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Two Obese Patients with Presumptive Diagnosis of Anaphylactoid Syndrome of Pregnancy Presenting at a Community Hospital

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
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Case series

Patient: Female, 21 • Female, 29
Final Diagnosis: Anaphylactoid syndrome of pregnancy
Symptoms: Coagulation dysfunctional
Medication: —
Clinical Procedure: Cardiac intensive care
Specialty: Obstetrics and Gynecology

Objective: Rare disease





Background: Anaphylactoid syndrome of pregnancy (ASP) is a rare but extremely serious complication, with an estimated incidence in North America of 1 in 15 200 deliveries. Despite its rarity, ASP is responsible for approximately 10% of all childbirth-associated deaths in the United States. At present, there is no validated biomarker or specific set of risk factors sufficiently predictive of ASP risk to incorporate into clinical practice. Toward the goal of developing a methodology predictive of an impending ASP event for use by obstetricians, anesthesiologists, and other practitioners participating in infant deliveries, physicians encountering an ASP event have been encouraged to report the occurrence of a case and its biologically plausible risk factors.

Case Report: Herein, we report on 2 patients who presented with a presumptive diagnosis of ASP to the delivery unit of a community hospital. Patient One was a 21-year-old, obese (5'11" tall, 250 lbs., BMI 34.9) white female, 1 pregnancy, no live births (G1P0), estimated gestational age (EGA) 40.2 weeks. Patient Two was a 29-year-old, obese (5'7" tall, 307 lbs., BMI 48.1) Hispanic female, second pregnancy, with 1 previous live birth via C-section (G2P1-0-0-1). Her pregnancy was at gestational age 38 weeks plus 2 days.

Conclusions: Patient One had 2 possible risk factors: administration of Pitocin to induce labor and post-coital spotting from recent intercourse. Patient Two suffered premature rupture of the placental membranes. Both Patient One and Patient Two had very high body mass indices (BMIs), at the 97th and 99th percentiles, respectively. In the relatively few cases of anaphylactoid syndrome of pregnancy described to date, this is the first report of a possible association with high BMI.

MeSH Keywords: Embolism, Amniotic Fluid • Pregnancy Complications, Cardiovascular • Pregnancy Complications, Hematologic

Full-text PDF: <http://www.amjcaserep.com/abstract/index/idArt/897984>

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Background

Anaphylactoid syndrome of pregnancy (ASP) is a rare but very serious event. The estimated incidence in North America is 1 in 15 200 deliveries and 1 in 53 800 in Europe. An estimated 13–30% of the affected mothers do not survive. Similarly, associated infant mortality is very high, at 9–44% [1]. Despite its rarity, ASP is responsible for about 10% of all maternal deaths in the US [2,3].

Based on 46 cases, Clark et al. (1995) [4] recommended that amniotic fluid embolism be renamed anaphylactoid syndrome of pregnancy to better describe the anaphylactoid rather than embolic aspects of the condition [5]. At that time, the recommended name change generated controversy, with M.D. Benson publishing a thoughtful letter to the editor suggesting the new nomenclature was premature, and elucidating the important difference between the term “anaphylactoid,” referring to a non-immune-mediated degranulation of mast cells, as contrasted with an antigen-antibody-mediated anaphylactic reaction [6]. In rebuttal, Clark described a number of incongruities in the Ig-mediated antibody hypothesis, including absence of cutaneous manifestations, bronchospasm, and upper airway swelling [7].

In the intervening years, a large number of studies have been conducted to identify the immunological mechanisms operant in, and risk factors associated with, ASP. From the first description of ASP in 1926, the conceptualization of the syndrome’s etiology has shifted from mechanical occlusion of the pulmonary vasculature toward an immuno-inflammatory pathogenesis [8]. Expression of complement C3a expression and tryptase degranulation have shown promise as biomarkers for diagnosing ASP [9,10]. Zinc coproporphyrin in maternal plasma has also been used as a diagnostic biomarker of ASP [11].

