CASE REPORT

Cannabinoid hyperemesis syndrome

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Accepted 4 January 2016

SUMMARY

The antiemetic properties of marijuana are well known, but there is increasing evidence of its paradoxical hyperemetic effects on the gastrointestinal tract and central nervous system, known as 'cannabinoid hyperemesis syndrome' (CHS). We report a case of CHS encountered in our outpatient clinic. We also completed a review of the literature using PubMed in patients over 18 years of age with CHS. Understanding the diagnostic criteria and risk factors associated with CHS may reduce the ordering of unnecessary and expensive investigations, and pursuing inappropriate medical and surgical treatments. Ultimately, abstaining from cannabis use leads to resolution of symptoms in the majority of patients.

BACKGROUND

Cannabis is the most widely used drug for recreational purposes in the USA and worldwide. Several states now allow the use of marijuana for medicinal purposes, and some have legalised its use for recreational purposes.¹ Coinciding with the increasing rate of cannabis use, there has been an increased recognition of an associated side effect termed 'cannabinoid hyperemesis syndrome' (CHS). CHS is characterised by cyclic episodes of nausea and vomiting in association with chronic cannabis use. Interestingly, patients with CHS have learned behaviour of compulsive hot water showers. We completed a detailed review of the literature in PubMed using the key words: Cannabinoid Hyperemesis Syndrome, cannabis, nausea and vomiting. Inclusion criteria were patients over the age of 18 years and a diagnosis of CHS. Our review of the literature found 76 cases. The first case was described in 2004 by Allen *et al.*² We present a case of CHS in a 38-year-old man encountered in our clinical setting and also provide a review of previously published literature.

CASE PRESENTATION

A 38-year-old African-American man presented to the emergency department with symptoms of acute onset nausea, continued vomiting and unrelenting epigastric pain for 5 days. The patient also reported continued bilious, non-bloody vomiting that occurred 10–12 times per day. The patient denied exacerbating factors but had partial relief with hot water baths. He experienced similar episodes for the past 20 years, which occurred 3–4 times a month and lasted for an average of 7 days. However, he subjectively felt this episode to be worse than the previous ones.

Medical history included hypertension and gastro-oesophageal reflux disease (GERD).

Hypertension was controlled with hydrochlorothiazide and lisinopril while GERD was controlled with pantoprazole. Of note, the patient was hospitalised multiple times in the past for similar episodes, in which extensive work up was unable to identify a pathology. The patient revealed he smoked marijuana regularly for the past 20 years. He smoked an average of 5–6 joints a day. He denied alcohol and tobacco use. Family history was unremarkable.

Physical examination revealed the patient to be diaphoretic and dehydrated. Vital signs consisted of a temperature of 36.6°C, pulse of 100 bpm, blood pressure of 159/122 mm Hg and a respiratory rate of 18 breaths/min. On abdominal examination, the patient had a soft, non-distended abdomen with mild epigastric tenderness on palpation. Laboratory work up was significant for leucocytosis (white cell count 24 000). Otherwise, electrolytes, pancreatic enzymes and liver function tests were within normal limits.

CT of the abdomen and pelvis revealed no abnormalities. Esophagogastroduodenoscopy (EGD) revealed bilious contents in the stomach, without visual evidence of gastritis. Gastric and distal oesophageal biopsies revealed mild inflammation.

The patient was resuscitated with isotonic saline, and given anti-nausea medications and ranitidine for mild gastritis. He responded well to this medical management. With a detailed review of the patient's history, and a close association between intractable vomiting and marijuana intake, a diagnosis of CHS was made.

OUTCOME AND FOLLOW-UP

The patient was educated about the diagnosis and was counselled to stop the use of marijuana completely if resolution of symptoms were to be desired. He was discharged the next day and was advised to follow-up with his general practitioner.

DISCUSSION

On reviewing the literature in detail, we found 76 previously published cases of CHS in patients over 18 years of age.^{2–45} Of the patients reported, 75% were men. There were three cases that occurred during pregnancy.^{3 21 26} The mean and SD of the current age of the reported patients were: mean 31.49, SD 7.69. The average duration of cannabis use was 12.9 years. The average age of onset of nausea and vomiting was 26.8 years, prior to which the respondents had smoked cannabis for an average of 9.4 years. Overall, patients were treated with different combinations of intravenous fluids, antiemetics, analgesics, antidepressants and anxiolytic drugs. In four studies, patients reported

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To cite: Parekh JD, Wozniak SE, Khan K, *et al.* *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2015-213620

significant improvement of their symptoms with lorazepam.^{6 7 13 26} In another study, a patient improved rapidly after haloperidol treatment.⁹

The main intervention that provided relief was hot showers or baths. There was one study in which the patient's symptoms improved with hot showers in the early stages of CHS but later on became refractory to them.¹⁵ Another case study of 10 patients reported 1 patient who did not benefit from hot showers.² The patient encountered in our clinical setting reported partial relief with hot water baths. Two patients developed a skin rash known as 'erythema ab igne (EAI)'^{8 32} and one patient suffered a second-degree burn secondary to excess hot water baths.²⁵

