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ANAPHYLACTIC SHOCK DUE TO PROPHYLACTIC ANTIBIOTICS IN PLANNED SECTIO CESAREAN: A CASE REPORT

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ABSTRACT

Introduction: *Anaphylactic reactions during pregnancy are complex to diagnose and manage, potentially ranging from mild symptoms to life-threatening situations for both the mother and fetus. With an incidence varying from 1.44 to 2.7 cases per 100,000 births and subtle, overlapping symptoms with other obstetric emergencies, accurate identification remains a challenge. Despite being underdiagnosed, severe anaphylactic events during pregnancy share symptoms with other critical conditions, making differentiation intricate. Prior reviews and recent data underscore the necessity for guidelines and public health actions, emphasizing the importance of vigilance and specific management strategies in obstetrics.*

Case report: *This case involves Ny. S, a 33-year-old pregnant woman undergoing an elective C-section, who developed an allergic reaction to Cefazolin, necessitating an emergency procedure and subsequent ICU admission due to anaphylactic complications. Patient at 38 weeks pregnant, encountered an unexpected allergic reaction during a planned C-section, necessitating an emergency procedure. Post-surgery, she experienced severe complications, including pulmonary and laryngeal edema, requiring intensive care. With prompt medical attention and a comprehensive treatment plan, including medications and careful monitoring, her condition stabilized over several days. By October 21, 2023, she showed significant improvement, allowing her discharge with scheduled follow-up care.*

Discussion: *The discussion encompasses the complexity of diagnosing anaphylaxis during pregnancy, highlighting challenges in laboratory confirmation, management protocols mirroring non-pregnant guidelines, and the importance of coordinated medical care to avert adverse maternal and fetal outcomes. It emphasizes the need for standardized protocols and consensus among healthcare providers to effectively manage maternal anaphylaxis, reflecting on the rarity of this condition and the potential risks it poses to both the mother and fetus.*

Conclusion: *Anaphylactic reaction during an elective C-section, prompting urgent medical intervention involving mechanical ventilator support and meticulous care. Patient's subsequent recovery and discharge, along with fluctuating lab results indicating an acute immune response, underscore the complexity of diagnosing and managing maternal anaphylaxis, emphasizing the need for standardized protocols and coordinated healthcare approaches.*

Keywords: *antibiotic allergy, anaphylaxis shock, fetal compromise, maternal anaphylactic, section caesarian*

INTRODUCTION

The diagnosis of an anaphylactic reaction, and determining the allergen responsible, is a clinically challenging situation. Anaphylactic reactions during pregnancy can range from subjective cutaneous symptoms to anaphylaxis and lethal anaphylactic shock. They are emergency situations requiring rapid diagnosis and management in obstetrics because of the unpredictable evolution from spontaneous resolution to serious maternal and fetal consequences, which may represent a life-threatening condition for both the mother and fetus, including severe neurological defects.[1] Based on European data, the reported incidence of anaphylaxis during pregnancy and labor varies from 1.44 to 2.7 cases per 100,000 births depending on case definition. The case fatality rate for anaphylaxis in the general population is low, <0.001%, but the specific anaphylaxis-related maternal mortality ratio during pregnancy is estimated to be 0.09 per 100,000 live births.[2,3]

The events may be underdiagnosed, as no consistently obvious signs and symptoms suggest improvement or lethality. Severe forms during pregnancy and labor are difficult to differentiate from severe hypotension due to spinal and epidural anesthesia, cardiopulmonary distress, amniotic fluid embolism, or placental abruption. The symptoms of anaphylactic shock may also involve subtle signs common for pregnancy, such as lower back pain, vulvar and vaginal itching, fetal distress, or premature birth.[4] Recent studies have also shown that painful uterine contractions can be a form of anaphylactic shock in both pregnant and non-pregnant women, but this manifestation is not frequently associated.[5]

This case highlights the need for standardized protocols and consensus in managing anaphylaxis during pregnancy, pointing to the limitations of maternal stabilization without adrenaline and the importance of swift intervention to prevent adverse fetal outcomes. The clinical criteria for diagnosing anaphylaxis delineate specific manifestations indicative of the condition. This case report focuses on occurrence of anaphylactic shock due to prophylactic antibiotics in planned sectio cesarean.

