ECRONICON OPEN ACCESS

EC GYNAECOLOGY
Case Report

Prolonged Isolated aPTT in Pregnancy: A Case Report

Lima Diogo*, Silva Daniel, Paiva Margarida, Silva Gisela, Vilhena Vera and Lopes Ana

Department of Obstetrics and Gynecology, Centro Hospitalar Barreiro Montijo, Lisboa, Portugal

***Corresponding Author:** Lima Diogo, Department of Obstetrics and Gynecology, Centro Hospitalar Barreiro Montijo, Lisboa, Portugal.

Received: September 14, 2023; **Published:** September 29, 2023

Abstract

Prolonged isolated activated partial thromboplastin time (aPTT) is among coagulation anomalies encountered during pregnancy. We report a case of a 31-year-old woman at 31 weeks of gestation initially admitted with intrahepatic cholestasis of pregnancy and preeclampsia. Additional manifestations, particularly an aPTT of 78.8 sec, led to further investigation. She was later diagnosed with systemic lupus erythematosus, secondary antiphospholipid syndrome and fetal growth restriction. She underwent urgent caesarean section at 34 weeks of gestation due to severe hypertension and a non-reassuring fetal status. This case reinforces the importance of recognizing coagulation disorders during pregnancy to correctly identify haemorrhagic or thromboembolic risk and ensure adequate management.

Keywords: *Activated Partial Thromboplastin Time; Antiphospholipid Syndrome; Lupus Anticoagulant*

Introduction

In addition to physiological changes, obstetric patients can suffer from congenital or acquired disorders of coagulation that impact haemostasis. As a result, standard coagulation tests such as prothrombin time (PT), international normalized ratio (INR), or activated partial thromboplastin time (aPTT) can be abnormal during gestation [1].

Prolonged isolated aPTT, meaning a prolongation accompanied by a normal PT and/or INR, is among coagulation test anomalies that may be encountered in clinical practice. The most common causes of prolonged isolated aPTT include anticoagulation effect, factor deficiency, or the presence of an inhibitor, either directed against a specific factor, such as factor VIII, or nonspecific, such as a lupus anticoagulant [2]. Recognizing the underlying cause of an abnormal isolated aPTT is fundamental in order to understand whether the patient has a haemorrhagic risk or, alternatively, is at risk for thromboembolism or fetal loss.

Case Report

We present a case of a 31-year-old caucasian woman, nullipara, admitted to the obstetric emergency department at 31 weeks of gestation with bilateral palmar pruritus and elevated blood pressure. She described intense itchiness, especially during the night, as well as palmar lesions with 1-week of evolution. Her blood pressure had been slightly elevated since 28 weeks of pregnancy. She denied headache, visual impairment, or epigastralgia. Her medical history included a deep vein thrombosis in the left lower limb at the age of 21, the cause of which was attributed to oral combined contraception after other risk factors were excluded, as well as a cervical conization due to a high-grade cervical intraepithelial lesion at the age of 30. She was taking subcutaneous enoxaparin in prophylactic dose since the

beginning of gestation due to her previous thrombosis. Her blood pressure was 148/99 mmHg. Physical examination showed red papules in the palms and a mild erythematous rash on the cheeks. Cardiotocography was normal and showed no uterine contractions. Blood workup showed Hb 11.9 g/dL, platelets 185*10^9/L, PT 11.3 sec, aPTT 78.8 sec, and total bile acids 26 umol/L. Uric acid, liver enzymes, total bilirubin, creatinine, and LDH were normal. Urinalysis showed 3+ proteinuria. Repeated PT and aPTT confirmed initial results. She was diagnosed with intrahepatic cholestasis of pregnancy and started on ursodeoxycholic acid and methyldopa. She was transferred to the obstetrics ward for further investigation and maternal-fetal surveillance.

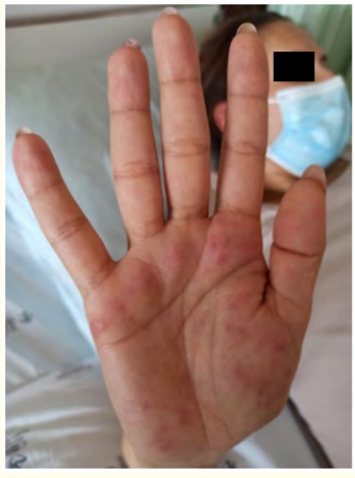

Figure 1: *Palmar red papules.*

Preeclampsia was confirmed after a 24-hour urine collection showed 2.5g of proteinuria. Further workup included: coagulation factors' activity, a complete autoimmune panel, skin biopsy from her palm lesions and renal ultrasound. VIII, IX and von Willebrand factors had normal or slightly increased activity. She had a positive antinuclear antibody (ANA) with a 1:320 titer. She also tested positive for all three antiphospholipid antibodies (lupus anticoagulant, anticardiolipin and anti-beta2 glycoprotein 1). The remaining autoimmune panel was negative. Skin biopsy was compatible with urticarial vasculitis. Renal ultrasound was unremarkable. Based on clinical and immunologic criteria, she was diagnosed with systemic lupus erythematosus. Antiphospholipid syndrome (APS) was also suspected. Enoxaparin was increased to 80 mg every 12 hours and the patient was started on azathioprine 25 mg twice a day. Serial obstetric ultrasounds showed a fetal growth under the 3rd centile with normal fetal doppler.

