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Post covid pregnancy related haemolytic Uraemic syndrome masquerading as HELLP syndrome-A twisted tale of gravid

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ABSTRACT

Pregnancy associated atypical haemolytic uremic syndrome (p-aHUS) is an infrequent condition to be encountered during the puerperium period and is associated with microangiopathic haemolytic anaemia, thrombocytopenia as well as acute kidney injury. This syndrome is triggered by pregnancy in the women who are predisposed genetically leading to an unfortunate haemolytic disease which is associated with endothelial diffuse damage and consumption of the platelets. This is a dangerous condition which required prompt diagnosis as well as management. Diagnosing p-a HUS can be challenging for the treating clinicians as it may mimic other conditions like HELLP Syndrome during the pregnancy as well as postpartum period. Plasma exchange should be started within 24 hours of diagnosing the condition in order to prevent mortality. With the emergence of the corona virus pandemic, atypical SARS Covid -2 presentations during pregnancy have emerged, ranging from COVID-19-associated HELLP syndrome to intrauterine death. COVID-19 has been linked to an atypical haemolytic uremic syndrome, with COVID-19 causing ischemic acute tubular necrosis or thrombotic microangiopathy through a complex complement activation process. We are presenting a case of 28 year old female with nine months amenorrhea who presented with bilateral pedal oedema and oliguria since one week and had severe thrombocytopenia along with acute kidney injury following 28 days of contracting COVID-19. She was diagnosed as Post COVID-19 p-a HUS following diagnostic work up and was treated promptly with plasmapheresis leading to complete recovery.

Keywords: pregnancy, Haemolytic Uremic Syndrome, plasmapheresis, HELLP syndrome

1. INTRODUCTION

COVID-19 has produced a state of stress amongst the health care workers with multiple organ dysfunction and varied presentations challenging the

diagnosis as well as management of the patients (Rajkumar et al., 2020; Mahajan et al., 2021). COVID-19's haematological manifestations, which range from simple neutropenia to atypical haemolytic uremic syndrome, have perplexed clinicians. Atypical haemolytic uremic syndrome is although rare is a severe disease which is potentially lethal and is associated with microangiopathic haemolytic anaemia, thrombocytopenia, and acute kidney injury that is not related with *Escherichia coli* 0157:H7 infections (Mayer et al., 2012).

Out of all the cases of haemolytic uremic syndrome, a HUS accounts for about five to ten percent of the cases. When triggered by pregnancy the resultant thrombotic microangiopathy or TMA is known as pregnancy associated atypical haemolytic uremic syndrome (p-aHUS). One out of twenty five thousand pregnancies is affected by p-a HUS especially during the postpartum period and is linked with adverse maternal outcomes (Fakhouri et al., 2010). The majority of patients with atypical haemolytic uremic syndrome suffer from renal damage, neurological impairment, and multiorgan dysfunction. According to a French cohort study, sixty to seventy percent of patients with atypical haemolytic uremic syndrome developed end-stage renal disease (Thurman et al., 2018).

2. CASE HISTORY

A 28 years old Gravida 2 Para 1 Live 1, nurse by occupation with 36 weeks gestational age with previous full term vaginal delivery presented with severe anaemia with thrombocytopenia with preeclampsia along with bilateral swelling in both feet since a week and oliguria. She had tested COVID-19 positive 28 days back when she had been home quarantined and was provided antipyretics and multivitamins. Her oxygen saturation was monitored throughout and she did not have any episode of hypoxia or breathlessness. Her previous antenatal and radiological investigations were normal. There was no history of diabetes mellitus, tuberculosis, Asthma, thyroid, epilepsy.

On admission she came with raised blood pressure 150/100mmhg with urine albumin with dipstick +2 with bilateral pedal oedema, clinically she appeared pale. On examination of the abdomen, the uterus was 36 weeks size, relaxed with a cephalic presentation, and the foetal heart rate was 142 beats per minute. A routine antenatal profile was sent, as well as a pregnancy-induced hypertension profile. Radiological investigation and Doppler was done to rule out any Doppler changes. Ultrasonography showed average gestational age of foetus as 36.1 weeks with effective foetal weight 2846gms with liquor index 9.5 with placenta anterior grade 3 with cephalic presentation. On admission haematological findings were haemoglobin of 6.9gm% total leucocytes count 11500/ cumm, platelet 52000/cumm. While the coagulation profile, liver and renal function tests all came normal, the lactic acid dehydrogenase level was elevated to 2000. On the dipstick, proteinuria was a +2. Non stress test of patient was done showed beat to beat variability with two or more acceleration with no deacceleration.

