist noted that the patient stated he had stopped taking his lithium in the preceding weeks, because he believed it was causing the vomiting. It was determined that there was no emergent reason for further investigation. He was determined to not be eligible for continued involuntary admission and was discharged after 3 days.

The patient returned, accompanied by his social worker, 3 days later for worsening of his psychiatric



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symptoms. His serum amylase was low at 15 mmol/L (reference range 20–110 mmol/L); lipase was within normal limits. A urine screen was positive for cannabinoids. His liver enzymes were mildly elevated. He received an abdominal X-ray, which was found to be normal. His abdomen continued to be tender. He was assessed as having frank mania and experiencing significant psychotic symptoms and prominent insomnia. He was transferred to the acute care psychiatric unit in the hospital.

He received three subsequent urine cannabinoid screens while in hospital. These were positive, although one of these positive screens was analysed by gas chromatography-mass spectrometry and found to be a false positive.

### DIFFERENTIAL DIAGNOSIS

The differential diagnosis in the context of a manic episode includes a first episode of cyclic vomiting syndrome (CVS), a syndrome characterised by idiopathic cyclic episodes of vomiting, and CH. It is unlikely that lithium alone was causing the gastrointestinal symptoms, given their spontaneous emergence following many years of treatment with lithium and resolution in hospital despite an increased dosage. Based on the patient's long history of cannabis use, vomiting that resolved on cessation of cannabis use, abdominal pain and symptomatic relief with extended, compulsive bathing, a diagnosis of CH was made. The hospital's addictions team was consulted and supported a diagnosis of CH based on diagnostic criteria.

### TREATMENT

During his stay in hospital, the patient was symptomatically titrated on standing doses of clonazepam (1–4 mg daily), quetiapine (50–700 mg nightly), methotrimeprazine (5–20 mg nightly) and zopiclone (7.5–22.5 mg nightly). Lithium was initially increased to 900 mg and then titrated to 1950 mg in order to attain therapeutic serum levels in context of his acute mania. At this dose, he reached a trough lithium level of 1.01, which was within the therapeutic range. His insight into his illness was initially poor; he often stated that he had come into hospital for his gastrointestinal concerns. He intermittently experienced cramping suprapubic pain that consistently resolved with lorazepam and psychotherapeutic intervention. He also experienced mild gastric reflux and was treated with pantoprazole. He vomited twice while in hospital. He initially had mild constipation, which resolved with daily sennosides. After 25 days of inpatient care, his manic symptoms subsided and his gastrointestinal symptoms largely resolved. He was subsequently discharged to the care of his community psychiatrist, with plans to optimise his maintenance lithium level.

### OUTCOME AND FOLLOW-UP

The patient was advised of the diagnosis and the need for cannabis abstinence. The patient disagreed with the diagnosis, as he found that cannabis tended to ease his gastrointestinal symptoms and thought his nausea could have been the result of alcohol consumption. He stated that his repetitive bathing was a cleanse he performed as an expression of his spirituality.

He expressed a desire to reduce his cannabis intake for personal and family reasons. During the admission, the addictions specialist discussed strategies with him for quitting or reducing his cannabis intake. The patient volunteered to follow-up with his outpatient social worker and to attend an addictions treatment group to work towards decreasing his use. The patient told the community psychiatrist that he had continued abstinence in the 3 weeks following discharge.

### DISCUSSION

The pathophysiology of CH remains speculative. Cannabinoids act on the CB1 and CB2 receptors in the central and enteric nervous systems. One proposed mechanism is that cannabinoid receptors involved in the hypothalamic–pituitary–adrenal axis respond abnormally due to long-term toxicity from chronic use.<sup>4</sup> This toxicity may increase corticotropin-releasing hormone levels, which has been proposed as a precipitating factor in a related condition called CVS.<sup>4–8</sup> Another hypothesis implicates enteric CB1 receptor activation that causes decreased gastric motility, which directly results in vomiting.<sup>4–9</sup> In both hypotheses, central CB1 receptors involved in thermoregulation are thought to account for the symptomatic improvement with hot water bathing.<sup>10</sup> Compulsive bathing is not typically found in other hyperemetic syndromes and has been previously described as pathognomonic of CH.<sup>10</sup>

This is the first reported instance of concurrent CH and bipolar I disorder. Since lifetime prevalence of cannabis use among people with bipolar I disorder has been estimated as 30–64%, CH may be an important determinant of prognosis in a subset of this population.<sup>7</sup> In patients who require tight control of the serum level of oral medications, periodic vomiting may result in chronic destabilisation by reducing drug absorption. Patients may continue to use cannabis, despite recurrences of CH, and management of addiction becomes a crucial dispositional consideration in order to prevent further mood destabilisation. While it may not be possible to establish a precise course leading to the onset of our patient's mania, we suggest that a combination of the tapering and possible cessation of mood stabilising medications, his increasing cannabis use and the ultimate onset of vomiting, resulted in the sharp decline in his lithium level and mental state. It is unlikely that lithium itself caused his gastrointestinal symptoms, as these greatly improved in hospital despite his dose increasing. As CH may significantly increase the risk of precipitation of manic episodes in patients with bipolar I disorder, we suggest that further investigation into these concurrent disorders must be performed in order to better manage outcomes.

### Learning points

- ▶ Cannabinoid hyperemesis syndrome (CH) is an uncommon, but important, diagnosis in patients with unexplained vomiting.
- ▶ CH is characterised by cyclic vomiting, chronic cannabis use, abdominal pain, symptomatic relief with hot water bathing and resolution with cessation of use.
- ▶ CH may result in mood destabilisation in patients who have bipolar I disorder, by reducing serum levels of medications.
- ▶ Addiction management is a crucial dispositional consideration in patients who have concurrent bipolar I disorder and CH.

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