Several reviews have been published in an attempt to improve the understanding of this complex syndrome. The 2009 review by Conde-Agudelo and Romero [1] is notable for its detailed description of both mechanisms and risk factors. In their comprehensive review, these authors recommend that the association between AFE and induction of labor deserves additional scrutiny. In the review of the 2 new cases described herein, following the guidance of Conde-Agudelo and Romero, we have examined a possible causal role for induction of labor, and have also noted possible sources of trauma to the relevant tissues.

Case Report

Patient One

Patient One was a 21-year-old, obese (5’11” tall, 250 lbs., BMI 34.9) white female, 1 pregnancy, no live births (G1P0),

estimated gestational age (EGA) 40.2 weeks. Patient One presented to triage with post-coital spotting that presented the previous night following intercourse. In anticipation of vaginal birth, Pitocin was administered on the morning of Day 1 to induce cervical ripening. Based on concerns emanating from her pregnancy-induced hypertension, Patient One was scheduled for induction of labor on the evening of Day 1 and was admitted. Patient One had been treated for the pregnancy-induced hypertension with Labetalol for 20 days prior to hospital admission on the evening of Day 1. As observed by nursing staff, the patient complained of lightheadedness and was cyanotic above the nipple line. The hypoxia resulted in the patient collapsing to the floor and subsequent initiation of cardiopulmonary resuscitation (CPR). A cardiologist met the anesthesiologist in the Operating Room (OR) to assist resuscitation during an emergency Cesarean delivery (C-section). By the time the cardiologist arrived in the OR, the patient had been intubated, was tachycardic, severely hypotensive, and was receiving epinephrine. While still in the OR, Neo-Syneprine was administered efficaciously, with systolic blood pressure remaining in the 130’s. The patient was then transferred to the Intensive Care Unit (ICU) for conduction of hypothermia protocol. The emergency C-section was successful, with delivery of a 9.4-lb. male infant followed by transfer to the neonatal intensive care unit (NICU). The baby required some respiratory support but recovered quickly, with an APGAR score of 2 at one and five minutes post-delivery, improving to APGAR score 8 by ten minutes. Both Patient One and Baby One experienced a complete recovery without neurologic deficit.

Patient One possessed several characteristics reported previously as possibly related to presentation of ASP [12]. These include history of gestational hypertension, which is a risk factor for placental abruption [13]; minor trauma (spotting following intercourse the night before); and induction of labor by cervical ripening [14]. Table 1 summarizes these risk factors and provides a description of Patient One.

Patient Two

Patient Two was a 29-year-old, obese (5’7” tall, 307 lbs., BMI 48.1) Hispanic female, second pregnancy, with 1 previous live birth via C-section (G2P1-0-0-1), with an estimated date of conception on December 1, 2014, who was scheduled for a second C-section. Her pregnancy was at gestational age 38 weeks plus 2 days. In preparation for the C-section, a spinal block consisting of 1.5 cc Bupivacaine (11.25 mg) and 0.3 mg Duramorph (preservative-free morphine) was administered with the patient in a slight reverse Trendelenburg position (in a supine position with the patient on a plane inclined with the head higher than the rest of the body). Just prior to the surgeon initiating an incision, the patient developed shortness of breath. The patient was intubated and noted to be experiencing severe bradycardia and hypotension.

Table 1. Patient characteristics at time of presumptive ASP presentation.

Age	21	29
Ethnicity	White	Hispanic
Height	5'11"	5'7"
Measured weight at delivery	250 lbs.	307 lbs.
Body mass index at delivery	34.9–97% of women aged 21 are below this BMI	48.1–99% of women aged 29 are below this BMI
Estimated pre-pregnancy weight*	230 lbs.	287 lbs.
Estimated pre-pregnancy body mass index	32.1–97% of women aged 21 are below this BMI	44.9–99% of women aged 29 are below this BMI
Previous births	0	1 via C-section
Estimated gestational age	40.2 weeks	38.3 weeks
Pitocin given	Yes – morning before event that night	No
Additional labor induction	None	None
Adverse events in labor	Gestational hypertension	Spontaneous rupture of placental membranes 6 hours pre-event
Relevant medical history	Post-coital spotting from night before	Previous C-section
Drugs administered prior to event	Labetalol for 20 days prior to event	1.5 cc Bupivacaine and 0.3 mgs Duramorph

* Mayo Clinic recommends a maximum pregnancy weight gain of 20 lbs. for women with BMI of 30 or more.

