

# A hot mess

## A case of hyperemesis

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### Case description

A 29-year-old previously healthy man presents to the emergency department (ED) for having more than 10 episodes of vomiting during the past 8 hours. He denies any headache, recent head injury, fever, chest pain, or abdominal pain. His bowel movements are normal. He has no sick contacts and has not recently traveled. He has had no intra-abdominal surgeries. He takes no medications. His social history is remarkable for prison tattoos, regular cocaine use (2 weeks since last use), and regular marijuana use (smoking 1 to 3 joints per day). He denies intravenous drug use and admits to occasional alcohol consumption (3 days since last use). On examination, he is nauseated and retching. His vital signs are within normal limits; respiratory and cardiovascular measurements are unremarkable. He is not jaundiced. Findings of his abdominal examination are unremarkable, with no masses or signs of bowel obstruction. After starting intravenous fluids and antiemetics, he requests a hot shower.

What is the diagnosis, and how should the condition be managed?

Since cannabinoid hyperemesis syndrome (CHS) was first described by Allen et al,<sup>1</sup> other case reports and series<sup>2,3</sup> have identified patients in whom marijuana (or cannabis) use has been associated, paradoxically, with cyclic vomiting in the absence of other pathology. **Box 1**<sup>1-5</sup> lists the current proposed criteria for this clinical syndrome.

In almost all patients with CHS previously described, chronic regular marijuana use is a requirement for

development of associated cyclic vomiting. The syndrome seldom manifests until after several years of daily marijuana use.<sup>2,4</sup> A case report suggests that CHS can also develop with the use of synthetic marijuana.<sup>6,7</sup> The cyclic vomiting manifests as multiple episodes of emesis that last for days, occur every several weeks to months, and are interspersed with periods of wellness.<sup>4</sup>

Hot bathing is effective in relieving patients' symptoms of nausea and vomiting temporarily. Patients will report multiple episodes of daily bathing or showers of several hours' duration.<sup>2</sup> Authors of several case series have suggested that hot bathing should be considered as pathognomonic for CHS.<sup>2,3</sup> Interestingly, in a case series of 98 patients, Simonetto et al<sup>3</sup> described a minority of patients who presented with atypical features, including those who developed CHS with less than 1 year of cannabis use or used cannabis less than once per week, and those whose symptoms were not relieved by hot bathing. Because CHS is a relatively newly described entity and not known to most physicians, patients presenting with CHS often experience a delay in their diagnosis and have undergone numerous investigations for their cyclic hyperemesis. With the increasing popularity and availability of marijuana in North America, along with possible decriminalization in the near future, it is important for health care providers to be aware of this syndrome.

### Pathophysiology

The pathophysiology of CHS is poorly understood. The cannabinoid type 1 (CB1) receptor is the receptor that is believed to be associated with CHS. Cannabinoid type 1 receptors are found in the brain and gastrointestinal (GI) tract.<sup>7,8</sup> Delta-9-tetrahydrocannabinol is the main active ingredient in cannabis. It has many effects in the central nervous system, including psychotropic properties and antiemetic effects that are believed to be due to the stimulation of CB1 receptors in the brain.<sup>9</sup> Delta-9-tetrahydrocannabinol also acts at CB1 receptors in the GI tract and results in gastroparesis.<sup>10</sup> With chronic use of cannabis, sensitization of the CB1 receptors in the brain might occur, leading to the pro-emetic CB1 activity in the gut overriding the antiemetic CB1 properties in the brain.<sup>11,12</sup>

Cannabidiol (CBD) and cannabigerol are other exogenous cannabinoids found in cannabis that might affect emesis. Low doses of CBD might produce an antiemetic

#### Box 1. Proposed diagnostic criteria for CHS

Diagnostic criteria for CHS include the following:

- Chronic regular use of marijuana
- Cyclic nausea and vomiting (might be accompanied by abdominal pain)
- Learned pattern of hot bathing
- Absence of organic pathology
- Resolution of symptoms within days of discontinued use
- Reliable return of signs and symptoms within weeks of resuming use

CHS—cannabinoid hyperemesis syndrome.