CASE REPORT

In the case of Ny. S, a 33-year-old woman at 38 weeks and 1 day of gestation, the anticipated delivery through elective Cesarean Section (C-section) faced an unforeseen complication on October 18, 2023. Initially scheduled for the procedure due to a lack of contractions and a history of a previous C-section, the situation took a sharp turn when she exhibited an allergic reaction to Cefazolin administered pre-operation in the observation room. This prompted an urgent transfer to the operating room (OR), where an emergency C-section was performed.

Unfortunately, despite the successful completion of the C-section, Ny. S's condition rapidly deteriorated post-operation. Upon admission to the Intensive Care Unit (ICU), she required immediate support from a mechanical ventilator due to an anaphylactic reaction, leading to pulmonary and laryngeal edema. Her initial condition upon ICU arrival revealed conscious responses, scoring a GCS of E3VxM6, with a blood pressure of 114/72 mmHg, a heart rate of 107 beats per minute, a respiratory rate of 14 breaths per minute, and optimal oxygen saturation at 100% while on the ventilator.

The medical team, led by Dr. Hatsari, an Obstetrician-Gynecologist, and Dr. Hendra, an Anesthesiologist, formulated a comprehensive treatment plan. Ny. S received intravenous fluids comprising Ringer's Lactate and Oxytocin at 20 units per minute. Additionally, she underwent a regimen of medications including Meropenem (1 gram every 12 hours), Metronidazole (500mg every 12 hours), Kalnex (1 amp every 12 hours), and Ketorolac (30mg every 12 hours). To manage potential blood pressure drops, the team monitored closely and was prepared to administer Epinephrine in diluted doses if her BP fell below 90.

Throughout October 19, 2023, Ny. S remained intubated in stable condition, maintaining a GCS of E3VxM6, a blood pressure of 118/72 mmHg, a heart rate of 107 beats per minute, a respiratory rate of 12 breaths per minute, and a satisfactory oxygen saturation of 99% while on the ventilator. Dr. Hendra advised a gradual approach to ventilator weaning until the patient could be safely extubated.

By October 20, 2023, Ny. S had shown sufficient progress to warrant a transfer from the ICU to a regular ward. Eventually, on October 21, 2023, she was discharged from the hospital with instructions for a follow-up appointment at the Obstetrics and Gynecology clinic scheduled for October 31, 2023.

Table 1. Laboratories Result on October 17th 2023

DR	Result	Normal	Unit
Leukosit	10.67	4-11	$X10^3$/uL
Eritrosit	4.71	4.6-6.2	$X10^6$/uL
Hb	12.6	12.5-18	g/dL
Hematokrit	**35**	40-50	%
Trombosit	241	150-400	$X10^3$/uL
Neutrofil	**75.9**	60-70	%
Limfosit	**14.7**	20-35	%
Monosit	7.8	2-8	%
Eosinofil	1.3	1-4	%
Basofil	0.3	0-1	%
MCV	73.5	82-92	fL
MCH	26.8	27-31	Pg
MCHC	36.4	32-36	g/dL
Hepatitis B	Non reaktif		

