

A CASE OF PUERPERAL PULMONARY EMBOLISM

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INTRODUCTION

Venous thrombo embolism remains one of the leading cause of direct maternal death in UK and other countries .Confidential enquiries highlighted delay in diagnosis and in adequate treatment leads to severe morbidity and mortality. Puerperium is the time of highest risk with estimates of relative risk approximately 20 fold. Venous thrombo embolism during pregnancy and puerperium can be one of the presenting features of Anti Phospholipid Antibody (APLA) Syndrome. APLA syndrome in pregnancy and puerperium can give rise to diagnostic and therapeutic challenges.

OBJECTIVE

To describe a case of puerperal pulmonary embolism presented on post-operative day 6 following emergency cesarean section and to discuss its therapeutic challenges.

CASE REPORT

This is a case of 33 year old staff nurse, mother of two children, both are born by emergency cesarean section presented on **post natal day 6 following second cesarean** with **progressively increasing breathlessness (started from 4th day post partum) orthopnoea and an atypical chest pain**.

During this present pregnancy, she was having regular ante-natal visits. History of COVID-19 infection resolved without hospitalisation during 5th month. Took 2 doses of COVID vaccine Pfizer at 4th and 7th month. She had **nutritional Iron deficiency** from 5th month of pregnancy onwards and was on Iron Supplements. She was admitted with labour pains at 38 weeks. During the admission stage there was single recording of high blood pressure with no impending symptoms and the blood investigations were normal except for haemoglobin 10g/dl. **Emergency cesarean section** was done in view of fetal distress (persistent late deceleration at 4cm cervical dilatation).No intra operative or post operative complications. Intra operative blood loss was about 200ml.As patient was ambulant, she was discharged on post natal day 3 with low molecular weight heparin prophylactic dose and hematinics.

When she presented with breathlessness on post operative day 6, her blood pressure was 160/90mm of hg. She was given Amlodipine for the blood pressure. Her chest was clear, she was afebrile, pulse was 98/minute, and oxygen saturation was 98%.ECG was normal, Troponin I was negative, Chest X- ray was clear & **Echo showed mild to moderate pulmonary hypertension with normal biventricular function** .CT pulmonary angiogram (CTPA) done as V/Q(ventilation perfusion scan) was not available. **CTPA showed thrombus 1.6 x1cm in left inferior lobar pulmonary artery extending in to left inferior lobar segmental branches. Venous Doppler of both lower limbs were normal**.

She was started with **low molecular weight heparin** according to body weight in therapeutic dose overlapped with **warfarin 5mg**. and was given Amlodipine 5mg for blood pressure. As the INR was persistently staying at 1.1, **warfarin dose increased to 10mg and later to 15mg**. Patient **stopped breast feeding** as the baby was refusing to suck breast probably due to nipple confusion due to the early introduction of bottle feeds .**Novel anticoagulant Rivaraxoban (Directly Acting Oral Anticoagulant - DOAC) at a dose of 15mg twice daily was started after appropriate counselling**.

25 days after Rivaraxoban (on 45th day post partum) **repeat Echo showed no pulmonary artery hypertension**, and normal left ventricular function. Hence Rivaraxoban twice daily continued for 3 weeks and 20mg once daily there after. On 53rd day post partum Anti phospholipid antibody testing (APLA testing) was done following **positive result of ANA**. APLA testing showed **positivity for lupus anticoagulant**, other antibodies were negative. Systemic lupus erythematosus (SLE) specific antibody Anti DsDNA found positive. After 3 months following the first test, **APLA testing** was repeated after stopping **Rivaraxoban** for 2 weeks. **APLA testing was negative including lupus anticoagulant**. ANA and Anti DsDNA remained positive even though no other features of SLE.

