A man in his 30s with recurrent vomiting and abdominal pain relieved by hot showers

Abdominal pain, nausea and vomiting are a common reason for admission to a medical ward. In our patient with recurrent symptoms, the medical history suggested a little known condition.

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A man in his 30s was admitted to the medical ward with nausea, retching, vomiting and abdominal pain. Seven years previously he had been admitted with stabbing retrosternal pain that worsened with intake of food and drink. At that time a small hiatus hernia of 1–2 cm and a small protrusion down towards the Z line were demonstrated. Over the following years the patient was admitted several times with corresponding symptoms. During the last admission it appeared that he smoked marijuana once a week. On examination on admission the patient had epigastric pain, he was sweating, felt nauseated and vomited green fluid. He had a lean stature. His blood pressure was 140/90 mm Hg, pulse 48 and the temperature measured in his ear was 35.4 °C. There was slight tenderness on light palpation in the epigastrium. There was no diarrhoea, he had had a normal bowel movement the same morning. His medication was pantoprazole 40 mg × 1. He had smoked marijuana on the day before admission.

Pantoprazole infusion was started. He had metabolic acidosis with base excess (BE) – 9.0 mmol/l (–3–3 mmol/l) and lactate 5.1 mmol/l (0.5–2.2 mmol/l) but the circulation was not affected. Blood tests showed a haemoglobin of 17.7 g/100 ml (13.4–17.0 g/100 ml), leukocytes 12.9 × 10^9/l (3.7–10.0 × 10^9/l), potassium 4.9 mmol/l (3.5–4.4 mmol/l) and glucose 8.4 mmol/l (4.2–6.3 mmol/l). The serum ethanol was negative. The other blood tests showed no significant abnormalities.

After receiving the results of the blood tests, the patient was re-examined in the ward. He had extreme motor restlessness, was sweating, felt nauseated, retched and had abdominal pain. Shortly afterwards he took a shower. After the shower he had no symptoms and was in good general condition and the clinical examination was normal. He admitted to smoking marijuana daily during the week before admission, but denied intake of other intoxicants including ethanol. Further, he said that he felt much better sitting in the shower, and that when he had similar symptoms he might shower 4 to 5 times a day. Not long after showering in the ward, the patient's symptoms returned. Analgesics and antiemetics had little effect.

On account of the metabolic acidosis, his urine was tested for ketones, and the osmolality and anion gaps were calculated. There were ketones in his urine. It was suspected that the ketonuria was due to inadequate nutrition. The osmolality gap was normal, but there was an anion gap of 20.1, which was attributed to the increased level of lactate and ketones. The reason for the increased lactate was not clear, but it may have been caused by muscular twitching/muscle activity. Porphyrins, porphobilinogen and δ-aminolevulinic acid in the urine were analysed, but the results were not available until after discharge when they were normal.

The symptoms were intuitively interpreted as probably related to intoxication. We were uncertain whether this could be normal abstinence as the patient had bradycardia, although this could also be due to increased parasympathotonia in connection with vomiting. A Google search using «cannabis» and «hyperemesis» revealed a description of cannabinoid hyperemesis that was relieved by compulsive bathing (1).

As his condition was still considered to be unresolved, CT of the abdomen and pelvis was carried out a little less than eight hours after admission, with a question of intestinal obstruction, ischaemic intestine or other aetiology of acute abdominal pain and vomiting. No abnormalities were found. Arterial blood gas analysis a little over 12 hours after admission showed that the pH and lactate had returned to normal, but there was still a slight base excess and mild hypocapnia, but normal oxygen values. The abdominal pain, nausea and retching diminished gradually. Two days after admission the patient was much better and wanted to leave, but remained in the ward for five days. A gastroscopy was performed with normal findings. When he was discharged he was feeling much better, though he still complained of nausea. He was told that we suspected cannabinoid hyperemesis. We recommended him to stop smoking marijuana.

