

CASE REPORT

## Cannabinoid hyperemesis syndrome: Clinical diagnosis of an underrecognised manifestation of chronic cannabis abuse

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### Abstract

Cannabis is a common drug of abuse that is associated with various long-term and short-term adverse effects. The nature of its association with vomiting after chronic abuse is obscure and is underrecognised by clinicians. In some patients this vomiting can take on a pattern similar to cyclic vomiting syndrome with a peculiar compulsive hot bathing pattern, which relieves intense feelings of nausea and accompanying symptoms. In this case report, we describe a twenty-two year-old-male with a history of chronic cannabis abuse presenting with recurrent vomiting, intense nausea and abdominal pain. In addition, the patient reported that the hot baths improved his symptoms during these episodes. Abstinence from cannabis led to resolution of the vomiting symptoms and abdominal pain. We conclude that in the setting of chronic cannabis abuse, patients presenting with chronic severe nausea and vomiting that can sometimes be accompanied by abdominal pain and compulsive hot bathing behaviour, in the absence of other obvious causes, a diagnosis of cannabinoid hyperemesis syndrome should be considered.

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### INTRODUCTION

Cannabis has been used recreationally for millennia and is the third most commonly used drug after tobacco and alcohol<sup>[1,2]</sup>. Research into the neurobiology of the compound has led to the discovery of an endogenous cannabinoid system. The therapeutic potential of cannabinoids has been recognized and these compounds are utilized as anti-emetics<sup>[3-5]</sup>. Recently, a distinct syndrome in chronic cannabis abusers characterized by recurrent vomiting associated with abdominal pain and a tendency to take hot showers has been increasingly recognised. This clinical manifestation is paradoxical to the previously identified therapeutic role of cannabinoids as anti-emetics. We describe the case of a young male seeking repeated emergency room care with recurrent nausea and vomiting.

### CASE REPORT

A 22-year male presented with recurrent episodes of nausea, refractory vomiting, and colicky epigastric pain for one week. The symptoms were characterized by treatment-resistant nausea in the morning, continuous vomiting, and colicky epigastric abdominal pain. Each episode lasted 2 to 3 h and increased with food intake. He often had two or more episodes a day during the symptomatic period. He had been treated for the severe nausea and vomiting in the emergency room on two occasions in the preceding two months. He also reported having learned to help himself by taking a hot bath each time the symptoms appeared, which dramatically

improved his symptoms. This habit had become a compulsion for him for symptom relief with each episode of hyperemesis. On physical examination his mucous membranes were dry, his pulse rate was 102/min and blood pressure was 140/100 with positive orthostasis. The remainder of the physical examination was unremarkable. His complete blood count and comprehensive metabolic panel were unremarkable. In addition, serum amylase and lipase levels were within the normal range. His urine drug screen was positive for tetrahydrocannabinol (THC). Abdominal X-ray series and ultrasonography were within normal limits.

Oesophagogastroduodenoscopy revealed Grade 2 distal oesophagitis and hiatal hernia. On further interviewing, he admitted to consistent marijuana abuse for the past 6 years, often smoking cannabis every hour or two on a daily basis. The patient and his mother did not recall any significant past illnesses or recurrent vomiting when he was a child. He was treated with intravenous fluids with steady improvement in symptoms, and metoclopramide, pantoprazole and morphine for the abdominal pain. It was explained that marijuana was the cause of his symptoms and he was advised not to resume marijuana abuse. On subsequent follow-up, he had abstained from cannabis and remained symptom-free.

## DISCUSSION

Cannabis is one of the most commonly abused drugs worldwide. Over the past decade, marijuana has remained the most commonly used illicit substance with close to 50% of high school seniors admitting use at some time<sup>[1]</sup>. It is estimated that each year 2.6 million individuals in the USA become new users and most are younger than 19 years of age<sup>[6]</sup>.

