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ATYPICAL HUS IN POSTPARTUM PERIOD

Obstetrics & Gynaecology

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ABSTRACT

Background: Hemolytic uremic syndrome (HUS) is a TMA defined by thrombocytopenia, microangiopathic hemolytic anemia, and acute renal failure with elevated serum creatinine levels, low glomerular filtration rates, microscopic hematuria, and subnephrotic proteinuria. The most frequent form is associated with infections by Shiga-like toxin-producing bacteria (Shiga-HUS). Atypical form of HUS (aHUS) is associated with defects in the immunological complement pathway and it's rare in the pregnant population.

Case Description: We present a case report of 21-year-old primigravida with 30 weeks of gestation with PIH with Abruptio Placenta, Emergency LSCS was done & patient was shifted to surgical ICCU and placed on a ventilator. Patient withstood the procedure well however, had oliguria & raised creatinine. AKD reference was done and hemodialysis was started. With further no improvement 4 cycles of plamapheresiswas given on alternate days with hemodialysis i/v/o Thrombotic thromcytopenicpurpura/Hemolytic uremic syndrome. Patient was started on Inj. Methyl Prednisolone followed by Tab. Prednisolone. Patient received a total 10 PRC'S, 12FFP, 10 Platelets. With due course, an improvement in urine output, platelets and hemoglobulin was seen with decreasing LDH and serum creatinine levels. Patient was symptomatically better and was discharged after a period of 3 weeks.

Conclusion: The distinction between HUS and preeclampsia picked up early reduces maternal morbidity and mortality by 90%.

Clinical Significance: As therapy is different, diagnosis and distinction between DIC and TMA is important because early initiation of plasmapheresis has better patient outcome.

KEYWORDS

HUS, Hemodialysis , Plasmapheresis , Thrombotic microangiopathies

BACKGROUND

Microangiopathic haemolytic anemia, thrombocytopenia and end organ damage are characteristic of Thrombotic microangiopathies (TMA). Although often associated with HELLP syndrome and preeclampsia, sometimes, it is seen with Hemolytic uremic syndrome (HUS) and thrombotic thrombocytopenic purpura (TTP). ADAMTS 13 cleaves von Willebrand factor in plasma. This enzyme is needed for cleavage of the ultralarge vWF multimers produced by the vascular endothelium to a smaller multimer normally present in the circulation. A congenital or acquired deficiency of ADAMTS13 can result in accumulation of the ultralarge vWF multimers leading to microangiopathic thromboses and severe thrombocytopenia with hemolytic anemia and thrombotic sequelae. The presence of antibody against ADAMTS 13 or its deficiency, activity (<10%) , causes Thrombotic thrombocytopenic purpura. [1]. Atypical haemolytic uremic syndrome (aHUS) seen in pregnancy is because of complement factor H deficiency leading to WVF-Platelet thrombi in the glomerular vasculature resulting in renal failure. This is not related to HUS caused by with *Escherichia coli* 0157:H7 and Shiga toxin [2]. Pregnancy-associated atypical hemolytic-uremic syndrome (p-aHUS) affects 1 in every 25,000 pregnancies, mostly in the postpartum period[3]. Disregulation of the complement system is triggered by infection, severe preeclampsia, placental abruption, surgical stimulation and hypercoagulable state of pregnancy. Diagnosis of P-aHUS is difficult and needs to be recognized early to reduce maternal morbidity and mortality.

CASE DESCRIPTION

A 21 year old female was referred in view of Pregnancy induced hypertension with antepartum hemorrhage with 30 weeks gestation. She had complaints of pain in abdomen, per vaginal bleeding and decrease fetal movement. She had received Cap. Depin (5); Tab Labet(100) Inj. Tranexa(1)gm and Inj. MgSo4(4)gm before being referred. O/E: Pallor+, Pulse: 100/min, BP 140/100mmHg, CVS/RS: NAD, Per Abdomen: Cephalic presentation, Tonically Contracted, FHS Not Localized, Per Vagina: OS Closed; poorly effaced; Membranes (+)/ Bleeding (+)/ clots (+) .USG showed an IUFD with Gestational Age of 31 week f/s/o Abrutio Placentae.

Patient underwent Emergency LSCS where 2 PRC and 4 FFP's were transfused and patient was transferred to surgical ICU. Post-operatively 6 platelets were given. Her general condition was fair, Pulse-100/minute, regular, BP-150/100, Pallor+, Pedal edema+, Facial puffiness+, CVS- NAD, RS-B/L crepts+, P/A-soft, non-tender and well contracted, P/v- nil active bleeding. **(TABLE 1)** Post-operatively, CXR-Within normal limits, USG (A+P)-Right Kidney 9.5*, Left Kidney 9.3*4, B/L grade2 Medullary Renal Disease with partial loss of CMD. BT-2.3 min /CT-5min, ECG-Normal sinus rhythm, No ST-T changes. Urine R/M- Protein+++, OB+, PC 20-30, RBC 4-5, EC 4-5, UPCR 2.7, PS for schistocytes-4.8%. D-Dimer-8213, Sr Fibrinogen – Normal, Sr LDH – raised, Blood C/S-No growth, Urine C/S-No growth, IPF -8.2%, Sr.Ca-6.4, PO4-5.4, ABG-7.399/29/140/18/99%, ESR-85, ANA- Negative, ANCA-Negative, Serum Haptoglobin<5 , DCT/ICT-Negative.

