



PERIMORTEM BEDSIDE HYSTERECTOMY: A SURVIVED PATIENT AND HER BABY AFTER FOUR CARDIAC ARRESTS. DOES EPINEPHRINE MAKE A CHANGE IN AMNIOTIC FLUID EMBOLISM MANAGEMENT?

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ABSTRACT

(Reviewer #1 abstract related, revised and replied comment no 3) In the labour room, our patient suddenly collapsed followed by immediate cardiac arrest during her labour course. Cardiopulmonary resuscitation done immediately including perimortum bedside CS followed by hysterectomy. Having an adult patient in labour made high suspicion about amniotic fluid embolism as a first possibility especially when we got the first severely deranged coagulation profile done within ~15 minutes of patient collapse. During her critical care journey, she had 3 successive cardiac arrests, a bedside perimortem CS and hysterectomy, 3 successive laparotomies in the following days. A fourth cardiac arrest happened 2 hours following cessation of epinephrine infusion. Epinephrine infusion was reinstated after regaining spontaneous rhythm and weaned gradually afterwards. Amniotic fluid embolism (AFE) is a rare obstetric catastrophe which represents about 15 % of all maternal deaths, incidence is about 7 per 100,000 births. Till now there is no definitive diagnostic tool hence, its diagnosis depends mainly on exclusion. An immunogenic theory describes the pathophysiology of AFE as an anaphylactic reaction, hence the name of "anaphylactoid syndrome of pregnancy". We suggest that properly timed aggressive resuscitation comprising perimortum bedside CS, then hysterectomy, plus the use epinephrine played a very important role in the successful outcome of our patient and her baby.

BACKGROUND

Amniotic fluid embolism (AFE) is a very rare obstetric disaster that threatens the life of pregnant; the recent reported incidence is 6.6-7.1 per 100,000 births.^[1] The mortality rate of AFE is more than 80% according to previous reports,^[2] which represents up to 15 % of all maternal deaths.^[3] The AFE results from the entry of the amniotic fluid into the maternal circulation due to disturbances of the barrier between amniotic fluid and maternal circulation leading to physical obstruction of the pulmonary vasculature like any pulmonary embolism, or firing of the immune and complements systems associated with the release of inflammatory mediators. Sudden seizure, maternal cardiovascular collapse up to cardiac arrest, respiratory failure, and rapid severe DIC is highly predictive of AFE.^[4] High suspicion of AFE, timely and aggressive supportive management, including CS is the cornerstone of reduction of both maternal and fetal morbidity and mortality. We report a case of a multiparous pregnant lady who got AFE during normal labor followed by four cardiac arrests and survived with her baby.

CASE PRESENTATION

A 42-years old woman, 90 Kg body weight, (gravid 12, para 9, and previous 2 abortions) with irrelevant medical history. Patient was admitted into the maternity department in Sohar Hospital/sultanate Of Oman at 36Th week gestation of her twelfth uncomplicated pregnancy as a result of labour pain. In the labour room; patient suddenly felt shortness of breath, immediately followed by grand mal seizure, cyanosis, loss of consciousness and cardiac arrest in asystole. The attendant labor nurse called for help, inserted an oral airway and supplied the patient with oxygen through a face mask.

Advanced cardiac life support (ACLS) team started prompt cardiopulmonary resuscitation (CPR) with external chest compressions with the maximum manual left uterine displacement on a backboard, while the patient's airway was secured with tracheal intubation by an anesthetist. CPR continued according to the ACLS guidelines in addition to administration of warm Ringer Lactate and gelfusine solutions very fast through 2 large bore peripheral IV channel using a plastic pressure bag. After 5 minutes of CPR with no return of spontaneous circulation, a bed side CS was decided; A bedside cesarean section (CS) was decided quickly, 3.7 Kg

female infant was delivered with Apgar scores were 4 and 7 at 1st and 5th minutes respectively; after 7 minutes of continuous CPR after delivery; carotid pulse was felt, and supra-ventricular rhythm pattern returned; HR recorded 147 beats /min. Blood pressure (BP) was unrecordable, the patient still unconscious having only gag reflex.

