Position Paper
Second Trimester Antenatal Maternal Sepsis; the Savita Halappanavar Case

Summary

1. Savita Halappanavar had spontaneous rupture of membranes complicated by chorioamnionitis, which resulted in maternal sepsis and septic shock. Unfortunately, this was not immediately detected and the patient was left to critically deteriorate before antibiotic treatment was escalated and the decision to deliver was considered.
2. The early recognition of the first signs of infection together with prompt and aggressive treatment can have a bearing on clinical outcome. Delays in recognition and treatment of obstetric sepsis will result in a rapidly deteriorating clinical situation.
3. If there are signs of sepsis then consideration needs to be given to urgently deliver the baby, even if the baby is not of viable age.
4. There is a clear distinction between abortion (termination), and the induced delivery of the foetus of non-viable age for the purposes of saving the mother's life. In the former, the purpose is to produce a dead baby, whereas with the latter the intention is to save the mother's life, while giving the baby full care, and a chance for life even if this chance is very small.

Background:

On the 21st of October 2012 a 31-year woman in her first pregnancy self referred to the gynaecology ward at The University Hospital in Galway, Ireland (accompanied by her husband) at 17 weeks of her first pregnancy complaining of lower backache radiating to the lower pelvic region for the previous 12 hours. Clinical examination indicated bulging membranes and no cervix to be felt. In the medical records the diagnosis noted was that of "an inevitable/impending pregnancy loss". The patient was admitted to the hospital for management of inevitable miscarriage on the 21st of October 2012.

The patient's membranes spontaneously ruptured at 00.30hrs on the 22nd of October. Her condition deteriorated on the 24th of October and a diagnosis of sepsis secondary to chorioamnionitis was made. She was admitted to the High Dependency Unit (HDU) from the Gynaecology ward at 16.45 hrs on the 24th of October. The patient was post miscarriage at 17 weeks when admitted to the HDU. On admission the patient was noted to be drowsy, but rousable.

During that night there was a clinical deterioration with an increasing oxygen requirement, vasopressor requirement, and worsening metabolic status. The patient was therefore transferred to the Intensive Care Unit (ICU) at 03:00 hrs on October 25th and was intubated and mechanically ventilated at 03:30 hrs on the 25th of October. The patient's condition further deteriorated despite appropriate management in the ICU and she sadly passed away at 01.09 hrs on Sunday, the 28th of October 2012.

Chronology of events:

Progression from sepsis to severe sepsis to septic shock can occur within hours and correlates with increasing mortality. Early diagnosis and management is essential to reduce the mortality rate. This can only occur if there is efficient and effective surveillance (through the utilization of Modified Obstetric Early Warning Score systems) of the mother at risk so that prompt and aggressive treatment can be instituted upon recognition of the early signs of sepsis.

Monday 22nd October

Unfortunately, in this case, the early signs of sepsis were missed. Savita had spontaneous rupture of membranes (SROM) on Monday 22nd of October at around midnight. At that point there was no sign of infection or sepsis and she was started on erythromycin at around 22:00 hrs.

Tuesday 23rd October

The first tell tale sign that the patient's clinical condition might be changing was when she developed a heart rate of 114 bpm, documented on Tuesday 23rd October at 19:00hrs.

Wednesday 24th October

Later on she developed rigors and a temperature of 37.7 degrees Celsius at 04:00hrs the following morning. The situation got worse by Wednesday 24th October at 06:30hrs where her heart rate shot up to **160bpm**, Temperature **39.6 degrees** Celsius and blood pressure of 94/55mmHg. There was a significant amount of foul smelling brownish discharge on vaginal examination.

Blood investigations, including FBC, blood cultures and serum lactate were taken at 07:00hrs. Augmentin and metronidazole were started at 08:30Hrs. Foetal heart was detected at 148bpm by doppler, at 11:45hrs.

Blood pressure at 12:00hrs was now **76/46 mm Hg**. WBC count result obtained at Noon (reported in the lab at 08:29HRS) was **1.7 x 10^9/L**. CRP was elevated. The patient became tachypnoeic and very unwell by 13:20hrs.

13:50hrs blood pressure dropped to 65/30 mmHg. **14:40hrs** Tazocin and Gentamycin were administered. Aggressive fluid resuscitation treatment comprising a total of 3L Hartmanns solution and 1 litre gelafundin was instituted. A good response was noted with a blood pressure of 140/66 being recorded.