Table 2. Laboratories Result on October 18th 2023

	Result	Normal	Unit
Leukocyte	**24.84**	4-11	$X10^3$/uL
Erythrocyte	5.36	4.6-6.2	$X10^6$/uL
Hb	14.4	12.5-18	g/dL
Hematocrit	40	40-50	%
Thrombocyte	234	150-400	$X10^3$/uL
Neutrophil	**94**	60-70	%
Lymphocyte	**2.8**	20-35	%
Monocyte	3.2	2-8	%
Eosinophil	0	1-4	%
Basophil	0	0-1	%
MCV	**73.6**	82-92	fL
MCH	**26.8**	27-31	Pg
MCHC	**36.4**	32-36	g/dL
Hepatitis B	Non reactive		
ELECTROLYTE	**Result**	**Normal**	**Unit**
Natrium	140.4	135-145	mEq/L
Kalium	**3.46**	3.5-5	mEq/L
Chloride	111.4	95-105	mEq/L
	Result	**Normal**	**Unit**
Urea	23	15-45	mg/dL
Creatinine	0.5	0.6-1.3	mg/dL
SGOT	18	0-37	U/L
SGPT	6	0-42	U/L
Albumin	3.5	3.8-5.1	g/dL

Table 3. Laboratories Result on October 20th 2023			
	Result	**Normal**	**Unit**
Leukocyte	**15.76**	4-11	$X10^3/uL$
Erythrocyte	**3.90**	4.6-6.2	$X10^6/uL$
Hb	**10.5**	12.5-18	g/dL
Hematocrit	29	40-50	%
Thrombocyte	160	150-400	$X10^3/uL$

DISCUSSION

The case of Ny. S, a 33-year-old woman at 38 weeks and 1 day of gestation, undergoing an elective Cesarean Section (C-section), unexpectedly experienced an allergic reaction to Cefazolin administered pre-operation. This led to an emergency C-section after transfer to the operating room. However, post-operation, Ny. S's condition rapidly deteriorated, necessitating ICU admission and immediate mechanical ventilator support due to anaphylactic reaction complications, resulting in pulmonary and laryngeal edema. The medical team formulated a comprehensive treatment plan including intravenous fluids, medications (Meropenem, Metronidazole, Kalnex, Ketorolac), and close monitoring for potential blood pressure drops, prepared to administer Epinephrine if needed. Ny. S remained stable and intubated in the ICU on October 19, with gradual plans for ventilator weaning, and by October 20, she showed sufficient progress to be transferred to a regular ward. Eventually, she was discharged with a follow-up appointment scheduled.

Laboratory results on October 17th, 18th, and 20th revealed notable changes, including leukocyte count elevations and variations in blood chemistry values across the days, indicating an acute immune response and physiological changes post-anaphylaxis.

The discussion delves into the rarity of maternal anaphylaxis, stressing its challenging diagnosis and potential complications for both mother and fetus. The management mirrors non-pregnant guidelines, emphasizing the importance of timely adrenaline administration despite concerns about placental perfusion. Skin testing for antibiotic sensitivity carries a risk of severe reactions and underlines the need for comprehensive emergency protocols in healthcare settings.

Diagnosing anaphylaxis during pregnancy relies on clinical criteria despite potential normal lab results, and management involves multifaceted interventions while considering potential adverse effects on the fetus. Immunological shifts during pregnancy might contribute to new sensitivities, necessitating vigilance in maternal stabilization and continuous fetal monitoring. The case highlights the need for standardized protocols and consensus in managing anaphylaxis during pregnancy, pointing to the limitations of maternal stabilization without adrenaline and the importance of swift intervention to prevent adverse fetal outcomes. The clinical criteria for diagnosing anaphylaxis delineate specific manifestations indicative of the condition. The mentioned sources further elaborate on various aspects of anaphylaxis during pregnancy, emphasizing the need for coordinated, timely, and careful management to mitigate potential risks to both mother and fetus.