A right internal jugular vein was successfully catheterized, for blood sampling, and administration of inotropes and vasopressors. Blood samples were sent for CBC, coagulation, renal function tests (RFT) electrolytes, liver function tests (LFT), random blood sugar (RBS), and cross matching. Dopamine and dobutamine infusion started at a dose of 15mic/Kg /min, uterine atony developed rapidly and managed by repeated intramyometrial injection of F2 α -prostaglandin with very transient improvement of uterine contraction. Vaginal bleeding was severe; estimated blood loss was about two liters within 5 minutes after skin closure. A 2nd cardiac arrest in asystole occurred a few minutes later; immediate CPR done by the ACLS team while available units of non-cross matched O-ve packed RBCs was transfused via a fast transfusion warmer device using a plastic pressure bag. Carotid pulse and supra-ventricular rhythm (HR 165 beats/min) returned after 8 minutes of continuous CPR; BP was still non-recordable.

Profuse vaginal bleeding continued, bedside hysterectomy discussed and done quickly. About 30 minutes after initiation of hysterectomy; a 3rd cardiac arrest in asystole occurred; again immediate CPR has done; within 5 minutes; HR returned back with severe supra-ventricular arrhythmia and frequent ventricular ectopics, carotid pulse was very faint. An epinephrine infusion started at a dose of 1mic /kg /min, 150 mg amiodarone was given to manage cardiac dysrhythmia; after few minutes sinus rhythm returned to HR 90-100 beats/ minute, and BP recorded 78/39 mmHg which was the first reading after collapse. Two incremental doses of ketamine 50 mg were given IV during hysterectomy, at the end of surgery, the pelvis was packed and abdomen was closed.

The patient was shifted into the ICU on a portable mechanical ventilator on FIO₂ 1.0; while dopamine, dobutamine and epinephrine were running with same infusion rates using infusion syringe pumps. In the ICU; radial artery cannulated, arterial blood gases (ABG) revealed: pH 7.16, pO₂ 73.2 mmHg, Sao₂ 96.3%, pCO₂ 36 mmHg, and HCO₃ 14 mEq/L. Haemodynamic monitoring of Invasive arterial blood pressure (IABP) and CVP recorded 89/51 mmHg, and 5mmHg; ECG revealed sinus rhythm with HR 102 /min.

Initial laboratory investigations were: Hb level 10 gm%, Platelet count was 233,000/ml, INR more than 10, ApTT more than 180 seconds (control 27.3), high D-dimer level which was diagnosed as a state of immediate and severe disseminated intravascular coagulopathy (DIC).

Laboratory testing of CBC , INR, and the ApTT was repeated frequently; concomitant with administration of FFPs, cryoprecipitate , and cross matched packed RBCs aiming at correction of coagulopathy and replacement of blood loss observed in abdominal drains, our target was INR level ~ 1.5, ApTT about 1.5 times normal, and Hb level ~ 10 gm%.

Pupils were initially fully dilated and no reactive, 4hours later pupils became 4 mm and reactive to light, sedation and analgesia started using a small infusion rates of midazolam. A stat dose of IV 100 mg hydrocortisone was administered for one week, 8 hourly first 4 days twice next 2 days and once last day then stopped.

Acute kidney injury and failure developed, managed by nephrologist who decided daily haemodialysis starting from 2nd day till the renal recovery on 9th day after which there was no need for haemodialysis; RFT and urine output returned to normal basal levels within the next week.

During the first day, chest showed bilateral lung infiltrations; diagnosed as transfusion related acute lung injury (TRALI), progressed to severe ARDS in the next few days before very gradual but significant improvement. Two-hour sedation vacation was allowed daily to assess the conscious level of the patient who became conscious, opening eyes spontaneously and obeying orders on the 3rd day.

After transfusion of 11 unites of packed red blood cells , 18 unites of FFPs; HB, INR, ApTT and platelet count values were 5.8 gm%, 1.9, 75.6 seconds (control 27.5), and 51.500/ml respectively. An emergent laparotomy; justified by bedside abdominal ultrasound was decided, done after~ 16 hours post-catastrophe; during which ; 4 unites of cross matched O+ve packed RBCs 4 unites FFPs in-addition to 6 unites platelet concentrates were transfused during surgery. Anaesthesia was achieved using increments of ketamine 25 mg and 20 mg of Atracurium in addition to fentanyl and midazolam with same infusion rates mentioned above. Surgical haemostasis and packing the hysterectomy bed were done, immediate postoperative Hb and platelet count levels was 8.7gm% and 81000/ml respectively. Platelets concentrates was given to achieve a platelet count ~ 100 000/ml. Gradual tapering of dopamine and dobutamine to a dose of 10 mic/Kg /min and adrenaline to 0.5 mic/kg /min was achieved within 10 hours of laparotomy.

