Cannabinoid Syndrome in the Pregnant Patient: Clinical Case and Literature Review

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Case report

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Abstract

**Background:** Cannabis use is on the rise. Several cases of cannabinoid syndrome, secondary to chronic cannabis intoxication, have been described worldwide, but few cases have described this entity in pregnant women.

**Case presentation:** We describe a 29-year-old pregnant patient that had consumed cannabis and experienced uncontrolled vomiting. The use of hot baths, the rapid improvement in symptoms, and results of complementary examinations suggested a diagnosis of cannabinoid syndrome. The patient could return home and she continued her pregnancy and childbirth without peculiarities.

**Conclusion:** Cannabinoid syndrome should be considered in the differential diagnosis of vomiting in pregnancy. Consumption of cannabis must be systematically included in the anamnesis. However, it seems to be somewhat unacceptable socially or medically. Consumption must be stopped to manage symptoms.

1. Background

Cannabinoid syndrome is a recent clinical entity (1) involving nausea and vomiting in chronic cannabis users. The syndrome is also frequently associated with abdominal pain and compulsive showers or hot baths, which can attenuate the symptomatology (1, 2).

The diagnosis of cannabinoid syndrome is based on the exclusion of other causes and the disappearance of symptoms once cannabis consumption is terminated (2). The diagnosis and treatment of cannabinoid syndrome presents a challenge to the clinician. We describe a rare case of a pregnant woman that was likely to have cannabinoid syndrome. We will review the cases published to date and the current therapeutic options and discuss the peculiarity of pregnancy. Finally, we emphasize the notion that this syndrome should not be ignored, when assessing other causes of vomiting during pregnancy, such as hyperemesis gravidarum.

2. Case Presentation

A 29-year-old patient in her first pregnancy, at 29 weeks and 1 day gestation, visited the emergency room for uncontrolled vomiting and epigastric pain. She reported no health problems, but she smoked tobacco and cannabis. She had consumed for about 2 grams per week for 6 years. She did not have any known allergies. She reported a decline in symptoms when taking a hot bath. The cardiopulmonary clinical examination was unremarkable. Abdominal palpation showed epigastric pain without guarding or rebound. The patient had a body temperature of 35.9 °C, and displayed stable hemodynamics.

Further examinations revealed normal blood biology, except for hyperleucocytosis; the leucocyte level was 14,700/mm³, including 12,850 neutrophils. An abdominal ultrasound showed no detectable pathology. Obstetrically, she had a normal ultrasound, normal cardio-fetal monitoring.

She was treated with paracetamol (1000 mg), tramadol (50 mg), metoclopramide (10 mg) and butylhyoscine bromide (10 mg). Based on the strong suspicion of cannabinoid syndrome and her clinical improvement in the emergency department, the details of this entity were explained to the patient, and she returned home.

The pregnancy was featureless, and she gave birth at 39 weeks 6/7 to a healthy 2650-g newborn. She returned home after 3 days of uneventful hospitalization.

3. Discussion
The classic clinical picture of cannabinoid syndrome is as follows: chronic, intensive use of cannabis, episodes of incoercible vomiting, and abdominal pain. A symptomatological and temporary improvement in symptoms is noted when taking a bath or hot shower. Finally, the syndrome is expected to cease when the patient stops cannabis use.

Cannabis use is increasing worldwide (3). Accordingly, the number of published cases of cannabinoid syndrome has increased, and the pathology is of interest in various related specialties, including pediatrics (4) and forensic pathology (5). Although the cause of the syndrome is being discussed continually and remains to be formally clarified, a few known factors are notable. First, Δ-9-tetrahydrocannabinol (THC) is a CB1 receptor agonist, and it is assumed that deregulation of the receptor could cause nausea.

More than half of pregnant women experience nausea and vomiting. Hyperemesis gravidarum, which affects only 0.3 to 1% of pregnant women, is defined as persistent vomiting, more than 5% weight loss, ketonuria, and electrolyte abnormalities (particularly hypokalemia). The physiopathology remains unclear, but it is linked to hormonal activity and the production of human chorionic gonadotropin (6, 7).

We conducted a literature search to identify clinical cases of cannabinoid syndrome in pregnant patients. We employed the search terms ‘Cannabinoid’ ‘Hyperemesis’ and ‘Pregnancy’ in PubMed and Google scholar. We identified five clinical cases (8–12) and extracted their characteristics (detailed in the appendix tables).