DISCUSSION

The absolute incidence of venous thrombo embolism(VTE) in pregnancy is about 1 in 1000 ² .Risk of VTE during pregnancy is 4-5 times higher than non pregnant .Even though VTE can occur at any stage of pregnancy ,puerperium is the time of highest risk^{3,4}. Acute VTE should be suspected during pregnancy in women with signs and symptoms consistent with possible VTE, particularly if there are other risk factors for VTE. Acute pulmonary embolism present with symptoms like chest pain, dyspnea, hemoptysis, and collapse. According to green top guideline 37b any women with symptoms and signs of VTE should have objective testing performed expeditiously and treatment with low molecular weight heparin given until diagnosis is excluded by objective testing . Emphasis is on rapid diagnosis and treatment to prevent maternal morbidity and mortality

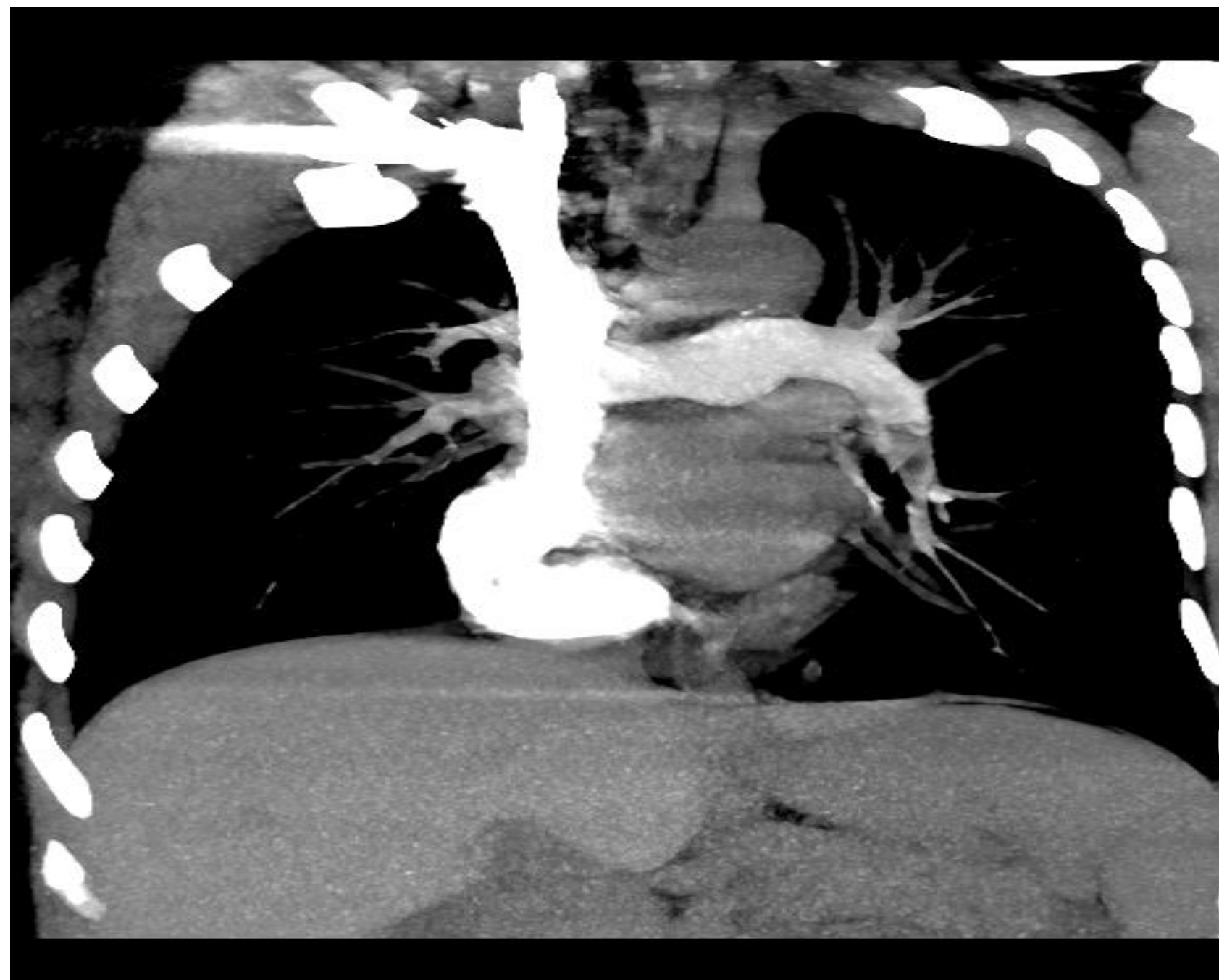
There are many risk factors for VTE including preexisting (heritable and acquired thrombophilia, medical comorbidities, and obesity) and obstetric risk factors (includes cesarean delivery ,operative vaginal delivery ,and new onset or transient risk factors like hyperemesis). Here in our case **emergency cesarean section and nutritional anemia** must have been the probable triggers for VTE. Patient presented with symptoms of breathlessness. Even though clinical examination ,ECG ,chest x ray were normal, **high index of suspicion and worsening of symptoms helped in clinching the diagnosis**.

