

Multidisciplinary Team Management of a Pregnant Woman With Newly Diagnosed Multiple Pulmonary Embolisms and Foetal Compromise, When to Deliver?

Anas Alojyli^{1*}, Michael Magro², Kingsley Mahendra² and Kunal Rathod²

¹Senior clinical Fellow at Queen's Hospital, Romford, UK

²Consultant in Obstetrics and Gynaecology at Queen's Hospital, Romford, UK

*Corresponding author: Anas Alojyli, Senior clinical Fellow at Queen's Hospital, Romford, UK

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ABSTRACT

Background: Thromboembolic disease, including pulmonary embolism (PE) is the leading cause of direct maternal mortality in the UK (UKOSS, [1]). In women with diabetes, there is usually an increase in resistance to insulin within the placenta and taking corticosteroids often causes an increase in insulin requirements. A sudden reduction at term is an indication of a failing placenta and increases the risk of sudden stillbirth, requiring an expedited delivery.

Case: Our case report concerns a pregnant woman, with insulin-controlled type 2 diabetes mellitus (DM), who developed multiple PEs and was treated with low molecular weight heparin (LMWH) but quickly developed signs of impending foetal distress. A multidisciplinary team (MDT) planned to expedite delivery due to a risk of sudden stillbirth in this high-risk woman with possible placental insufficiency. As the PEs were recently diagnosed (Clexane had only been administered for seven days), risks of clot embolisation and maternal death would increase if the Clexane was stopped to allow induction of labour and vaginal delivery; there was also the risk of excessive bleeding if the last dose was 12 hours before the Caesarean section. The treatment dose of Clexane was therefore changed from twice to once daily and delivery was performed by Caesarean section. This made it easier to time and minimise the duration of delivery to minimise time off anticoagulation medication.

Results: A baby girl was born in good condition, weighing 3,070 g. The mother remained in a stable condition. Prophylactic Clexane 40 mg was given subcutaneously six hours after surgery with full treatment dose 150 mg subcutaneously once daily for 24 hours after delivery.

Conclusion: This case was complicated by a new diagnosis of multiple PEs and risks of maternal morbidity and mortality that had to be balanced with risks to the foetus. An MDT approach to management of multiple comorbidities resulted in a safe outcome for both mother and child.

Keywords: Diabetes; Pregnancy; Pulmonary Embolism; Multidisciplinary Team

Introduction

Thromboembolic disease, including PE, is the leading cause of direct maternal mortality in the UK (UKOSS, [1]). In women with diabetes, there is usually an increase in resistance to insulin within the placenta and taking corticosteroids often causes an increase in insulin requirements. A sudden reduction at term is an indication of a failing placenta and increases the risk of sudden stillbirth, requiring an

expedited delivery. We discuss the importance of multi-professional input in determining the safest way to expedite delivery without risking maternal wellbeing and clot propagation or embolisation. The aim of presenting this case is to show the dilemma over when and how to deliver in the case of a pregnant woman, who had experienced a recent PE with suspected foetal compromise secondary to placental insufficiency and who was on insulin for type 2 DM. Expediting delivery to minimise risks of clot propagation and maternal death due

to ceased or reduced anticoagulation medication must be weighed up against the risks of stillbirth, keeping in mind the risk of haemorrhage at or after delivery. The MDT approach to this case is presented.

