

Case of cannabinoid hyperemesis syndrome with long-term follow-up

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Abstract

Long-term cannabis use may be associated with attacks of severe nausea and vomiting, and a characteristic learned behavior of compulsive hot bathing, termed cannabinoid hyperemesis syndrome (CHS). Long-term follow-up and prognosis of CHS have not been reported previously. A 44-year-old Caucasian man with a long history of addiction to marijuana presented with chronic abdominal pain complicated by attacks of uncontrollable vomiting for 16 years. He had a compulsion to take scalding hot showers, as many as 15 times a day, to relieve his symptoms. All previous therapies had been ineffective. However, abstinence from marijuana led to rapid and complete resolution of all symptoms and his compulsive hot showering behavior. He has been followed for nine years, and is still doing well without recurrence of symptoms. Physicians should have a high index of suspicion for this under-recognized condition, as excellent long-term prognosis of CHS can be achieved when abstinence is maintained.

Key words: Cannabinoids; Hyperemesis; Prognosis; Abdominal pain; Adverse drug effect

Core tip: Cannabinoid hyperemesis syndrome (CHS) can be diagnosed with characteristic clinical features, including long-term cannabis use, severe cyclical abdominal pain, nausea and vomiting, and temporary relief of symptoms with hot showers or baths. Excellent long-term prognosis of CHS can be achieved when abstinence from cannabinoid is maintained. Physicians should have a high index of suspicion in patients with unexplained chronic abdominal pain and vomiting.

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INTRODUCTION

According to the World Health Organization, drug abuse remains prevalent around the globe, and about 27 million individuals worldwide are addicts^[1]. Although legal recreational drugs, such as tobacco and alcohol, boast higher rates of consumption, cannabis is the most commonly used illegal recreational drug in the world^[2,3]. In some patients, long-term cannabis use is associated with severe episodes of nausea and vomiting, and a characteristic learned behavior of compulsive hot bathing. So-called cannabinoid hyperemesis syndrome (CHS) was first described in 2004 by Allen *et al*^[4] and its features were confirmed by several other subsequent reports^[5,6]. This condition may be underdiagnosed because of relatively recent recognition and lack of awareness. Physicians should be vigilant for this unique cluster of symptoms to avoid misdiagnosis even after a protracted, invasive and costly workup. Long-term follow-up and prognosis of

CHS has not been previously reported, therefore we now present a case of CHS with follow-up of nine years.

CASE REPORT

A 44-year-old Caucasian man with a long history of marijuana use presented to our clinic with chronic episodic abdominal pain complicated by attacks of uncontrollable vomiting for the past 16 years. His abdominal pain centered in the epigastrium or periumbilical region, occurred abruptly without provocation, was often aggravated by eating in the morning, and lasted anywhere from three hours to two days. Because of his abdominal pain, his weight fluctuated between 50-68 kg. In recent years, all his symptoms had increased in intensity and frequency. He had a compulsion to take scalding hot showers, as many as 15 times a day, to relieve his symptoms. When he ran out of hot water at home, he would drive to his mother's house, his sister's house, or visit his neighbors, even in the middle of night. Four years prior to his presentation to us, he had been hospitalized with second degree burns on his back because of the showers. In the last few years, he had undergone a massive workup from five previous gastroenterologists, and had visited the emergency room more than 20 times. He denied tobacco, alcohol or illegal drug use, with the exception of regular marijuana use for the past 20 years, consuming at least 4-8 marijuana doses ("joints") per day. He had no specific family history, except for Crohn's disease in a cousin.