Since then, over a year since he was admitted, we have been in touch with him by telephone several times. He has not managed to stop using marijuana, but says that his consumption is considerably reduced. His symptoms have not recurred. In the telephone conversations he explained his symtomatology in greater detail, and said that he had been smoking marijuana daily for 16 to 17 years. During these years, he has periodically isolated himself at home and smoked marijuana and drunk coffee with minimal food intake. He described that this behaviour evoked nausea, vomiting and abdominal pain with the feeling that his intestines were twisting, often accompanied by bouts of sweating – and relief of symptoms by a hot shower. He denied polydipsia. During periods before and during episodes of symptoms he has not tried to reduce his marijuana smoking.

Discussion

Cannabis is a generic term for intoxicants, for example hashish and marijuana, made from the plant Cannabis sativa or hemp. The active substance in cannabinoids from C. sativa is Δ^9-tetrahydrocannabinol (Δ^9-THC). Δ^9-THC binds itself to the membrane receptors CB_1 and CB_2. CB_1 receptors are localised in central and peripheral neurones, and also in the enteric nervous system in the digestive tract. CB_2 receptors are involved in immune functions and are expressed in plasma cells and macrophages, but are also found in areas of the brain connected with emesis (2).

The effects of cannabis in humans include mood changes (euphoria and dysphoria), impaired awareness, disturbed ability to

perceive, cognitive and psychomotor changes, tachycardia and conjunctival injection. Some of the effects of cannabinoids may be useful for medical treatment, for example the antiemetic and analgesic effects.

The cannabinoid hyperemesis syndrome was first described in 2004, when clinical observations led to a desire to investigate the connection between chronic cannabis abuse and cyclic vomiting (3). We have found 24 articles with case histories and collections of case histories that deal with the cannabinoid hyperemesis syndrome – 13 of these are from 2009–2010. The manifest disease picture is often preceded by a long prodromal period with nausea, vomiting and often loss of weight. During the course of the disease, hyperemesis develops accompanied by nausea, sweating, colic-like abdominal pain and polydipsia. A special acquired bathing behaviour has also been observed, the symptoms are relieved in the course of a few minutes by a hot bath or shower. Hospitalisation usually occurs when there is no more hot water or when there is general bodily weakness because of vomiting. The vomiting is intractable and refractory to antiemetic medication (3).

The condition improves after 24–48 hours with intravenous fluid therapy, but sometimes lasts for several days (4). The syndrome is seen in chronic, daily and considerable abuse for several years (often cannabis abuse for 10 to 20 years) and may thus be dose dependent (3, 5, 6). The incidence of cannabinoid hyperemesis is not known. In a collection of case histories by Soriano-Co and colleagues from the William Beaumont Hospital in Michigan, USA, with 1,065 beds and about 60,000 admissions per year, reference is made to eight diagnosed cases in the course of eight months (5). The symptoms are described as being chronically recurrent, with new attacks after weeks or months with persistent use of cannabis. The only known treatment is to stop using cannabis. Sontineni and colleagues have suggested criteria for the clinical diagnosis of the cannabinoid hyperemesis syndrome (frame 1) (7). The reason why the syndrome was not known until 2004 may be increased availability and higher global use in recent years, as well as the fact that cannabis has become stronger with a higher level of Δ^9-THC (6).

It is not known why some cannabis users develop the syndrome while others who smoke just as much for a long time do not develop the syndrome. There is no evidence to suggest that the syndrome is due to multi drug abuse as this has been investigated by toxicological screening tests in other published descriptions of case histories. Even so it is unfortunate that we failed to examine the urine for cannabinoids or other intoxicants. This was because the patient had already admitted to smoking marijuana and denied intake of other intoxicants. Δ^9-THC is excreted as Δ^9-THC acid, which can be demonstrated in urine in chronic abusers of cannabis for several weeks after the most recent intake (8). Urine analysis can be useful in patients with similar symptoms who deny use of intoxicants.