Hemodynamic parameters were treated with atropine and epinephrine. Given the extreme rarity of an ASP event, the initial suspicion was that the adverse response might be due to high spinal anesthesia, wherein the level of sensory denervation inadvertently extends to the second or third thoracic dermatome, or sometimes even as high as the cervical dermatomes. Based on this initial suspicion, repeated epinephrine bolus infusions were given, without an immediate response. Chest compressions were started to assist in circulation of already administered medications. The chest compressions assisted in increasing pulse and blood pressure, but these increases were accompanied by a sustained reduction in end-tidal carbon dioxide (ETCO₂). A sudden decrease in ETCO₂ was possibly indicative of acute right heart failure secondary to extreme pulmonary vasospasm. This observation of sudden onset of hypoxia, hypotension, and cardiovascular collapse raised the suspicion of ASP. Hypotension persisted, with an electrocardiographic reading of ST-segment depression (indicating cardiac ischemia). A code was called, with a cardiologist arriving to assist. A diagnosis of ASP was presumed based on the acute onset of dyspnea, bradycardia, decreased ETCO₂, cardiovascular collapse, and ST-segment depression.

Six hours before the initiation of the code, the patient had experienced spontaneous rupture of the placental membranes (at 6:30 pm). The aforementioned chest compressions began at approximately 1 am. The code was initiated at 1:07 am. At 1:08 am, a female infant was delivered from a vertex presentation via emergency C-section. The infant's APGAR score at

one minute was 0, improving to 5 at five minutes, to 7 at ten minutes, and peaking at 8 at twenty minutes. The female infant weighed 7 lbs., 2.3 oz. Patient Two had not yet received Pitocin. Unfortunately, Patient Two did not recover from the neurological insult, and died after 3 months of intensive care. However, Baby Two experienced a complete recovery.

The most significant risk factor possessed by Patient Two was a spontaneous rupture of the placental membranes experienced approximately 6 hours prior to the ASP episode. Characteristics of Patient Two are summarized in Table 1.

Discussion

The notable commonality between Patient One and Patient Two is a very high BMI. Patient One had a higher BMI than 97% of other women her age, and Patient Two had a BMI higher than 99% of age-comparable women. Adjusting the body weight of Patient One and Patient Two by subtracting the maximum recommended pregnancy weight gain of 20 lbs. for a woman with a BMI of 30 or greater did not change these percentile rankings [15]. Although Patient One and Two had very high BMIs, BMI itself is inversely associated with risk for development of placental disruption (i.e., obese women have lower risk [16].

The lack of a statistical association between severe obesity during pregnancy and disruption of placental membranes [16]

does not preclude a possible role for obesity as a risk factor for ASP in a subset of patients. Much recent evidence has led to the idea that obesity is characterized by chronic low-grade inflammation [17]. Further, obesity is known to adversely affect a wide variety of immune responses [17]. Immune responses associated with obesity that have been related to an increased tendency toward inflammation include increase in effector CD4 and CD8 cells, activation of M1 macrophages, and increase in the inflammatory mediators TNF- α , IL-6, and MCP-1.

Although the precise nature of the immunological dysfunction in ASP is not well understood, several mediators of inflammation have been hypothesized to play a role in the pathophysiology of ASP [18]. A subset of the proposed actors includes depletion of C3 and C4 complement [9,19,20], release of histamine [19], bradykinin [21], endothelin [22,23], leukotrienes [24], and other arachidonic acid metabolites [25]. Whether the tendency toward an inflammatory state seen in morbidly obese individuals places a subset of these patients at increased risk for ASP is unknown.

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Conclusions

We would encourage physicians at major medical centers participating in large numbers of deliveries to note pre-existing medical conditions characterized by an inflammatory state, and to measure biomarkers of inflammation and mast cell degranulation [26] in the rare cases of ASP that sometimes present. In the community hospital setting, an ASP event is a profound challenge to the patient, infant, and the treatment team. Developing predictive methodology or better understanding risk factors [27] might help reduce the mortality associated with this rare but serious condition. Advances in understanding the chain of pathophysiologic causation is an essential component of developing ASP-specific therapeutic strategies [28-30].

Statements

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