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A Case report of acute pulmonary embolism in pregnancy managed by systemic thrombolysis

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Abstract
A case of a 37-year-old pregnant woman at 29 weeks of gestation presented to our hospital with syncope and shortness of breath. We diagnosed her as a case of bilateral pulmonary thromboembolism. Due to Persistent hypotension, thrombolytic therapy with tenecteplase was administered. The clinical and hemodynamic response was excellent, with no maternal or fetal hemorrhagic complications.
The clinical presentation of pulmonary embolism is sometimes challenging to identify due to resemblance to physiological pregnancy changes. The diagnosis gets delayed by the reluctance to expose the fetus to ionizing radiation. Systemic thrombolysis is considered a high-risk treatment in pregnancy, and very few women have received it. However, the complication rates of thrombolytic therapy are acceptable in the view of the underlying disease.

Keywords: Pulmonary embolism, Thrombolytic therapy, Tenecteplase

Introduction
Around 0.2- 4% of India's pregnancies are complicated by cardiovascular disease, and this figure is increasing. There is frequently a need for diagnostic and therapeutic cardiological interventions in pregnant women. It is always a challenge because most cardiologists lack experience with this patient group and because few cardiological interventions have been thoroughly validated in this population.
The recently published ESC guidelines on the management of cardiovascular diseases during pregnancy were developed more by extrapolating the evidence for non- pregnant patients than based on the limited data available, and most of their recommendations are level of evidence C (consensus of the experts and small studies, retrospective studies, registries) [1].

Case report
A 37-year-old pregnant woman at 29 weeks of gestation (gravida two para 1), with a history of overweight, no relevant family history, and not taking any regular medication, presented with fatigue and pain in the side and back of the left thigh 24 hours after prolonged sitting work for about 3 hours. The clinical setting was interpreted as a possible herniated disc with inflammation of the left sciatic nerve, and she was medicated with analgesics and anti-inflammatory agents. Her fatigue worsened, with shortness of breath on successively less exertion; on a ninth day, she suffered a brief loss of consciousness at home and oppressive chest pain and went to the emergency department.
On physical examination, she was agitated, hypotensive (73/35 mmHg), tachycardia (115 bpm), hypoxemia (oxygen saturation in room air 80%), and tachypneic (50 CPM). No signs of deep vein thrombosis (DVT) were observed. Laboratory tests revealed hemoglobin 12.3 g/dl; platelets 170 × 10^9/l; D-dimers 2962 ng/ml; and troponin I 0.43 ng/ml (reference value <1.50 ng/ml). Arterial blood gas analysis (with the patient on 5 l/min supplementary oxygen) showed respiratory alkalosis (pH 7.49); pO_2 105 mmHg; pCO_2 28 mmHg, HCO_3^- 20.9 mmol/l; and O_2 saturation 98%. The electrocardiogram (ECG) showed sinus tachycardia and signs of right ventricular (RV) overload, confirmed by bedside transthoracic echocardiography (TTE) The fetus was in a transverse position, with good vital signs; the cardiotocograph was reactive, with good variability and no uterine contraction. The ultrasound scan showed concordant fetal growth. Doppler ultrasound of the lower limbs excluded DVT. According to the Wells score, the patient's clinical probability of acute pulmonary thromboembolism (PTE) was intermediate.

She was medicated with subcutaneous enoxaparin 1 mg/kg, and fluid therapy was initiated It was decided to perform thoracic computed tomography (CT) with the administration of intravenous contrast in the pulmonary arterial phase; the fetus is protected from radiation by lead shielding. CT angiography confirmed acute bilateral PTE

The patient was transferred to the coronary care unit, where after four hours, she was still agitated, hypotensive (80/45 mmHg), tachycardia (115 bpm), and tachypneic (60 CPM). After weighing the hemorrhagic risk against the greater risk of irreversible clinical decompensation, it was decided to administer thrombolytic therapy with tenecteplase (40-mg bolus over 5 minutes). Within three hours, the clear clinical and hemodynamic improvement was seen, with blood pressure 95/65 mmHg, heart rate 100 bpm, breathing rate 25 CPM, and decreasing need for supplementary oxygen therapy.