Data from Allen et al,<sup>1</sup> Wallace et al,<sup>2</sup> Simonetto et al,<sup>3</sup> Galli et al,<sup>4</sup> and Sullivan.<sup>5</sup>

effect, while high doses induce emesis.<sup>13</sup> Cannabigerol reverses the antiemetic effects of low-dose CBD.<sup>14</sup> Therefore, the emetic effects of high-dose CBD and the emesis-enhancing effects of cannabigerol might contribute to the nausea and vomiting seen in CHS. There are many other exogenous cannabinoids found in cannabis, the effects of which are still unknown.

Hot bathing in CHS is a behaviour learned by patients in order to alleviate their symptoms. Cannabinoid type 1 receptors in the hypothalamus are located near the thermoregulatory centre, and chronic CB1 receptor stimulation in the hypothalamus might lead to thermodyregulation.<sup>11</sup> Thermoregulation might also be disrupted by chronic cannabis use through a mechanism of disequilibrium in the limbic system unrelated to the CB1 receptors.<sup>1</sup> The exact mechanism of hot bathing for relief of GI symptoms is unclear. However, a “cutaneous steal syndrome” has been hypothesized.<sup>15</sup> Hot bathing might divert blood from the gut to the periphery, reducing the stimulation of CB1 receptors in the gut and offering temporary relief to the patient.<sup>15</sup>

### Differential diagnosis

The differential diagnosis of CHS should include other causes of cyclic vomiting, including cyclic vomiting syndrome, hyperemesis gravidarum, migraines, metabolic disorders, motility disorders, psychogenic vomiting, and bulimia.<sup>1,2,4</sup>

**Table 1** describes the unique characteristics of these diagnoses.

### Assessment

A history of hyperemesis that is consistent with the diagnostic criteria listed in **Box 1**<sup>1-5</sup> should trigger the clinician to consider CHS. Patients might complain of a prodromal illness of early-morning nausea (sometimes accompanied by vomiting) and abdominal pain that might predate the hyperemesis by months to years.<sup>1,4,16</sup> Patients also report polydipsia and abdominal pain, often episodic and colicky.<sup>1,16</sup> The physical examination might reveal signs of dehydration and weight loss secondary to nausea and vomiting, flushing, and low-grade pyrexia,<sup>1</sup> but findings are otherwise unremarkable for a focus causing the patient's symptoms.

While the diagnosis of CHS is made in the absence of organic pathology, hot bathing that results in the relief of symptoms practically denotes CHS. Therefore, the diagnosis can be made without further investigation if this behaviour is present, and if history and physical examination are consistent with CHS and do not suggest another underlying medical cause.<sup>2</sup> Supplementary investigations should be performed to evaluate the extent of dehydration and electrolyte or acid-base abnormalities caused by hyperemesis, or if the history and physical examination do not support CHS as the most likely cause of vomiting. Investigations that would be appropriate for initial workup of vomiting presenting to the ED are listed in **Box 2**. Case reports of some patients who have undergone endoscopy have revealed esophagitis and gastritis; however, it is unclear whether this is a comorbid disorder or secondary to hyperemesis.<sup>4,5,15</sup>

### Management

Because little is known about the pathophysiology of CHS, it remains difficult to treat and current treatments are not evidence-based. Management includes rehydration with intravenous fluids and correction of hypoglycemia, electrolyte, and acid-base abnormalities. Antiemetics (eg, diphenhydramine, ondansetron, metoclopramide, prochlorperazine) are used routinely for attempted symptomatic relief of nausea and vomiting, often with little effect.<sup>17</sup> A different class of antiemetics might be considered if one class is ineffective. Three case reports<sup>16-18</sup> have suggested that haloperidol and