On the next- day early morning and because of significant blood loss followed by marked reduction of HB and platelet count levels; a second laparotomy was decided. Needed blood products were given, at the end of 2nd laparotomy; BP improved significantly which encouraged us to stop adrenaline infusion keeping dopamine and dobutamine with the same preoperative infusion rates, again hysterectomy bed and pelvis were packed, abdomen closed and patient shifted to the ICU.

In the ICU BP level was 143/87 mmHg, two hours later; a 4th cardiac asystole happened, CPR has immediately carried on according to ACLS guidelines. Sinus tachycardia returned on ECG with full radial pulse 5 minutes after asystole, BP was 125/74 mmHg. Epinephrine infusion restarted with 1 mic/Kg/min. In the next 24 hours, both dopamine and dobutamine were gradually tapered and stopped while adrenaline tapering was more gradual within the next 48 hours.

The patient was shifted back to the OT for 3rd laparotomy for removal of the abdominal packs on the 6th day of collapse; intraoperative anaesthesia was maintained using oxygen/air, isoflurane, and atracurium.

On the seventh postpartum day; the patient was put on CPAP mode of MV as a trial of weaning, the patient was on minimum sedation, arousable, obeying orders. Neurological examination revealed motor weakness grade I in upper and lower limbs. CT brain was done to exclude central lesion and it was free; limb and chest physiotherapy program was planned, the patient started moving upper and lower limbs voluntarily with a limited range within the next few days.

On the day 14 and after the failure of weaning from mechanical ventilator, after exclusion of a cardiac cause by bedside echo; tracheostomy was decided and done on the next day after taking consent. On the 21st day; patient was shifted to the OT for closure of a wound gap under local anaesthesia and mild sedation and analgesia using 2 mg of midazolam and 40 mic. of fentanyl.

On 22nd day, patient was discharged from ICU to High dependency unit (HDU) where tracheostomy tube was connected to oxygen with a flow rate 4 L/min. In the ward; daily limb and chest physiotherapy continued. The patient started walking dependently on the 25th day, walked independently On the 30th day with a full range of motor power as reported by the physiotherapist.

On the 35th day; skin wound sutures removed, on the Day 41 and after complete wound healing; and tracheostomy was closed. On day 42; patient was discharged without any physical or neurological disabilities, her delivered baby was normal, started formula milk feeding normally and does not have any neurological problem as per pediatrician. All over this long trip; patient was given 21 units of packed RBCs, 28 unites of FFPs and 17 units of platelet concentrates, 10 units of cryoprecipitates. Thrombo-prophylactic measures with enoxaparin started from day 3 of the disaster and continued till the patient was discharged from the hospital.

On the day of discharge, patient and her family were very happy. An informed consent was taken from patient and her husband for permission of publication, we informed them thoroughly about all details of publication, thankfully they appreciated the managing team efforts and agreed for publication.

DISCUSSION

Amniotic fluid embolism (AFE) is a rare disaster that occurs as a result of disruption in the barrier between amniotic fluid and maternal circulation leading to entry of amniotic fluid through endocervical veins, placenta and uterine trauma sites and threatens the life of pregnant ladies.^[4] In 1926; Meyer reported the first case of AFE,^[5] which was described later as a syndrome in 1941 by Steiner and Lushbaugh.^[6]

Diagnosis of AFE depends mainly on exclusion, any peripartum lady having sudden seizures or disturbed level of consciousness, cardio-respiratory collapse is suspicious.^[4] In our patient; the rapid development of DIC as well as uterine atony in-addition to above manifestations were highly indicative of AFE triggering us to start prompt and aggressive management of the condition.

The following differential diagnoses were excluded clinically and laboratory: pregnancy-induced hypertension (PIH) and HELLP syndrome, anaphylaxis and transfusion reactions, uterine rupture and abruptio placenta. Uterine rupture or abruptio placenta exclusion was confirmed intra-operatively during CS. Neither medications nor transfusion of blood products was given before the catastrophe which excluded anaphylactic and transfusion reactions respectively. The immediate post-catastrophe HB level, platelet count, and normal liver enzymes which were very close to the basal levels of the patient, in addition to clinical examination before catastrophe helped us to rule out PIH, and HELLP syndrome.