Case

A 30-year-old Bangladeshi finance broker in her second pregnancy presented in March 2022 to Queen's Hospital at 37 weeks of gestation with shortness of breath and wheezing for three days. Additionally, she complained of a productive cough with green sputum and had flu-like symptoms. Her obstetric history included a low-risk full-term pregnancy with assisted vaginal (vacuum) delivery of her first child. She received consultant led antenatal care due to having a BMI of 37 kg/m² and type II DM treated with insulin (Humulin + NoVo Rapid). The foetal growth scans were normal. She had no prior history of asthma, venous thromboembolism (VTE), or cardiac disease. She had coronavirus disease 2019 (COVID-19) in the first trimester but had declined vaccination. Relevant family history included type 2 DM of her father. On admission, she had pleuritic chest pain, palpitations, and felt feverish but her temperature and observations were normal (blood pressure, 118/71; heartrate, 95; temperature, 36.3°C; respiratory rate, 20; saturation, 99%). The first clinical impression was PE and differential diagnosis was a chest infection, asthma, or heart failure. On examination, there was wheezing throughout both lungs but no other abnormal signs. She was started on a treatment dose of LMWH, subcutaneous Clexane 100 mg twice daily for seven days, amoxicillin, and salbutamol nebulisers due to the lack of clarity about her diagnosis. A chest X-ray showed no obvious consolidation, but a prominent right hilum. An electrocardiogram (ECG) showed sinus tachycardia but no evidence of heart strain.

Blood results demonstrated no evidence of infection or myocardial infarction (Troponin 4ng/l, Hb: 110, WBC: 10,7, Neutrophils: 8.6, Lymphocyte: 1.0). Cardiotocography (CTG) was normal. The initial perfusion aspect of a ventilation-perfusion (V/Q) scan demonstrated features suspicious for multiple PEs involving both lungs. A subsequent lung ventilation study performed two days later demonstrated a pattern of uptake which suggested infective exacerbation of asthma. The conclusion was that the unmatched perfusion abnormalities were either due to coexisting PEs or changes in the airways because of asthma. She was reviewed by the respiratory consultant whose clinical impression was the same, and who recommended prednisolone 40 mg per orally for five days and to switch the amoxicillin to clarithromycin. Over the next 24 hours it was noted that her insulin requirements were dropping despite taking prednisolone, which has the converse effect on blood sugar control. This raised concerns about rapidly deteriorating placental function and the risk of a sudden stillbirth due to foetal compromise. A multidisciplinary meeting was held, which included two maternal medicine obstetric consultants, an obstetric physician, a labour ward lead consultant, midwives, and an anaesthetist. Concerns were

twofold. Firstly, the reduction in insulin requirements, especially when on prednisolone, which would usually increase requirements, can be a sign of impending placental insufficiency prior to sudden stillbirth. For this reason, it was felt that delivery within 24 hours was required. Secondly, the PEs were recently diagnosed, and the woman had only been on therapeutic Clexane for seven days. Continuing therapeutic Clexane would increase the risk of significant haemorrhage at or after delivery, whilst stopping the Clexane would risk clot embolisation and an increased risk of maternal death (UKOSS, [1]). The multi-professional team discussed these concerns with the woman and her partner, and a shared decision was made to balance the risks to both mother and baby.

It was planned to amend the treatment dose of Clexane to a 150 mg once daily dose subcutaneously on the day before delivery, rather than 100 mg twice daily, and to perform the delivery by Caesarean section. This would make it easier to time delivery to ensure there was a 24-hour gap after the last dose of Clexane to reduce the risk of bleeding, whilst also ensuring delivery was as quick as possible to minimise time off anticoagulation medication, thereby reducing the risk of clot embolisation and enlargement. An echocardiogram was performed preoperatively to exclude pulmonary hypertension. A baby girl was born, weighing 3,070 g, in good condition 12 days after her initial presentation and ten days after the PE was first diagnosed. Blood loss at delivery was 700 ml. The mother remained in a stable clinical condition throughout her stay in the hospital. Prophylactic Clexane was given 40 mg subcutaneously six hours after surgery with the full treatment dose 150 mg once daily subcutaneously, given 24 hours after delivery, which continued for six weeks.

Discussion

This was a complex situation in a woman with a recent PE, where there had been little time for clot stabilisation and a potentially high risk existed for embolisation or clot enlargement if anticoagulation was stopped, but who needed early delivery due to suspected placental insufficiency secondary to type 2 DM and risk of sudden stillbirth. In such situations, the expertise of a full MDT is required to plan (Knight, et al. [2]). A plan was drawn up and then discussed with the woman, and a shared decision was agreed.