**Table 1. Differential diagnoses of cyclic vomiting**

| DIFFERENTIAL DIAGNOSIS   | ASSOCIATED CHARACTERISTICS   |
|--------------------------|--|
| CHS                      | Chronic cannabis use<br>Learned behaviour of hot bathing   |
| Cyclic vomiting syndrome | Family history of migraines<br>Psychiatric comorbidities<br>Psychosocial stressors   |
| Hyperemesis gravidarum   | Pregnancy  |
| Migraines                | Unilateral headache<br>Photophobia or phonophobia with or without aura   |
| Metabolic disorders      | Addison disease (symptoms include fatigue, hypotension, hyperkalemia, hyponatremia)<br>Porphyria (symptoms include neurovisceral symptoms, red or brown urine, elevated urinary porphobilinogen)   |
| Motility disorders       | Gastroparesis (symptoms include early satiety, postprandial fullness, bloating, decreased gastric motility; it can be an idiopathic or postsurgical condition or associated with diabetes)<br>Ogilvie syndrome (symptoms include constipation, abdominal distention; plain film results reveal dilated colon)<br>Intestinal obstruction (symptoms include constipation, obstipation, abdominal distention; plain film results reveal dilated loops of bowel) |
| Psychogenic vomiting     | Associated with conversion disorders, depression   |
| Bulimia                  | Binging or purging behaviour   |

CHS—cannabinoid hyperemesis syndrome.

benzodiazepines might be effective in cases of vomiting refractory to common antiemetic drugs. Inpatient admission might be warranted in cases where emesis cannot be controlled in the ED. Usually, hyperemesis resolves within 12 to 48 hours.<sup>1,2,5</sup> Discontinuation of cannabis use is the only known definitive management of CHS, and patients should be counseled about their cannabis use being a cause of their hyperemesis and to cease its use. Patients can expect resolution of CHS within days of discontinuing cannabis; however, symptoms can persist up to 2 weeks after last use. Within weeks to months of resuming use of marijuana, symptoms reliably return.<sup>1,6,15</sup> It is worthwhile to note that most chronic marijuana users will reject the association between their cannabis use and hyperemesis because of having been asymptomatic despite years of use and the cultural belief that cannabis has antiemetic properties.

**Box 2. Initial investigations for the patient presenting with hyperemesis**

Investigations that would be appropriate for initial workup of vomiting presenting in the ED are as follows:

- Complete blood count
- Routine electrolytes (Na, K, Cl, HCO<sub>3</sub>)
- Calcium
- Glucose
- Urea, creatinine
- Liver enzymes (AST, ALT, ALP, GGT, bilirubin, amylase)
- β-hCG
- Abdominal x-ray scan
- Urine toxicology screen, serum drug levels

ALP—alkaline phosphatase, ALT—alanine aminotransferase, AST—aspartate aminotransferase, β-hCG—β-human chorionic gonadotropin, Cl—chloride, ED—emergency department, GGT—γ-glutamyl transpeptidase, HCO<sub>3</sub>—bicarbonate, K—potassium, Na—sodium.

**Case resolution**

The patient refused to accept his chronic cannabis use as the cause of his hyperemesis. After receiving intravenous rehydration and taking antiemetics, his vomiting resolved and he was discharged. 🌿

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**Competing interests**

None declared

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## BOTTOM LINE

- Cannabinoid hyperemesis syndrome is a diagnosis of exclusion that is characterized by episodes of persistent vomiting in chronic users of marijuana.
- Patients will report obtaining some relief through the practice of prolonged or repeated hot bathing.
- Treatment of these patients in the emergency department includes correcting metabolic derangements, reversing volume depletion, providing antiemetics, and counseling patients to cease delta-9-tetrahydrocannabinol consumption. Accepting that regular delta-9-tetrahydrocannabinol consumption is the cause of their plight will be difficult for many patients with cannabinoid hyperemesis syndrome.

## POINTS SAILLANTS

- Le syndrome de l'hyperémésie cannabinoïde est un diagnostic d'exclusion caractérisé par des épisodes de vomissements persistants chez des consommateurs chroniques de marijuana.
- Les patients signalent obtenir un certain soulagement en prenant des bains chauds prolongés ou répétés.
- Le traitement de tels patients à l'urgence comporte de corriger les perturbations métaboliques, de renflouer la déplétion des volumes, de fournir des antiémétiques et de conseiller aux patients de cesser leur consommation de delta-9-tétrahydrocannabinol. Il pourrait être difficile pour de nombreux patients atteints du syndrome de l'hyperémésie cannabinoïde d'accepter que leur consommation régulière de delta-9-tétrahydrocannabinol soit la cause de leur problème.

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