Table 1: Baseline Investigations

INVESTIGATIONS	PRE-OPERATIVE	POST-OPERATIVE	POST-TRANSFUSION
HB(gm/dl)	6.5	4.7	5.4
TLC	19,000	15,500	17,000
PLATELETS	1,49,000	22,000	47,000
SR CREATININE	0.9	2.3	

Table 2: Investigation Flowchart

	HEMODIALYSIS STARTED		PLASMAPHERESIS 4 CYCLES WITH ALTERNATE DAY HEMODIALYSIS GIVEN				DISCHARGE
	1ST CYCLE	1ST CYCLE	1ST CYCLE	2ND CYCLE	3RD CYCLE	4TH CYCLE	
HB	8.5	6	6.4	7	8	7.5	9
TLC	18K	11K	10K	12K	13K	14K	12K
PLT	47K	56K	65K	88K	168K	223K	256K
PT/INR	16/1.4	17/1.3	16/1.4	15/1.4		16/1.3	17/1.2
T BIL	0.7	0.6	0.5			0.5	0.6
SGOT	90	56	45			34	25
SGPT	70	60	40			36	20
BUN	41	104	98	109	70	72	14
CREAT	3	6.5	6.9	8	5.9	3.9	1.8
Sr LDH	6370	4070	2000	2272	1353	879	

FIBRINOGEN	195			642		587	

Our provisional diagnosis was P1IUFD1 post emergency LSCS in view of Pregnancy Induced Hypertension with Abruptio Placenta with thrombotic microangiopathy? aHUS/TTP. A team of nephrologist, hematologist and intensivist was involved. With oliguria and rising creatinine, Hemodialysis was started. Fluid was restricted and higher antibiotics were given, however, with no benefit with hemodialysis, plasmapheresis was started. Four cycles of plasmapheresis on alternate day with hemodialysis was given. Inj. Methyl Prednisolone 1mg/kg was added. Improvement in urine output, platelets and hemoglobulin was seen with decreasing creatinine and Sr LDH **(TABLE 2).** Patient was symptomatically better, discharged and twelve weeks later her ADAMTS level and complement H factor levels were sent. She follows up in the OPD.

DISCUSSION

In pregnancy, aHUS may overlap with symptoms of TTP, HELLP, preeclampsia, ALFP and DIC[3]. Factors that helped in the diagnosis include onset, often postpartum, severe renal impairment, evidence of hemolysis and thrombocytopenia. There is no fever, hypoglycaemia, purpura and neurological involvement. Bilirubin levels, SGOT, SGPT and clotting pathway are not affected. P-aHUS is usually seen postpartum, comprising 80% of the cases. Dysregulation of the complement system especially due to factor H mutation and deficiency causes endothelial cell activation and production of procoagulative factors. This leads to tissue damage and kidney failure. A-HUS kidney biopsy shows glomerular thrombosis, intracapillary foamy cells, endocapillary swelling, mesangiolysis, and double basement membranes. Arterioles have thrombosis, endothelial swelling and fibrinoid necrosis[4]. Platelet aggregation in thrombus and lysis results in thrombocytopenia. Reduced blood flow to the brain due to microthrombi and uremia from kidney dysfunction can give rise to neurological symptoms. End-stage renal disease is common in majority of these patients. A-HUS diagnosis depends on clinical features and laboratory results; Kidney biopsy is impossible because of bleeding (uremia, thrombocytopenia) diathesis. Ideally, pre-treatment ADAMTS13 activity should be sent and PEX therapy should be started monitoring platelets, Sr LDH and creatinine levels. In patients with good response, PEX therapy should be continued and complement mutations should be assessed. In patients with poor response, if ADAMTS13 levels <10%, immunosuppression should be intensified. If ADAMTS 13 levels > 10%, consider a-HUS, initiate Eculizumab therapy and obtain complement mutation studies. Our patient was diagnosed clinically. She received a combination of plasma exchange and hemodiafiltration therapy and her condition improved. Additionally, glucocorticoid were used to reduce hemolysis process and restore kidney function[5]. Laboratory investigations for complement factors were sent 12weeks post-delivery because of intra and postoperative transfusion given to her. She had Factor H deficiency with ADAMTS13 levels >10%. Eculizumab, a monoclonal antibody stops complement activation by inhibiting production of C5a and C5b by binding to C5 [4]. Hematological remission and increase in the glomerular filtration is seen in patient not responding to plasmapheresis. Besides these interventions, active treatment of obstetric complications and anticoagulation therapy should also be considered. Women with aHUS with serum creatinine above 1.5 mg/dL develop chronic kidney disease. They have a high rate of recurrence and a poor pregnancy outcome. Hence, Pregnancy care, and decisions regarding future pregnancy, should be made in conjunction with obstetrician-gynaecologists, maternal–fetal medicine specialists, hematologists, and nephrologists.

CLINICAL SIGNIFICANCE

Urgent and accurate diagnosis of TMAs is exceedingly important because of associated organ damage and mortality. Early diagnosis of atypical uremic–hemolytic syndrome is challenging since it mimics other diseases that occur during pregnancy. As treatment varies, early diagnosis and initiation of plasmapheresis is important.

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