Non-immune mediated anaphylaxis to Syntocinon during labour

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Case Report

A 26-year-old Caucasian primigravid woman presented at 38 weeks and 4 days after the onset of spontaneous labour. She did not have any medical conditions and was not on regular medications prior to pregnancy. She had an uneventful antenatal course, with well managed hypothyroidism and iron deficiency anaemia. Ultrasound at the 34th week of gestation was within reference ranges, with an estimated foetal weight of 2.8 kg (85^{th} percentile). She had no known drug allergies or history of hay fever, asthma or eczema. However, had a strong family history of atopy on her maternal side. Drug doses were administered as per hospital guidelines.

After 2.5 hours of an uncomplicated first stage of labour, she required 10 units of intravenous (IV) Syntocinon (as per hospital protocol) augmentation during the second stage of labour. Cardiotocography showed a baseline foetal heart rate of 140 beats per minute, normal variability, and recurrent variable decelerations. Eight minutes later, she complained of facial oedema, the Syntocinon infusion was immediately ceased. Over the next ten minutes, the facial swelling subsided with stable vital signs. Due to prolonged foetal bradycardia down to 80 beats per minute, mediolateral episiotomy and vacuum extraction was performed. This was complicated by one minute of shoulder dystocia which was managed using the McRoberts manoeuvre. An infant weighing 4.1 kg was born in good condition, with Apgar scores of 8 and 9 at 1 and 5 minutes, respectively. To augment delivery of the placenta, 10 units of intramuscular (IM) Syntocinon was administered. However,

postpartum haemorrhage (PPH) developed shortly afterwards due to uterine atony and a fourth-degree vaginal tear, with an estimated blood loss of 2 litres. This was controlled with IV fluid resuscitation, 1g of IV tranexamic acid, and 250mcg of IV and IM doses of ergometrine, with a plan to repair the fourth-degree tear urgently in the operating theatre. Sixteen minutes later, there was worsening throat discomfort and chest tightness. The midwife noted facial oedema, patchy erythema on her back, increased work of breathing, and dysphonia. No gastrointestinal symptoms or urticaria were noted. Anaphylaxis was suspected and a rapid response was initiated. Oxygen was administered through a non-rebreather mask at 15 litres/minute. Vital signs were stabilised with an oxygen saturation of 100%, blood pressure of 140/84 mmHg (systolic blood pressure/diastolic blood pressure), heart rate of 108 beats/min, and respiratory rate of 16 breaths/minute. Electrocardiography (ECG) demonstrated sinus tachycardia with no concerning features. Two 500mcg doses of IM 1:1000 adrenaline and 200mg of IV Hydrocortisone were administered, the airway was stabilised with endotracheal tube intubation in the operating theatre. Of note, no laryngeal swelling was visualised during intubation by the Anaesthesiologist.

The patient was transferred to the intensive care unit (ICU) after the operation. She was extubated six hours later with a patent airway and no increased work of breathing. The results of serial tryptase measurements, absolute basophils, serum immunoglobulin-E (IgE), and complement C3 and C4 levels post-surgery were all within normal limits (Table 1). Serum electrolytes were normal throughout her admission. Mobile chest x-ray immediately post-surgery demonstrated extensive subcutaneous emphysema, but no other significant abnormalities. She recovered well in ICU with 24 hours of 4mg IV dexamethasone three times per day, and 2 units of packed red blood cells due to haemorrhage. She was discharged from the hospital after a four-day admission.

Discussion

Syntocinon is a widely used synthetic oxytocin that stimulates contractions of uterine smooth muscle. It is used for induction and augmentation of labour, and prevention of PPH.[1]Syntocinon rarely causes anaphylaxis, but reported side effects include nausea, vomiting, reflex tachycardia, hypotension, headache, and uterine rupture.[2] There are very few documented reports of anaphylactic reactions to Syntocinon, and these were hypothesized to precipitate from concurrent latex exposure,[9-21] and chlorobutanol exposure,[3, 4] a formulated ingredient in Syntocinon.[5] This case involved a rare non-immune mediated anaphylactic response to Syntocinon that was recognised early and responded well to appropriate treatment. The only drug that was administered prior to the onset of anaphylaxis was Syntocinon and the rapid abatement of symptoms following its withdrawal suggested that the patient had suffered an allergic reaction to the drug.