15:15hrs, the patient had a **spontaneous delivery**. Patient was then transferred to HDU at 17:06hrs and further support with noradrenaline given. Hydrocortisone and vasopressin were also administered. pH at this time was 7.27 and lactate 7.3 mmol/l.

Thursday 25th October

03:30hrs patient transferred to ITU and intubated. DIC and ARDS were noted to have developed. Further aggressive support and antibiotics continued.

The patient partially responded to treatment with improvements in oxygen requirements, pH and lactate.

Friday 26th October

The patient's cardiac output was noted to have decreased by the afternoon and adrenaline was commenced. Indices improved but the patient remained pyrexial (39 – 40 degrees Celsius) with a WCC of 23.4 that morning. Ultrasound scan did not show any residual products. This was confirmed on CT scan.

By 18:30hrs the patient deteriorated again with increased oxygen and inotropic and vasopressor requirements.

Saturday 27th October

Continuous renal replacement therapy was commenced. pH dropped to 7.14 at 15:00Hrs. Antibiotic management was further enhanced with an increase in meropenem dose and the addition of vancomycin.

Transoesophageal echocardiogram (TOE) was performed showing a dilated right ventricle and severe tricuspid regurgitation and hypokinetic left ventricle thus noting the possibility of a pulmonary embolism. The patient was thus heparinised.

The patient's condition continued to deteriorate despite on-going measures, including further volume challenge, blood products, increase in vasopressor infusion dosage, continuous renal replacement therapy, bicarbonate infusions, insulin and dextrose for hyperkalaemia, and muscle relaxation to assist mechanical ventilation.

Sunday 28th October

00:45Hrs the patient suffered a cardiac arrest and CPR was continued till 01:09Hrs, when the patient was declared dead.

Discussion:

There is a widespread misconception that pro-life doctors are prepared to risk the mother's life in order to preserve that of the unborn child, at all costs. Similarly, pro-abortion advocates project the utility of abortion in such situations, as the only possible way of saving the mother's life.

The case of Savita Halappanavar illustrates how easily such patients could be mismanaged with delays and untimely action, possibly leading to catastrophic consequences.

Yet, the burning question remains **"Could this case have had a different outcome within the current Ethical and Legal framework here in Malta?".** But in order to answer this question there are a number of other clinical considerations that need to be made, namely:-

Q. What are the chances of survival of a foetus once spontaneous Premature Preterm Rupture of Membranes (PPROM) has occurred?

A. Survival of the foetus varies with gestational age at diagnosis of PPROM (from 12% when diagnosed at 16-19 wk, to as much as 60% when diagnosed at 25-26 wk).

Ref; Vergani P, Ghidini A, Locatelli A, et al. Risk factors for pulmonary hypoplasia in second-trimester premature rupture of membranes. Am J Obstet Gynecol. 1994 May. 170(5 Pt 1):1359-64. [Medline].

The major morbidity in the foetus with mid-trimester ROM is lethal pulmonary hypoplasia from prolonged, severe, early oligohydramnios, which occurs in about 20% of cases. Other morbidities such as RDS (66%), sepsis (19%), grade III-IV IVH (5%), and contractures (3%) also occur with significant frequency.

Ref; Waters TP, Mercer BM. The management of preterm premature rupture of the membranes near the limit of fetal viability. Am J Obstet Gynecol. 2009 Sep. 201(3):230-40. [Medline].

Older studies have reported that approximately 50% of all remaining pregnancies deliver each subsequent week after PPROM. More recent studies have shown better prognosis and may be more relevant to today's clinical practice. With appropriate therapy and

conservative management, more recent studies have reported less than 40% delivering in a week and more than 30% remaining pregnant after 5 weeks.

Ref; Mercer B, Milluzzi C, Collin M. Periviable birth at 20 to 26 weeks of gestation: proximate causes, previous obstetric history and recurrence risk. Am J Obstet Gynecol. 2005 Sep. 193(3 Pt 2):1175-80. [Medline].

Q. What is the *long term* prognosis of a foetus that survives mid-trimester PPROM?

A. A study by Lorthe et al that included 1435 women with a diagnosis of PPROM reported that of the 427 foetuses at 22-25 weeks' gestation, 51.7% were survivors at discharge, 38.8% were survivors at discharge without severe morbidity, and 46.4% were survivors at 2 years without cerebral palsy.