Unlike studies in non-pregnant individuals (2), the low number of studies in pregnant patients makes it difficult to perform statistical analyses. On the other hand, there are similarities between non-pregnant and pregnant individuals. Most individuals with cannabinoid syndrome have consumed cannabis for years, mostly daily, and the symptoms tend to improve after taking a shower or hot bath. However, cannabinoid syndrome is particularly complex in pregnant women. Women that use cannabis during pregnancy are more likely to experience severe nausea than those that do not (13). Nevertheless, and paradoxically, antiemetic effects have been attributed to cannabis, in both the general population (14) and pregnant women (15). Some authors have recommended cannabis for treating hyperemesis gravidarum (16). One hypothesis suggested that endocannabinoids played a role in the latter pathology. However, that hypothesis was refuted in a prospective study that did not find any changes in plasma endocannabinoid levels in patients with gravidarum hyperemesis (17).

Cannabis use is increasing among pregnant women (18). However, it seems to be somewhat unacceptable socially or medically. This stigma might lead them to hide it during an anamnesis. This possibility was reinforced by the absence of a link between symptomatology and cannabis use (8). The prevalence of cannabis use in parturition is likely to be generally underestimated (19). Some patients diagnosed with classical nausea and vomiting during pregnancy or even gravidarum hyperemesis might actually have cannabinoid syndrome. These entities might be differentiated clinically by the sensitivity of hyperemesis gravidarum to certain antiemetic drugs (20, 21).

Potentially beneficial therapies for treating common cannabinoid syndrome, such as lorazepam (22) and haloperidol (23), are contraindicated in parturient women (24). Capsaicin cream is not recommended in pregnant women. However, its usefulness could be discussed, in light of its supposed safety. Capsaicin treatment requires low dosages, and it cannot pass the placental barrier (25). Similarly, ondansetron (26) appeared to have some efficacy. Although ondansetron is not recommended in the first quarter of pregnancy, its use might be permissible thereafter (24). Metoclopramide, which can be used in any term of pregnancy, has been used to treat cannabinoid syndrome and showed some efficacy.

This case study serves to remind physicians of the need to insist on recounting cannabis use in anamnesis, particularly in parturient women with vomiting. Fortunately, the compulsive use of hot baths or showers seems specific
to this clinical entity (2) and can help discriminate cannabinoid syndrome from other diseases.

There is a need for prospective studies that aim to determine the proportion of cannabinoid syndrome among a parturient sample with vomiting and characterize potential differences in this subpopulation.

Randomized, controlled therapeutic trials should also be conducted to find a functional treatment for symptoms. On one hand, an effective treatment could obviate the potential consequences of drugs of equivocal safety. On the other hand, an effective treatment is needed to avoid serious consequences of incoercible vomiting, which range from pneumomediastinum (27) to death (5) and acute renal insufficiency (28).
| Number | Reference                          | Age, y | Obstetric Status | Gestation period, weeks; days | Nausea and vomiting | Showers effect | Usual consumption (how long/how many times per week) | Antiemetic/Effect | Other Examinations | Delivery |
|--------|-----------------------------------|--------|------------------|-------------------------------|---------------------|----------------|-----------------------------------------------------|-----------------|------------------|----------|
| 1      | Schmid SM et al, 2010             | 26     | G2P0A            | 10; ?/ ?                      | All 3               | Beneficial | 13 years/daily | Metoclopramide | Chlorpromazine | NICU for hypoxia. |
|        |                                   |        |                  |                               |                     |               |                                                     |                 |                  | Hospital discharge on the second day in good condition |
|        |                                   |        |                  |                               |                     |               |                                                     |                 |                  | Hospital discharge on the second day in good condition |
| 2      | Alaniz VI et al, 2015             | 28     | G5P3A            | 30; 5/7                       | All 3               | Beneficial | 12 years/daily | Unspecified molecule/ineffective | Blood test + Cerebral and abdominal Magnetic Resonance imaging |
|        |                                   |        |                  |                               |                     |               |                                                     |                 |                  | NICU for hypoxia. |

