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Atypical hemolytic-uremic syndrome in pregnancy: a case report

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ABSTRACT

Introduction: The diagnosis of Atypical hemolytic-uremic syndrome (aHUS) is largely imprecise. Improving outcomes requires accurate diagnosis and timely management. Acute kidney damage, thrombocytopenia, and microangiopathic hemolytic anemia are all signs of aHUS. The condition is brought on by pregnancy, and in genetically susceptible women, it progresses to a terrible hemolytic illness marked by widespread endothelium damage and platelet consumption. The sickness is a potentially fatal ailment that demands quick identification and treatment.

Case Presentation: Our facility provided treatment for severe anemia, thrombocytopenia, and acute renal damage in a 24-year-old G1P1A0 postpartum lady with Caesarean sectio and a HELLP syndrome suspicion. An aHUS diagnosis was later verified. The condition of the patient failed to improve in the first 24 hours after birth. Inside this presence of TMA, the patient began on daily TPE and ran in parallel prednisone medication (1 mg/kg/day). After six TPE cycles, the laboratory values began to rise.

Conclusion: AHUS can be challenging to diagnose early since it frequently mimics other illnesses. To enhance results, proper diagnosis and prompt management are essential. The management strategy includes a multidisciplinary team, early plasmapheresis, and complement inhibition. To lessen the effects of aHUS, TPE should be carried out as soon as feasible on a daily basis.

INTRODUCTION

The overactivation of the alternative complement pathway results in the dangerous but uncommon condition known as an atypical haemolytic-uremic syndrome (aHUS) (Yan et al., 2020). aHUS is a condition that mainly impacts renal function and results in the formation of abnormal blood clots (thrombi) (Saad et al., 2016; Schramm et al., 2015). A triad of symptoms characterizes this thrombotic microangiopathy: thrombocytopenia, acute renal impairment, and microangiopathic hemolytic anemia, which can take place at any age, mostly in the tiny blood bloodstream of the kidneys. If these clots restrict or obstruct blood flow, they can cause serious medical problems (Bhandari & Sedhai, 2023).

aHUS appear to be associated with disorders in complement genes in genetically susceptible patients (Salvadori & Bertoni, 2013), non-Shiga-toxin-HUS, and accounts for 5-10% of children but a large percentage throughout adults (Loirat & Frémeaux-Bacchi, 2011). When pregnancy causes thrombotic microangiopathy (TMA), the condition is known as pregnancy-

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associated aHUS (p-aHUS). Probably one in every 25,000 pregnant women, primarily in the postnatal, and also linked to poor maternal results (Saad et al., 2016).

aHUS is frequently due to a combination of innate gene mutation and environmental factors that activate the innate immune pathway (Vieira-Martins et al., 2016). The investigation of familial aHUS has linked genetic change in multiple complement system genes to disease pathogenesis (Bu et al., 2012). Mutations in genes encoding complement regulators or activators have been identified as the cause of aHUS (Feitz et al., 2018; Waters & Licht, 2011). Function loss mutation (affecting factor H, factor H-related proteins, membrane co-factor protein, and factor I) and function gain (involving factor B and C3) are the two types of aHUS mutations (Feitz et al., 2018). Genetic aHUS is thought to account for 60% of all aHUS cases (Noris et al., 1993).

The pathophysiology of aHUS is characterized by excessive activation of the complementary alternative route (Wong et al., 2013). Complement appears to be a sophisticated innate immune surveillance system that is crucial for maintaining the health of the host, eliminating pathogens quickly, causing cell death (apoptosis), determining the scope and limits of the inflammatory immune response, bridging innate and adaptive immunity, and producing anaphylactoid reactions (Merle et al., 2015; Schartz & Tenner, 2020; Walport, 2001). Complement should be strictly regulated so that it only targets unwanted materials and does not attack healthy cells (Walport, 2001).

A primary defect in complement occurs in complement-mediated aHUS, usually after exposure to an environmental trigger (Brocklebank & Kavanagh, 2017). Infections, chemotherapy, systemic lupus erythematosus, pregnancy, HSCT, and GvHD have all been identified as triggers in the patients for the progress of aHUS (Tomazos et al., 2020). Any family of aHUS can have healthy carriers, but it is uncertain whether or not they will go on to acquire aHUS.

The early complement inhibitor licensed for the treatment of aHUS was eculizumab (Ardissino et al., 2021). Clusterin, cystatin-C, 2-microglobulin, and liver fatty acid binding protein-1, in addition to inflammatory processes (soluble tumor necrosis factor receptor-1), blood coagulation (prothrombin fragment F1+2 and D-dimer), and endothelial damage, were all decreased to near-normal levels with eculizumab (thrombomodulin) (Gurevich & Landau, 2023). However, because of the financial implications for healthcare systems, therapy that inhibits C5 shouldn't be viewed as a cure-all (Brocklebank & Kavanagh, 2017).