The long-term and short-term toxicity of cannabis abuse is associated with pathological and behavioural effects. However, cannabis has also been suggested to have therapeutic properties with anticonvulsive, analgesic, antianxiety and anti-emetic activities. Cannabis has also been used to treat anorexia in patients with acquired immunodeficiency syndrome<sup>[3-5]</sup>. The actions of cannabis are mediated by specific cannabinoid receptors. The first of the cannabinoid receptors-CB-1-was identified in 1990 and this finding revolutionized the study of cannabinoid biology. Since then, a multitude of roles for the endogenous cannabinoid system has been proposed. A large number of endogenous cannabinoid neurotransmitters or endocannabinoids have been identified, and the CB-1 and CB-2 cannabinoid receptors have been characterized<sup>[7]</sup>. The CB-1 receptors exert a neuromodulatory role in the central nervous system and enteric plexus<sup>[8]</sup>. Cannabinoid type 2 receptors have an immunomodulatory effect and are located on tissues such as microglia<sup>[5]</sup>. The presence of other receptors, transporters, and enzymes responsible for the synthesis or metabolism of endocannabinoids are being recognised at an extraordinary pace. Cannabinoids have a wide variety of effects on the body systems and physiologic states (Table 1) due to their actions on the

**Table 1** Harmful effects of cannabinoids on body systems<sup>[1,6,7]</sup>

Cognitive and mental health
Impaired memory
Impaired attention, organization and integration of complex information
Association with schizophrenia
Increased risk for depression
Pulmonary
Carcinogenic effect
Obstructive lung disease
Increased propensity toward infections
Acute and chronic bronchitis
Behavioural
Weapon possession and physical fighting
Unwanted and unprotected sexual encounters
Unwanted pregnancies
School dropout
Amotivational syndrome
Impairment of driving skill and coordination
Endocrine
Decreased testosterone, sperm motility and production, disruption of ovulatory cycle
Pregnancy
Low birth weight
Problems with attention, memory and higher cognitive function
Cardiovascular
Stroke
Dose-dependent increase in HR
Orthostasis
Decreased exercise tolerance
Precipitation of angina or myocardial infarction

receptors as well as direct toxic effects.

The anti-emetic effect of cannabinoids is largely mediated by CB-1 receptors in the brain and the intestinal tract, although some of their effect may also be receptor-independent. However, in this report, we were presented with the paradoxical effect of hyperemesis in a susceptible chronic cannabis abuser. Such a paradoxical response has previously only been demonstrated following acute toxicity to an intravenous injection of crude marijuana extract<sup>[9]</sup>. Proposed mechanisms of cannabinoid hyperemesis include toxicity due to marijuana's long half-life, fat solubility, delayed gastric emptying, and thermoregulatory and autonomic disequilibrium *via* the limbic system<sup>[10]</sup>. Cannabinoids are known to impair peristalsis in a dose-dependent manner<sup>[11,12]</sup>, which can theoretically override the centrally mediated anti-emetic effects, thus leading to hyperemesis. It is not known why the hyperemesis syndrome surfaces after several years of cannabis abuse. The effects of cannabinoids on the functions of the thermoregulatory and autonomic mechanisms of the brain can lead to behavioural changes<sup>[10]</sup>. Such effects might be the underlying mechanism for the compulsive hot bathing behaviour. There is also a supposition that the syndrome could represent a type of cyclic vomiting. Cyclic vomiting syndrome (CVS) in adults is now very well recognized, and it has been proposed that marijuana contributes to CVS<sup>[13]</sup>. However, unlike the other forms of CVS, patients with cannabinoid hyperemesis are not likely to have a history of migraine or other psychosocial stressors and the peculiar behaviour of hot showers is

**Table 2 Clinical diagnosis of cannabinoid hyperemesis**

## Essential for diagnosis:

History of regular cannabis use for years

Major clinical features of syndrome

Severe nausea and vomiting

Vomiting that recurs in a cyclic pattern over months

Resolution of symptoms after stopping cannabis use

## Supportive features

Compulsive hot baths with symptom relief

Colicky abdominal pain

No evidence of gall bladder or pancreatic inflammation

unique to this syndrome.

Based on the published research and case reports<sup>[10,14-16]</sup>, we propose the set of clinical characteristics for the diagnosis of cannabinoid hyperemesis syndrome shown in Table 2. Allen *et al*<sup>[10]</sup> first noted this condition in a group of nineteen patients from Australia with chronic cannabis abuse and cyclical vomiting illness. An earlier case report by de Moore *et al*<sup>[17]</sup> described a chronic cannabis abuser with psychogenic vomiting, which was complicated by spontaneous pneumomediastinum. Subsequent reports have identified similar clinical presentations<sup>[7-9,18]</sup>. Given the high prevalence of chronic cannabis abuse worldwide and the paucity of reports in the literature, clinicians need to be more attentive to the clinical features of this underrecognised condition.

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