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Case Report

Marijuana in Pregnancy; its Relationship to Nausea, Emesis, and Hyperemesis

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Abstract

Background: Approximately 4.6 - 11% of patients admit to marijuana use during pregnancy. Marijuana is used both medicinally and recreationally. Historically, marijuana has been used as an anti-emetic. However, the growing literature of Cannabinoid Hyperemesis Syndrome necessitates attention to the paradoxical proemetic effects of this drug. As marijuana use increases, the effect on pregnancy and neonatal outcomes is a topic of ongoing investigation.

Case: We present a case of a 25-year-old female with twenty-eight hospital visits for hyperemesis during her pregnancy. On review of her case, she met criteria for diagnosis of Cannabinoid Hyperemesis Syndrome, which if diagnosed sooner, may have altered the course of her admissions and treatment.

Conclusion: Marijuana use is associated with nausea and vomiting in pregnancy. However, whether it is the causative agent or the treatment option has yet to be established. Cannabinoid Hyperemesis Syndrome can be seen in pregnant patients and treatment during pregnancy remains the same as in the non-gravid state.

ABBREVIATIONS

CHS: Cannabinoid Hyperemesis Syndrome; FGR: Fetal Growth Restriction; THC: Tetrahydrocannabinol

INTRODUCTION

In 2004, Allen et al. aimed to explore the association between chronic cannabis abuse and a cyclical vomiting illness. He published a case series of 10 patients all with chronic cannabis use and cyclical vomiting whom after discontinuation of cannabis use experienced cessation of vomiting illness. A novel finding was that 9 of the 10 patients displayed an abnormal washing behavior during episodes of active illness [1]. This is the first report of what is now known as Cannabinoid Hyperemesis Syndrome (CHS). To this date, there are approximately 100 published cases of CHS. This syndrome continues to gain publicity as legislation that governs the use of marijuana evolves. Currently in the United States, there are twenty-six states that allow medicinal marijuana use and five that have legalized marijuana for recreational use [2].

CASE PRESENTATION

The patient was a 25 year-old gravida 1, para 0 who first

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presented to the Emergency Department at 6 weeks gestation with complaints of nausea and vomiting. At this initial visit her weight was 122 lbs. She was given Zofran and pyridoxine and discharged home. At her obstetrics intake visit at approximately 10 weeks gestation, her weight was 109 lbs and she complained of severe nausea and refractory emesis for the past 4 weeks. Her medical history was significant for resolved hepatitis C infection and post-traumatic stress disorder from a violent attack as a teenager. She reported quitting tobacco and marijuana after knowledge of pregnancy and denied any other illicit drug use.

Throughout her pregnancy, she had twenty-eight hospital triage visits with fifteen hospital admissions all with the chief complaint of nausea and vomiting. She had an extensive evaluation for other causes of nausea and vomiting. She had normal thyroid studies, normal liver enzymes and lipase, as well as normal ultrasound of liver and gallbladder. She frequently had electrolyte abnormalities, which were corrected with intravenous supplementation and at each admission treated with intravenous fluid hydration, Zofran, Raglan, Phenergan, scopolamine patch, vitamin B6, and proton pump inhibitors. She had one attempt at steroid therapy with very minimal relief, so never completed an entire steroid course. After episodes of

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hematemesis she underwent further evaluation and was found to be positive for *H. pylori* infection. She received treatment with triple antibiotic therapy without improvement in symptoms and her hematemesis was attributed to Mallory-Weiss esophageal lacerations. Given poor nutrition and maternal weight gain, she had naso-duodenal feeding tube placed for supplemental feeds. This ultimately was dislodged with episodes of emesis after hospital discharge. Her weight fluctuated extensively throughout pregnancy, with her maternal weight at delivery 118 lbs. This was 3 lbs less than her pre-pregnancy weight.

She reported temporary relief of nausea and emesis by taking hot showers. She routinely requested to get in the shower as soon as possible after being admitted and reported improvement in her nausea. She repeatedly denied marijuana use despite all urine drug screens from 12 weeks gestation to 29 weeks gestation being positive for THC. Further evaluation of her past history revealed recurrent THC positive urine drug testing for five years prior to pregnancy. After discussion of these results, she admitted to marijuana use "every now and then" to aid with appetite and nausea. She was strongly advised to cease all THC use, as there was concern for possible Cannabinoid Hyperemesis Syndrome. Her first negative drug screen was at 31 weeks gestation.

Ultimately, the patient developed fetal growth restriction (FGR) thought to be secondary to malnutrition. At 28 weeks gestation she had estimated fetal weight of 1275 grams at

The $43^{\rm rd}$ percentile. This declined to 1789 grams which was the $11^{\rm th}$ percentile at 32

Weeks gestation and then to 2269 grams which was the 2nd percentile at 37 weeks gestation. At that time she underwent induction of labor for poor fetal growth and delivered a male infant via vaginal delivery with birth weight 2460 grams, appropriate for gestational age. At her 4-week postpartum visit she was doing well with no complaints of nausea or emesis after delivery.