? indicates no data available. Abbreviations: NICU: neonatal intensive care unit; y: years; wks: weeks; g: grams.
| Number | Reference  | Age, y | Obstetric Status | Gestation period, weeks; days | Nausea and vomiting | Shower effect | Usual consumption (how long/how many times per week) | Antiemetic/Effect | Other Examinations | Delivery |
|--------|------------|--------|------------------|------------------------------|---------------------|--------------|---------------------------------------------------|----------------|-------------------|----------|
| 3      | Andrews KH et al, 2015 | 24     | G5P2A 2          | 26; 2/7                      | All 3               | Beneficial  | 8 years / several times per week                  | Metoclopramide effectiveness associated with stopping cannabis use and a prescription of hot showers | Blood test Abdominal x-ray abdominal and pelvic CT scan | 37 wks   |

APGAR 9/9; No complications described

? indicates no data available. Abbreviations: NICU: neonatal intensive care unit; y: years; wks: weeks; g: grams
| Number | Reference          | Age, y | Obstetric Status | Gestation period, weeks; days | Nausea and vomiting | Showers effect | Usual consumption (how long/how many times per week) | Antiemetic/Effect | Other Examinations | Deliver y |
|--------|--------------------|--------|------------------|-----------------------------|---------------------|----------------|-----------------------------------------------------|-----------------|-------------------|-----------|
| 4      | Manning Meurer M et al, 2017 | 21     | G1P0A0           | 6;?/?                       | Shower/bath not described | ?              | ?                                                   | ?               | Induced at 36 wks 6/7 for Pre-eclampsia. | Induced at 36 wks 6/7 for Pre-eclampsia. |

2430 g

Fetal deceleration

Shoulder dystocia

APGAR 1/5

19 days in NICU

Baby intracranial hemorrhage and spontaneous resorption.

At 10 months of life, normal baby evolution.

? indicates no data available. Abbreviations: NICU: neonatal intensive care unit; y: years; wks: weeks; g: grams
| Number | Reference | Age, y | Obstetric Status | Gestation period, weeks; days | Nausea and vomiting | Showers effect | Usual consumption (how long/how many times per week) | Antiemetic/Effect | Other Examinations | Delivery |
|--------|-----------|--------|------------------|-----------------------------|---------------------|----------------|------------------------------------------------------|------------------|-------------------|----------|
| 5      | Kim HG et al, 2018 | 20     | G7P0A 6          | 14; 3/7                     | All 3               | Beneficial    | ?                                                     | Ondansetron      | Blood test        | 40 wks 1/7 |
|        |           |        |                  |                             |                     |                |                                                      | Famotidine       |                   | 3190 g  |
|        |           |        |                  |                             |                     |                |                                                      | Metoclopramide   |                   | APGAR 8/9 |
|        |           |        |                  |                             |                     |                |                                                      | Ondansetron per os |                   | No complications described |
|        |           |        |                  |                             |                     |                |                                                      | Promethazine IR |                   |                      |
|        |           |        |                  |                             |                     |                |                                                      | All ineffective  |                   |                      |
| 6      | This Case | 29     | G1P0A 0          | 29                          | All 3               | Beneficial    | 6 years/daily                                        | Metoclopramide/ no effect | Blood test | 39 wks 6/7 |
|        |           |        |                  |                             |                     |                |                                                      | Abdominal and pelvic ultrasound |                   | 2650 g  |
|        |           |        |                  |                             |                     |                |                                                      | No complications. Hospital discharge on the third day in good condition |                   |                      |

? indicates no data available. Abbreviations: NICU: neonatal intensive care unit; y: years; wks: weeks; g: grams
Table 2  
Demographic Characteristics

| Characteristic                                      | Average/median |
|-----------------------------------------------------|----------------|
| Age, years                                          | 24.6/25        |
| Pregnancy at diagnosis, weeks                       | 19.1/20        |
| Time since first consumption, years                 | 9.75/10        |
| Consumption at least several times a week, n        | 4/4            |
| Beneficial showers/hot baths, n                     | 6/6            |
| Need for neonatal intensive care, n                 | 2/6            |

**Declarations**

**Consent for publication**

The patient provided consent to the publication of all the material referenced here.

**Availability of data and materials**

All data generated or analysed during this study are included in this published article [and its supplementary information files].

**Competing interests**

The authors declare that they have no competing interests

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**Authors' contributions**

JF was the major contributor in writing the manuscript. NS and HT corrected the text. All authors read and approved the final manuscript.

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