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Cannabinoid hyperemesis syndrome

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Accepted 13 March 2024

Summary Cannabis use is legalised in many countries. We present a patient in their 40s who complained of recurrent abdominal pain and associated nausea and vomiting. The patient was previously seen in various hospitals, treated symptomatically, and discharged with a diagnosis of non-specific abdominal pain. The patient had a chronic history of smoking cannabis and nicotine and drinking alcohol. Abdominal examination revealed no masses, and abdominal X-ray was normal. Blood tests and gastroduodenoscopy revealed no obvious aetiology. Intravenous fluids, together with antiemetics and proton pump inhibitors, were administered. The patient also received counselling and was advised to stop cannabis use. At discharge, the patient was well and asked to come back for review in 2 weeks, and, thereafter monthly for a period of 6 months after stopping cannabis use. The patient reported no recurrent symptoms despite continued cigarette and alcohol use. A suspected cannabinoid hyperemesis syndrome (CHS) became a consideration. Awareness of cannabis-related disorders such as CHS may assist in avoiding costly hospital workups.

BACKGROUND

Cannabinoid hyperemesis syndrome

The first description of cannabinoid hyperemesis syndrome (CHS) was in 2004. It is characterised by cyclical nausea and vomiting, accompanied by abdominal pain after a prolonged high dose of cannabis use.[1] Patients generally have a history of multiple emergency department visits and hospitalisations followed by extensive workups, including diagnostic imaging and invasive procedures. The recent legalisation on cannabis in many countries raises a concern about increased use.

CASE PRESENTATION

A patient in his mid-40s presented to the emergency department, where he complained of a 48-hour history of nausea and uncontrollable bilious vomiting with no blood. The patient also reported burning abdominal pain but no diarrhoea or fever. There was a history of similar episodes, the most recent being a year ago, when extensive tests were done with no specific positive findings. The patient was admitted, treated symptomatically, and discharged with a diagnosis of non-specific abdominal pain. The patient had an over 10-year history of smoking cannabis and cigarettes and alcohol consumption of 4–5 units a week. The patient had stopped drinking and smoking cigarettes 2 years earlier because of the suspicion that these might be the cause of the symptoms, but continued to smoke cannabis.

Examination revealed an ill-looking patient who also appeared to be anxious. His temperature, heart rate and blood pressure were 36.6°C, 60 beats per minute and 139/82 mmHg, respectively. His respiratory rate was 20 breaths per minute. Abdominal examination revealed mild epigastric tenderness and normal bowel sounds with no succussion splash and no masses. Examination of other systems was unremarkable. Several differential diagnoses were considered. Pancreatitis was one possibility because of the history of chronic alcohol use; however, his presentation and the reported character of pain were not typical of pancreatitis. Peptic ulcer disease, because of alcohol intake and smoking, was also considered; however, he had been treated for this condition previously without any improvement in symptoms. Lastly, acute hepatitis was considered unlikely as there was no jaundice and no typical right upper quadrant pain.

Blood tests revealed normal full blood count (FBC), C-reactive protein (CRP) of <5.0 mg/dL, and normal renal and liver functions with normal serum amylase and lipase. Abdominal X-ray was normal. Gastroscopy revealed only evidence of mild gastritis. Because of the past admissions, workups and current clinical and laboratory test results, no further tests such as ultrasound and CT scanning were done.

The following treatment was initiated: intravenous (IV) fluids; IV proton pump inhibitor, pantoprazole 40 mg daily; and antiemetic, metoclopramide 10 mg IV three times daily, changed later to ondansetron 4 mg IV three times daily after vomiting continued despite metoclopramide. The patient also received counselling and was advised to stop cannabis use completely. Despite this treatment, vomiting continued for a further 2 days, and on the third day of hospital admission the patient reported that their symptoms were subsiding, and they were feeling better. CHS was suspected. The patient was later discharged in a stable condition.

OUTCOME

The patient responded well to supportive care and cessation of cannabis use. Initial follow-up was every month, where the patient was seen by clinicians and counsellors, both of whom reported good compliance. The patient remained symptom-free, with no further hospital visits 6 months after discharge.

DISCUSSION

Cannabis var. *sativa* is widely distributed in our country, occurring in seven of the nine provinces;

To cite: Elnagar A, Kgomo M, Mokone M, *et al*. *BMJ Case Rep* 2024;**17**:e256921. doi:10.1136/bcr-2023-256921

var. *indica* and *spontanea* occur each in one province only. The patient lived in a province where only var. *sativa* is available on the market, and it can be assumed they smoked the var. *sativa* type of cannabis.

The Rome IV criteria state that non-organic nausea and vomiting disorders be subclassified into three categories:

1. Bothersome nausea and vomiting syndrome lasting for at least 6 months with no evidence of other organic aetiology. This is referred to as chronic nausea and vomiting syndrome.
2. Episodes of vomiting with at least three discrete episodes in the prior year and two episodes in the past 6 months, occurring at least 1 week apart in a stereotypical pattern named cyclical vomiting syndrome.[2]
3. The last subclass is characterised by stereotypical episodic vomiting, occurring in individuals who chronically use cannabis daily. Cessation of cannabis use leads to relief of vomiting episodes (CHS).[3]

The diagnostic standards for CHS required by Rome IV are:

1. Episodic and stereotypical vomiting resembling cyclical vomiting syndrome in start, duration and frequency.
2. This should follow prolonged and excessive cannabis use.
3. This should improve after cessation of cannabis use.
4. It is associated with "pathological" washing behaviour.