Various proposals have been offered to explain the mechanism by which hot showers provide relief from gastrointestinal discomfort, but no study has identified the exact explanation for this phenomenon. One suggested mechanism is that hot baths may increase body temperature enough to reverse the chronic hypothalamic cannabinoid receptor stimulation that may have caused nausea.¹ Another mechanism states that, as splanchnic cannabinoid receptors mediate vasodilation in the gut, hot showers may divert blood to the periphery, resulting in 'cutaneous steal syndrome'.^{1 14}

The majority of patients reported abdominal pain in association with cyclic nausea and vomiting, and some patients also reported significant weight loss.^{2 6 7 11 16 40} The majority of the patients had normal laboratory tests, apart from mild leukocytosis, hypokalaemia and ketonuria resulting from dehydration. Amylase, lipase and liver function tests were reportedly normal in all patients. Four patients developed acute renal failure as sequelae of CHS.^{32 36 42} Endoscopic findings were normal in the majority of patients except for mild oesophagitis, gastritis and erosions. Almost all of the reported patients had undergone extensive evaluation of their cyclic nausea and vomiting with multiple CT scans of the abdomen/pelvis, MRI of the brain, colonoscopies, gastric emptying study, barium swallow, abdominal X-ray, ultrasound and barium swallow; all of which revealed no pathology.

A majority of the patients smoked natural cannabis. We found three cases in which synthetic cannabis (K2, Kryptonite) was the cause of CHS.^{5 30 36} All of the patients were counselled about ceasing cannabis use at discharge. Patients who stopped smoking cannabis reported complete resolution of their symptoms. A few patients were lost to follow-up and some patients who did not quit cannabis reported relapse of their symptoms.

Cannabis is known to have antiemetic effects, and has been used to relieve nausea and vomiting associated with chemotherapy. The mechanism for this antiemetic effect is unknown, but may be related to cannabinoid receptors exerting a neuromodulatory effect in the brain. The main active chemical of cannabis is delta-9-tetrahydrocannabinol (THC). THC is highly lipophilic and, with chronic use, can accumulate in high concentrations in the body, including in cerebral fat. This can cause severe nausea and vomiting in sensitive patients. THC binds to cannabinoid receptors in the brain, but also to those in the enteric nervous system. Additionally, it slows peristalsis and gastric emptying. Chronic, heavy cannabis use may cause cannabinoid receptors in the gut to override the effect of cannabinoid receptor stimulation in the brain, thereby leading to paradoxical hyperemesis.^{1 14}

Our patient fits the diagnostic criteria proposed by Simonetto *et al.*⁴⁶ Our patient was a chronic marijuana smoker for the previous 20 years. He had been hospitalised multiple times in the past with episodes of abdominal pain, cyclic nausea and vomiting, and had an extensive work up completed that was negative

for any underlying pathology. However, our patient had only partial relief of symptoms with hot water baths.

Thus, our case and literature review suggest that we have come to a greater understanding of CHS, however, some aspects still remain unclear. For example, the exposure of cannabis in terms of dose and duration needed prior to the emergence of CHS is unclear. The duration of cannabis use prior to onset of symptoms varies from months to >25 years in reported cases. Further, the majority of chronic marijuana users do not seem to develop CHS. Diagnostic tests have consistently been shown to be of no benefit in the diagnosis of CHS. In spite of this, the majority of patients are still subject to multiple costly investigations and are eventually unable to reach a diagnosis. This highlights the importance of eliciting a detailed history of cannabis use in patients reporting cyclic nausea, vomiting and abdominal pain. We conclude by saying that—even though further research needs to be undertaken to understand the risk factors, pathogenesis and epidemiological characteristics of this syndrome—increasing awareness of this condition among physicians and patients will go a long way in cutting the healthcare costs of patients with CHS, and will ultimately help in diagnosing and treating this condition.

Learning points

- Diagnostic tests (CT, MRI, X-ray, colonoscopies, gastric emptying study, ultrasound and barium swallow) have consistently been shown to be of no benefit in the diagnosis of cannabinoid hyperemesis syndrome (CHS). In spite of this, the majority of patients are still subject to multiple costly investigations and are eventually unable to reach a diagnosis.
- Chronic, heavy cannabis use may cause cannabinoid receptors in the gut to override the effect of cannabinoid receptor stimulation in the brain, thereby leading to paradoxical hyperemesis.^{1 29}
- Our literature review found that 99% of patients with CHS had symptom relief with hot water showers or baths. Hot water may increase body temperature to reverse the chronic hypothalamic cannabinoid receptor stimulation that may have caused nausea.¹ Additionally, as splanchnic cannabinoid receptors mediate vasodilation in the gut, hot showers may divert blood to the periphery resulting in 'cutaneous steal syndrome'.^{1 29}

Competing interests None declared.

Provenance and peer review Not commissioned; externally peer reviewed.

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