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RESEARCH ARTICLE

JAUNDICE AND OLIGURIA IN HELLP SYNDROME WITH LOW COMPLEMENT C3 LEVELS: A FORGOTTEN ENTITY

Anusha Devalla[1], Pallavi Ullur[2], Bharghavi Muddam[3,*] and Anitha Swamy[4]

[1]Assistant Professor, Department of Obstetrics and Gynecology, All India Institute of Medical Sciences, Bibinagar, India; [2]Senior Resident, Department of Obstetrics and Gynecology, All India Institute of Medical Sciences, Bibinagar, India; [3]Senior Resident, Department of Obstetrics and Gynecology, All India Institute of Medical Sciences, Bibinagar, India; [4]Assistant Professor, Department of Nephrology, All India Institute of Medical Sciences, Bibinagar, India

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****Corresponding author: Bharghavi Muddam***

ABSTRACT

HELLP syndrome (Hemolysis, Elevated Liver enzymes, Low Platelet count) is a severe complication of pre-eclampsia. Atypical hemolytic uremic syndrome rarely presents during pregnancy and is characterized by low C3 complement levels. Low complement levels are also observed in HELLP syndrome and is thought to be due to increased complement activation and a disruption of its regulatory mechanisms. We present a case of 27-year-old Primigravida of Asian ethnicity at 34 weeks gestation, who initially was diagnosed with HELLP syndrome based on jaundice, thrombocytopenia, elevated blood pressure, and abnormal liver function. However, subsequent investigations revealed a progressive decline in renal function, thrombocytopenia and low C3 complement levels raising suspicion for atypical hemolytic uremic syndrome (aHUS). This case highlights the diagnostic challenges and the importance of differentiating between HELLP syndrome and aHUS, particularly in the setting of complement abnormalities, as management strategies differ significantly.

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INTRODUCTION

HELLP syndrome (Hemolysis, Elevated Liver enzymes, Low Platelet count) is a severe variant of preeclampsia. HELLP syndrome incidence range from 0.5 to 0.9 % of all pregnancies. aHUS, a rare disorder associated with complement system dysregulation presents with thrombocytopenia, microangiopathic hemolysis, and acute renal failure. In HELLP syndrome, there is an increased activation of the complement system, particularly the alternative pathway.[1]This activation, along with a potential decrease in regulatory proteins, lead to tissue damage and inflammation, abnormal breakdown of red blood cells (hemolysis) and damage to the liver. Due to this, low complement levels are observed in HELLP syndrome.

Link to Atypical Hemolytic Uremic Syndrome (aHUS): There is a growing understanding that HELLP syndrome may have a connection to aHUS, a disease also involving excessive activation of the alternative complement pathway. Both conditions can lead to similar manifestations, such as microangiopathic hemolytic anemia, thrombocytopenia, and renal dysfunction. However, the overlap of clinical features between HELLP syndrome and atypical hemolytic uremic syndrome (aHUS) can lead to diagnostic confusion, especially in presence of low complement levels.[2]We describe a rare case of a woman with clinical features of HELLP syndrome, later developed renal failure with low C3 levels raising the suspicion of atypical hemolytic uremic syndrome.

CASE PRESENTATION

A 27-year-old primigravida, at 34+3 weeks gestation, presented to the antenatal outpatient department for a routine checkup. The patient reported no obstetric complaints, but on examination, deep icterus in the sclera and pallor in the conjunctiva were noted. Additionally, mild fetal growth restriction (FGR) and reduced amniotic fluid index (AFI) were observed on obstetric examination. The patient had elevated blood pressure of 150/100 mmHg, but there were no imminent symptoms such as headache, visual disturbances, or edema. A Urinary dipstick suggested +3 proteins. The patient was admitted for further investigations and Initial Diagnosis of pre-eclampsia was made. The patient's clinical presentation, including jaundice, elevated liver enzymes, low platelet count, and high blood pressure, raised concern for HELLP syndrome (Table 1).

Table 1. Laboratory investigations done for the patient

	ANC	PRE OP	PRE OP	POD -0	POD -1	POD -2
Hb (g/L)	13.9	14.4	13.4	13.4	10.2	10.5
Platelet count(10^9/L)	214	150	85	67	62	55
Wbc (10^9/L)	9.3	11.8	16.09	21.59	24.13	27.3
TB /DB (mg/dL)	-	6.4 / 5.1	5.9 / 3.3	4.9 /2.7	3.3/1.8	3/1.5
PT/INR	-	21.3 /1.64	18.9/1.46	-	19.7 /1.52	19.6 /1.59
Blood urea (mmol/L)	20	29	45	38	48	86
Creatinine (mg/dL)	1.3	2	2	1.9	1.8	1.9
Total protein (g/L) Albumin	-	7.5/2.8	6.6/2.7	-	4.5/2	4.9/2.0
AST/ ALT (IU/L)	315/227	69/43	64/30	56/26	67/21	73/23
ALP (IU/L)	461	556	705	578	323	323
LDH (IU/L)	843	358	884			
PCR (IU/mL)	0.15	0.13	0.37			
Spot urine protein (mg)	8.01	10.30	14.7			
Urine Creatinine (mmol/day)	54.2	76.2	39.8			
Procalcitonin(microg/L)					0.634	
Complement C3 (CAU/mL)					<40	
Complement C4 (CAU/mL)					18.9	
Sr.Haptoglobin (mg/dL)					108	

an obstetric ultrasound revealed stage 1 fetal growth restriction (FGR), and betamethasone injections were administered to facilitate fetal lung maturation in anticipation of preterm delivery. The patient was closely monitored, and she went into spontaneous labor. An emergency cesarean section was performed due to Grade III meconium-stained liquor and fetal bradycardia. A live male child of 1.7 kg was delivered and shifted to the neonatal intensive care unit (NICU) for management of low birth weight.