Non-immune mediated anaphylaxis, also known as an anaphylactoid reaction is a non-IgE mediated immune response.[6,7] In this case, immunological blood testing of serial tryptase, IgE and Complement assays (C3 and C4) levels were all within normal range suggesting the diagnosis.[8] Inflammatory mediators such as bradykinin and prostaglandin modulate mast cell and basophil degranulation resulting in vasodilation and bronchoconstriction, resulting in anaphylaxis.[9] These reactions are rare, with an incidence of less than 1 in 20,000 in anaesthesia, however, their life-threatening outcomes present concern for anaesthesiologists.[10-12] While in pregnancy IgE does not cross the placenta, maternal haemodynamic instability can jeopardize placental perfusion.[13] Laboratory tests may be used to support the diagnosis, but it is important to note that anaphylaxis is a clinical diagnosis,[8] and results of tests are not specific and may not be quick enough to impact acute management. Further, it has been shown that serum tryptase levels are more likely to be elevated in those with hypotension and shock, than in those with anaphylaxis who are normotensive.[14]

Another hypothesized cause of anaphylaxis during delivery is an allergic sensitivity to latex.[15] In obstetrics and gynaecological surgical procedures, a high incidence of latex anaphylaxis (1 in 310) has been observed.[16]Interestingly, previous case reports have suggested that allergic sensitization to latex may be an important predisposing factor for anaphylaxis or systemic reactions to Syntocinon.[17]However, our patient had frequent exposure to latex in her workplace and prenatal check-ups with no documented reactions. Other differential diagnoses at the time were pulmonary thromboembolism and air embolism, however, the absence of typical risk factors, suspicious ECG changes, and normal central venous pressure and right ventricular

function on Echocardiogram did not support the diagnosis. The most common symptoms of pulmonary embolism are dyspnoea (73%), pleuritic pain (66%), and cough (37%), however, haemodynamic collapse is only present in less than 10% of cases.[18,19] Another possible diagnosis was amniotic fluid embolism, but with an incidence of 1 in 40,000 delivery, it is a difficult diagnosis to make.[20,21]The Society for Maternal-Foetal Medicine (SMFM) states the diagnosis for amniotic fluid embolism must have all of the four following: sudden cardiorespiratory arrest, documentation of overt dissemination (platelet counts <50,000/mL, fibrinogen <200 mg/L), clinical onset during labour, and absence of fever during labour.[22] In this case, amniotic fluid embolism was unlikely, given the SMFM criteria and normal findings on blood panel, Echocardiogram, ECG, and chest x-ray. Other differential diagnoses of acute respiratory distress during pregnancy included aspiration of gastric contents and acute heart failure, both of which were ruled out clinically.

Non-immune mediated anaphylaxis to Syntocinon is extremely rare and only a few case reports exist. Here, we presented a case of non-immune mediated anaphylaxis to Syntocinon in the setting of vacuum-assisted birth, shoulder dystocia and PPH in a healthy 26-year-old primigravid woman. The patient developed novel symptoms including patchy erythema, bronchospasm, angioedema, and laryngeal oedema. Although the symptoms resolved on withdrawal of Syntocinon, the mechanism(s) which precipitated this response warrants further investigation.

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Ethics statement: Appropriate written informed consent (available upon request) was obtained for publication of this case report and accompanying images.

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Table 1. Results of the immunological assay.

Test	**Test**	**Result**	**Comment**
Tryptase	2.5 hrs post-Syntocinon	2.2 μg/L	Normal range <11.0 μg/L
	6 hrs post-Syntocinon	1.9 μg/L	Within laboratory normal ra
	10 hrs post-Syntocinon	1.3 μg/L	Within laboratory normal ra
	22hrs post-Syntocinon	1.2 μg/L	Within laboratory normal ra
Absolute Basophils	6 hrs post-Syntocinon	$0.2x10^9$/L	Above normal range
	10 hrs post-Syntocinon	$0.1x10^9$/L	Within normal range
IgE – 2hrs post-Syntocinon	IgE – 2hrs post-Syntocinon	12 KU/L	Within laboratory normal ra
Complement 3 – 2hrs post-Syntocinon	Complement 3 – 2hrs post-Syntocinon	1.1 g/L	Within laboratory normal ra
Complement 4 – 2hrs post-Syntocinon	Complement 4 – 2hrs post-Syntocinon	0.2 g/L	Within laboratory normal ra

μg= micrograms; L= litres; g= grams; KU= kilounit, hrs= hours, IgE= immunoglobulin-E. The actual

reference range and grading may vary with the laboratory.