The criteria are satisfied if the symptoms last for 12 weeks, with symptoms starting 6 months before diagnosis.

Patients with CHS go through three stages[4]:

1. The first stage is the prodromal stage, which includes nausea without vomiting, loss of appetite, apprehension of vomiting, and abdominal discomfort. Patients usually tolerate a liquid diet.
2. In the second stage, the hyperemesis stage, they have intractable vomiting and dry retching. Hot showers or baths sometimes relieve these symptoms and the stage can last for days. This stage is also associated with sympathetic overactivity.
3. During the third stage, the recovery stage, the symptoms resolve and the patient recovers.

Cannabinoid has several types of receptors. The active ingredients (cannabinoids) of cannabis are tetrahydrocannabinol, cannabidiol and cannabigerol, and they are thought to be responsible for CHS by interacting with the receptors listed below. Their interaction has yet to be fully understood, but tetrahydrocannabinol is thought to exert the most effect.[5]

1. Type 1 (CB-1) causes cannabis-related cognitive and memory disturbances with nausea and vomiting. Chronic cannabis use can result in derangement of the endogenous CB-1 system, downregulating this receptor and causing rebound vomiting and spasmodic pain. This resolves and recovers on cannabis cessation.
2. Transient receptor potential vanilloid 1 (TRPV1) is a non-selective cation channel activated by noxious heat and capsaicin. This receptor is present throughout the gastrointestinal tract, including in several sensory neurons, enteric neurons in the myenteric plexus and epithelial cells in the gastric mucosa.[4] It is also found in the central nervous system, especially in the area postrema, also known as the chemoreceptor trigger zone. Activation of this receptor has a potent antiemetic effect, which is thought to be mediated by the depletion of substance P from neural circuits travelling to the nucleus tractus solitarius.[4]

Both CB-1 and TRPV1 are activated by exogenous cannabinoids.[5] Laboratory studies show that exogenous cannabinoids lead to dephosphorylation and subsequent receptor desensitisation.[4] Chronic exposure to cannabinoids could lead to downregulation or desensitisation of TRPV1 signalling, explaining how prolonged exposure to cannabinoids might result in decreased TRPV1 signalling, altered gastric motility and emesis (figure 1).[4 5]

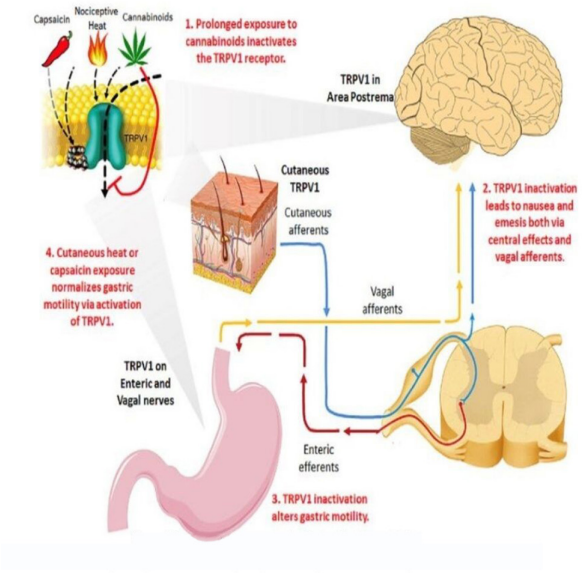

Figure 1 Diagrammatic representation of the pathophysiology of cannabinoid hyperemesis syndrome (CHS).[4 5] TRPV1, transient receptor potential vanilloid 1.

MANAGEMENT

The following expert consensus treatment guideline is available to assist with the diagnosis and appropriate treatment of CHS:

- Cessation of cannabis use, which is the only standard treatment reported in the current literature. CHS can recur on the resumption of cannabis use if the patient is in the recovery phase. Generally, it is thought that cannabinoid receptors return to normal levels after 4 weeks of cessation.
- Avoiding opioids to avoid addiction.
- These actions should be aided by supportive therapy, which includes:
  - IV fluids for dehydration.
  - Antiemetic medication such as ondansetron 4–8 mg IV or orally, promethazine 12.5 mg IV and metoclopramide 10 mg IV.
  - Benzodiazepines such as lorazepam 1 mg IV, diazepam 5–10 mg IV and diphenhydramine 25–50 mg IV have also been found to be helpful.

A hot shower may alleviate symptoms and be beneficial to the patient.

The application of capsaicin cream to the abdomen may provide some symptomatic relief for patients.

- Education, reassurance and referral to cessation programmes are important factors in management.[6–8]
- For refractory and severe nausea or vomiting in CHS, haloperidol should be considered.[9 10]

Awareness of this condition can prevent unnecessary investigations, save costs, and reduce hospital admissions in selected patients.

Learning points

The following are essential points of in-patient care:

- Good history taking, including illicit cannabis use, may reduce health costs.
- Cessation of cannabis use is the only known successful cure for this recurrent condition, as demonstrated in this patient.
- Cannabinoid hyperemesis syndrome is not a common condition, so whenever it is diagnosed it needs to be reported so that new manifestations can be recorded and patients can be appropriately managed.

Contributors Drafting of the text, sourcing and editing of clinical images, investigation results, drawing original diagrams and algorithms, and critical revision for important intellectual content: AE, MK, MM, BY. Final approval of the manuscript: AE, MK, MM, BY.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Consent obtained directly from patient(s)

Provenance and peer review Not commissioned; externally peer reviewed.

Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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