The patient was admitted for close observation, and injections of dexamethasone 6mg 4 doses 6 hours apart were given for foetal lung maturation, as well as injections of magnesium sulphate 4gm in 100ml normal saline for foetal neuroprotection. She was shifted for caesarean section male baby 2.5 kg was delivered with vertex presentation with two loop of cord around neck with freshly passed meconium preperitoneal straw coloured 200cc fluid present, bilateral tubal ligation was done by modified Pomeroy method. Baby was shifted to relative side. Post operatively haemoglobin was 6.9gm % and there was leucocytosis with count of 27400/cumm, thrombocytopenia with platelet 34000/cumm (Table 1).

Table 1 Blood Investigations of the case

Sr. No.	Investigation	Measured Value(20/11/21)	Measure Value (30/12/21)	Measure Value (20/12/21)
1.	CBC	Hb 6.9 gm% Tlc 11500/cumm Plt 52000/cumm	Hb 8 gm% Tlc 41400/cumm Plt 61000/cumm	Hb 10.4 gm% Tlc 15000/cumm Plt 125000/cumm
2.	KFT	Urea 39 Creatnine 0.61 Sodium 140 Potassium 4.1	Urea 70 Creatnine 2.8 Sodium 130 Potassium 4.9	Urea 18 Creatnine 1.1 Sodium 142 Potassium 4.2

3.	LFT	Alkaline phosphatase 128 SGOT 266 SGPT 111 Total protein 4.9 Albumin 2.5 Globulin 2.4 Total bilirubin 1.1	Alkaline phosphatase 78 SGOT 105 SGPT 64 Total protein 4 Albumin 2 Globulin 1.8 Total bilirubin 1.4	Alkaline phosphatase 80 SGOT 30 SGPT 36 Total protein 4 Albumin 2 Globulin 2.3 Total bilirubin 1.2
4.	LDH	2000	1765	264
5.	C3,C4		160,42	
6.	ANA		0.97	
7.	ADAMTS13		More than 10%	

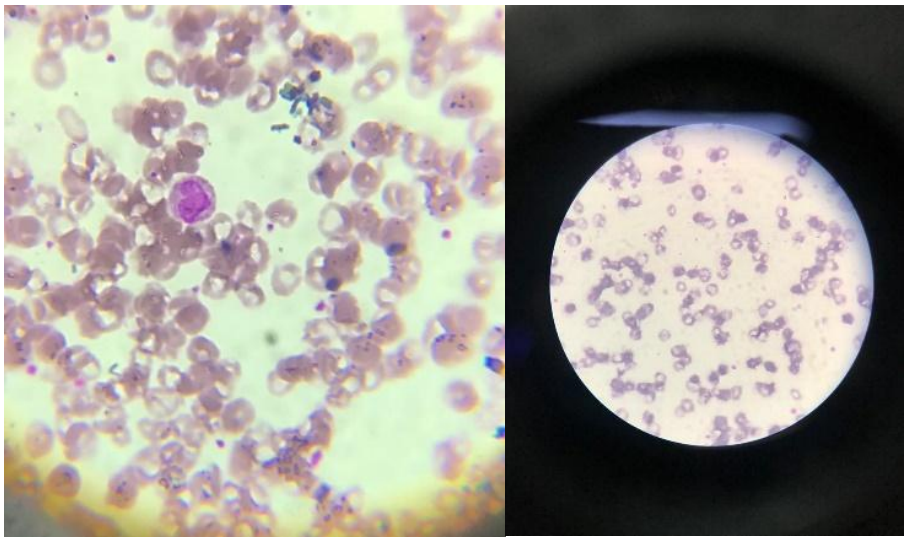

Figure 1 peripheral smear showing schistocytes

Peripheral smear showed split red cells with schistocytes (figure 1) suggestive of microangopathic haemolytic anaemia, Platelets–Reduced on smear. APC- 34,000 cells/mm3 as per cell counters No Haemoparasite seen. WBCs – Neutrophilic leucocytosis with mild shift to left up to the stage of band forms. Post operatively she was diagnosed as haemolytic uraemic syndrome. Patient was shifted to intensive care unit in view of oliguria, thrombocytopenia, HUS syndrome with puerperal sepsis, and started on plasmapheresis. Complement c3 c4 and Anti-nuclear antibody factor and ADAM13 level was sent for investigation clinching the diagnosis toward haemolytic uraemic syndrome.