Ref; Lorthe E, Torchin H, Delorme P, Ancel PY, Marchand-Martin L, Foix-L'Hélias L, et al. Preterm premature rupture of membranes at 22-25 weeks' gestation: perinatal and 2-year outcomes within a national population-based study (EPIPAGE-2). Am J Obstet Gynecol. 2018 Sep. 219 (3):298.e1-298.e14. [Medline].

Q. What is the risk to a mother with spontaneous rupture of membranes in the second trimester of developing major complications?

A. The major maternal risk is infection, namely chorioamnionitis, which occurs in about 35%; abruption, which occurs in 19%; and sepsis, which is rare and occurs in less than 1%. The prophylactic use of antibiotics in the expectant management of PPROM may reduce the incidence of infection and the best evidence based approach available at the time needs to be considered.

Ref; Waters TP, Mercer BM. The management of preterm premature rupture of the membranes near the limit of fetal viability. Am J Obstet Gynecol. 2009 Sep. 201(3):230-40. [Medline].

Ref; Muris C, Girard B, Creveuil C, Durin L, Herlicoviez M, Dreyfus M. Management of premature rupture of membranes before 25 weeks. Eur J Obstet Gynecol Reprod Biol. 2007 Apr. 131(2):163-8. [Medline]

Q. If a mother receiving expectant management of PPROM is diagnosed with intrauterine infection, which is the best course of action?

A. There is a significant risk of chorioamnionitis (30-40%) when PPROM happens at the limit of viability. Furthermore, chorioamnionitis can be a cause or a result of PPROM before or at the limit of viability.

The maximum clinical occurrence of chorioamnionitis is on the second through fifth day after rupture. After the first week of latency, the incidence of clinical chorioamnionitis falls dramatically.

Ref: Beydoun SN, Yasin SY. Premature rupture of the membranes before 28 weeks: conservative management. Am J Obstet Gynecol. 1986;155(3):471.

Ref; McElrath TF, Allred EN, Leviton A, Development Epidemiology Network Investigators. Prolonged latency after preterm premature rupture of membranes: an

evaluation of histologic condition and intracranial ultrasonic abnormality in the neonate born at <28 weeks of gestation. Am J Obstet Gynecol. 2003;189(3):794.

There is no clear evidence base on the management of uncomplicated chorioamnionitis. While antibiotic Rx with the foetus in utero may temporize sequelae of chorioamnionitis, extended latency (time to delivery) can lead to maternal sepsis. The mortality of pregnant women with septic shock is significant and ranges between 3 and 50%.

Ref; Fernández-Pérez, Evans R. MD; Salman, Salam MD; Pendem, Shanthan MBBS; Farmer, J Christopher MD. Sepsis during pregnancy. Critical Care Medicine: October 2005 - Volume 33 - Issue 10 - p S286-S293

Clinicians must therefore bear in mind that once the mother is severely compromised then the lives of both the mother and baby are at stake. Hence, if the clinical condition of the mother is deteriorating then consideration needs to be given to urgently deliver the baby, even if the baby is not viable and the premature delivery will, or could result in the tragic death of the baby.

Q. Is it ethically acceptable to induce premature delivery in such circumstances?

A. Yes, it is ethically and legally acceptable to induce premature delivery in such circumstances. There is a clear distinction between abortion and the induced delivery of the non-viable foetus for the purposes of saving the mother's life. In the former case, the intention is to kill the foetus and involves a direct attack on the life of the unborn child. In the latter case, the intention is to save the mother's life, and the act of separating the foetus from the mother, even if the unborn child is too premature to live, does not constitute a direct action intended to kill the child.

Such a procedure is in fact ethically justified by the principle of double effect, since the foreseen death of the unborn child is not intended and the death of the foetus is only a consequence to saving the mother's life.

Q. Could this case have had a different outcome within the current Ethical and legal framework here in Malta?

A. So, back to our original question regarding how this unfortunate young mother could have been managed within the Ethical and Legal framework currently available in Malta.

In essence, earlier recognition and aggressive treatment of infection might have altered the clinical course. Yet, evidence of sepsis would have justified the delivery of the baby in spite of the early gestation and non-viability.

It is clear, therefore, that pregnant women who need a medical intervention to save their life will not be denied the necessary medical care they need. Indeed, the illegality of abortion in Malta does not jeopardise women's health simply on account of being pregnant.