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Thrombotic Thrombocytopenic Purpura in Pregnancy Presented with Stroke at 29 Weeks: A Case Report

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Abstract

Thrombotic thrombocytopenic purpura (TTP) is a rare but acute, life-threatening condition which may be precipitated by pregnancy. This disorder that presents with thrombocytopenia, haemolytic anemia, and clinical consequences of microvascular thrombosis such as stroke. The exact cause is not known but it is associated with a deficiency of ADAMTS13 enzymes. Immune mediated TTP is more common and can present in pregnancy. The aim of this case is to bring awareness as many clinicians are unaware of this condition in pregnancy, its diagnosis may be missed or delayed, leading to fetal loss or serious maternal implications. In this case the patient presented at 29 weeks with stroke in Emergency department, referred to delivery suit for Obstetric review, with suspicion of Pre-eclampsia/HELLP. The diagnosis of TTP was achieved by a multidisciplinary team who worked tirelessly together. The patient was transferred to a Specialist Tertiary Care Centre for further management. The pregnancy continued until 33 weeks and 5 days. She underwent an emergency caesarean section for fetal distress. Steroids and Rituximab were continued postnatally. The outcome was favourable due to fast and efficient multidisciplinary care. Awareness of this rare but important condition can lead to recognition of clinical presentation, prompt diagnosis and appropriate management.

Keywords

Thrombotic Thrombocytopenic Purpura, Pregnancy, Ischemic Stroke, Caesarean Section

1. Introduction

Thrombotic Thrombocytopenic Purpura (TTP) is a life-threatening, multi-system

disease. It is characterised by widespread intraluminal and sub-endothelial platelet thrombin in capillary and pre-capillary arterioles. TTP occurs in 1 in 25,000 - 100,000 pregnancies, mostly in the third trimester. TTP in pregnancy may be congenital or acquired. Of those women with undiagnosed congenital TTP, 66% present with acute late onset TTP in pregnancy. This condition carries a 90% mortality rate if untreated [1]. Symptoms often consist of the pathogenic triad: thrombocytopenia, macroangiopathic haemolytic anaemia and neurological symptoms. 40% of these patients present with additional symptoms of renal impairment and high temperature, making up the full pentad [2].

2. Case Presentation

Mrs XX was 23 years of age booked in her first pregnancy at Luton and Dunstable NHS Hospital. She was referred for consultant-led care as she was a smoker and there was a history of anxiety and depression. She was placed under the perinatal mental health team and was taking Mirtazapine. Her BMI was 29. There was no other medical history of note. Regular fetal growth scans were arranged to screen for fetal growth problems.

Her routine 28weeks bloods revealed unexpectedly low platelet count of 26 × 10^9. XX confirmed the recent appearance of significant bruising over her abdomen and legs. She was diagnosed as having ITP and the obstetric Haematology team recommended a course of oral prednisolone.

She presented acutely at 28 + 3 weeks to Maternity Triage with reduced fetal movements, dizziness, and blurred vision. CTG was performed and was normal. Fetal movements were felt and so she was discharged home. There was no medical review performed.

XX re-presented at 29 + 4 weeks in the emergency department in September 2022. She had signs and symptoms suggestive of stroke i.e. left sided weakness, headache, visual disturbance, and drooping of the mouth. Some of the symptoms were transient however, the headache and weakness persisted. She denied any abdominal pain/contractions, vaginal bleeding and reported good fetal movements. She was referred for an obstetric review; suspecting HELLP syndrome (a serious version of pre-eclampsia).

Her blood results were as follows: haemoglobin was 78 g/L, platelet counts 15 × 10^9, reticulocytes 275.8, white blood count was 32, neutrophils were 28, ferritin was risen to 465, Lactate dehydrogenase was 312 and Alanine transferase was raised to 75. Her renal function, electrolyte and clotting were normal. However, her urine dip was positive for 1+ protein and 4+ of blood. Her blood pressure remained normal.

Abnormal liver function, haemolysis, thrombocytopenia, and neurological symptoms raised the suspicion of a non-obstetric cause. Advice was sought from the Obstetric Physician. Differential considered included ITP, TTP, HUS, PET, Acute fatty liver, and infection e.g. Hepatitis (**Figure 1**).

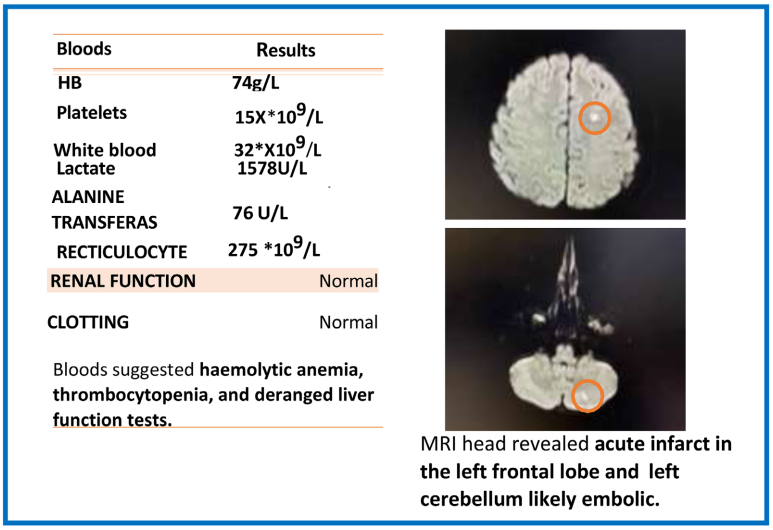

Figure 1. Blood results and MRI head revealed acute infarct in the left cerebellum and left frontal lobe, likely emboli.

