Two lives at stake: Obstetric anaphylactic shock resulting in acute respiratory distress syndrome – A case report

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Abstract
Maternal anaphylaxis is rare albeit life-threatening critical incident dreaded by many due to negative effects on not only the mother but the foetus as well. Antibiotics and anaesthetic agents still contribute to majority of the episodes. Consequences of anaphylaxis such as placental insufficiency and subsequent foetal neurocognitive deficits are devastating outcomes. Acute respiratory distress syndrome following anaphylaxis is even rarer among the normal population. The management of maternal anaphylaxis does not differ from routine recommendations even though close monitoring and preparedness for early delivery should be embedded in the protocols. This is a rare case report of a primi mother who developed anaphylactic shock following intravenous penicillin in the background of negative allergic history, resultant foetal distress requiring emergency lower segment caesarian section and delayed onset acute respiratory distress syndrome which was later attributed to anaphylaxis. Pertinent identification and management which included a multidisciplinary team culminated in favourable outcomes.

Keywords
Obstetric, anaphylactic shock, acute respiratory distress syndrome, allergen skin test, penicillin sensitivity

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Introduction
Anaphylaxis during pregnancy is rare.1 The incidence is quoted around 1.6 in 100,000 mothers in a UK-based study1 and 3.8 per 100,000 in the United States.3 The inherent maternal physiological changes and the foetus hindering venous return especially towards the latter part of the pregnancy contribute to poorer outcomes following anaphylaxis. The effect on neonates is found to be much worse with an increased incidence of intensive care admissions and hypoxic-encephalopathy. The use of antibiotics is implicated in the majority of these critical incidents5 while neuromuscular blocking agents5,6 and latex7 are also implicated. Some advocate pre-pregnancy identification of high-risk patients and confirming sensitivity to allergens5 albeit their practicality is questionable in low resource countries. This article entails the events of a maternal anaphylactic shock precipitated by intravenous penicillin, foetal distress warranting emergency delivery and acute respiratory distress syndrome (ARDS) following anaphylaxis compounding maternal health. Early identification, protocol-based individualized management and follow-up led to a favourable outcome for both the mother and the neonate.

Case description
A 22-year-old primigravida, in her 36 weeks of period of amenorrhoea, presented to the obstetric unit with preterm labour. She did not have any significant past medical or past surgical history. There was no history of allergies. She was averagely built with a body mass index of 26 kg m–2. For Group B streptococci coverage, intravenous crystalline penicillin was opted and a skin sensitivity test was performed per institutional protocol. After 20 min, it was read by the obstetric unit doctor which was found to be negative following which the first dose of the intravenous antibiotic (1.5 g) was administered. Five minutes later, the mother complained of shortness of breath. She was conscious, rational and found to be tachycardic (116 per minute) and hypotensive (non-invasive blood pressure 70/30 mm Hg) by the same doctor. Her respiratory rate was 30 per minute while the peripheral
oxygen saturation was noted as 97%. Immediate clinical diagnosis of anaphylactic shock was made. Emergency protocol was activated. Intramuscular adrenaline 0.5 mg was administered to the lateral thigh. Supplemental oxygen and 10 mL/kg crystalloid bolus were administered simultaneously with left manual displacement of uterus and leg elevation. She was catheterized and urine was noted in the bag. Hourly input and output monitoring was commenced. Following two further intramuscular adrenaline doses, her blood pressure was stabilized (121/72 mmHg), 15 min following the onset of her symptoms. Intravenous steroids and an antihistamine dose were administered (the former was repeated 6 hourly up to 24 h). Continuous foetal monitoring during the episode did not indicate any features suggestive of distress. Following stabilization, she was transferred to the intensive care unit. Serum for tryptase was collected at 1, 6 and 24 h. Intravenous clindamycin was substituted for penicillin. She was transferred to the ward after 24 h where intramuscular dexamethasone was administered. Six hours later, a pathological cardiotocography trace with late decelerations warranted emergency caesarean section under subarachnoid anaesthesia as the mother was haemodynamically stable and did not show any features of biphasic reaction following the initial episode of anaphylactic shock and to avoid polypharmacy during general anaesthesia. Foetal scalp sampling was not performed as it was not the routine practice in our centre. Standard monitoring including non-invasive blood pressure monitored at 3-min intervals, continuous electrocardiogram and peripheral oxygen saturation monitoring was commenced. Anaesthesia and the operating theatre team were briefed on the recent maternal anaphylactic shock. Emergency protocol which was to be deployed during an event of a repeated episode of anaphylaxis was clearly communicated and displayed on a notice board with dedicated roles allocated to each member of the team. Maternal clindamycin dose had already been administered; thus, repeated dose was not suggested by the microbiologist. The rest of the drugs were clearly labelled and read out loud during administration. Non-latex gloves were utilized. The mother was administered 2.5 mL of 0.5% heavy bupivacaine at L3-4 intervertebral space during the spinal anaesthesia. Consultant paediatrician was present during the caesarian section and a single, live foetus was delivered. APGAR (Appearance, Pulse, Grimace, Activity and Respiration) scores were 9 and 10 at 1 and 5 min which were reassuring, and maternal haemodynamics were stable. The baby and the mother were admitted to the premature baby unit and the intensive care unit, respectively, for observation where vital parameter monitoring was continued. Over the next 12 h, the mother became oxygen dependent with fine bi-basal crepitations in the absence of bronchospasms or stridor. Her haemodynamics were stable. Cardiac assessment by way of electrocardiogram, two-dimensional (2D) echocardiogram and troponin I test yielded normal results. Her fluid status was assessed utilizing ventricular filling and inferior vena cava collapsibility which suggested euvolaemia. Urine output was normal. The arterial blood gas analysis revealed a PaO2/FiO2 ratio of 180. The ultrasound chest revealed increased B lines. Chest X ray showed hilar congestion with ‘bats wing’ appearance (Figure 1). The rest of the inflammatory markers, routine cultures and COVID-19–PCR were unremarkable (Table 1).