Ultrasonography of Kub was done suggestive of grade 1 renal parenchymal disease, hepatosplenomegaly and sludge with polyp, minimal ascites, and mild pleural effusion. Ophthalmologist opinion was done suggestive of hypertensive retinopathy. Post plasmapheresis patient started improving and there was decreasing trend of profile. Patient was treated conservatively, with plasmapheresis performed every third day, discharge on day 30, and weekly follow-up advised.

3. DISCUSSION

The importance of preventing maternal mortality in a case of renal impairment seen in pregnancy due to haemolytic uremic syndrome is in this report. Schistocytes on a peripheral smear have been associated with to thrombocytopenia, haemolysis, and renal impairment. In our case, the diagnosis of haemolytic uremic syndrome was confirmed. In haemolytic uremic syndrome, uncontrolled activation of the alternate complement pathway results in diffuse endothelial damage, platelet activation, and finally

TMA with multiple organ failure due to distal ischemia (Angioi et al., 2016). Regulatory proteins malfunction as a result of mutations in the genes encoding C3, CFI, MCP, and CFH, resulting in excessive complement pathway activation.

The main form of therapy entails replacing the dysfunctional forms of proteins with normal and regular proteins, which was done in our case via plasma exchange. Even if plasma exchange therapy is initiated early in the course of the disease, some patients may not experience a recovery in renal function as the disease progresses to end-stage renal disease. In cases of p-a HUS, an anti-c5 therapy known as eculizumab has recently been developed, which is based on the terminal blockage of the complement system due to uncontrolled activation of the alternative complement pathway in p-aHUS. Eculizumab is a monoclonal antibody that binds to the C5 complement component and prevents it from being cleaved into C5a and C5b. There has been a significant improvement in the outcomes of atypical haemolytic uremic syndrome since the use of plasmapheresis and eculizumab. These findings match the clinical course described in a case report of three children with Shiga toxin-associated HUS and neurological involvement who were treated with Eculizumab (e Lars et al., 2016). The complement system is activated in COVID-19, resulting in systemic thrombotic microangiopathy. Thurman (2018) demonstrated hyperactivation of complement in typical HUS. In the past, it has been reported that thrombotic microangiopathy or atypical haemolytic uremic syndrome can recur in the context of viral infections like influenza (Valentina Fanny et al., 2022). Some cases of COVID-19 associated with this syndrome have been reported suggesting the addition of SARS CoV-2 as a possible trigger for haemolytic uremic syndrome.

Another important aspect of our case is the rural background of our health care Centre. Our patient had oliguria and oedema since a week however she had avoided visiting health care centres to seek help for the same. This show cases the lack of awareness amongst pregnant patients in the rural outskirts of India regarding the warning symptoms and signs during pregnancy. The policy makers should therefore pay more attention towards conducting awareness programs and providing means of transportation for such patients to ensure regular follow up especially during the pandemic era of COVID-19 when the lockdown restrictions have made it difficult for the patients based in remote areas to reach health care facilities.

4. CONCLUSION

Thus a case of atypical haemolytic uremic syndrome associated with pregnancy was diagnosed and managed successfully on time with early plasmapheresis to prevent maternal mortality. We emphasize on the importance of regular antenatal check-ups and covid related health problems and follow ups in rural India along with education of the patients to ensure early presentation to the health care set ups of such cases so that they can be managed on time.

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Informed Consent

Informed Consent was obtained from the patient.

Author's contribution

All the authors contributed equally to the case report.

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Conflicts of interest

The authors declare that there are no conflicts of interests.

Data and materials availability

All data associated with this study are present in the paper.

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