The major focus of therapy is therapeutic plasma exchange (TPE) or plasmapheresis, which includes substituting normal, regular proteins for mutant, defective proteins. Despite early TPE with platelet count recovering, a sizable number of patients did not recoup renal role and are probably ESRD (Saad et al., 2016). We describe a patient with normal blood pressure, without any neurological symptoms, who underwent a caesarian section and initially displayed symptoms of apparent HELLP syndrome (hemolysis, increased liver enzymes, and low platelet count). The patient was later found to have p-aHUS. This is the first incident we have diagnosed and is an inherently uncommon case, so we exercise greater caution in treating it.

CASE PRESENTATION

A 24-year-old G1P1A0 postpartum with a suspected HELLP syndrome, a caesarian sectio, severe anemia, thrombocytopenia, and acute renal injury was treated at our clinic. Afterwards, an aHUS diagnosis was verified. At the time of admission to the hospital, based on the polyclinic medical

record, she had normal blood pressure (120/80), pulse of 84 beats/minute, respiratory rate of 20 breaths per minute, temperature of 36.8 ^{o}C and denied having any neurological symptoms. She was given the preeclampsia diagnosis on the first day in the hospital because of high blood pressure (180/115) and proteinuria (+3). Apart from that, platelet levels were 86,000 µl, serum creatine 1.6 mg/dL, serum aspartate aminotransferase 68 µ/L, urine production in 24 hours 450 cc, blurry eyes, headache, and heartburn. A straightforward Caesarean section birth was performed on the patient. The patient experienced acute kidney damage, hemolytic anemia, and severe thrombocytopenia on the first postpartum day. She was then given treatment for possible HELLP syndrome.

According to a laboratory test, serum creatinine was 3.32 mg/dL, haemoglobin was 5.3 g/dL, lactate dehydrogenase (LDH) was >4,550 U/L, serum aspartate aminotransferase was 116 IU/L, total bilirubin was 2.2 mg/dL, and platelet count was $5x10^4/mm^3$. The condition of the patient failed to improve in the first 24 hours after birth. Inside this presence of TMA, the patient began on daily TPE and ran in parallel prednisone medication (1 mg/kg/day). For the course of the therapy, packed red blood cells were transfused as necessary to maintain haemoglobin levels above 7.0 g/dL. On day four of her inpatient, her platelet count fell to $2.5x10^4/mm^3$, and her creatinine level peaked at 3.8 mg/dL. After six TPE cycles, the laboratory values began to rise.

In spite of refusing further genetic testing, a diagnosis of aHUS was taken into consideration because of an atypical presentation for TTP, which improved with subsequent TPE. On hospital day 10, when the patient's haemoglobin levels were stable, and his platelet counts were over $15x10^5/mm^3$ for two consecutive days, the decision was taken to halt plasmapheresis. With a platelet count of $19x10^4/mm^3$ and a creatinine count of 1.2 mg/dL, the patient was discharged from the hospital 14 days after being admitted. Dialysis was not required.

DISCUSSION

Haemolytic uremic syndrome is typically classified as typical (caused by STEC infection), atypical (resulting from unchecked complement activation), or secondary (with a concurrent illness) (Cofiell et al., 2015). Thrombocytopenia, microangiopathic haemolytic anemia, and renal failure are all symptoms of aHUS, and a TMA is brought on by unchecked complement activation in the alternative route (AP) (Jokiranta, 2017). The varied collection of thrombotic microangiopathies known as secondary HUS is linked to a number of different underlying diseases (Yoshida et al., 2019); involving autoimmunity, pregnancy, some cytotoxic medications, cancer, infection, or transplantation (Cofiell et al., 2015). Figure 1 shows the types of thrombotic microangiopathy lesions.