A clinical diagnosis of moderate ARDS was made. She was started on intermittent continuous positive airway therapy and gradually weaned off. Both the mother and baby were discharged 4 days later and referred for further immunological studies. Maternal tryptase levels were elevated (1 h: 24.3, 24 h (baseline): 3.8, reference < 11.4 µg/L). The intradermal skin test at 6 weeks confirmed sensitivity to benzylpenicilloyl polylysine component (major determinant penicillin). With the temporal association, ARDS subsequent to anaphylactic shock was made. This particular critical incident led to a retrospective institutional survey with collaboration from other major specialties to ascertain documented episodes of anaphylaxis in patients with initial negative penicillin skin testing. Close liaison with microbiology team for optimal antibiotic stewardship and vigilance following administration of antibiotics was reinforced as penicillin use was quite common and intradermal skin testing was not available in our centre.

**Discussion**

Being considered a rare occurrence, maternal anaphylaxis may be unsuspected due to multiple pregnancy-related and non-related conditions which may mimic the former.8 The resultant haemodynamic compromise will threaten the well-being of not only the mother but the foetus as well. Swift management which includes a multidisciplinary team with obstetricians, neonatologists, anaesthetists, intensivists and immunologists plays a crucial role in prevention and/or acceptable outcomes following maternal anaphylaxis.
Management of anaphylaxis in pregnancy does not differ from the recommended guidelines for the non-pregnant cohort. Adrenaline is the mainstay of therapy, however, delay in its use in fear of compromising placental perfusion and poor foetal outcomes are not uncommon. Delays in instituting adrenaline could lead to worse maternal outcomes, and thus should be avoided at all costs. Oxygen therapy and intravenous fluid loading are pivotal adjuncts in resuscitation. After the 20th week of pregnancy, the aortocaval compression could further hinder the resuscitative efforts; thus, manual displacement of the uterus and left lateral tilt may be additionally adopted. In the worst-case scenario where the maternal cardiac arrest occurs, a perimortem section should be considered within 4 min while cardiopulmonary resuscitation is continued. Intrauterine foetal monitoring should be continued during an episode where early delivery should be considered cautiously in cases of foetal distress especially in preterm pregnancies. In our patient, foetal distress warranted emergency delivery where APGAR score, a validated scoring system utilized to determine the level of immediate neonatal care scored out of 10, was satisfactory.

The skin test for antibiotic sensitivity is the conventional practice in developing countries. In local setup, it is the minor constituent of penicillin that is used for skin test. Even though systemic adverse events are quoted to be around 1%, a full-blown anaphylactic shock after this test dose in previously undocumented patients is still a possibility. Moreover, antibiotics have been attributed as the leading cause of maternal anaphylaxis. Documenting past allergies, use of antibiotics wisely, monitoring and having emergency management protocols ready at wards, labour rooms and operating theatres are essential in preventing and mitigating such occurrences. Biphasic reactions following anaphylaxis have been witnessed in around 20% of the general population; thus, close monitoring is appropriate following the initial stabilization. Our patient developed moderate ARDS 12 h after the partus. The authors of this monograph, with their prior experience of a similar event, are in the view that in the absence of any other aetiology, unexplained deterioration of respiratory parameters in post-anaphylactic patients should be attributed to ARDS, employing the ‘Occam’s razor’ principle. The management consisted of supplemental oxygen therapy and non-invasive ventilation with meticulous monitoring and exclusion of secondary causes for maternal hypoxia, which included cardiogenic pulmonary oedema, peripartum cardiomyopathy and thromboembolism.

The subsequent investigations to identify the aetiology are as important to initial management following an anaphylactic shock. Immunological inputs are vital. A rise in serum tryptase levels and serum IgE levels, and drug-provocation tests are utilized in this aspect, and the mother should be educated regarding the critical incident.

