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Successful management of thrombotic thrombocytopenic purpura associated with pregnancy

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ABSTRACT

Thrombotic thrombocytopenic purpura (TTP) is an uncommon, severe, potentially life-threatening disease characterized by microangiopathic hemolytic anemia, thrombocytopenia, altered mental status, fever, and renal abnormalities. It can be seen at any age or sex but affects women of childbearing age more commonly. Pregnancy is known as one of the most common precipitating events for the onset of TTP and occurs mostly in the late third trimester or during the puerperium. Because of relatively low prevalence of pregnancy-related TTP, here we report the clinical characteristics and successful outcomes of 7 women with pregnancy-related TTP. Median age of patients was 25 (19–32). While 4 out of 7 women were primiparous, others were multiparous. Total plasma exchange (TPE) procedure was started within 24 h after admission to our hospital. All patients got into complete remission without any maternal mortality. Fetal mortality was found to be 28%. Pregnancy-related TTP is still associated with high maternal and fetal mortality rates. However, the prognosis of TTP has improved dramatically with early diagnosis and plasma-based therapies.

1. Purpose

Thrombotic thrombocytopenic purpura (TTP), described for the first time in 1924 by Moschcowitz [1], is a rare, potentially life-threatening disease. The classical pentad of clinical features of TTP are microangiopathic hemolytic anemia, thrombocytopenia, altered mental status, fever, and renal abnormalities [2,3]. It can be seen at any age or sex, but is characterized by a female predominance and occurs with an increased frequency during pregnancy. Women who are pregnant or in the postpartum period constitute approximately 10–25% of all TTP patients [4–6]. Until the introduction of plasma infusion and total plasma exchange (TPE) therapy, maternal and fetal survival rates in pregnancy related TTP were very low [7]. Currently, the prognosis of the disease has changed dramatically with the use of plasma-based therapies.

Because of the relatively low prevalence of pregnancy-related TTP, here we presented the clinical characteristics and outcomes of 7 women with pregnancy-related TTP who were successfully treated with plasma-based therapies.

2. Materials and methods

We evaluated the results of therapeutic plasma exchange (TPE) in 7 women (pregnant: 5, postpartum period: 2) diagnosed with TTP at the Department of Hematology, Meram Medicine School, Necmettin Erbakan

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University, between 2011 and 2013. Clinical signs on admission and laboratory characteristics including WBC, INR, aPTT, BUN, creatinine and LDH values were obtained from patients' charts. All patients and/or first-degree relatives were given information about the process and TPE information/consent forms were filled out by patients or first-degree relatives before process.

In all patients, TPE procedure was started within 24 h after admission to our hospital. Fresh frozen plasma was used as a replacement fluid. The exchange volume varied between 1 and 1.5 calculated plasma volumes (40–60 mL/kg). TPE procedure was carried out with Haemonetics MCS +900 (2003, Deerfield, USA). Patients were monitored about complications of TPE (volume overload, signs and symptoms of hypocalcaemia, fever, hypotension, hypertension, skin and allergic reactions, hematoma, bleeding, catheter infection etc.). The platelet count, LDH levels and clinical signs of disease were evaluated daily. The number of TPE procedures and sessions' range were determined according to the clinical and laboratory findings and TPE was continued on a daily basis until the level of platelet count reached $\geqslant$ 150.000 and the level of LDH $\leqslant N$ as well as by the absence of clinical signs of disease. Following complete remission, the process was stopped, with a tapering schedule.

3. Results

The median age of patients was 25 (19–32). While 4 out of 7 women were primiparous, others were multiparous. Microangiopathic hemolytic anemia (prominent red cell fragmentations on peripheral blood smear) and severe thrombocytopenia were present in all of the patients. Direct and indirect antiglobulin test were also negative in all patients. Acute renal failure and/or neurological symptoms occurred in four patients and only one patient had the evidence of fever. The results of coagulation test (PT/INR and PTT) for differential diagnosis of disseminated intravascular coagulation were normal ranges in all patients. Liver function tests (ALT/AST) for differential diagnosis of HELLP (hemolysis, elevated liver enzyme levels, and low platelet levels) were normal levels in 6 patients. ALT were detected about 5 times higher than normal in only one patient (Case: 4). Although we could not rule out HELLP syndroms in this patient, TTP was diagnosed due to profound thrombocytopenia, microangiopathic hemolytic anemia (presence of prominent red cell fragmentations), renal failure and elevated serum LDH levels. In addition she was referred to our hospital in postpartum period. Table 1 describes abnormal laboratory findings and the symptoms on presentation.

TTP developed in two patients during early period of the pregnancy. Both of those pregnancies were terminated because of fetal death (Cases 2 and 7). Two patients who suffered from TTP during the third trimester of pregnancy gave birth to preterm infants. Two were in the postpartum period and delivered healthy babies. One out of 7 women was in the second trimester of pregnancy and gave birth to a premature baby. Overall, fetal mortality rate was 28%. Seven patients got into complete remission without any maternal mortality. In only one patient TTP relapsed twice during the pregnancy. Gestational age and follow up information of the patients are given in Table 2.

Five patients were admitted to the intensive care due to dyspnea, hemoptysis, tachypnea and severe bleeding. In 2 of 5 patients, mechanical ventilation was needed because of depressed blood oxygen saturation (Cases 1 and 3). Adjunct to plasma exchange therapy, 90 mcg/kg of rFVIIa (Novoseven RT, Novo Nordisk) was given to these patients as thorax CT also showed diffuse alveolar hemorrhage. Median length of stay in ICU was 14 (1–23) days.

Only in one patient, Plasmapheresis was performed 2 times daily for 5 days due to the high risk of hemorrhage and the severity of disease (Case 1). Median number of plasmapheresis was 11 (3–24).

ADAMTS 13 activity was studied in only 2 patients and one case was proved to be acquired while the other case was congenital.

Case 6: ADAM TS 13 Activity: 8 (40–130%), ADAM TS 13 Antigen:<0.02 (0.50–1.60 μg/mL), ADAM TS 13 Inhibitory test: 0.9 (<15).

Case 7: ADAM TS 13 Activity: 8 (40–130%), ADAM TS 13 Antigen:<0.02 (0.50–1.60 μg/mL), ADAM TS 13 Inhibitory test 23: (<15).

3.1. Case 1

A 27-year-old, 26 weeks of pregnant woman was referred to the emergency department with massive vaginal bleeding. Cesarean section (C/S) was performed because of fetal distress and a premature baby was delivered. Immediately after delivery, the patient developed dyspnea, hemoptysis, tachypnea, consciousness symptoms and blood oxygen saturation was depressed. Therefore, she was transferred to the intensive care unit (ICU) and was put on a mechanical ventilator. Laboratory values showed

Table 1
Abnormal laboratory findings and symptoms of patients on presentation.

Patient no.	Platelet count (10^3/μL)	Hemoglobin level (g/dL)	Neurological symptom	Renal function disorder	Need for mechanical ventilation	Need for intensive care unit
1	17.4	9.96	+	+	+	+
2	21.3	8.75	–	+	–	+
3	11.4	7.58	+	+	+	+
4	33.9	10.9	–	+	–	+
5	31	10.6	–	–	–	–
6	21.4	9.85	–	–	–	–
7	17.8	5.93	–	–	–	+

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