APLA syndrome is one of the acquired thrombophilia syndromes(leading to arterial ,venous ,or microvascular thrombosis)or obstetric morbidities due to the presence of persistent anti phospholipid antibodies .Main Antiphospholipid antibodies are Lupus anticoagulant, Anti cardiolipin and Anti beta 2 glycoprotein. **Revised Sapparo criteria**(Sydney 2006)is used for **diagnosis of APLA syndrome** needs **one clinical and one lab parameters to be positive. Antibodies need to be retested after 12 weeks** to confirm the diagnosis. **In our case even though initially lupus anticoagulant was positive while on DOAC ,repeat testing after 3 months (after stopping DOAC for 2 weeks) showed it to be negative** .So according to Sydney criteria in our patient APLA syndrome was ruled out as a cause for pulmonary embolism.

In a review published in British journal of Hematology by Deepa R.J. Archillage ,Mike Laffran shares a possibility of **Lupus anticoagulant estimation being false positive while on DOAC**.(Merimann et al 2011).A possible method to detect Lupus anticoagulant in sample containing factor Xa inhibitor is Taipan **snake venom/Ecarin clotting time** combination as theses tests are insensitive to factor Xa. (Archillage et al 2015).How ever these tests are not widely available.



Axial section of CT pulmonary angiogram showing thrombus in left interior lobar pulmonary artery



MIP image, coronal section showing filling defect in left inferior pulmonary artery.

Some studies have shown that **absorption methods to remove the effects of DOAC** are useful for avoiding false positive Dilute Russells Viper Venom time test while on DOAC(Exner et al in 2018,cox mortan et al 2019).These are currently used in clinical practice in some centres. Prior to recommendations of these methods for routine **use they should be validated in large enough samples from the patients**. This probably explains the initial positive lupus anticoagulant report in our patient .

The treatment of pulmonary embolism involves using low molecular weight heparin dose titrated according to body weight . In our case patient was given 80mg twice daily. Maintenance treatment may be needed for at least 3-6months .In view of daily injections being difficult patient was overlapped with warfarin. Started with 5mg dose increased progressively till 15mg. **Even with 15mg warfarin desired INR was not achieved**. According to a case control study⁵ regarding warfarin dosage in post partum period it is found that significantly higher doses of medicine and more number of days are required to reach the desired INR(RCOG GTG 37b).**The probable cause may be altered coagulation parameters in pregnancy persisting** in puerperium antagonizing warfarin. After discussing with patient regarding advantages disadvantages and uncertainties about novel anticoagulants Rivaraxoban was initiated at a dose of 15mg twice daily. Prior to starting Rivaraxoban breast feeding was stopped .(As patient was not keen to continue heparin injections).Patient had her symptoms fully resolved with rivaraxoban in our case

Warfarin is a drug with **narrow therapeutic index requires frequent INR monitoring** and food and drug interactions .**Rivaraxoban** is an oral factor Xa inhibitor is a novel anticoagulant(DOAC) is indicated for maintenance treatment following **venous thrombo embolism in non pregnant patients** as an alternative to traditional Vitamin K antagonist Warfarin. **Advantages of Rivaraxoban being fixed dose prescription, no need for monitoring anticoagulant effect ,simplified peri operative management** ,reduced major intra cranial bleeding and fewer food drug interactions. **But, latest RCOG green top guidelines and several recent papers published on Rivaroxaban not recommending its use in pregnancy or non lactating lady**.NO recommendations came out regarding DOAC use in post partum non lactating lady. The reason for such uncertainties are lack of RCTS on effect of novel anticoagulants on altered pathophysiology of pregnancy and lactation ,fetal and neonatal effects.

CONCLUSION

High index of suspicion is required in any post partum patient presenting with symptoms of breathlessness. Involvement of **multi disciplinary team** is an important part of care .More RCTS and **trials are needed regarding use of direct thrombin inhibitors in puerperium** in both lactating and non lactating mothers. More researches also needed in case of **tests for diagnosing lupus anticoagulant in patients on DOAC** .Also there is a need for research regarding potential use of DOAC in single antibody positive thrombotic APS.

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