An Unusual Cause of Thrombotic Thrombocytopenic Purpura in Pregnancy

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Thrombotic thrombocytopenic purpura is a disseminated form of thrombotic microangiopathy. Although most cases are assumed to be idiopathic, its association with malignancy is well-recognized and it usually occurs at the terminal stage of cancer. The condition is characterized by microangiopathic hemolytic anemia and thrombocytopenia. It is generally idiopathic, and its association with adenocarcinomas is extremely rare.

Herein, we report on a pregnant woman with the rare association of TTP and clinical manifestations of a metastatic gastric adenocarcinoma.

Case Report

Our patient was a 28-year-old lady, G 7P6A1L6, with a gestational age of 27 weeks. She gradually developed diplopia, headache, myalgia, hypertension, and one episode of hematemesis. She was then referred to a medical center far from Shiraz, southern Iran. After 20 days, she was transferred to Nemazi Hospital affiliated to Shiraz University of Medical Sciences, Shiraz.

Because of severe preeclampsia, her pregnancy was terminated at 30th week of gestation. After cesarean section, the patient developed persistent fever, hypertension, and mild respiratory distress, which was corrected with nasal administration of O2 in the recovery room. Her hemoglobin level dropped to 5.5 g/dL, with a mean corpuscular volume of 89 fl, reticulocyte count of 5.2%, and a significant drop in platelet count (45,000/µL). Due to decreased level of consciousness and worsening of her hypoxia, she was referred to ICU. She was then intubated and received O2 by endotracheal tube with no need for mechanical ventilation. In her routine peripheral blood smear, she had 4% schistocytes with a mild increase in lactate dehydrogenase (LDH). With suspicion of TTP, she underwent a 20-liter plasmapheresis in five consecutive sessions. Pelvic ultrasonography showed free fluid in the posterior cul-de-sac. Five days after the admission, she was connected to the mechanical ventilator for severe respiratory failure.

In spite of using broad-spectrum antibiotics with negative culture results, her fever persisted. So, all drugs were discontinued except metronidazole, cephalothin (Keflin), and methyldopa.

Two days later, her general condition became better and her fever subsided. Then, we decided to wean her off the mechanical ventilation. Feeding was started by nasogastric tube. Her hemoglobin level increased to 10 g/dL but her platelet count did not raise rapidly (~70,000/µL).

After one day, her diplopia recurred.
Ophthalmologic examination showed papilledema indicating raised intracranial pressure (ICP). Her new brain computed tomography (CT) demonstrated a linear hypodense lesion in the periphery of the left frontal lobe with mild subdural effusion. Therefore, mannitol and acetazolamide were administered and she was put on hyperventilation.

Thereafter, the patient’s condition deteriorated rapidly and she experienced four episodes of convulsions with massive gastrointestinal (GI) bleeding that could not be controlled easily (Figure 1). At that time, peripheral blood smear showed many fragmented red blood cells (RBCs) (Figure 2). Fibrin degradation product (FDP) level was <20 µg/dL. The prothrombin time and partial tromboplastin time were normal. LDH level reached 2500 IU/L. Direct and indirect Coombs' tests were negative. Serum CEA level was 105 ng/mL (normal range: 0 – 10 ng/mL). Serum alkaline phosphatase level was 1541 IU/L (normal range: 30 – 110).

With high suspicion of TTP, plasmapheresis with exchange was restarted for her. Reticulocyte count was around 0.5%.

The gastroscopic exploration found a neoplasm diffusely spreading through the whole gastric wall. Pathologic study revealed a poorly differentiated adenocarcinoma.

In her new abdominal ultrasonography there was a large hematoma extending from the site of cesarean section to the umbilicus. She had hydronephrosis of the right kidney.

Bone marrow biopsy proved necrosis and sparse isolated clumps of undifferentiated carcinoma cells and nearly absent hematopoietic tissues.

Due to severe GI bleeding, endoscopy with sclerotherapy was repeated. Unfortunately, a few days later the patient died of severe GI bleeding and thrombocytopenia not responsive to plasmapheresis and exchange.

**Discussion**

Thrombotic microangiopathy, manifesting as TTP or hemolytic uremic syndrome, is relatively uncommon in cancer patients. It shares the pathogenic microvascular occlusive lesion and many clinical manifestations as the classical TTP. However, the spectrum of complications varies widely. Several subsets are seen, including a MAHA in advanced cancer, chemotherapeutic drug-associated microangiopathy, and those with the transplant setting. The prognosis is not as favorable as in classical TTP. Anecdotal reports indicate that responses are seen with plasma exchange and with immuno-adsorption.1, 2

The mechanism of secondary TTP is different from the idiopathic one. Idiopathic TTP is believed to be due to a deficiency in ADAMTS13 (von Willebrand factor [vWf]-cleaving protease), which results in the accumulation of unusually large vWf multimers, which then causes platelet agglutination and microvascular thrombi. In contrast, in cancer-associated TTP, the ADAMTS13 activity and the multimeric pattern of vWf are normal. The pathogenesis of secondary TTP remains poorly understood.3 Probably, tumor cell emboli could generate endothelial damage with platelet agglutination and thrombocytopenia, implying microangiopathic hemolytic anemia and leukoerythroblastosis.
aggregation. MAHA is considered to be attributed to mechanical fragmentation of RBCs traversing the injured microvasculature. The role of plasma exchange in these patients should be re-evaluated. In conclusion, patients with TTP who do not initially respond to plasma exchange must be investigated meticulously to rule out an underlying disorder. Moreover, if alkaline phosphatase is increased, such as in our case, bone marrow biopsy should be performed to rule out metastasis. Finally, the assay of ADAMTS13 activity can help to discriminate between idiopathic and secondary TTP.

References