DISCUSSION

Cannabinoid Hyperemesis Syndrome (CHS) is a cluster of symptoms characterized by cyclic nausea and vomiting with abdominal pain without an obvious organic cause and compulsive hot water bathing behavior induced by long-term cannabis use (more than 1 year) [3]. The etiology of CHS is not well understood. However, there are numerous theories that attempt to explain this paradoxical adverse emetic effect of marijuana use. Theories range widely. Some advocate that genetic variation in cannabinoid metabolism leads to toxic accumulation [4]. Alternatively, long-term marijuana use leads to THC accumulation in cerebral fat causing toxicity and emesis in sensitive patients [5]. Still others indicate that the enteric pro-emetic effects of cannabis may override its central nervous system-mediated antiemetic effects to promote emesis [4,6]. CHS is divided into three phases [6]. The prodromal phase lasts for months or years and is characterized by morning nausea, a fear of vomiting, and abdominal discomfort. Intensely persistent nausea, vomiting, and retching characterize the hyper-emetic phase. Patients experience weight loss and dehydration due to inability to tolerate solid food. During this phase patients may take multiple hot water showers or a single shower lasting hours

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in attempt to quell the hyperemesis. This learned compulsive bathing is characteristic of CHS. It is not yet well understood why patients experience relief with hot showers. Finally, the recovery phase begins with cannabis cessation and can last from days to months. Return to cannabis use lead to recurrence of CHS. The treatment of hyperemesis is largely supportive with anti-emetics, IV hydration, and supplementing electrolytes. The hallmark of treating CHS specifically is cannabis cessation and the addition of lorazepam, which has been proven to aid in cessation of nausea, abdominal pain, and food aversion [7].

In 2011, the first case of cannabinoid hyperemesis syndrome in pregnancy was reported by Schmid et al., [8]. Since this time, only two other cases of CHS in pregnancy have been added to the literature [9,10]. We do believe our patient met criteria for diagnosis of CHS.

The patients in previous CHS in pregnancy reports along with this patient, range from age 24-28 years old. Patients were not of the same race, did not report similar past medical or social history, and no inference could be made of their social economic status. Three of the four patients initially denied marijuana use. All patients were initially diagnosed with hyperemesis gravidarum and treated in this manner. All patients began habitual marijuana use in their teenage years. Improvement of symptoms with hot showers was described in each case. No similarities in pregnancy or neonatal outcomes could be made due to lack of this information presented in all cases. Resolution of symptoms after decreasing marijuana use or complete abstinence was noted in the previously published cases. However, the timing from abstinence to resolution of symptoms was not specified.

Nausea and vomiting affects approximately 85% of pregnant patients. Severe nausea and emesis with associated weight loss, referred to as hyperemesis gravidarum, affects approximately 2% of pregnant patients [11]. Depending on the patient population, marijuana use during pregnancy varies from 4.6% to 11% [12,13]. The majority of marijuana users propose marijuana as a potential treatment for nausea, emesis, and hyperemesis. While investigating cannabis use among childbearing women, Westfall et al. found that 92% of respondents who used cannabis therapy for morning sickness considered it 'extremely effective' or 'effective' [14]. Yet, a retrospective study by Roberson et al. found that women who reported severe nausea during pregnancy were more likely to report marijuana use when compared to women who did not report severe nausea. They also found that women who reported severe nausea during pregnancy also had a higher prevalence of marijuana use before pregnancy compared to women who did not report severe nausea during pregnancy. This result was not statistically significant [15]. These results leave us to question whether patients with severe nausea and emesis attempted to use marijuana as an anti-emetic or if chronic marijuana users are at greater risk of severe nausea and emesis during pregnancy. Further research is still needed for us to answer the question of marijuana's effect on nausea and emesis or to identify which patients are at risk of the paradoxical proemetic effects of marijuana.

The incidence of CHS is not well established. Given the similarities of CHS with hyperemesis gravidarum, it is suspected that CHS is under diagnosed in the pregnant population. The

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presence of compulsive hot water bathing is an important major diagnostic feature of CHS, because no other known vomiting syndrome shares this phenomenon [3]. Our patient had been treated for hyperemesis gravidarum without success. As we looked back on her case, it was the peculiarity of hot water bathing that led us to the diagnosis of CHS rather than hyperemesis gravidarum. A high index of suspicion is imperative in order to direct questioning and toxicology to differentiate between these syndromes.

In July 2015, The American College of Obstetricians and Gynecologists released a Committee Opinion on Marijuana Use During Pregnancy and Lactation. Pregnancy-specific safety data is difficult to obtain given the numerous cofounding exposures such as tobacco, alcohol, other illicit drugs, or adverse socioeconomic conditions. The Committee reviews conflicting data that suggest impaired cognition and increased sensitivity to drug abuse, negative effects on brain development, decreased attention span and behavioral problems, association with low birth weights, and preterm birth. Current research is slowly elucidating the association with marijuana and these outcomes that have not yet been firmly established. However, "because of concerns regarding impaired neurodevelopment, as well as maternal and fetal exposure to adverse effects of smoking, women who are pregnant or contemplating pregnancy should be encouraged to discontinue marijuana use. Because the effects of marijuana use may be as serious as those of cigarette smoking or alcohol consumption, marijuana use should be avoided during pregnancy" [16].

Marijuana use is increasing and its effect on pregnancy and neonatal outcomes is not yet clear. For cases of refractory hyperemesis, a thorough history and high index of suspicion is necessary to diagnose CHS. As we learn more about marijuana in pregnancy, recommendations may change. Currently, the use of marijuana during pregnancy and lactation is strongly discouraged.

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