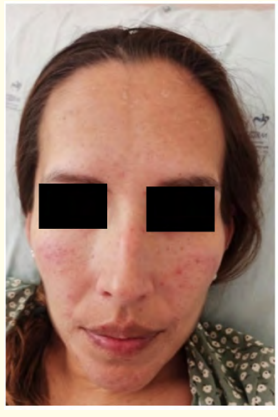

Figure 2: *Maculopapular rash over the malar eminences.*

At 34 weeks of gestation, due to severe hypertension and a non-reassuring fetal status, the patient underwent an urgent caesarean section without complications. The outcome was a male newborn with 1760g and an Apgar score of 8 in the 1st minute and 10 in the 5th minute. He was transferred to the neonatal intensive care unit due to prematurity. She was discharged at 72 hours postpartum. Diagnosis of antiphospholipid syndrome was confirmed after follow-up laboratory workup at 12 weeks postpartum reaffirmed triple-positive antiphospholipid antibodies.

Discussion

We present a case of prolonged isolated aPTT secondary to lupus anticoagulants, a class of autoantibodies that target phospholipid-binding proteins such as beta2-glycoprotein I or prothrombin. Lupus anticoagulants form complexes on coagulation active phospholipids, slowing down coagulation reactions *in vitro.* As a result, they prolong phospholipid-dependent coagulation tests such as aPTT. Curiously, their presence *in vivo* results in multiple proinflammatory and prothrombotic changes which lead to inflammation, vasculopathy, thrombosis, and pregnancy complications [2,3].

Enoxaparin might have influenced this patient's coagulation abnormalities as well, but low-molecular-weight heparin fractions prepared from standard commercial-grade heparin have a reduced effect on aPTT [4].

Current guidelines for definite antiphospholipid syndrome require proof of vascular thrombosis or pregnancy morbidity as well as a positive antiphospholipid antibody on two or more occasions separated by at least a 12-week period [5]. Although this patient had a previous history of vascular thrombosis, the clinical manifestation was separated more than 5 years from the positive antiphospholipid test, meaning it could not be appreciated under current guidelines, as a causative relationship between test and event would be difficult to ascertain, risking misdiagnosis. However, this patient fulfilled clinical criteria for pregnancy morbidity by having a premature birth at 34 weeks of gestation because of severe pre-eclampsia with features of placental insufficiency (non-reassuring fetal status and postnatal birth weight under the 10th percentile for the gestational age) [5].

Additional diagnosis of systemic lupus erythematosus was based on her maculopapular rash over the malar eminences, proteinuria greater than 500 mg/24h, high titer of ANA, and positive antiphospholipid antibodies [6].

It is worth noting this patient has a substantial risk of recurrent thromboembolic events, as demonstrated by her triple positivity for antiphospholipid antibodies, and may require long-term anticoagulation [7].

Conclusion

Although the prolonged isolated aPTT initially led us to believe this patient was at risk for haemorrhagic complications, the presence of lupus anticoagulants quickly replaced our initial presumption and confirmed she was in fact at risk for thromboembolism or fetal loss. This case reinforces it is of great importance to recognize coagulation disorders during pregnancy and thus, ensure adequate management as clinical consequences from differential diagnoses can be completely different.

Disclosure

The authors don't have any conflict of interest in this topic.

Bibliography

1. Katz D., *et al*. "Disorders of coagulation in pregnancy". *British Journal of Anaesthesia* 115 (2015): ii75-ii88.

2. Rasmussen K., *et al*. "Unexpected, isolated activated partial thromboplastin time prolongation: A practical mini-review". *European Journal of Haematology* 104.6 (2020): 519-525.

3. Garcia D., *et al*. "Diagnosis and management of the antiphospholipid syndrome". *New England Journal of Medicine* 378.21 (2018): 2010-2021.

4. Hirsh J., *et al*. "The seventh ACCP conference on antithrombotic and thrombolytic therapy". *Chest* 126.3 (2004).

5. Miyakis S., *et al*. "International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS)". *Journal of Thrombosis and Haemostasis* 4.2 (2006): 295-306.

6. Aringer M., *et al*. "2019 European League against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus". *Arthritis and Rheumatology* 71.9 (2019): 1400-1412.

7. Pengo V., *et al*. "Clinical course of high-risk patients diagnosed with antiphospholipid syndrome". *Journal of Thrombosis and Haemostasis* 8.2 (2010): 237-242.

Volume 12 Issue 10 October 2023