Due to its rarity, maternal anaphylaxis often goes undetected, as it can mimic various conditions related and unrelated to pregnancy. This leads to potential hemodynamic complications, posing risks not just to the mother but also to the fetus. Swift and coordinated management involving obstetricians, neonatologists, anesthetists, intensivists, and immunologists is pivotal in averting adverse outcomes from maternal anaphylaxis.[4,5,6]

The approach to managing anaphylaxis during pregnancy aligns with non-pregnant guidelines. Adrenaline remains the cornerstone of treatment; however, apprehensions about compromising placental perfusion often cause delays in its administration, potentially resulting in poorer maternal outcomes. Essential adjuncts in resuscitation involve oxygen therapy and intravenous fluid administration. The latter part of pregnancy presents challenges due to aorto-caval compression, requiring manual uterine displacement and left lateral tilt. In extreme cases of maternal cardiac arrest, considering a perimortem section within 4 minutes while continuing cardiopulmonary resuscitation becomes crucial. Continuous intrauterine fetal monitoring and cautious consideration for early delivery in cases of fetal distress, especially in preterm pregnancies, are vital.[7]

Skin testing for antibiotic sensitivity is a common practice in developing countries, typically using a minor component of penicillin. Despite a low incidence of systemic adverse events (around 1%), there remains a possibility of a full-blown anaphylactic shock following this test, particularly in undocumented patients. Antibiotics stand as a primary cause of maternal anaphylaxis, emphasizing the importance of documenting allergies, prudent antibiotic use, and prepared emergency protocols across healthcare settings to prevent and manage such incidents. Post-stabilization, monitoring for biphasic reactions, seen in about 20% of the general population after anaphylaxis, is crucial. Our patient developed

moderate Acute Respiratory Distress Syndrome (ARDS) post-partum, prompting the application of oxygen therapy, non-invasive ventilation, and meticulous monitoring to exclude secondary causes for maternal hypoxia.[8]

Following an anaphylactic shock, subsequent investigations are vital for identifying the underlying cause. Immunological assessments such as serum tryptase and IgE levels, along with drug-provocation tests, play a crucial role. Educating the mother about the critical nature of the incident becomes integral in such scenarios.[9,10]

The spectrum of causative factors and clinical presentations associated with anaphylactic shock during pregnancy and the peripartum period emerges distinctly from existing studies. This highlights the challenge of differentiating it from conditions like amniotic fluid embolism or other hypotensive causes before or during labor. Consequently, there's a justified call for validated markers for decision-making and a standardized treatment protocol. Confirming the diagnosis of anaphylaxis amidst challenges in clinical laboratory tests can be aided by increased levels of MC tryptase within 1–4 hours post-event, along with serum allergen-specific IgE tests, retrospectively validating the diagnosis. However, around 50% of patients with perianesthesia hypersensitivity reactions may show normal tryptase levels, necessitating encouragement for skin testing in cases of high clinical suspicion despite negative results.[11,12]

Recent studies, spanning 2012–2015, underscore a significant proportion of anaphylaxis occurrences during cesarean sections and subsequent to antibiotic and anesthetic drug administration, aligning with literature findings between 1985 and 2021. However, the mortality rates between the two periods exhibit minimal variance, showcasing the ongoing risks associated with this condition.[1,2]

Management of anaphylactic shock during pregnancy involves prompt cessation of the triggering substance, ensuring adequate oxygenation, ventilatory support, bronchodilators, intravenous fluids, adrenaline administration, antihistamines, corticosteroids, and positioning the woman in left lateral decubitus to optimize blood flow to the heart and fetus. Despite the lack of consensus on defining anaphylaxis in clinical cases, a uniform approach akin to non-pregnant subjects is adopted. Notably, delayed administration of adrenaline correlates with adverse outcomes in the general population, making its use controversial in pregnancy-related anaphylaxis due to potential adverse effects on both the mother and fetus.[13]

While epinephrine remains a contentious choice for treating anaphylactic shock during pregnancy due to its impact on uterine vasoconstriction and potential adverse effects on the fetus, its administration has been noted in cases with mixed outcomes. Studies propose ephedrine as an alternative due to its weaker uterine vasoconstrictive effects compared to adrenaline. However, the latter's superior efficacy in resolving maternal hypotension and ensuring better uteroplacental perfusion continues to make it a consideration despite associated risks.[14,15]

