



CASE REPORT

Acquired thrombotic thrombocytopenic Purpura diagnosed during first trimester of pregnancy with excellent outcome after plasma exchange and rituximab, a case report

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Key Clinical Message

Acquired thrombotic thrombocytopenic purpura is a life-threatening condition that rarely presents during pregnancy. Early diagnosis and treatment with plasma exchange is needed to achieve a good pregnancy outcome.

KEYWORDS

hematology, plasma exchange, pregnancy, rituximab, thrombotic thrombocytopenic purpura

1 | INTRODUCTION

Acquired thrombotic thrombocytopenic purpura (aTTP) associated with pregnancy is a rare antibody-mediated thrombotic microangiopathy with high maternal and fetal mortality. Acquired TTP debut is uncommon during the first trimester, but it is especially severe in this situation, and it causes high fetal mortality, even with appropriate treatment. We describe a rare case of aTTP diagnosed during the first trimester of pregnancy, in which early diagnosis followed by thorough plasma exchange, steroids, and rituximab led to an excellent pregnancy outcome.

Thrombotic thrombocytopenic purpura (TTP) is a rare disease characterized by hemolytic anemia, thrombocytopenia, and clinical manifestations of microvascular thrombosis, caused by ADAMTS13 deficiency. ADAMTS13 is a metalloprotease which cleaves von Willebrand Factor (VWF), and its deficiency leads to the accumulation of ultra-large VWF multimers in plasma.¹ This produces platelet aggregation,

thrombocytopenia, small vessel occlusion, and secondary mechanical hemolytic anemia.

ADAMTS13 deficiency can be either congenital, due to different mutations in *ADAMTS13* gene, or acquired, resulting from the production of neutralizing IgG autoantibodies directed toward ADAMTS13 protein. Acquired TTP (aTTP) is usually diagnosed during the third or fourth decade of life and around 5% of cases are diagnosed during pregnancy. In this setting, it is a severe disease, which can result in high maternal and fetal mortality. Acquired TTP is uncommon during the first trimester, and pregnancy outcomes are worse than those of later onset aTTP.²

2 | CASE REPORT

A 35-year-old Caucasian female with a past medical history of chronic mastitis was admitted to obstetric emergency department at week 7 of her first pregnancy with vomiting,

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asthenia, and malaise. Blood test showed anemia, severe thrombocytopenia, incipient kidney damage, and elevated hemolysis biomarkers (Table 1). Neurological examination was normal. A thrombotic microangiopathy was suspected, and she was admitted to Intensive Unit (ICU). ADAMTS13 activity was low, and she had Anti-ADAMTS13 antibodies, which established the diagnosis of aTTP. No ADAMTS13 mutation was found. The patient was referred to the prenatal counseling team, and she decided to carry on pregnancy.

Daily plasma exchange (PE) of one volume of plasma per day with fresh-freeze plasma replacement using a COBE Spectra and Spectra OPTIA apheresis system (Terumo BCT®), and high dose methylprednisolone (1 mg/kg/d) was started at the ICU. We used a subclavian tunneled central venous catheter (CVC) for PE. Prophylactic low-molecular-weight heparin (enoxaparin 40 mg daily) and aspirin 100 mg daily were administered for the whole duration of pregnancy.

After 7 days of daily PE hemolysis, biomarkers and platelet count improved ($178 \times 10^9/L$). PE was continued every 2 days for 1 week, and steroids were slowly tapered down. However, after reduction of PE frequency to one every 3 days, an abrupt fell in platelet count (to $88 \times 10^9/L$) was observed with normal ADAMTS13 activity. Daily PE was reinitiated, and intravenous rituximab $375 \text{ mg}/\text{m}^2$ was administered weakly for 3 weeks. After 13 sessions of daily PE, at week 11 of pregnancy, platelet count started to progressively rise and PE frequency was gradually reduced and was finally discontinued at week 16 of pregnancy. The patient received a total of 40 PE sessions. She only presented a mild allergic reaction to plasma and a CVC infection at week 23, that required CVC

removal. Follow-up consisted of complete blood count every 2 days and weekly ADAMTS13 activity determination.

At 37 weeks, ADAMTS13 activity had decreased to 35%, with normal platelet count, and induction of labor was programmed. However, an emergency cesarean section was performed due to fetal bradycardia. The patient delivered a healthy 2260 g female baby (Apgar score 7 after 1 minute and 9 after 5 minutes). The patient has remained in complete remission since delivery, and the baby has shown normal growth and neurological development.

3 | DISCUSSION

Few cases of pregnancy-associated TTP occur during the first trimester, the majority occurring at the time of delivery or during postpartum period, and most of them are the late-onset congenital TTP, being aTTP extremely rare in this setting.²

Acquired TTP in the first trimester frequently leads to miscarriage, and only few cases of successful pregnancies have been reported.^{3,4} PE is considered the first-line treatment for aTTP and should be initiated as soon as possible.^{5,6} Adjuvant treatment consist mainly of steroids and rituximab. Rituximab has shown efficacy as second-line treatment for refractory or relapsing aTTP,⁷ and it has also been proposed in combination with PE as first-line treatment to reduce the risk of relapse.^{8,9} In pregnancy, the use of rituximab is associated with congenital transitory hematological alterations in the newborn (mainly B-cell aplasia), that could lead to severe infections and perinatal sepsis. However, these adverse events are manageable and the frequency of serious malformations is low.¹⁰ To our knowledge, this is the first reported case of a new onset aTTP treated with rituximab in the first trimester of pregnancy.

In conclusion, aTTP in pregnancy is a life-threatening condition that requires prompt diagnosis and treatment with PE. The present case suggests that thorough plasma exchange and administration of rituximab could reduce relapse rate and help to achieve successful delivery, even in the first trimester, without severe adverse events. Moreover, ADAMTS13 activity and platelet count should be monitored during pregnancy and after delivery to allow for early intervention in case of relapse.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

JA and MM wrote the manuscript. JJM performed plasma exchange to the patient and provided relevant data to write the manuscript. MV, MD, RADO, EA, BA, and JCG performed the clinical management of the patient and provided

TABLE 1 Blood test results at the time of diagnosis

Test	Result	Normal value
Hemoglobin	8.1 g/dL	12-16 g/dL
Platelet count	$15 \times 10^9/L$	$135-450 \times 10^9/L$
Lactate dehydrogenase	>2000 U/L	26-245 U/L
Haptoglobin	Undetectable	50-200 mg/dL
Creatinine	1.16 mg/dL	0.55-1.10 mg/dL
Estimated Glomerular Filtration Rate	63 mL/min/1.73 m ²	>60 mL/min/1.73 m ²
Indirect bilirubin	8.0 mg/dL	0.2-1.2 mg/dL
ADAMTS13 activity	<3%	40%-130%
Anti-ADAMTS 13 antibodies (ELISA)	Positive	
Lupic anticoagulant	Negative	
Direct antiglobulin test	Negative	
Anti-nuclear cytoplasm antibodies	Negative	
Anti-neutrophil cytoplasm antibodies	Negative	

the relevant data to write the manuscript. All authors read and approved the final manuscript.

ETHICAL APPROVAL

This report is in accordance with the Declaration of Helsinki. The patient gave her informed consent prior to inclusion in this report.

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How to cite this article: Arzuaga-Mendez J, Moreno M, Mateos-Mazón JJ, et al. Acquired thrombotic thrombocytopenic Purpura diagnosed during first trimester of pregnancy with excellent outcome after plasma exchange and rituximab, a case report. *Clin Case Rep*. 2021;9:1304–1306. <https://doi.org/10.1002/ccr3.3752>