Table 1. Investigation summary.

| Investigation                        | Result          | Reference |
|-------------------------------------|-----------------|-----------|
| Full blood count                    |                 |           |
| White cells                         | $11 \times 10^9/L$ | $4–11 \times 10^9/L$ |
| Neutrophils                         | 62%             |           |
| Lymphocytes                         | 35%             |           |
| Red cells                           | $5.2 \times 10^9/L$ | $4–5.5 \times 10^9/L$ |
| Platelets                           | $380 \times 10^9/L$ | $150–450 \times 10^9/L$ |
| C-reactive protein                  | 6 mg/L          | <6 mg/L   |
| Blood urea                          | 4.1 mmol/L      | 2–7 mmol/L |
| Serum creatinine                    | 90 µmol/L       | 60–110 µmol/L |
| Serum Na\(^+/K^{+}/Mg^{2+}/Ca^{2+}\) | $140/4.1/1.0/1.25$ mmol/L | $135–145/3.5–5.5/0.8–1.0/1.1–1.3$ mmol/L |
| Serum Aspartate aminotransferase    | 45 µ/L          | <50 µ/L   |
| Serum Alanine aminotransferase      | 35 µ/L          | <40 µ/L   |
| Prothrombin time and International normalized ratio | 1.2 | |
| Random blood sugar                  | 130 mg/dL       | 140–180 mg/dL |
| Urine full report                   |                 |           |
| Red cells                           | Nil             |           |
| Protein                             | 1–2/High power field |           |
| Urine culture                       | No growth       |           |
| Blood culture                       | No growth       |           |
| COVID-19–Polymerase chain reaction  | Negative        |           |
| D-dimer                             | 0.3 mg/L        | <0.5 mg/L |
| Venous duplex of lower limbs        | No deep vein thrombosis detected | |
| Blood picture                       | Normal main cell lines; no features suggestive of consumptive coagulopathy | |
Conclusion

Maternal anaphylaxis is frequently an unforeseen event that could lead to maternal and foetal morbidity and mortality. Other pregnancy-related and non-related differential diagnoses should also be considered simultaneously as symptoms and signs can essentially overlap in such conditions. Careful history taking to identify mothers who are at risk of anaphylaxis, optimum antibiotic stewardship in pregnancy and rapid deployment of protocol-driven resuscitation, early administration of adrenaline when indicated, multidisciplinary inputs and continuous maternal and foetal monitoring to detect complications of anaphylaxis would invariably improve both the maternal and foetal outcomes.

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Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed consent

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References

1. McCall SJ, Bunch KJ, Brocklehurst P, et al. The incidence, characteristics, management and outcomes of anaphylaxis in pregnancy: a population-based descriptive study. BJOG 2018; 125(8): 965–971.
2. McCall SJ, Bonnet M-P, Äyräs O, et al. Anaphylaxis in pregnancy: a population-based multinational European study. Anaesthesia 2020; 75(11): 1469–1475.
3. McCall SJ, Kurinczuk JJ and Knight M. Anaphylaxis in pregnancy in the United States: risk factors and temporal trends using national routinely collected data. J Allergy Clin Immunol Pract 2019; 7(8): 2606–2612.e3.
4. Reiner K, Zah Bogović T, Ćaćić M, et al. Anaphylaxis during pregnancy. Psychiatr Danub 2019; 31(Suppl. 1): 60–62.
5. Hepner DL, Castells M, Mouton-Faivre C, et al. Anaphylaxis in the clinical setting of obstetric anesthesia: a literature review. Anesth Analg 2013; 117(6): 1357–1367.
6. Chaudhuri K, Gonzales J, Jesurun CA, et al. Anaphylactic shock in pregnancy: a case study and review of the literature. Int J Obstet Anesth 2008; 17(4): 350–357.
7. Shingai Y, Nakagawa K, Kato T, et al. Severe allergy in a pregnant woman after vaginal examination with a latex glove. Gynecol Obstet Invest 2002; 54(3): 183–184.
8. Simons FER and Schatz M. Anaphylaxis during pregnancy. Journal of Allergy and Clinical Immunology 2012; 130(3): 597–606.
9. Levy N and Weiniger CF. Anaphylaxis in pregnancy. In: Einav S, Weiniger CF and Landau R (eds) Principles and practice of maternal critical care. Cham: Springer, 2020, pp. 577–581.
10. Savic LC and Lucas DN. Anaphylaxis in obstetrics – double the trouble. Anaesthesia 2020; 75(11): 1424–1427.
11. Simon LV, Hashmi MF and Bragg BN. APGAR score. Treasure Island, FL: StatPearls Publishing, 2022.
12. Fox S and Park MA. Penicillin skin testing in the evaluation and management of penicillin allergy. Ann Allergy Asthma Immunol 2011; 106(1): 1–7.
13. Berenguer A, Couto A, Brites V, et al. Anaphylaxis in pregnancy: a rare cause of neonatal mortality. BMJ Case Rep 2013; 2013: bcr2012007055.
14. Fernando UPM, Dharmawardhane MP, Subramaniam N, et al. Acute respiratory distress syndrome following anaphylactic shock – ‘a deadly duel’ – case report and literature review. Open J Anesthesiol 2021: 11: 33–38.