Case Report

Thrombotic Thrombocytopenic Purpura (TTP) In Pregnant Patient

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Abstract

A 22 years old primigravida presented with loose motion, fever and atonic seizures at home. Patient was markedly pale and dehydrated. Her blood pressure was 110/70 mmHg, temp 100F and pulse 100/min. On obstetric examination baby was corresponding to dates and liquor was adequate. Her complete blood count and serum electrolytes were done. Platelet count was only 16,000/uL. Patient was admitted for evaluation and management. Urgent hematological and medical consultation was done and diagnosis of Thrombotic thrombocytopenic purpura was made. Patient was put on steroids and daily plasma transfusion. Her platelet count improved dramatically and pregnancy was taken to 35 weeks of gestation and baby delivered by cesarean section.

Keywords: Thrombotic thrombocytopenic purpura. Pregnancy. Plasma Transfusion.

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Introduction

Thrombotic thrombocytopenic purpura (TTP) is very rare multi-organ system disorder due to deficiency of ADAMTS-13 (a Distntegrin and Metalloproteinase with a Thrombospondin Type 1 motif, member 13) also known as Von willebrand factor cleaving protease.[1] It typically affects females and atleast half of episode of TTP are in females of child bearing age. Incidence of TTP is 3.7 cases per million people each year.[2,3]

Untreated TTP has a mortality rate as high as 90%. Risk of recurrence of TTP in a future pregnancy is 100% in women with congenital TTP and 47% in women with acquired TTP.[4] First case of TTP was reported in 1924 described by Dr.Eli Moschcowitz first described a 16-year-old girl presenting with fever, neurological symptoms, and severe thrombocytopenia.[5]

Autopsy findings revealed widespread thrombi in the terminal arterioles and capillaries of multiple organs, though the underlying cause of this enigmatic disease remained unknown. In 1947, Singer named the condition *Thrombotic Thrombocytopenic Purpura (TTP)*.[6] Two decades later, Amorosi and Ultmann introduced classic diagnostic pentad of TTP consisting of fever, thrombocytopenia, hemolytic anemia, renal injury and neurological manifestation. In our case platelet count was reduced and rest of coagulation profile was normal. Diagnosis could have been easily missed if multidisciplinary approach would not have been adopted.

Case Report

A 22 years old married woman for 1 year regularly booked from first trimester. Her pregnancy was uneventful except that she was beta thalassemia trait and was maintaining her hemoglobin around 9g/dL. At 28 weeks of gestation she presented in outpatient department (OPD) with multiple episodes of loose motions accompanied with low grade fever and history of drop attacks at home. She was pale with sunken eyes and dry cracked lips. On General physical examination (GPE) her blood pressure was 110/70 mmHg, temp 100F and pulse 100/min, rest of the GPE was unremarkable. On abdominal examination fundal height was corresponding with dates and fetal heart was positive.

Her ultrasound was done which was normal with biometry corresponding to dates and adequate liquor.

Her complete blood count and electrolytes were done on urgent basis and patient was retained for IV fluids and antibiotics. Her hemoglobin was 6.7g/dL and platelet count 16,000/uL. Patient was admitted on urgent basis and multidisciplinary team was involved for further evaluation. Her peripheral film showed abundant shistocytes, red blood cell (RBC) fragmentation (shown in figure 1) and 15% reticulocyte count. Her PT ApTT was normal, lactate dehydrogenase (LDH) 479 U/L, Coombs (Direct Indirect) Negative, Uric acid 7.62mg/dL and alanine transaminase (ALT) levels were normal. Diagnosis of TTP was made as she had fever, neurological manifestation, thrombocytopenia and hemolytic anemia which falls in the pentad of TTP and according to revised criteria only two (thrombocytopenia and hemolytic anemia) are needed for diagnosis.

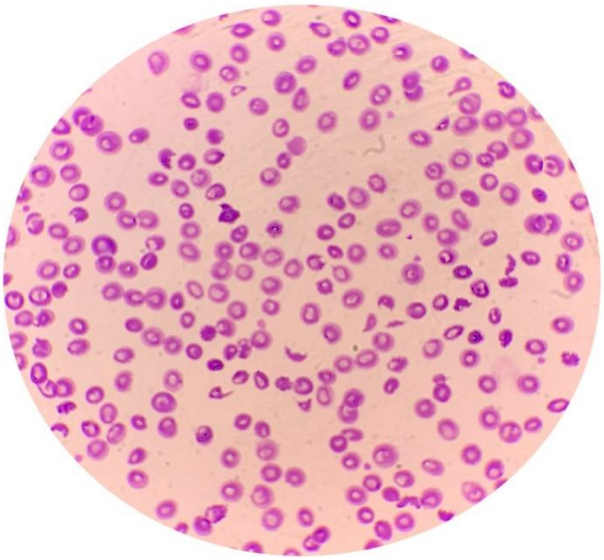

Figure 1. Slide showing RBC fragmentation and thrombocytopenia.

