Cannabinoid Induced Intractable Cyclic Vomiting Syndrome in a 14.5-Year-Old Child

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Abstract
Cyclic Vomiting Syndrome (CVS) is characterized by recurrent, discrete episodes of vomiting between periods of completely normal health. Cannabinoid-induced CVS have been documented in adults but the link is often overlooked in children. To our knowledge this one of the youngest reported cases of cannabinoid induced CVS.

A 14.5-year-old male had been admitted to the hospital 9 times with episodes of CVS over a period of 24 months. Diagnostic tests including several imaging studies and laboratory tests were unremarkable except positive urine toxicology for cannabinoids at each hospitalization. Marijuana abuse is on the rise among adolescents in United States. It should be considered in young adolescents presenting with episodes of CVS prior to costly diagnostic testing which is a significant financial burden to the healthcare system.

ABBREVIATIONS
CVS: Cyclic Vomiting Syndrome; THC: Tetrahydrocannabinol; CNS: Central Nervous System; CB: Cannaboid

INTRODUCTION
Cyclic Vomiting Syndrome (CVS) is characterized by recurrent, discrete episodes of vomiting between periods of completely normal health. The costly and extensive work-up is a serious burden to the healthcare system. Cannabinoid-induced cyclic vomiting and hyperemesis have been documented in adults but the link is often overlooked in children. We report the youngest case of cannabinoid induced CVS. To our knowledge this one of the youngest reported case of cannabinoid induced CVS.

CASE PRESENTATION
A 14.5-year-old patient had been admitted to the hospital 9 times with episodes of cyclic vomiting over a period of 24 months. These episodes were abrupt in onset and resolved within 3-17 days. Physical examination was normal except for intermittent hypertension and abdominal tenderness. During each hospitalization, he was treated with IV fluids, acid-suppressing medications, and anti-emetics. Diagnostic tests including Upper GI series, colonoscopy, Head MRI-MRA, Abdominal CT, Abdominal MRA, Abdominal US, HIDA scan, and Head CT were within normal limits. Upper endoscopy showed mild erosions in the distal esophagus. Laboratory tests including amylase, lipase, liver function tests, metabolic panel, 24-hour urine catecholamines, and blood count were all normal. Urine toxicology was positive for cannabinoids at each hospitalization. Patient was counseled to discontinue marijuana use, however he continued to abuse marijuana. Interestingly unlike the adult cases, he did not have a history of compulsive bathing.

DISCUSSION
Cannabis is one of the most frequently abused illicit substances in the United States with over 16.7 million users. It is estimated that each year 2.6 million individuals in the USA become new users and most are younger than 19 years of age [1]. Cannabinoids are often used to treat nausea and vomiting, however recent published reports clearly describes that marijuana induces vomiting in chronic users. Cannabis induced hyperemesis syndrome was first described in 2004 by Allen and colleagues in 10 adult patients [2]. All patients used cannabis daily for 3-27 years. These patients had cyclic vomiting that often begins years after the initiation of the drug, abdominal pain, and compulsive hot showering with symptom relief, and resolution of the symptoms with abstinence from marijuana. In 2012 case series from Mayo Clinic described 98 adult patients from 2005-2010 with history of cyclic vomiting and chronic cannabis use [3]. In another case report described a 22 year old...
with refractory vomiting, colicky abdominal pain who had been abusing marijuana for six years. After cessation of marijuana the patient reported complete resolution of symptoms [4].

It is unclear if marijuana triggers or cause episodes of cyclic vomiting syndrome. Various theories have been hypothesized to explain the mechanism of cannabinoid induced vomiting. Delta-9 tetrahydocannabinol (THC), the main active cannabinoid acts on endogenous cannabinoid receptors CB-1 and CB-2 [5]. CB-1 receptors are expressed mainly in Central Nervous System (CNS) and Enteric Nervous System. CB-2 receptors are expressed in immune system. CB-1 receptors are thought to be involved in the most of the known effects. In animal models, CB-1 receptor activation in the dorsal vagal complex of the brainstem mediates the anti-emetic effect. In the CNS, marijuana is commonly used for the treatment of chemotherapy-induced nausea and vomiting [6].

The gastrointestinal effects of the cannabinoids are mediated mainly by CB-1 receptors. Activation of CB-1 receptors result in inhibition of gastric acid secretion, lower esophageal sphincter relaxation and altered motility. CB-1 receptor activation reduces gastric motility and results in delayed gastric emptying in rat models. THC when used to at an antiemetic dose causes significant gastroparesis. Dronabinol (synthetic THC) has been shown to delay gastric emptying in humans [7].

CVS seems to be a paradoxical reaction with chronic THC abuse, resulting in episodes of recurrent vomiting with completely symptom free period in between the episodes. While mechanism of this syndrome is not well known, it may be related to dysregulation of the endogenous cannabinoid system due to sustained stimulation of the receptors overtime. The cannabis plant contains hundreds of components with sixty posing cannabinoid structures, only two CBD and CBG have been studied extensively, the effects of other components in the humans are not known. There is also a possibility that the contamination of the marijuana with chemicals and toxins might be the culprits [8].

It is unclear why these patients have dramatic episodes of vomiting and severe colicky abdominal pain every few weeks rather that daily. Our patient similar to the other cases reported had significant colicky epigastric pain in addition to the vomiting which is not a classic pattern seen in children with CVS. Most of the children with CVS have self-limited episodes of vomiting which does not require ER visits. However patients with marijuana induced CVS tend to have longer episodes with severe colicky abdominal pain requiring hospital stay or ER visits.

Marijuana abuse should be considered in young adolescents presenting with episodes of cyclical vomiting prior to costly diagnostic testing which is a significant financial burden to the healthcare system. Our case is the youngest patient in the literature with marijuana related CVS. Recognition of this syndrome among the clinicians and scientist is important to prevent repeated diagnostic testing and decrease morbidity. We are expecting a surge of these cases presenting to ER, gastroenterologists and primary care physicians due to legalization of the medical use of marijuana in some states. We do advocate routine urine drug screen in young adolescents presenting with CVS. Since symptoms resolve with cessation of marijuana, these patients would need counseling and frequent follow up to ensure that they stop abusing marijuana. More pharmacological research is needed to understand the exact mechanism of the pro-emetic effect of cannabinoids and their metabolites on the gut and how it overrides the its antiemetic CNS properties.

REFERENCES