Importance of Multidisciplinary Team Approach

MDT is an important tool in such cases (Andretta, et al. [3]). Literature on interdisciplinary teams in obstetrics and gynaecology mostly recommend the use of multidisciplinary approaches when managing complex medical cases (Andretta, et al. [3]). Researchers, such as (Easter, et al. [4]), emphasise the improved outcomes for women in complex medical or obstetric cases, when managed by an MDT. In fact, such outcomes have inspired national guidelines to support the creation of a Pregnancy Heart Team for women (Easter, et al [4]). Blondon, et al. [5] claim that in all cases, pregnancy-associated

high-risk PE requires an MDT approach, which should involve both PE response teams and obstetricians. Important points that required MDT consideration focused on balancing the risks to the mother versus the risks to the foetus. In life and death situations, the life of the mother is always put first, but in this situation, with MDT expertise and full involvement of the mother and partner, it was possible to discuss all the potential risks, the benefits of all options, and come to a shared decision.

Risk of Death from PE

PE varies in presentation from being asymptomatic to causing shock or sudden death. The highest risk for recurrence following VTE is in the first two weeks after presentation (McIntock, et al. [6]). PEs are at their most unstable in the first few weeks, which is when the risks of clot migration or embolisation and potentially death are highest (Bělohávek, et al. [7]). Subacute massive PE is caused by numerous small emboli (Bělohávek, et al. [7]). Pulmonary bed obstruction takes longer to develop (approximately one to two weeks) and presents as increasing exertional dyspnoea and fatigue (Bělohávek, et al. [7]). The possibility of subacute massive PE should be considered in all patients experiencing progressive exertional dyspnoea over a period of one to two weeks (Bělohávek, et al. [7]). Stopping anticoagulation medication to reduce the risk of bleeding at birth could increase the risk of clot migration. Induction of labour was considered as an alternative to Caesarean section but would have been a lengthier process with a more unpredictable timeframe for Clexane dose planning. It is reported in The Royal College of Obstetricians and Gynaecologists' Green-top guideline, Thrombosis and Embolism during Pregnancy and the Puerperium: Acute Management, that when VTE occurs at term, the risk of recurrent thrombosis may be increased if anticoagulant therapy is discontinued to allow a planned induction of labour or a Caesarean section (UKOSS, [1]). Research suggests that the risk of recurrent VTE is higher within two weeks of the initial thrombosis (UKOSS, [1]). Knight et al. [2] emphasise the vital role that MDT management plays in making complex decisions such as in the case reported here. There should always be close liaison with the obstetric anaesthetist and consultant obstetrician when considering the time without LMWH, while waiting for and undergoing induction of labour or delivery (Knight, et al. [2]). For women at high risk of VTE, who are aiming for a vaginal delivery with induction of labour, LMWH should not be withheld until labour is established, and a discussion regarding the necessary 12-hour window prior to regional analgesia should be individualised. Consultant prioritisation of women awaiting labour induction must include consideration of the length of time they have been without thromboprophylaxis (Knight, et al. [2]). Despite this advice, it was felt in the case reported here that a Caesarean section would offer a quicker delivery and therefore minimise time off treatment. It is also important to note that LMWH can be promptly and appropriately restarted after birth. Most women can start LMWH

soon after delivery (four hours after a spinal block or removal of an epidural catheter, after discussion with the anaesthetist). In women with a confirmed PE, it is recommended in the MBRRACE report of 2017-2019 on thromboembolism management (Knight, et al. [2]) that anticoagulation with unfractionated heparin, including a weight-adjusted bolus injection, be initiated without delay to reduce the risk of complications.