An urgent MRI head was performed, which revealed acute infarct on left cerebellum and left frontal lobe. The Stroke team advised against Thrombolysis and critical care were informed of her condition. Her GCS remained 15 out of 15. Repeat blood results showed progressive decline in both haemoglobin and platelets. This was managed conservatively through blood and platelet transfusion. Steroids were administered for fetal lung maturation, in preparation for early delivery.

Due to the complex nature of her presentation and difficulty coming to a definitive diagnosis Multidisciplinary discussion involving Obstetrician, Haematologist, Obstetric Physician and Anaesthetist, proposed the diagnosis of TTP. This was based on triad of Thrombocytopenia, Haemolytic anemia, and Ischemic Stroke. The patient was transferred to a tertiary centre for diagnostic ADAMTS13 testing and ultimately, plasma exchange.

A combination of plasma exchange and high dose steroid treatment stabilised her platelet count. The pregnancy continued until 33+5wk when she underwent an emergency caesarean section for fetal concerns. The surgery was uneventful, and she made a full recovery. Postnatally the steroids were gradually reduced and XX remains under Haematology surveillance.

3. Discussion

This case highlights the importance of multi-disciplinary involvement to achieve the correct diagnosis and managing patients in a time-sensitive manner. Diagnosis was a significant challenge because of her heterogeneous clinical presentation, which includes TTP, Haemolytic uremic syndrome, disseminated intravascular coagulation, HELLP syndrome and immune thrombocytopenia.

Pregnancy related TTP can be congenital TTP and acquired TTP. Patients diagnosed with TTP may have additional disorders including autoimmune dis-

eases. In this group systemic lupus erythematosus (SLE) is the most common, followed by antiphospholipid antibody syndrome, adult-onset still's disease, rheumatoid arthritis, systemic sclerosis, polymyositis, and dermatomyositis scleroderma Sjogren's syndrome [3]. Acquired TTP in pregnancy may be associated with autoimmune disease such as Systemic lupus erythematosus, Rheumatoid arthritis, Scleroderma, dermato-myositis and Sjogren's syndrome [4] [5]. Our patient had a normal auto-immune screen.

Correct and prompt diagnosis of TTP in pregnancy is crucial for both maternal and fetal outcomes. Delayed management may have significant sequelae such as placental infarction, miscarriage, 2nd trimester loss, fetal growth restriction, stillbirth, and even maternal mortality [6].

Delivery of the fetus would have been appropriate for severe cases of pre-eclampsia/HELLP syndrome however, not for TTP and other non-obstetric causes. Although our patient in our case underwent preterm delivery, this was for fetal indications and not directly related to her TTP condition.

TTP is diagnosed by a deficiency of the specific ADAMTS13 antigen and the presence of antibodies against it. ADAMTS13 is an enzyme which breaks down Von Willebrand factor (VWF). Without this enzyme, VWF stays in circulation and can increase platelet coagulation and blood cell destruction.

The treatment of pregnancy associated TTP does not differ from non-pregnancy associated TTP. It is diagnosed by a deficiency of the specific ADAMTS13 antigen: assay and presence of antibodies. Daily therapeutic Plasma exchange must be started. Plasma infusion should be considered only if Plasma Exchange is not available which will be sufficient to correct severe deficiency of ADAMTS13. For acquired TTP immunosuppressive therapy is recommended including Steroids and azathioprine. Rituximab should only be considered postpartum due to lack of safety evidence in pregnancy. Most recently caplacizumab is used as it inhibits the interaction between VWF and platelets hence reducing platelets aggregation and thrombosis but the safety in pregnancy is unclear [7] [8] [9].

Rituximab may be considered postpartum due to lack of safety evidence in pregnancy. This was also used as part of the treatment in this case [10] [11].

More recently, caplacizumab is used as it inhibits the interaction between VWF and platelets, hence reducing platelets aggregation and thrombosis. Its safety in pregnancy is also unclear [12].

We recommend pre pregnancy counselling in the future to provide health education, an opportunity to optimise her condition prior to conception and to plan pregnancy care under specialist centres. Specifically, Obstetric complications include miscarriage, 2nd trimester losses, fetal growth restriction and stillbirth, recommended maintenance ADAMTS13 activity level of >20% to 25% holds the best outcome. Levels should be monitored before, during and after pregnancy and provide prognostic information regarding the risk of relapse.

4. Conclusion

Acute TTP is a medical emergency and requires a Multidisciplinary team ap-

proach in pregnancy and the postpartum period. Clinical judgement and ADAMTS13 measurement are crucial for correct diagnosis and appropriate therapeutic management. Current treatment options including Plasma-Therapy/ Plasma Exchange and immunosuppressants have dramatically improved maternal and fetal outcomes.

Methodology

The data was collected prospectively initially followed by retrospective collection of investigations, follow up appointments and the outcome from Evolve and ICE, online hospital electronic software.

Ethical Approval and Statement of Informed Consent

Research was conducted in accordance with the **World Medical Association Declaration of Helsinki**. Informed consent was obtained from the patient for publication of this case report.

Conflicts of Interest

The authors declare no conflicts of interest.

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