His previous gastrointestinal workup had been extensive, including numerous abdominal and pelvic computerized tomographs (CTs), at least two small bowel follow-through studies, multiple abdominal ultrasounds, and a barium swallow and head CT. All were negative. Twenty-four hour urine porphyrin levels were normal and urinalysis did not show occult blood. Three years ago, he underwent upper endoscopy and colonoscopy, which were also unremarkable. In the past, treatment attempts had been made with psychotropic and neuromodulatory medications (including amitriptyline, paroxetine hydrochloride, sertraline and tegaserod), dietary manipulation, and alternative medical therapies. However, all of these efforts had been ineffective. This condition adversely affected all aspects of his life, including his relationship with family, friends and peers, making him unemployable. His workup was estimated to have cost tens of thousands of dollars.

He was thin with a weight of 50 kg, and his physical examination was otherwise unremarkable. His laboratory and radiological tests were within normal limits. Blood tests showed no abnormalities, including a liver functional panel, amylase and lipase. Stool occult blood tests were negative. Repeat abdominal ultrasound and abdomen and pelvic CT were normal. A repeat small bowel follow-through and capsule endoscopy were performed to exclude small bowel Crohn's disease, as he had a history of unexplained perirectal fistulae as well as a distant relative with Crohn's disease. The small bowel follow-through was negative, but multiple small ulcerations

scattered throughout the small intestine were noted on capsule endoscopy. However, the mucosa did not appear to be inflamed, and there were no strictures, masses, or signs of bleeding, therefore the small ulcers were considered an incidental finding. The gastric emptying time for the capsule was only three minutes. A urine toxicology screen was done to rule out other recreational drugs, and was negative.

He was asked to stop marijuana use because of the concern for CHS. Abstinence led to a dramatic improvement within one week, with complete resolution of all symptoms and compulsive hot showering behaviors. Since then, he has gained 20 kg, completed a college degree, found employment, gotten married and started a family. We have had 9 years of follow-up so far, and he is still doing well without recurrence of symptoms. He speaks at educational events on the impact of marijuana on his life.

DISCUSSION

Large, population-based surveys suggest that illicit drug use is relatively common in the population, with initial use typically starting in mid to late adolescence: cannabinoids are the most commonly used illegal substances^[7,8]. Cannabinoids have also been used for the treatment of nausea, vomiting, anorexia and anxiety^[5]. Its mechanism of action for inhibiting nausea and vomiting is not precisely known, but is probably related to stimulation of cannabinoid receptors in the brain. Given the nationwide increase in cannabinoid use for recreational and medical reasons, adverse drug effects associated with cannabinoid have become more prominent.

Chronic use of cannabinoids in some individuals can paradoxically cause severe episodic abdominal pain, nausea and vomiting^[4]. Recently, Simonetto proposed clinical criteria for CHS^[6]: Major diagnostic features include long-term cannabis use, severe cyclical abdominal pain, nausea and vomiting, resolution with cannabis cessation, and temporary relief of symptoms with hot showers or baths. The patient in our case report demonstrated all these features; in particular, he indulged in compulsive hot bathing behavior during acute attacks, a phenomenon prominently seen in almost all prior reports in the literature^[9-14]. Supportive diagnostic features include age younger than 50 years, weight loss of greater than 5 kg, morning predominance of symptoms, normal bowel habits and negative findings on diagnostic testing. Our case also showed all the secondary features, with his social and work life severely affected by CHS. In the past, long-term follow-up and prognosis for this condition have not been reported because CHS has only recently been recognized and the recidivism rate is high in patients who are not determined to get better. It should be noted that some patients are psychologically addicted to marijuana and exhibit considerable denial when confronted with the possibility that marijuana, which has purported anti-nausea properties, may be the cause of their chronic nausea and abdominal pain symptoms. Patients who are not determined to get

better may have difficulty maintaining abstinence from marijuana for long periods of time. Our case demonstrates that prolonged abstinence leads to sustainable improvements in all symptoms over a period as long as nine years.

