

## Lesson of the month 1: A rare case of cannabis hyperemesis syndrome relieved by hot water bathing

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### OVERVIEW

We present here a case of cannabinoid hyperemesis syndrome (CHS), which is an under-recognised disorder presenting in chronic abusers of cannabis typically as cyclical vomiting relieved by frequent hot baths. Increased awareness of CHS allows for earlier recognition by emergency departments, leading to prompter treatment and the prevention of future recurrence through cannabis cessation.

**KEYWORDS:** Vomiting, cannabis, hyperemesis, bathing

### Lesson

Our patient was a 28-year-old Caucasian man who presented acutely with vomiting and abdominal pain. His past medical history included a frontal skull fracture 6 years previously, which was treated conservatively. He was taking no medication, smoked 10 cigarettes and drank two cans of lager daily.

Physical examination was unremarkable other than epigastric tenderness. Initial blood tests were normal (including liver function tests, electrolytes, blood sugar and amylase) except for a high white cell count of  $18.4 \times 10^9/l$  (4.0–11.0). Radiology, including a chest X-ray and plain X-ray of abdomen, were also normal.

He was subsequently discharged the same day but returned twice over the following 3 months with identical symptoms. Hot baths would relieve his pain and nausea within minutes. This led to compulsive bathing during his admission.

On each admission routine bloods, as well as viral screen, *Helicobacter pylori* serology, thyroid function tests, coeliac screen, porphyria screen and stool cultures, were all normal. An ultrasound scan of abdomen was also normal. He underwent two oesophagogastroduodenoscopies (OGDs), which showed mild gastritis with normal duodenal biopsies. He started treatment with an oral proton pump inhibitor. A computed tomography (CT) scan of chest, abdomen and pelvis showed only a small solitary peripheral lung nodule. A colonoscopy and a small bowel meal were all normal. The patient self-discharged on both

admissions, frustrated that no cause for his symptoms was given and that no effective treatment had been provided.

The patient was seen in the outpatient clinic 6 months later and, for the first time, he reported occasional use of cannabis. He again presented as an emergency admission 4 months later with symptoms identical to those described during the other admissions. By that point, he had lost 25 kg in weight. He admitted to smoking cannabis every day.

A literature search on this strange ‘hot bath’ phenomenon discovered case reports of vomiting associated with heavy cannabis use. Discussing this possibility with the patient, he admitted to smoking approximately 1.5 g of cannabis almost every day for the past 13 years. With this being a possible cause for his symptoms, he vowed to stop. Since stopping cannabis use, he has remained well without recurrence of his previous symptoms and has now regained weight.

### Discussion

First described in 2004 by Allen *et al*<sup>1</sup> this increasingly recognised syndrome is relatively unknown by staff in emergency departments. Currently in the UK, there are 2.3 million cannabis users. In our area of Brighton and Hove, although cannabis use is an obvious problem, there have been recent calls by local politicians for the opening of cannabis cafes;<sup>2</sup> therefore, cannabis use might be on the rise. Its use is heaviest among 18–25-year-olds. The syndrome of cannabinoid hyperemesis syndrome (CHS) is described by Sontineni *et al* in 2009<sup>3</sup> as having specific diagnostic criteria of: recurrent nausea and vomiting, with relief after stopping cannabis and supportive features of compulsive hot bathing and colicky abdominal pain. Hepatobiliary disease must be excluded. Sullivan *et al* reported several such cases and described how CHS can also evoke symptoms of diarrhoea, temporary gastroparesis and polydipsia with diaphoresis.<sup>4</sup>

Cannabis mainly contains the exogenous-acting compound  $\Delta^9$ -tetrahydrocannabinol (THC), which is metabolised by cytochrome P450<sup>5</sup> in the liver (half life 20–30 h)<sup>6</sup> to acid metabolites that are excreted in urine and faeces. Before metabolism, THC is stored in body fat, which periodically can be broken down during times of stress or food deprivation, to produce a so-called ‘reintoxification effect’.<sup>7</sup> This might explain why CHS occurs periodically in patients precipitated by stress.

THC has antiemetic effects by acting on both the central and enteric nervous system via cannabinoid-1 and -2 receptors (CB1 and CB2). Although initially these effects delay gastric

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motility, thereby promoting nausea and vomiting, these effects become desensitised and most antiemetic effects occur through central nervous system activity. Two other active compounds of cannabis are cannabidiol (CBD) and cannabigerol (CBG), which have effects on the antiemetic properties of THC. In animal models, low doses of CBD enhance the antiemetic effect of THC, whereas higher levels enhance vomiting. Likewise, CBG antagonises CB1 receptors, reversing the antiemetic effects of THC and low doses of CBD. This could explain the mechanism by which chronic use of cannabis causes periodic hyperemesis and, therefore, the syndrome of CHS.

Classically, patients who present with CHS have been abusers of cannabis for several years. In one study, this was shown to be up to  $16.3 \pm 3.4$  years,<sup>8</sup> whereas the shortest reported length of abuse before CHS onset has been 18 months.<sup>9</sup> A retrospective case series of 98 patients found that 32% of patients reported less than 1 year of abuse.<sup>10</sup> However, this study might have been prone to memory bias. Use of cannabis is typically required to be above three times daily for CHS to develop.

CHS is a cyclical disorder separated by symptom-free periods. There are three phases to CHS<sup>7</sup>: the prodromal phase, lasting up to several months to years and characterised by early-morning nausea; the hyperemesis phase, which lasts up to 48 h; and the recovery phase, which can take weeks or months. During the hyperemesis phase, patients become dehydrated and are admitted to hospital. Through learned behaviour, they find relief through frequent hot bathing in up to 90% of cases.<sup>10</sup> Patients with CHS can remain misdiagnosed, with the average number of hospital admissions being  $7.1 \pm 4.3$ .<sup>8</sup> Early diagnosis leads to a reduction in morbidity and in the cost of unnecessary investigations.

Differential diagnoses for CHS include: cyclical vomiting syndrome itself (a disorder of which the mechanism remains unknown and classically occurs in young infants with anxiety or depression), abdominal migraine, pregnancy, gastrointestinal and pancreaticobiliary disorders (eg sphincter of Oddi dysfunction) and central nervous system diseases. A full history, examination and blood panel, as well as urine tests for glucose and  $\beta$ -human chorionic gonadotropin, must be carried out before a diagnosis of CHS can be considered, and only in those patient who meet the profile.

Treatment for CHS is with intravenous fluids and supportive care. Given the high frequency of oesophagitis and gastritis,<sup>3,4,8,11,12</sup> when these patients have endoscopies, acid suppression with proton pump inhibitors should be used routinely. Hot showers offer a short-lived relief of all symptoms, including pain, although the mechanism behind this is unknown. There have also been cases of relief with parental benzodiazepines.<sup>13</sup>

Relapse among this patient group is high because patients continue to abuse cannabis. In fact, patients resort back to cannabis because, in the prodromal phase, cannabis use eases nausea.

Our case is typical of CHS and was at first not recognised by our department. There is only one other case report of CHS in the

UK.<sup>14</sup> Although the debate around legalisation continues, there is a move certainly in the west (eg Washington state legalised cannabis in 2012) for cannabis use to become legalised to avoid black-market trading. There is an argument that this might increase the prevalence of users and, if so, CHS might become an increasing phenomenon. If this does occur, we might see more patients such as ours in emergency departments. However, knowledge that such a disorder exists will improve the lives of such patients.

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