Postoperative Course and Diagnostic Dilemma: Postoperatively, the patient developed a falling platelet count, progressively low hemoglobin levels, elevated LDH, and reduced urine output over the next 72 hours.

These findings raised suspicion for an underlying renal failure considering a continuous rise in creatinine. Nephrology consultation was sought, and C3 complement levels were checked, revealing significantly low levels (<40 mg/dL).

Clinical Features

- **Renal Dysfunction:** The patient's renal function progressively worsened with rising blood urea and creatinine levels.
- **Thrombocytopenia:** Platelet count decreased from 2.14 lakh/µ L to 0.62 lakh/µL by Day 5 and further dropped to 55,000/µL.
- **Microangiopathic Hemolysis:** Elevated LDH and falling hemoglobin levels indicated hemolysis.
- **Complement Testing:** The patient's low C3 levels and normal C4 levels were consistent with complement dysregulation, a hallmark of aHUS.

The diagnosis of atypical hemolytic uremic syndrome (aHUS) was suspected based on these findings, and the arrangement for plasma exchange or higher monoclonal antibody treatment (Eculizumab) was made, but patient showed improvement with supportive care with high grade antibiotics and serial monitoring of clinical signs with renal and liver function tests suggesting HELLP syndrome and exclusion of atypical hemolytic uremic syndrome (aHUS) was made.

DISCUSSION

This case presents a diagnostic dilemma between HELLP syndrome and atypical Hemolytic uremic syndrome (aHUS), two pregnancy-related conditions that share many similarities such as thrombocytopenia, hemolysis and renal dysfunction. In both conditions, endothelium disturbance is clearly involved followed by complement and coagulation activation. Typically, in pregnancy-related TMA (Thrombotic Microangiopathy), clinical findings of hemolysis and thrombocytopenia resolve in ~ 3 days. If disease activity lasts longer, differential diagnostics are to be considered and only then is alternative treatment (eg., Eculizumab) considered. On one hand, Eculizumab is a very expensive medication, but on other, the cost of intensive care treatment, plasmaexchange, hemodialysis, possible kidney transplantation, not to mention the emotional consequences for mothers and families remain inestimable.[3] While HELLP syndrome is primarily a pregnancy-induced hypertensive disorder associated with placental ischemia, endothelial damage, and activation of the coagulation system, aHUS results from dysregulated activation of the complement system, leading to endothelial injury, thrombosis, and microangiopathic hemolysis.[4] The presence of renal involvement (progressively worsening creatinine and oliguria) and complement abnormalities in this patient made aHUS a more likely diagnosis, but the patient did not require plasma exchange or monoclonal antibody therapy (eculizumab), improved with only supportive treatment , made exclusion.[5] Vaught AJ et al.in a study used a functional complement assay, modified Ham test, to analyze sera of women with classic or atypical HELLP syndrome, pre-eclampsia with severe features, normal pregnancies, and healthy nonpregnant women, tested the in vitro ability of eculizumab to inhibit complement activation in HELLP serum. Increased complement activation was observed in participants with classic or atypical HELLP compared with those with normal pregnancies and nonpregnant controls. Mixing HELLP serum with eculizumab-containing serum resulted in a significant decrease in cell killing compared with HELLP serum alone, found that HELLP syndrome is associated with increased complement activation as assessed with the modified Ham test.[6] Gunawan et al presented a case report of 32-year-old, 38 weeks pregnant Caucasian woman admitted to Eberswalde Hospital with signs of preeclampsia and HELLP Syndrome. Caesarean Section was performed due to HELLP syndrome and fetal distress. Acute renal failure occured shortly after a successful delivery. After a diagnosis of p-aHUS is established, the patient was given Eculizumab, which yielded significant improvements.[7] Kanmounye et al presented a case report of 31-year-old, 38 weeks pregnant high blood pressure, bilateral pitting edema, and low fetal heart rate, cesarean section was performed. On postoperative day 2, based on the history, clinical presentation, acute kidney injury,

declining liver function and standard laboratory results team made a presumptive diagnosis of aHUS. patient was given four sessions of hemodialysis after which renal function and platelet count gradually increased.[8]

CONCLUSION

This case illustrates the importance of early recognition and differentiation between HELLP syndrome and aHUS, as both conditions share overlapping clinical features but require distinct management approaches. Low complement C3 levels, HELLP syndrome, jaundice, and oliguria can occur together in pregnancy, and this combination is a serious sign of potential liver and kidney dysfunction. Prompt recognition and management, including delivery, are crucial to improve maternal and fetal outcomes by ensuring appropriate treatment, particularly in managing complement dysregulation in aHUS.[9]

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