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(CASE REPORT)

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Multidisciplinary management of severe hyperemesis gravidarum complicated by cannabinoid and opioid use: A case report on the complex interplay of hyperemesis gravidarum, opioids and treatment challenges

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Abstract

Hyperemesis gravidarum (HG) presents a significant management challenge in pregnancy due to its debilitating effects on maternal health and fetal outcomes. This case report details the presentation and management of a 34-year-old primigravida at 17 weeks and 4 days gestation with severe HG. The patient's history includes significant gastrointestinal procedures, a prior child with lissencephaly, and continued opioid use during pregnancy. Her symptoms were refractory to conventional treatments and further complicated by cannabinoid use. A multidisciplinary approach involving gastroenterology, surgery, obstetrics, pharmacists, and dietitians was employed, resulting in significant improvement. This case highlights the importance of a comprehensive care strategy in managing refractory HG complicated by substance use.

Keywords: Hyperemesis Gravidarum; Opioids; Cannabinoids; Antiemetics; Multidisciplinary Approach.

1. Introduction

Hyperemesis gravidarum (HG) is a severe form of nausea and vomiting in pregnancy, leading to dehydration, electrolyte imbalance, and ketonuria, and posing a substantial clinical challenge in obstetric care [1-2]. While various treatment modalities, such as antiemetic medications and intravenous fluids, are commonly employed, refractory cases demand a deeper exploration of contributing factors [3]. Opioid and cannabinoid overuse, though not typically associated with HG, can complicate management due to their potential to exacerbate nausea and vomiting or mask underlying symptoms and significant weight loss. This report presents a complex case of HG exacerbated by cannabinoid and opioid use, managed through a multidisciplinary approach emphasizing the importance of tailored interventions to optimize maternal and fetal outcomes.

2. Case Presentation

A 34- year-old primigravida (G4 P0302) at 17 weeks and 4 days gestation presented with severe nausea, vomiting, and dehydration. Her medical history included multiple gastrointestinal procedures: laparoscopic cholecystectomy, esophago-gastro-duodenoscopy (EGD), Nissen fundoplication, and esophagus dilation and biopsy. Additionally, she had a history of a child with lissencephaly who passed away at 21 months.

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2.1. Obstetric History

- **First Pregnancy:** Complicated by lissencephaly (Dandy-Walker syndrome) and preterm delivery, resulting in the child's demise at 21month.
- **Second Pregnancy:** Complicated by COVID-19 with gastrointestinal symptoms, decreased fetal movements, and emergent preterm delivery via cesarean section.
- **Third Pregnancy:** Complicated by severe HG, mid-epigastric pain, TPN requirement, premature preterm rupture of membranes, chorioamnionitis, emergent cesarean delivery, postoperative sepsis, ICU admission, and identification of a large hiatal hernia leading to Nissen fundoplication.

2.2. Current Pregnancy Presentation

The patient presented with acute worsening of nausea, vomiting, and mid-epigastric pain at 17 weeks and 4 days. She reported continued opioid use during pregnancy for chronic back pain, albeit at lower doses. Urine toxicology was positive for cannabinoids, opioids, and benzodiazepines.

2.2.1. Labs and Diagnostics

Laboratory investigations revealed electrolyte imbalances (Table A) consistent with dehydration, hyponatremia, and hypokalemia secondary to excessive vomiting. Urine toxicology screening (Table C) confirmed the presence of cannabinoids and opioids. The patient's hematology and renal functions were however, non-significantly changed. (Table B).

2.2.2. Chemistry

Table 1 Laboratory chemistry findings at GA (17 weeks) – Day 1 through Day 5

GA weeks (17)	Na mEq/L	K mEq/L	Cl mEq/L	CO_2 mEq/L	Anion gap mEq/L	Glucose mg/dl
D1	136	3.7	104	21.6	10	90
D2	135	3.7	106	18..8	8	91
D3	135	3.3	106	21.5	8	86
D4	133	3.6	106	19.8	7	107
D5	141	3.6	108	19.6	13	101

2.2.3. Hematologic and kidney function test

Table 2 Laboratory hematologic/renal findings at GA (17 weeks) – Day 1 through Day 5

GA weeks (17)	Creatinine mg/dl	eGFR ml/min	Total protein g/dl	Albumin g/dl	Bilirubin mg/dl	BUN mg/dl	BUN/ Creatinine
D1	0.64	119	6.6	3.1	0.5	19	29.7
D2	0.57	122	6.4	3	0.7	17	29.8
D3	0.49	127	5.5	2.6	0.6	15	30.6
D4	0.57	122	6	2.8	0.5	16	28.1
D5	0.64	119	6.9	3.2	0.5	19	29.7

2.2.4. Toxicology (Urine)

Table 3 Laboratory toxicology findings at GA (9W D1) and (17W D4)

GA weeks	Cannabinoids	Opioids	Benzodiazepines	Cocaine metabolites	Amphetamines
9W D1	Pos	Pos	Neg	Neg	Neg
17WD4	Pos	Pos	Neg	Neg	Neg

2.3. Management and Follow-Up

As conventional antiemetic therapy and fluid resuscitation failed to alleviate her symptoms, she was initiated on a multimodal pharmacotherapy approach, including ondansetron (scheduled and continuous infusion pump), promethazine, trimethobenzamide, diphenhydramine, and topical capsaicin cream, which provided moderate relief. Additional supportive care included intravenous fluids, total parenteral nutrition (TPN), and regular fetal monitoring.