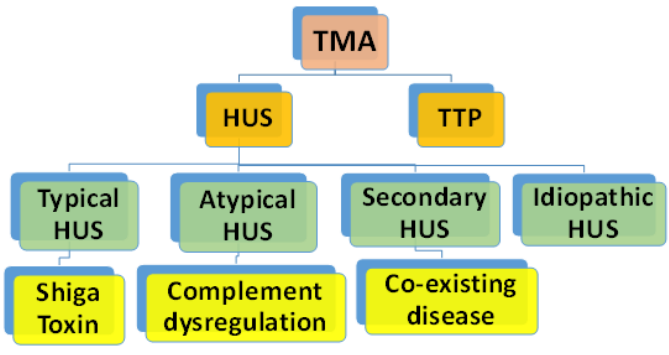

Figure 1. Types of thrombotic microangiopathy lesions

Due to its ability to mimic a range of illnesses present during pregnancy and the postpartum period, p-aHUS is difficult to diagnose (Saad et al., 2016). There are several p-aHUS symptoms that are also present in HUS and secondary HUS (Jokiranta, 2017). Although it can be difficult, at times, to properly treat patients, it is essential to make the proper diagnosis as soon as possible. Even though these diseases share certain clinical characteristics, several laboratory tests can help the doctor make the proper diagnosis (Le Clech et al., 2019). The flow of diagnosis and management of HUS can be seen in Figure 2.

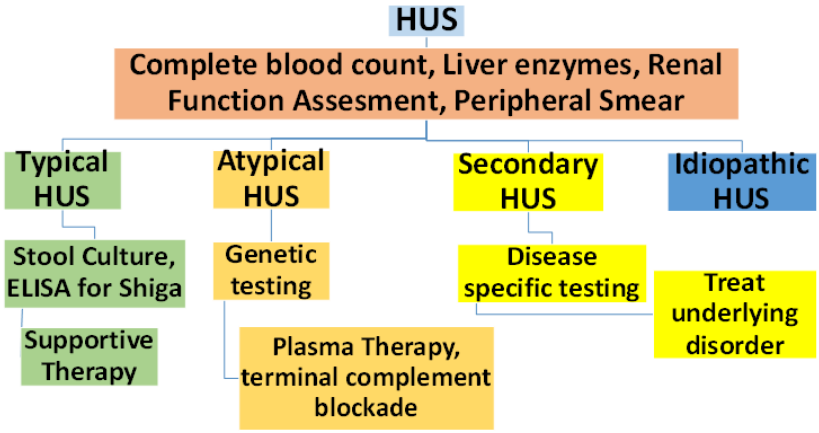

Figure 2. Diagnosis and management of HUS

Due to the high incidence of complement gene mutations in the population, a thorough genetic and molecular analysis of the alternative complement pathway is advised in order to establish the diagnosis (Saad et al., 2016). The fact that complement gene mutant carriers only have a 40–50% penetrance and impart propensity rather than cause should also be known to doctors. Instead of predicting future occurrences of the syndrome, the finding of these mutations should be utilized to emphasise how crucial it is for doctors to closely monitor expectant mothers and new mothers both during pregnancy and after delivery (Fakhouri et al., 2010; Loirat et al., 2016).

TPE was given to the patient after the first 24 hours postpartum, as recommended, that TPE should be performed daily for the whole career. TPE has been the standard therapy for patients with aHUS (Fakhouri et al., 2010; Nester et al., 2015), and according to current American Society for Apheresis (ASFA) criteria, this is considered first-line therapy (Hans et al., 2016). TPE should be continued until the blood parameters are fully normalized (platelets > $15x10^4$/mm3 for two days in a row and LDH normalization); the length of time is often customized depending on the patient's reaction. TPE failures are generally understood to be deteriorating clinical states despite treatment or persistent thrombocytopenia (Faguer et al., 2013; Fakhouri et al., 2010). However, the treatment of 6 times TPE in this case has succeeded in increasing laboratory parameters. This is slightly more than Hans et al. statement, where TPE is a safe and effective therapy method in pediatric aHUS if started early in the disease's progression with four to five operations (Hans et al., 2016).

Initial recommendations for treating aHUS include:

- Maintaining adequate nutrition, electrolyte balance, and fluid balance through intravenous feeding,

- Starting plasma exchange,
- Transfusing packed red blood cells when necessary,
- Avoiding platelet transfusions whenever possible,
- Considering high-dose steroids (1 mg/kg/d prednisone),
- If aHUS is diagnosed, begin renal replacement treatment as necessary and consider continuing complement therapy.

CONCLUSION

Atypical haemolytic-uremic syndrome can be challenging to diagnose early since it frequently mimics other illnesses. In this case, the six TPE cycles succeeded in increasing laboratory parameters, platelets returned to normal, and renal function improved. To enhance results, proper diagnosis and prompt management are essential. A multidisciplinary team, early plasmapheresis, and complement inhibition are all part of the management strategy. To lessen the effects of aHUS, TPE should be carried out as soon as feasible daily. Various technical problems might compromise TPE therapy due to significant hemolysis, which is typical in aHUS patients, such as the continual activation of the blood leak alarm due to hemolysis.

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