Anaphylaxis, characterized as a rapid and potentially fatal allergic reaction, presents a lifetime prevalence in the general population estimated between 0.05–2%. However, data concerning its prevalence among pregnant women remains limited, with an approximate occurrence of 2.7 cases per 100,000 deliveries. Anaphylaxis during pregnancy poses significant risks to both the mother and the fetus, increasing the potential for fatality or fetal hypoxic/ischemic encephalopathy. The triggers for anaphylaxis in pregnant women mirror those in non-pregnant individuals, particularly during labor and delivery, often linked to interventions like oxytocin or commonly, antimicrobial agents such as penicillin or cephalosporin used in preventing neonatal group B hemolytic streptococcal (GBS) infection.[16]

Diagnosing anaphylaxis in pregnant women aligns with methods used for non-pregnant patients, primarily reliant on clinical criteria despite potentially normal laboratory results. While positive skin tests or heightened serum-specific IgE levels indicate sensitization, they do not confirm the diagnosis due to common asymptomatic sensitization in the general population. The clinical criteria for diagnosing anaphylaxis are applicable to pregnant women, considering any one of three criteria indicative of a highly likely diagnosis. Anaphylactoid or pseudoanaphylaxis terminologies are discouraged, and a confirmed case was evident in the mother in this particular neonatal scenario.[17]

Maternal anaphylaxis poses significant concerns for obstetricians and neonatologists, possibly due to altered immune status during pregnancy despite protective mechanisms like heightened placental histaminase levels. Immunological shifts during pregnancy may potentially lead to new sensitivities, evident in cases where previous antibiotic use without allergic reactions may trigger sensitization during pregnancy. Notably, while maternal IgE antibodies aren't transmitted across the placenta, fetal central nervous system development remains vulnerable, often affected in severe cases, leading to neurological impairments.[18]

Managing anaphylaxis during pregnancy remains contentious, with controversies surrounding optimal timing and mode of neonatal delivery following such episodes. Continuous fetal monitoring post-anaphylaxis is vital to detect signs of distress, considering potential biphasic reactions within the first 72 hours. Additionally, increased umbilical and cerebral arteries resistance index (RI) can signal poor outcomes, further complicating the management and outcome prediction in such cases.[19,20]

Establishing consensus and protocols for managing anaphylaxis in pregnant women remains crucial, highlighting the need for standardized approaches across healthcare services. The presented case underscores the potential limitations of maternal stabilization without adrenaline, indicating the importance of effective and swift intervention in preventing adverse fetal outcomes.[20]

The clinical criteria for diagnosing anaphylaxis, indicate the likelihood of anaphylaxis when any of the following three criteria are met: [20]

1. Acute Onset with Skin or Mucosal Involvement:
   An abrupt onset of symptoms (within minutes to hours) involving the skin, mucosal tissue, or both (e.g., widespread hives, itching, flushing, or swelling of lips-tongue-uvula).
   Accompanied by at least one of the following:
   - Respiratory compromise (e.g., difficulty breathing, wheezing, bronchospasm, stridor, reduced peak expiratory flow, or low oxygen levels).
   - Reduced blood pressure or signs of end-organ dysfunction (such as hypotonia/collapse, fainting, or loss of bladder control).
2. Rapid Onset of Multiple Symptoms after Exposure to Allergen:
   - The occurrence of two or more symptoms shortly after exposure to a likely allergen for that individual (within minutes to hours).
   - Symptoms can involve skin/mucosal tissue, respiratory system, reduced blood pressure, or persistent gastrointestinal issues (e.g., abdominal pain, vomiting).
3. Decreased Blood Pressure following Known Allergen Exposure:
   - Manifestation of reduced blood pressure after exposure to a known allergen (within minutes to hours).
   - Criteria for infants/children: Low systolic blood pressure as per age-specific standards or more than a 30% drop in systolic blood pressure.
   - Criteria for adults: Systolic blood pressure lower than 90 mm Hg or a decrease of over 30% from the person's baseline blood pressure.