2.4. Multidisciplinary Approach

Given the complexity of the case, a quick multidisciplinary approach was utilized, involving input from gastroenterology, surgery, obstetrics, and dietetics. The patient was initially admitted for hydration and nutritional support through TPN. Regular fetal monitoring and ultrasound assessments ensured fetal well-being. The patient's symptoms improved with the comprehensive care approach, including ondansetron infusion and topical capsaicin cream, eventually allowing her to transition to oral nutrition.

2.5. Psychiatric Evaluation

A psychiatric consult indicated that the patient did not have anxiety or depression; her symptoms were deemed medical in nature, and her emotional responses were appropriate.

3. Outcome and Discussion

Hyperemesis gravidarum is characterized by dehydration, nutritional deficiency, poor oral intake, and weight loss, typically managed by combinational pharmacologic agents with variable success [4-5]. Alternative approaches involve using scheduled and as-needed prescription medications (pyridoxine-doxylamine, promethazine, diphenhydramine, and metoclopramide) for mild to moderate symptom control, followed by ondansetron for a range of severity and maternal wellbeing during pregnancy [6]. Ineffective control of anxiety and depression can worsen hyperemesis [7-8]. Although interpregnancy interval does not significantly influence HG recurrence risk, factors like unplanned pregnancies and ineffective control of ongoing postpartum depression can accentuate HG recurrence [8-10].

The patient's depression was minimally controlled with an Edinburgh postnatal depression score of 17, significantly impacting her mental wellbeing. She continued on sertraline outpatient, and buspirone was added to her regimen, thereafter sertraline was increased from 25 mg to 50 mg daily. Sertraline and buspirone, use was associated with significant gastrointestinal symptoms, further complicating intractable hyperemesis [11-12].

Discussions with hospital providers confirmed tetrahydrocannabinol THC-induced nausea and vomiting. THC can mediate effects on CB1 receptors in the enteric nervous system, resulting in decreased peristalsis and gastric emptying, accentuating hyperemesis [13]. Ondansetron infusion, together with as-needed antiemetic therapy and topical capsaicin cream, afforded significant emesis control.

The Surgeon General of the United States and the American College of Obstetricians and Gynecologists strongly discourage cannabinoid use during pregnancy due to potential risks to the developing fetus and adverse fetal outcomes [14-17]. Benzodiazepine use is also discouraged in HG due to risks of congenital malformations and behavioral abnormalities [18]. Despite the patient's continued outpatient use of these medications, we implemented a comprehensive, multimodal approach, utilizing combinational pharmacotherapy, fluid and electrolyte replacement, and intermittent use of opioids and antipsychotic agents like olanzapine, resulting in positive maternal outcomes and resolution of symptoms.

Upon follow-up, the patient reported minimal to zero episodes of hyperemesis, demonstrating significant improvement. The positive outcome highlights the effectiveness of a multidisciplinary approach and tailored pharmacotherapy in managing refractory HG. This case highlights the need to weigh the risks and benefits of cannabinoid and opioid use in patients with persistent hyperemesis. It underscores the importance of coordinated care and tailored treatment strategies for refractory hyperemesis gravidarum, considering the complexities of comorbid conditions and medication interactions. A personalized approach like this can significantly enhance patient outcomes.

Table A - C. Abbreviations

- GA, Gestational age;
- W: weeks,
- D: days,

- Pos: Positive,
- Neg: Negative,
- BUN: Blood urea nitrogen,
- Na: Sodium,
- K: Potassium,
- Cl: Chloride,
- CO_2: Carbon dioxide, Agap: Anion gap,
- eGFR: estimated Glomerular filtration rate.

4. Conclusion

This case emphasizes the complex interplay between cannabinoid and opioid use in exacerbating hyperemesis gravidarum. It demonstrates the necessity of a multidisciplinary approach to achieve successful management and underscores the potential benefits of individualized treatment strategies in refractory cases.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors have no conflict of interest to disclose.

Statement of ethical approval

If studies involve use of animal/human subject, authors must give appropriate statement of ethical approval. If not applicable then mention 'The present research work does not contain any studies performed on animals/humans subjects by any of the authors'.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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