The mechanism of CHS is still unknown. Most cannabinoids act through two receptors, CB1 and CB2, which reduce anterior pituitary hormone and increase corticotrophin release^[15]. Disturbances of the hypothalamic-pituitary-adrenal axis and the presence of autonomic instability have been proposed as possible mechanisms of CHS^[6]. The central effect of long-term cannabis use is thought to be similar to that seen in cyclic vomiting syndrome, which is characterized by the increased secretion and activation of corticotrophin-releasing factor^[16]. In addition, relief of symptoms with compulsive hot bathing might be due to impairment of physiologic thermoregulatory mechanisms by cannabinoids^[6], as CB1 receptors of the preoptic area have been reported to be involved in the hypothermic effects of cannabinoids^[17,18]. As peripheral CB1 receptors in the gastrointestinal tract have also been implicated in slowing gastrointestinal transit^[19], it is suggested that slowed gastric emptying might be responsible for the severe vomiting seen in CHS^[4]. However, only 30% of CHS patients had delayed gastric transit, with the majority having either normal or increased gastric transit on gastric scintigraphy^[6].

The diagnosis of CHS can be made if there is a high index of suspicion; the pathognomonic feature of compulsive bathing is particularly useful because this phenomenon is not seen in any other condition. As diagnosis of CHS is based on only clinical criteria^[6], laboratory or radiological data are not required for its diagnosis except to rule out other gastrointestinal conditions. Although blood or urine cannabinoid metabolites were not measured in our case, they may be helpful in ruling out the use of other recreational drugs. The correct diagnosis can often prevent an extensive and fruitless medical workup and lead to complete resolution of symptoms once abstinence from marijuana is achieved. Therefore, the index of suspicion amongst the medical profession should be raised, as this may be only the tip of the iceberg given the increasing use of marijuana associated with its legalization in several American states^[1].

In conclusion, physicians should have a high index of suspicion in patients with unexplained chronic abdominal pain and vomiting, because an excellent long-term prognosis of CHS can be achieved when abstinence is maintained. Since the mechanism by which cannabis induces hyperemesis is unknown, further research is required in patients with CHS.

COMMENTS

Case characteristics

A 44-year-old man with a history of marijuana use presented with chronic abdominal pain complicated by attacks of uncontrolled vomiting for 16 years.

Differential diagnosis

Cyclic vomiting syndrome or small bowel inflammatory bowel disease.

Laboratory diagnosis

All laboratory findings were unremarkable, including normal 24-h urine porphyrin levels and urinalysis.

Imaging diagnosis

Repeat abdominal ultrasound, abdomen and pelvic computerized tomograph as well as small bowel follow-through were all normal.

Treatment

All previous treatments were ineffective, including psychotropic and neuro-modulatory medications (amitriptyline, paroxetine hydrochloride, sertraline, and tegaserod), dietary manipulation, and alternative medical therapies, however, abstinence of marijuana led to a dramatic improvement of all symptoms within one week.

Related reports

Cannabinoid hyperemesis syndrome (CHS), which is caused by chronic use of cannabis, may be associated with severe episodes of nausea and vomiting, and a characteristic learned behavior of compulsive hot bathing. This condition may be underdiagnosed because of relatively recent recognition and lack of awareness. Physicians should be aware of this unique cluster of symptoms to avoid misdiagnosis even after a protracted, invasive and costly workup.

Term explanation

CHS can be diagnosed based on major clinical features including long-term cannabis use, severe cyclical abdominal pain, nausea and vomiting, resolution with cannabis cessation, and temporary relief of symptoms with hot showers or baths.

Experiences and lessons

This case report highlights the excellent prognosis of CHS when abstinence from cannabis is maintained. Physicians should have a high index of suspicion for this rare condition in patients with unexplained chronic abdominal pain and vomiting. This report provides useful information on a rare disease as the cause of chronic abdominal pain and vomiting.

Peer review

This is an interesting case study of cannabinoid hyperemesis syndrome, which is characterized by chronic, heavy use of cannabis, recurrent episodes of severe nausea and intractable vomiting, and abdominal pain. Overall, the paper is well written.

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