Case in Point

Cannabinoid Hyperemesis Syndrome

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The convergence of legislative efforts, increasing prevalence, and tetrahydrocannabinol toxicity make this difficult-to-diagnose condition important to consider.

Given the recent rise in marijuana legalization efforts and an overall increase in the prevalence of marijuana use, it is becoming increasingly important to recognize conditions that are associated with its use. Data obtained from the National Survey on Drug Use and Health show the prevalence of marijuana use within the past month among those surveyed was 8.4% in 2014 This represents a 35% increase from the same study in 2002. Based on this survey, 2.5 million people (or ~7,000 per day) used marijuana for the first time.[1]

Following the liberalization of marijuana in Colorado, the prevalence of presentation to the emergency department (ED) for cyclic vomiting nearly doubled.[2] During the 2016 election season, several states included legislation that increased access to marijuana on the ballot, most of which passed. There are now 28 states plus the District of Columbia that permit medical marijuana usage, and 8 of those states and the District of Columbia have laws allowing for recreational use of marijuana.[3]

First described in a case series by Allen and colleagues in 2004, cannabinoid hyperemesis syndrome (CHS) is indicated by recurrent episodes of nausea and vomiting with vague abdominal pain and compulsive hot bathing in the setting of chronic, often daily, cannabis use.[4] A case of a middle-aged veteran with chronic marijuana use and recurrent, self-limited nausea and vomiting is presented here.

CASE PRESENTATION

A 45-year-old man presented to the ED with a 5-day history of persistent nausea and vomiting that began abruptly. The symptoms had been constant since onset, resulting in very little oral intake. The patient reported no hematemesis or coffee ground emesis. He noted a drop in his urine output over the previous 2 days. He also reported abdominal pain associated with the nausea. The patient characterized his pain as "dull and achy" diffuse pain that was partially relieved with emesis. His bowel movements had been regular, and he reported no diarrhea, fever, chills, or other constitutional symptoms. Additional 10-point review of systems was otherwise negative. The patient reported smoking marijuana multiple times daily for many years. The patient reported he had not used alcohol for several months.

A physical exam showed a pale and diaphoretic patient. Vital signs were significant for mild hypertension (150/75), but the patient was afebrile with a normal heart rate. An abdominal exam revealed a nontender, nondistended abdomen with no signs of rebound or guarding. The remainder of the examination was unremarkable. An initial workup showed a mild elevation of serum creatinine to 1.36 mg/dL (baseline is 1.10 mg/dL). Other workups, including complete blood count (CBC) with differential, complete metabolic panel, lipase, amylase, and urine analysis, were all unremarkable.

The patient's urine drug screen (UDS) was positive for tetrahydrocannabinol (THC). A computed tomography (CT) scan of his abdomen and pelvis with contrast was unremarkable. The patient was admitted for his inability to tolerate

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Table. Proposed Criteria for Cannabinoid Hyperemesis[5]

Essential to diagnosis
Long-term cannabis use (often daily)
Major features
• Cyclic nausea and vomiting
• Resolution with marijuana cessation
• Hot showers/baths relieve symptoms
• Abdominal pain
• At least weekly use of marijuana (often daily)
Supportive features
Age < 50 y
Weight loss > 5 kg
Morning predominance of symptoms
Normal bowel habits (lack of diarrhea)
Work up unremarkable (including laboratory, radiographic, and endoscopy)

oral intake and dehydration and treated supportively with IV fluids and antiemetics.

Overnight, the nursing staff reported that the patient took multiple, prolonged hot showers. Upon further questioning, he reported the hot showers significantly helped the nausea and abdominal pain. He had learned this behavior after experiencing previous episodes of self-limited nausea, vomiting, and abdominal pain.

Extensive review of his medical record revealed that the patient had, in fact, presented to the ED with similar symptoms 11 times in the prior 8 years. He was admitted on 8 occasions over that time frame. The typical hospital course included supportive care with antiemetics and IV fluids. The patient's symptoms typically resolved within 24 to 72 hours of hospitalization. Previous evaluations included additional unremarkable CT imaging of the abdomen and pelvis. The patient also had received 2 esophagogastroduodenoscopies (EGDs), one 2 years prior and the other 5 years prior. Both EGDs showed only mild gastritis. On every check during the previous 8 years, the patient's UDS was positive for THC.

Most of his previous admissions were attributed to viral gastroenteritis due to the self-limited nature of the symptoms. Other admissions were attributed to alcohol-induced gastritis. However, after abstaining from alcohol for long periods, the patient had continued recurrence of the symptoms and increased frequency of presentations to the ED.

The characteristics, signs, and symptoms of CHS were discussed with the patient. The patient strongly felt as though these symptoms aligned with his clinical course over the prior 8 years. At time of writing, the patient had gone 20 months without requiring hospitalization; however, he had a recent relapse of marijuana use and subsequently required hospitalization.

DISCUSSION

As in this case, CHS often presents with refractory, self-limited nausea and vomiting with vague abdominal pain that is temporarily relieved by hot baths or showers. In the largest case series, it was noted the average age was 32 years, and the majority of subjects used marijuana at least weekly for > 2 years.[5] Many studies categorize CHS into 3 phases: prodromal, hyperemetic, and recovery.

The prodromal, or preemetic phase, is characterized by early morning nausea without emesis and abdominal discomfort. The hyperemetic phase begins when the patient accesses the health care system via either the ED or primary care physician. This phase is characterized by intractable nausea and vomiting and may be associated with mild diffuse abdominal pain. The nausea and vomiting typically do not respond to antiemetic medications. Patients in this stage also develop a compulsive behavior of hot showers that temporarily relieve the symptoms. These behaviors are thought to be learned through their cyclical periods of emesis and may not be present during the first few hyperemetic phases.