Byrne and colleagues have expressed scepticism about the syndrome (9). In 2008, Izzo & Camillieri argued that the condition was caused by cannabis abstinence (2). There is solid documentation demonstrating the existence of a cannabis abstinence syndrome (10). It has now been suggested that cannabis abstinence should be included in the Diagnostic and Statistical Manual of Mental Disorders (DSM)-5. However, none of the patients in the original description of the cannabinoid hyperemesis syndrome had wanted or tried to stop using cannabis before they became ill, on the contrary many increased their consumption (3). This was also true of our patient.

The mechanism behind the syndrome is not known. Cannabinoids have a long half life, are lipophilic and bind themselves to cerebral fat, and regular use may lead to accumulation and toxicity (3). Cannabis can also affect the hypothalamus via CB_1 receptors and thus disturb normal thermoregulation (1, 3). Δ^9-THC leads to dose-dependent hypothermia in mice (11). In none of the cases where the body temperature is mentioned, have there been strikingly high or low temperatures. Our patient had an ear temperature of 35.4 °C and has explained that he developed increased sweating and chills during his episodes of symptoms. Since the intake of cannabis has traditionally been associated with antiemetic properties, the syndrome is apparently a paradox – however some patients who are given cannabis as an antiemetic or appetite stimulating remedy may experience nausea, vomiting and abdominal pain (1).

The most characteristic feature of the syndrome is perhaps the bathing behaviour. It is not known why hot baths relieve the symptoms. Various suggestions have been put forward to explain this. Chang & Windish suggest that the brain reacts to reduced core body temperature caused by the hypothermic action of cannabis or that the patient attempts to increase skin temperature because of direct action of Δ^9-THC on the CB_1-receptors in the hypothalamus, and that this is not necessarily is a response to reduced core body temperature (1). Patterson and colleagues consider that CB_1-mediated vasodilatation in the visceral region contributes to the symptoms and that a hot shower leads to a redistribution of blood to the skin and therefore relieves symptoms (12).

It has also been shown that cannabinoid receptor agonists delay stomach emptying and intestinal transit. This can explain some of the symptoms, however gastric retention was not described on endoscopy of our patient.

There is a discussion of possible explanations of the syndrome in a review article by Darmani. Cannabis contains 60 substances with a cannabinoid structure, so that it could be one or more of these and not Δ^9-THC that causes vomiting. Moreover, genetic differences in the cytochrome P-450 system may lead to accumulation of cannabinoid metabolites that can in turn lead to vomiting in some individuals. It is also possible that Δ^9-THC has a paradoxical biphasic emetic/antiemetic effect and can act both as a partial agonist and as an antagonist. Chronic exposure to cannabis can also lead to desensitization and reduction in receptor density, which can threaten endocannabinoid receptor inhibition, resulting in increased tendency to vomit. Some individuals may be extra sensitive to the stimulating effect of Δ^9-THC on the liberation of endocannabinoids and inflammatory substances, for example arachidonic acid, which may have a pro-emetic effect (13).

In brief: The cannabinoid hyperemesis syndrome is a relatively recently described clinical picture with unknown pathogenesis. Some have wondered whether the clinical picture described in this syndrome is a consequence of cannabis abuse. The condition may be under-diagnosed and may also occur more frequently in the future, as the abuse of cannabis has increased in Norway. Clinicians should therefore be aware of the condition and the possibility of cannabinoid hyperemesis should be considered when evaluating patients with (cyclic) vomiting and abdominal pain of unknown origin. Knowledge of the syndrome leads to avoidance of extensive evaluation and unnecessary repetitions of the same examinations. The case history also illustrates the benefit of rapidly available medical information via the Internet in patients with unclear conditions (14).

Frame 1

Suggested criteria for the cannabinoid hyperemesis syndrome (7)

- Essential for the diagnosis
  - Regular use of cannabis for several years
- Main clinical features of the syndrome
  - Considerable nausea and vomiting
  - Vomiting with a cyclic pattern for months
  - Improvement of the symptoms after stopping use of cannabis
- Supplementary findings
  - Relief of symptoms by compulsive bathing/showering in hot water
  - Colic-like abdominal pain
  - No sign of cholecystitis or pancreatitis

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The patient has given permission for the article to be published.

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