She was discharged from the coronary care unit on the fourth day and transferred to the Obstetrics and Gynecology Department. She remained hemodynamically stable throughout her hospital stay, with 96% oxygen saturation in room air. No maternal or fetal hemorrhagic complications occurred.

ECG Showing Sinus Tachycardia

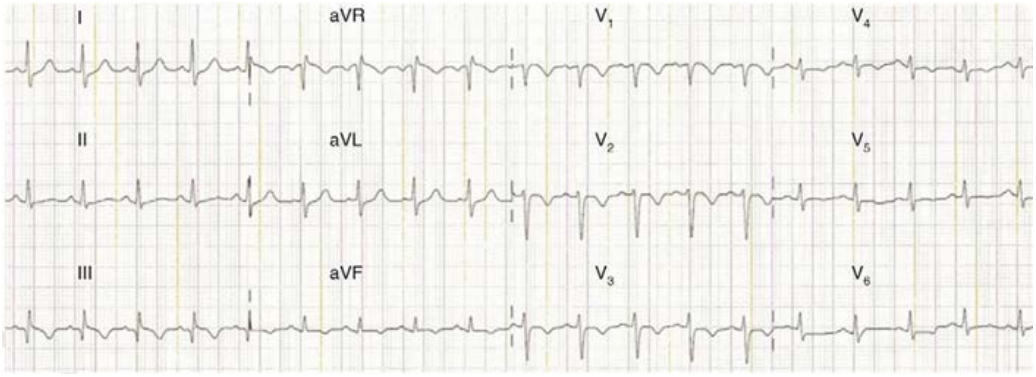


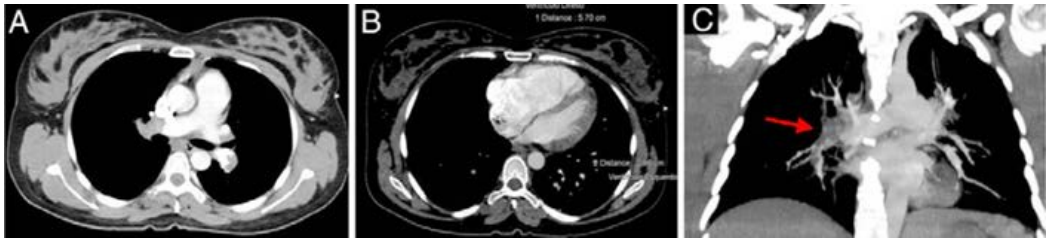
Table 1: The well scoring System for Diagnosis of PTE

Table 1 The Wells scoring system for diagnosis of PTE.

Findings	Points
Clinical signs of DVT	3.0
No alternate diagnosis likely or more likely than PTE	1.5
Heart rate >100 bpm	1.5
Immobilization in the previous 3 days or surgery in the previous 4 weeks	1.5
Previous diagnosis of DVT/PTE Hemoptysis	
Cancer	

DVT: deep vein thrombosis; PTE: pulmonary thromboembolism.

Occlusive thrombus in RT pulmonary artery



Discussion

The most feared manifestation of venous thromboembolism (VTE) is PTE, a joint entity with a mortality of 30% if untreated, mainly due to recurrence. Oral anticoagulation (OAC) at therapeutic doses within 24 hours reduces mortality.

VTE, which includes DVT and PTE, is the leading cause of maternal death (20%) in developing countries, accounting for 1.2-4.7 deaths per 100 000 pregnancies. The precise incidence of

VTE is unknown but is estimated at 0.5-- 2 cases per 1000 pregnancies [7]. The risk is most significant in the first three weeks after birth by cesarean section, two, but the risk is still high between the third and sixth week after delivery and is the same as during pregnancy. From the sixth week, the risk is the same as for non-pregnant women [8].