During the recovery phase, the patient returns to a baseline state of health and often ceases utilizing the hot shower. The recovery phase can last weeks to months despite continued cannabis use prior to returning to the hyperemetic phase (Figure).[6,7]

Simonetto and colleagues proposed clinical criteria for the diagnosis of CHS based on their case series as well as on previously proposed criteria presented by Sontineni and colleagues.[5,8] Long-term cannabis use is required for the diagnosis. In the Simonetto and colleagues case series, the majority of patients developed symptoms within the first 5 years of cannabis use; however, Soriano and colleagues conducted a smaller case series that showed that the majority of subjects used marijuana for roughly 16 years prior to the onset of vomiting.[5,7]

The major CHS features that suggest the diagnosis are severe cyclic nausea and vomiting, relief of symptoms with abstinence from cannabis, temporary symptom relief with hot bathing, abdominal pain, and at least weekly use of marijuana. Other supportive features include aged < 50 years, weight loss > 5 kg, symptoms that are worse in the morning, normal bowel habits, and negative evaluation, including laboratory, radiography, and endoscopy (Table).[5]

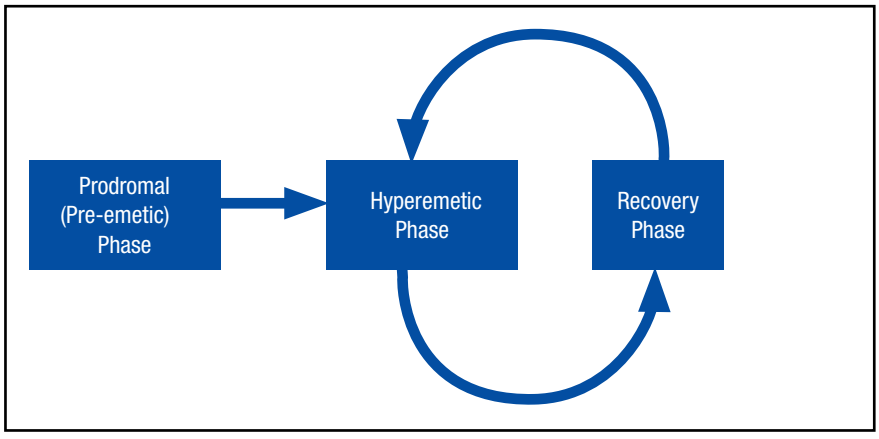
The differential diagnosis for nausea and vomiting is very broad,

including several gastrointestinal, peritoneal, central nervous system, endocrine, psychiatric, and metabolic causes. The suggested initial workup includes laboratory evaluation with CBC with differential, complete metabolic panel, lipase, urine analysis, UDS, and abdominal series. Further imaging and EGD may be indicated in certain patient populations, depending on the patient presentation.[6] When performed, the EGD can show a mild, nonspecific gastritis or distal esophagitis.[7]

Treatment often is supportive with emphasis placed on marijuana cessation. Intravenous fluids often are used due to dehydration from the emesis. The use of antiemetics, such as 5-HT3 (eg, ondansetron), D2 (eg, prochlorperazine), H1 (eg, promethazine), or neurokinin-1 receptor antagonists (eg, aprepitant) can be tried, but these therapies often are ineffective. Diet can be advanced as the patient tolerates. Given that many patients are found to have a mild gastritis, H2 blockers or proton pump inhibitors may be used. Extensive counseling on marijuana cessation is needed as it is the only therapy shown to have prolonged relief of the hyperemetic phase.[6] The length of cessation from marijuana for resolution of the cyclical hyperemesis varies from 1 to 3 months. Returning to marijuana use often results in the returning of CHS.[5]

The pathophysiology of CHS is largely unknown; however, there are several hypothesized mechanisms. Many theorize that due to the lipophilicity and long half-life of THC, a primary compound in marijuana, it accumulates in the body over time.[4,6] It is thought that this accumulation may cause toxicity in both the gastrointestinal track as well as in the brain. Central effects on the hypothalamic-pituitary axis may play a major role, and the reason for the symptom relief of hot baths is due to a change in thermoregulation in the hypothalamus.[5] One interesting mechanism relates to CB1 receptor activation and vasodilation within the gastrointestinal track due to chronic THC accumulation. The relief of the abdominal pain, nausea, and vomiting with hot showers can be secondary to the vasodilation of the skin, causing a redistribution from the gut. This theorized mechanism has been referred to as "cutaneous steal."[9]

Figure. Phases of Cannabinoid Hyperemesis Syndrome



CONCLUSION

With the increased prevalence of marijuana use in the U.S. over the past decade and reform in legislation taking place over the next couple of years, it is increasingly important to be able to recognize CHS to avoid frequent hospital utilization and repeated costly evaluations. Cannabinoid hyperemesis syndrome is recognized by the triad of chronic cannabis use, cyclical hyperemesis, and compulsive hot bathing.[4]

The syndrome has 3 phases. In the prodromal phase the patient has morning predominance of nausea, usually without emesis. This is followed by the hyperemesis phase, which is characterized by hyperemesis, vague abdominal pain, and learned compulsive hot bathing.

The third phase is the recovery phase, which is a return to normal behavior. During the recovery phase, if patients cease marijuana use, they remain asymptomatic; however, if patients continue to use marijuana, they often have recurrence of the hyperemesis phase.[5] The diagnosis of cannabinoid hyperemesis syndrome is difficult as it is a diagnosis of exclusion. Patients may present to the ED many times prior to diagnosis. With the changing climate of marijuana laws, it is an important condition to consider when establishing a differential. More studies will be required to evaluate the overall prevalence of this condition as well as if there are any changes following the liberalization of marijuana laws in many states. ●

Author disclosures

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