Pathophysiology

An alteration in immunological status during pregnancy due to increased progesterone levels can predispose pregnant patients to anaphylaxis. Hormonal changes, especially during lactation and prenatal periods, have shown a causal relationship with recurrent anaphylaxis in some cases. Immunological changes, including altered cytokine signaling, depressed T-cell response, and shifts in cellular immunity, are thought to contribute to increased predisposition to anaphylaxis during pregnancy. [22]

Maternal hypotension during anaphylactic shock can significantly affect fetal perfusion and oxygenation due to its direct impact on uterine blood flow. This can lead to hypoxic damage to the fetal central nervous system, with the extent and site of injury possibly influenced by the duration of maternal hypotension and fetal maturity.[22]

Current Recommendations

Managing acute anaphylactic episodes involves discontinuation of the allergen, airway maintenance, prevention of hypoxia with oxygen support, aggressive fluid resuscitation, and administration of medications like epinephrine, antihistamines, H2 blockers, and corticosteroids. While corticosteroids may not directly manage acute anaphylaxis, they might prevent protracted or future attacks. [22,23]

Epinephrine and Pregnancy

The use of intravenous (i.v.) epinephrine, the standard therapy in non-pregnant patients, remains controversial during immediate resuscitation of anaphylactic shock in pregnancy. Despite its effectiveness in improving maternal hypotension, concerns about its impact on uterine vasoconstriction and potential harm to the fetus exist. There's a debate about its appropriate dosage, route of administration, and its effects on both maternal and fetal health.

Other Vasopressors

Alternative vasopressors like ephedrine, metaraminol, methoxamine, etilefrine, phenylephrine, and vasopressin have been used in non-pregnant patients for anaphylaxis. Their efficacy and safety in pregnant patients during anaphylactic episodes remain uncertain, although some have shown positive results in resuscitating patients with cardiovascular collapse due to anaphylactic shock. [22,23]

Intrapartum Antibiotic Prophylaxis

Intrapartum chemoprophylaxis for group B streptococcal infections during pregnancy has significantly reduced neonatal infections. However, routine chemoprophylaxis with antibiotics carries risks of anaphylactic reactions and bacterial resistance, prompting careful consideration of risk factors, choice of antibiotics, and potential adverse effects when administering such prophylaxis during labor. This breakdown separates the information into distinct sections, covering

pathophysiology, current recommendations, the use of epinephrine, alternative vasopressors, and the considerations around intrapartum antibiotic prophylaxis during pregnancy. [22,23]

CONCLUSION

The case of Ny. S, a 33-year-old woman at 38 weeks and 1 day of gestation, faced a critical situation during an elective Cesarean Section (C-section) due to an allergic reaction to Cefazolin. Despite successful completion of the C-section, she experienced an anaphylactic reaction leading to pulmonary and laryngeal edema. Immediate medical intervention was necessary, involving mechanical ventilator support, intravenous fluids, and a careful medication regimen.

Her subsequent progress in the ICU, stability, and eventual discharge with a follow-up appointment indicated a positive outcome. The laboratory results across different days showed fluctuations, signaling an acute immune response post-anaphylaxis. The comprehensive discussion highlights the rarity of maternal anaphylaxis, emphasizing the diagnostic challenges and potential risks to both mother and fetus. Managing anaphylaxis during pregnancy involves multifaceted interventions and vigilant fetal monitoring due to immunological shifts and potential adverse effects. It underscores the need for standardized protocols in healthcare settings, especially in cases like antibiotic sensitivity testing, where the risk of severe reactions exists. Furthermore, it stresses the importance of post-stabilization monitoring for complications like biphasic reactions and additional investigations to identify underlying causes.

Despite controversies regarding adrenaline administration and alternative vasopressors, the case echoes the criticality of prompt intervention to prevent adverse outcomes. Overall, the case study emphasizes the complexities of diagnosing and managing anaphylaxis during pregnancy, necessitating a coordinated and careful approach across medical specialties.

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