Risk of Stillbirth in Type 2 DM

Type 2 diabetes in pregnancy is associated with a poor pregnancy outcome, including an increased risk of perinatal mortality (Coulthard, et al. [8]). In general, pregnant women with type 2 DM require a much greater increase in insulin dose from the start to the end of each trimester, with the percentage change progressively increasing with advancing gestation. As compared to women with type 1 DM, who often display an insulin sensitising phenomenon in early and late pregnancy, women with type 2 DM often require almost double the increase in dose from the second trimester onwards. In the first trimester there can be a fall in insulin requirements, thought to be due to a transient reduction in progesterone levels as hormonal production shifts from the corpus luteum to the placenta, as well as decreased prandial requirements due to hyperemesis (Coulthard, et al. [8]). Pregnancy affects insulin requirements differently (Padmanabhan, et al. [9]). However, in the third trimester, a fall in insulin requirement (FIR) can indicate placental insufficiency and impeding placental failure, resulting in stillbirth (Padmanabhan, et al. [9]). FIR is an important clinical sign among women with pre-existing diabetes, which should alert the clinician to investigate underlying placental dysfunction (Padmanabhan, et al. [9]). Moreover, Siassakos, et al. [10] report that in the UK, one in 250 pregnancies end in stillbirth. Abnormal placental villous maturation, commonly associated with gestational diabetes, is a risk factor for stillbirth (Siassakos, et al. [10]). In the case reported here, the only sign of placenta dysfunction was the reduction in requirement of insulin, despite prednisolone intake. Of more concern was the FIR despite prednisolone treatment having been started, which often worsens diabetic sugar control and has the opposite effect (Suh, et al. [11]). In a study reported by Suh, et al. [11], prednisolone administration for seven days in healthy volunteers led to a 50% reduction in insulin sensitivity, as assessed using the insulin clamp methodology. Most inpatients given glucocorticoids at a dose at least equivalent to 40 mg daily for more than two days develop hyperglycaemia (Suh, et al. [11]). Glucocorticoid therapy may provoke new-onset type 2 DM and invariably worsens hyperglycaemia in patients with pre-existing DM (Suh, et al. [11]).

Predicting Timing of Stillbirth in Pregnant Women With Type 2DM

According to the National Institute for Health and Care Excellence's (NICE) Guidelines for diabetes in pregnancy (2015):

Unexpected intrauterine death remains a significant contributor to perinatal mortality in pregnant women with diabetes. Conventional tests of foetal wellbeing (umbilical artery doppler ultrasound, cardiotocography and other biophysical tests) have been shown to have poor sensitivity for predicting such events (p.35). Siassakos, et al. [10] report that additional placental histopathological lesions also present in women with diabetes in pregnancy. Accelerated villous maturation and distal villous hypoplasia are associated with maternal vascular malperfusion lesions, which represent hypoxic ischaemic damage to the placenta. Foetal thrombotic lesions, including foetal vascular malperfusion, have also been reported more frequently in placentas of women with diabetes in pregnancies. The literature demonstrates a link between diabetes and abnormal villous maturity putting women at increased risk of stillbirth. However, less is known about women with DVI without a formal diagnosis of DM. Women with dysregulated glucose metabolism may be underdiagnosed and suffer adverse outcomes as a result (Siassakos, et al. [10]).

Conclusion

There are always multiple ways individual cases can be managed. In this case, the risks of death to the mother or the baby had to be balanced. Input by the MDT was vitally important to this situation; everyone contributed their experience and combining this expertise lead to a management plan [12-15]. Equally important was the full involvement of the woman and her family in the decision-making process so that a fully informed decision could be made. This case resulted in a very good outcome for both mother and baby, yet it highlights some of the challenges which may be faced in similar cases, including: how to manage delivery after a recent PE diagnosis, what needs to be considered in women with type 2 DM with FIR, and how to manage both simultaneously. In this case, the FIR despite corticosteroid use was a red flag. This should trigger prompt action to prevent morbidity and mortality. The case could also have been managed in other ways, as all situations are unique and should be individualised. However, the case highlights some of the key points to consider in similar situations.

Ethical Considerations

Written informed consent was obtained from the patient, who agreed for the case to be published for the benefit of patients and doctors.

Data Availability

All data underlying the results are available within this article and no additional source data are required.

Competing Interests

The authors report no conflicts of interest.

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Anas Alojyli. Biomed J Sci & Tech Res



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