Her treatment was started by 5 Fresh frozen plasma (FFPS) infusions on daily basis and injection methylprednisolone 1g intravenous (IV) daily. 3 units of red cell concentrate (RCC) were also transfused. Steroids were given intravenously for 3 days and later switched over to oral prednisolone. Broad spectrum antibiotics were started by physician. Patient remained admitted and daily Complete blood count (CBC) was done. Platelet count started improving and she was discharged on 30 weeks of gestation on oral steroids. Hemoglobin increased to 10.4g/dL, platelet count 161,000/uL and reticulocyte count 3%. Fetomaternal surveillance was continued on OPD basis, initially twice weekly visits followed by weekly visits. Steroids were gradually tapered off and stopped at 33 weeks.

At 34 plus week gestation, her platelets again dropped to 20,000/uL. Patient was readmitted with plan of delivery after stabilization. During her hospital stay she again developed fever. Detailed workup was done to exclude other causes of fever. Her CRP was 45mg/L, ALT 256 U/L and coagulation profile was normal except platelet count. Broad spectrum antibiotics again started. Plasma infusions were continued and on sixth day of readmission her platelet count improved to 147,000/uL. Her delivery was planned when maternal compromise started that was around 35 weeks. Induction of labour was planned in view of maternal safety. Induction was done with tab dinoprostone but emergency cesarean was performed due to fetal tachycardia and failure to progress. Intraoperatively patient went into intermittent uterine atony, B-lynch suture was applied. 1RCC and 5FFPs were transfused intra-operatively. Vigilant post-operative monitoring was done with daily CBC. Baby was healthy (APGAR score 7/10, 9/10 at birth and 5 min) and shifted to mother after few hours of observation in neonatal intensive care unit (NICU).

Her post-operative period remained uneventful. Her laboratory parameters improved, hemoglobin 8.8g/dL, platelet count 187,000/uL, ALT 67 U/L and Uric acid 8.7mg/dL on third postop day. She was discharged on fifth postoperative day in good health. Her complete blood count was repeated again on 10th post-operative day and platelets were 243,000/uL. Six weeks follow-up was done and both mother and baby were fine with normal platelet count.

After three months, she had a relapse and presented in emergency with stroke. Computed Tomography (CT) scan showed multiple microthrombi in brain. She was treated on similar lines and fully recovered.

Discussion

Thrombotic thrombocytopenic purpura can be divided into congenital and immune mediated on basis of ADAMTS-13 deficiency. Congenital TTP (Upshaw-Schulman syndrome) is defined by a persistent severe deficiency of ADAMTS-13 caused by biallelic pathogenic mutations in ADAMTS13 gene.[7] Immune mediated TTP is caused by ADAMTS13 deficiency mediated by autoantibodies. However overt enzyme deficiency is not a universal finding and its estimation is not recommended for diagnosis. Medications associated with precipitation of TTP include quinine

and estrogen containing drugs.[8] As pregnancy is a hyperoestrogenic state so it is a well-known precipitating factor.

Late presentation of TTP during pregnancy is often linked to a milder form of the disease and better placental reserve. In contrast, cases occurring in the second trimester are more likely to involve significant placental dysfunction, resulting in severe fetal growth restriction (FGR) and an increased risk of stillbirth. Fetal death is secondary to placental infarction.[9]

Though the pentad mentioned before are the classical features of the disease but the revised criteria for the diagnosis is thrombocytopenia and microangiopathic hemolytic anemia (MAHA) alone.[10,11] Gold standard treatment is plasmapheresis with controversial beneficial effects of steroids.[12] Platelet transfusion has been contraindicated.[13] Immunosuppression targeting ADAMTS13 autoantibodies with humanized anti-CD20 monoclonal antibody rituximab is frequently added to initial therapy. Rituximab is a new drug and its safety in pregnancy is weighed against the benefit. In our case we could not offer her gold standard treatment option that is plasmapheresis as it was an expensive treatment and patient could not afford but isolated plasma infusion and steroids worked miraculously and we had very good outcome.

Conclusion

We recommend a high index of suspicion for the disease in each case of thrombocytopenia in pregnancy as it is a fatal condition if untreated. Such women should be managed in tertiary care setups where experienced multidisciplinary team and facility of plasma transfusion is available. Long term follow-up after the acute episode is critical to monitor for relapse and to diagnose and manage chronic sequel of this disease.

Patient consent: The informed consent is obtained from the patient to publish the data concerning this case

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