Pulmonary thrombo-embolism was excluded in view of the absence of DVT as evidenced by duplex US later on; but not confirmed by either pulmonary angiography or spiral CT because of the unstable condition of the patient and the contraindication of the use of radio-contrast materials in the presence of acute renal shutdown. Bedside echocardiography revealed normal echo-findings apart from mild to moderate pulmonary hypertension which is concomitant with AFE manifestations.^[7]

According to a recent retrospective review in both Canada and United States, the incidence of AFE is 6.6-7.1 per 100,000 births,^[1] Early studies recorded mortality incidence of AFE 60-86%,^[2] more recent researches reported mortality incidence of 26%,^[8] AFE represent a sizable fraction of all maternal deaths (5-15%).^[3] According to the best of our knowledge; no study correlated the incidence of mortality to the number of AFE-related cardiac arrests which would be more higher than the previous figures if cardiac arrest numbers is 4 times as in our patient. The high awareness of AFE associated with aggressive and timely resuscitation may help in improving maternal and fetal outcome.

There are two theories behind AFE, first is a mechanical obstruction of the pulmonary vasculature by fetal squamous cells like any pulmonary embolism causing cardiovascular collapse. However Clarks SL *et al.*,^[9] in their study on 16 pregnant ladies using pulmonary catheter for different indications, they detected squamous cells in the pulmonary vasculature of all ladies without having AFE hence their conclusion was: detection of fetal squamous cells in pulmonary vasculature is not pathognomonic for AFE.

The second theory is an immunogenic theory.^[10] which states that entry of amniotic fluid cells and fetal materials into maternal circulation activate the immune and complement systems resulting in release of pro-inflammatory cytokines, serotonin, histamine, and pro-coagulants.^[10] The result is an inflammatory cascade process like anaphylaxis which is behind the description of the AFE as “anaphylactoid syndrome of pregnancy”,^[11] The pro-coagulant effect of amniotic fluid and/or the complement activation may explain the prevalence of DIC in AFE.^[12] while cardiovascular collapse may be due to pulmonary vasoconstriction with subsequent right ventricular failure or due to myocardial depressant effects of the released inflammatory mediators.^[13,14]

Respiratory failure in AFE could be related to the marked ventilation perfusion mismatch either because of pulmonary vasoconstriction, pulmonary edema,^[13] or transfusion related acute lung injury.^[15]

The anaphylactic and allergic nature of AFE and the immunogenic release of histamine as a result of stimulation of immunoglobulin E was behind our use of epinephrine not only to augment vasopressor and inotropic effects of both dopamine and dobutamine. Through its agonistic action on α and β adrenoceptors; epinephrine reverses the immediate symptoms of anaphylaxis like hypotension, oedema, bronchoconstriction, in addition to its positive inotropic action on myocardium and suppression of release of further anaphylactic mediators, so epinephrine is the drug of choice in anaphylaxis.^[16,17] In this case we used hydrocortisone because of its known anti-inflammatory effect.

In our patient; initiation of epinephrine infusion was associated with improvement of BP, hence decrease the rate of dobutamine and dopamine. An epinephrine infusion started after the 3rd cardiac arrest, continued about 40 hours, stopped 2 hours followed by the 4th cardiac arrest, restarted immediately and tapered during the next 3 days. The beneficial haemodynamic support of epinephrine infusion in this case as documented by the appearance of the first reading of BP after the initiation of epinephrine infusion could be explained by its potent anti-anaphylactic action, inotropic, and its vasopressor effects.

The 4th cardiac arrest 2 hours after cessation of epinephrine may be related to a biphasic anaphylaxis which is a known criterion of anaphylaxis syndrome even with no further exposure to the allergen up to 72 hours after the first episode.^[18] This biphasic anaphylactic reactions are sometimes more serious and fatal than initial episode as reported by Samson *et al.*,^[19] in a case series. Many authors recommend post-anaphylactic observation of at least 24 hours before discharge; with the facility to administer epinephrine if deemed necessary for the patient in the next 48-72 hours post discharge.^[20]

CONCLUSION

Early prediction, prompt aggressive well organized prompt resuscitation, including perimortum CS and (hysterectomy if deemed necessary), is the cornerstone of successful management and good outcome for the mother and her in case of AFE. To prove epinephrine efficacy in AFE, its optimal dose, method and duration of its administration; we need further prospective randomized controlled studies which is extremely difficult to do. The successful use of epinephrine boluses and infusion in this case might give a clue for possible application of the whole algorithm for treatment of anaphylaxis whenever AFE is diagnosed.

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