There are three pathophysiological mechanisms, known as Virchow's triad, that together or in isolation may be responsible for the high incidence of VTE in pregnancy [9].

1. **Venous stasis:** This begins in the first trimester and reaches a maximum of 36 weeks. It is caused by progesterone-induced vasodilation, compression of the pelvis by the gravid uterus, and pulsatile compression by any of the iliac arteries on the left iliac vein (which explains why 80% of cases of DVT in Pregnancy are on the left, a phenomenon known as May-Thurner syndrome) [10].
2. **Vascular injury:** During childbirth, the veins of the pelvic region may be distended and/or traumatized, mainly when a cesarean section is performed (which explains the more significant risk described above);
3. **Hypercoagulability:** The production of several coagulation factors (I, II, VII, VIII, IX, and X) increases in pregnancy, while protein S output and the activity of the inhibitors of fibrinolysis PAI-1 and PAI-2 are reduced. These physiological changes are crucial to the hemodynamic challenges of birth (peripartum bleeding is the leading cause of maternal death in developing countries) [11]. This prothrombotic state will be further exacerbated by the presence of hereditary thrombophilia such as factor V Leiden, the G20210A mutation in the prothrombin gene, ant thrombin III or protein C or S deficiency, or the presence of antiphospholipid antibodies [12].

Based on risk factors and physical examination, the clinical probability of PTE can be calculated using the Wells or Geneva score. This then guides the choice of diagnostic exams (Table 1).2 These tools have not been validated in the pregnant patient, although one study has found three variables that appear to predict DVT in pregnant women: left leg symptoms, >2 cm difference in thigh circumference, and first trimester.14

Laboratory results such as respiratory alkalosis or elevated fibrin degradation products are also commonly found in healthy pregnant women; levels of the latter increase with gestational age and reach a maximum at the time of birth, but such tests should be performed due to their ability to exclude disease and to avoid unnecessary exposure to ionizing radiation.1,15

Peripheral venous Doppler ultrasound

The deep venous system of the lower limbs is difficult to assess by physical examination, and when DVT and/or PTE are suspected, the techniques used are B-mode echocardiography and compression venous ultrasonography together with color Doppler in transverse view [1, 2]. Magnetic resonance imaging has 100% sensitivity in diagnosing DVT and appears to be safe in pregnancy. Documented DVT in a hemodynamically stable pregnant woman is sufficient motive to begin OAC without needing to exclude or confirm PTE, although at least 70% of patients with PTE do not have DVT at the time of diagnosis.

Radiography

Investigations using ionizing radiation in women of childbearing age should be performed during the first ten days after a menstrual cycle, and if there is a possibility that the woman is pregnant, this must be excluded first. Exposure of the ovaries to radiation pre-conception has no measurable effects on future gestations, and the risk from ionizing radiation to pregnant women is the same as to those who are not pregnant. However, for the fetus, ionizing radiation can cause death, malformations (particular ocular),

A major problem with the diagnosis of PTE is clinicians' reluctance to expose the fetus to ionizing radiation, often due to the overestimation of the risk of harm. When faced with the clinical probability of PTE, the primary diagnostic modalities are pulmonary ventilation-perfusion scintigraphy (VPS) and thoracic CT. The estimated radiation dose from CT absorbed by the fetus is 0.003-0.13mGy, while from VPS, it is 0.mGy. There is no evidence that doses of up to 50mGy lead to fetal abnormalities, low IQ, growth restriction or miscarriage. Less radiation is absorbed by the mother's mammary and pulmonary tissue with VPS than with CT. Although VPS and CT appear to be safe for the fetus, it should be noted that some studies suggest that exposure to low radiation doses *in utero* can increase the risk of childhood leukemia (1 in 2000 compared to the baseline risk of 1 in 2800), which does not correspond with the risk of maternal death from undiagnosed and untreated PTE (15%).

