Hemolytic Uraemic Syndrome Associated with Pregnancy

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Abstract:
Hemolytic uraemic syndrome (HUS) and thrombotic thrombocytopenic purpura (TTP) are described as acute syndromes with multisystem abnormalities and pentad of thrombocytopenia, microangiopathic hemolysis, neurological symptoms, renal impairment and fever. Both diseases were believed to form a continuum of the same disease, but recently it was found, that they were having a different pathophysiology, as TTP patients have a deficiency in von willbrand factor (vWF) cleavage protease.

When renal involvement is severe with little or no neurological manifestation, this microangiopathy is termed as haemolytic-uraemic syndrome. If the hemolytic uraemic syndrome is not associated with diarrhea, it is called D-negative or atypical HUS. This subdivision is of etiological and prognostic importance.

TTP-HUS is associated with high maternal and fetal morbidity and mortality. Treatment of these syndromes differs from syndrome of hemolysis with elevated liver enzymes (HE LLP syndrome) and acute fatty liver during pregnancy, hence accurate diagnosis is important for optimal therapy.

Plasma transfusion and plasmapheresis have revolutionized management of TTP and HUS by increasing survival 80% to 90%.

Here we are reporting a case of D-negative hemolytic uraemic syndrome associated with pregnancy, which was successfully managed in the surgical intensive care unit of our hospital.

Illustrative Case:

Thirty-three years old patient admitted with intrauterine fetal death (IUFD), dropped her hemoglobin and platelet count, her coagulation profiles were normal and there was no vaginal bleeding.

She underwent vaginal delivery of fetus next day there was significant blood loss, resuscitated with packed red blood cell, fresh frozen plasma and platelet concentrate. She was stable hemodynamically, but started to become oliguric, with thrombocytopenia and anaemia in spite of transfusions so she was transferred to Surgical Intensive Care Unit.

In Intensive Care Unit she was fully awake, no neurological abnormality, her vital signs were stable, blood pressure and central venous pressure were on higher side. She became anuric, started on lasix infusion and labetalol infusion to control her blood pressure. She responded to lasix and started to pass urine,
blood pressure controlled with labetalol. But serum creatinine was raising, she was febrile, thrombocytopenic and anaemic even with transfusion of blood and blood product according to complete blood count data. Her lactic dehydrogenase (LDH) were very high and liver function were normal, coagulation profiles was not deranged, septic workup was negative, ultrasound abdomen not showed any collection only both renal cortex were hyperechogenic and peripheral smear showed schistocyte >21%, hemolytic uraemic syndrome suspected. Hematologist and Nephrologist confirmed the diagnosis and decided to start plasmapheresis. On third day of admission she was passing good amount of urine lasix was stopped, creatinine levels were stable, LDH levels decreasing and by sixth day platelet increased to more then 100,000. Started her on oral tenormine and Norsac and weaned from labetalol infusion. Plasmapheresis stopped on 7th day.

She was started on normal diet and transferred to the ward from there she was discharged home one week later and was followed in by the Nephrologist in the Outpatient Department for her residual renal impairment.

Discussion:
Thrombotic microangiopathy typically present with classic pented of thrombocytopenia, microangiopathic hemolysis, neurological manifestation, renal impairment and fever\(^{(3)}\).

When thrombotic microangiopathy associated with pregnancy two entities have to be considered, first thrombotic thrombocytopenic purpura (TTP)-hemolytic uremic syndrome (HUS) and secondly severe preeclampsia with hemolysis, elevated liver enzymes and low platelets. The differential diagnosis in these two entities is important for therapeutic and prognostic reasons. In our case clinical, hematological parameters and timing of presentation were suggesting diagnosis of hemolytic uraemic syndrome.

TTP-HUS often occurs in postpartum period symptoms often delayed for 48 hours or more after delivery\(^{(4)}\).

TTP-HUS used to be considered as a variant of the same disease but recent evidence suggests, that patients with TTP are having a deficiency of protease enzyme, responsible for cleavage of larger vWF\(^{(5)}\). Till this test is freely available, the differentiation between this two diseases is based on involvement of neurological symptoms in TTP and more severe renal impairment in HUS\(^{(6)}\). As our patient was having renal shutdown, thrombocytopenia, fever and hemolysis without CNS symptoms, the diagnosis was hemolytic-uremic syndrome.

HUS was first described in 1955\(^{(7)}\). HUS is subdivided in two forms: the typical form, which is associated with infectious diarrhea and an atypical or D-negative form without diarrhea\(^{(8)}\). This subdivision is important for diagnosis and prognostic value\(^{(9)}\). Our case was D-negative hemolytic-uremic syndrome.

TTP-HUS is associated with high maternal and fetal mortality and morbidity. Weiner in review of 40 cases of TTP and HUS reported maternal mortality of 44% and associated fetal loss rate of 80%\(^{(10)}\).

Plasma transfusion and plasmapheresis have revolutionized the management of TTP and HUS.

The use of plasma transfusion as first line of therapy during pregnancy yielded response rate of 64%\(^{(11)}\). Plasmapheresis should be started as early as possible. Onundarson et al demonstrated initial response rate to plasmapheresis was 81%; seventy four percent of initial nonresponders died and 38% of those responded initially needed additional therapy\(^{(12)}\).

Other therapies have a lower response rate, glucocorticoids are less effective than plasma transfusion\(^{(13)}\). Other treatments include immunoglobulin, vincristine\(^{(14)}\), cyclosporine and azathioprine\(^{(15)}\). Lastly to mention in spite of hazard of thrombosis, massive hemorrhage can occur in TTP and HUS. It is advisable to infuse platelets in case of life threatening bleeding\(^{(16)}\). Spleenectomy has been reported to induce long-term remission inpatients refractory to plasmapheresis.

Our case responded initially to plasmapheresis and did not require any other additional therapy.

Conclusion:
Early accurate diagnosis with aggressive treatment with plasmapheresis is cornerstone of management of TTP and HUS.
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References:


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