In a pregnant woman with a normal chest X-ray, VPS may be more valuable in diagnosing PTE than CT, since in the latter test, the contrast material can be interrupted by unopacified blood from the inferior vena cava. Conversely, CT should be used when the chest X-ray is abnormal since it can diagnose other conditions such as pneumonia or another lung disease. Pulmonary angiography should not be used in pregnancy.

Iodinated contrast agents may lead to fetal thyroid dysfunction (although this has never been reported with isolated use), and this should be assessed in the first week after birth

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Acute treatment

OAC, together with unfractionated or low molecular weight heparin, should be administered to achieve therapeutic doses within 24 hours. This reduces mortality by preventing the recurrence of PTE and improving RV function. There is no evidence of differences in mortality between OAC alone or in combination with thrombolytic, although in patients with signs of RV dysfunction thrombolysis is associated with less clinical deterioration (10% vs. 25%), more rapid resolution of hemodynamic alterations, and probable long-term improvement in pulmonary artery pressure and pulmonary vascular resistance [24]. Thrombolysis is indicated in PTE when there is severe clinical instability (i.e. with shock or systolic blood pressure <90 mmHg or a fall of >40 mmHg in 15 minutes not caused by new-onset arrhythmia, hypovolemia or sepsis), a situation associated with high early mortality (>15%). Although it may be considered in other conditions such as severe hypoxemia, severe scintigraphic perfusion defects, RV dysfunction, massive PTE on CT, free-floating thrombus in the right atrium or RV, and patent foramen ovale, there is general agreement on the use of thrombolysis only in the case of persistent hypotension [2]. Current thinking is to prescribe thrombolysis not on the basis of the extent or severity of PTE but solely to counteract its hemodynamic repercussions. Pregnancy is a relative contraindication to the use of thrombolytics [2], but successful thrombolysis has been reported in at least 200 pregnant women [1].The reported risks are 1% for maternal death, 6% for fetal loss and 8% for hemorrhage, mostly from the genital tract. At the time of delivery, thrombolytic treatment should not be used except in extremely severe cases and if surgical embolectomy is not immediately available. The thrombolytics most com- monly used in pregnancy are streptokinase, urokinase and recombinant

tissue plasminogen activator (rt-PA). If OAC is absolutely contraindicated, as in the immediate postoperative or postpartum period, possible treatments include an inferior vena cava filter, thrombus fragmentation with or without local thrombolysis, or surgical embolectomy. The use of fluid challenge in PTE-induced hemodynamic compromise is controversial; it should not exceed.

Maintenance therapy

Warfarin should not be used in pregnancy, particularly in the first trimester due to the risk of embryopathy and the third trimester due to placental abruption or fetal and neonatal hemorrhage. Still, it can be used after delivery and during breastfeeding. Vaginal delivery is preferable to cesarean section, which should be reserved for specific fetal or maternal indications. It is safe to begin OAC 12 hours after delivery; it should be continued for at least three months [1, 2].

Tenecteplase (TN Kase) is a genetically engineered glycoprotein derived from rt-PA by substituting three amino acids, which confers slower plasma clearance, longer half-life, more significant fibrin binding, less fibrinogenolysis and coagulopathy, and more excellent resistance to inactivation by PAI-1. Tenecteplase does not cross the blood-placenta barrier, and single-bolus administration results in more rapid plasmin formation and hence to the clinical setting's resolution.

correction of 500-1000 cm

Conclusion

Pulmonary thromboembolism is common in pregnancy and is associated with significant maternal morbidity and mortality. It should always be considered in the presence of suspicious symptoms and signs and confirmed by appropriate diagnostic tests, including VPS or CT. Oral anticoagulation should be begun immediately, and thrombolysis should be considered in cases of hemodynamic instability as it is useful in the few cases described in the literature and the case presented here.

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