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POST PARTUM ASSOCIATED HAEMOLYTIC UREMIC SYNDROM : FROM HELLP SYNDROM TO ATYPICAL POSTPARTUM UREMIC HEMOLYTIC SYNDROM

BY

MARWEN NADIA[1*], ALOUANE CHOUROUK[1], FDHILA SANA[2], DHOUIBI MARYAM[1], AMROU DINARI[1], TARHOUNI KHOULOUD[1], BALSAM BRAIEK[1]

[1]Gynaecology obstetrics, Department of Obstetrics and Gynecology, Ibn El Jazzar University Hospital, Kairouan, Tunisia, Kairouan, Tunisia
[2]Faculty of Medicine of Monastir

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Abstract

Thrombotic microangiopathy (TMA) disorders are characterized by endothelial injury, microvascular thrombosis, and end-organ injury. Since they are often fulminant and contribute to maternal and neonatal morbidity they should be diagnosed and treated in time. Haemolytic Uremic Syndrome (HUS) is included in the spectrum of thrombotic microangiopathy (TMA).

In effect, the Objective of this study is to describe a rare case of pregnancy-associated HUS (p-aHUS) initially diagnosed as presumptive HELLP Syndrom. The aim of this citation is also to help the reader to differentiate between these similar symptomatic conditions threw a review of literature for a correct diagnosis and management.

INTRODUCTION

Thrombotic microangiopathy (TMA) disorders are characterized by endothelial injury, microvascular thrombosis, and end-organ injury. Since they are often fulminant and contribute to maternal and neonatal morbidity they should be diagnosed and treated in time. Haemolytic Uremic Syndrome (HUS) is included in the spectrum of thrombotic microangiopathy (TMA), first described by Gasser in children [1] in 1968. it is defined typically by the triad of microangiopathic hemolytic anemia, thrombocytopenia, and acute kidney injury. HUS is a rare faced problem in the obstetric emergency department that can signal a life-threatening condition during pregnancy and puerperium. pHUS recuire the appropriate interventions to improve maternel and fetal outcomes. Therefore, differential diagnosis among pregnancy-related TMAs is crucial to ensure a correct management. In effect the Objective of this study is To describe a rare case of pregnancy associated HUS (p-aHUS) initially diagnosed as presumptive HELLP Syndrom. The aim of this citation is also to help the reader to differentiate between these similar symptomatic conditions threw a review of literature for a correct diagnosis and management.

The diagnosis of pregnancy-associated TMA (HUS)

There is currently no international consensus regarding the classification of diseases under TMA. Therefore, Scully M. and al [2] Worked on Standardizated definitions of TMA including HUS, they developed a document based on robust criteria for future clinical use.

TMA in pregnancy is diagnosed based on the presence of :

- platelet count <100 × 10^9/L
- hemoglobin level <10 g/dL
- lactate dehydrogenase (LDH) serum level >1.5 upper limit of normal
- undetectable serum haptoglobin
- negative direct erythrocyte antiglobulin test and
  - the presence of schistocytes on blood smear or
  - TMA features in kidney (or another organ) biopsy.

Hemolytic uremic syndrome (HUS) is a comparatively rare hematological abnormality that accompanies microangiopathic hemolytic anemia (MAHA), thrombocytopenia, and acute kidney injury (AKI)[2]

Acute kidney injury: AKI is frequently encountered in most types of pregnancy-associated TMA. There is no universally

*Corresponding Author: **MARWEN NADIA.**

accepted definition of AKI during pregnancy. The various available definitions refer to the Kidney Disease Improving Global Outcomes (KDIGO) guidelines[3]: a doubling or >26 µmol/L increase in serum creatinine, a level of serum creatinine >90 µmol/L and/or a >25% increase compared with baseline values.

Typical HUS is characterized by HUS syndrome with bloody diarrhea, and it is associated with, Escherichia coli O157:H7 is a Shiga-toxin-producing bacteria. it was predominately implicated in 73% to 83% of HUS cases in major epidemiologic studies [2], [3].

Atypical HUS is characterized as HUS syndrome without bloody diarrhea, and its underlying pathophysiology is due to defective complement system activation and regulation. the emergence of postpartum HUS entity complicated the concept of atypical HUS further.

pregnancy associated HUS (p-aHUS) is a HUS that occurs in pregnancy after 20 weeks or in postpartum period less than 10 weeks[4] or even up to 12 weeks postpartum [5] according to other authors.

The following conditions were excluded from aHUS by Scully and Goodship [2]: STEC-HUS, and secondary HUS induced by medications, infections, organ transplants, cobalamin deficiency, systemic lupus erythematosus, antiphospholipid syndrome, scleroderma, and other causes. Based on findings reported by numerous publications, the definitions of aHUS and HUS have been significantly revised in the current aHUS clinical guides [4], [6].

The term "aHUS (complement-mediated HUS)" has been used to refer specifically to aHUS associated with congenital and acquired "complement regulation abnormality".

CASE PRESENTATION

A 30-year-old Tunisian woman, with no previous family history of hemorrhage syndrom , gravida 4 para 3 with 3 vaginal deliveries , and no previous personal history except for the second pregnancy complicated with moderate preeclampsia transferred to our institution for initially presumed severe preeclampsia complicated with eclampsia.

Patiente had no Fetal growth restriction or abnormal umbilical artery Doppler wave around delivery but she had a platelet count <150 × 10^9/L at the time of delivery.

She presented a generalized tonic clonic seizure at her local hospital after a symptom free interval of 10 hours post vaginal delivery, with Systolic blood pressure >180 mm Hg, a sudden onset of headache and vision loss as well as increased deep tendon reflexes.

The patient was therefore transferred to our institution for further care. She was in the meanwhile treated with intravenous (IV) Nicardipine and an IV magnesium bolus of 4 g and started on a 2-g/h magnesium drip. She denied any underlying disease, medication history or familial history of renal impairment

First inspection at arrival had noted moderate edema on face and limbs.

After prompt diagnosis of TMA and recognition of HUS in this case, treatment with antibiotics was associated with improvement in both hematologic parameters and renal function.

Upon presenting her blood pressure (BP) was 140/90 mm Hg and heart rate of 90 beats/min. The rest of postpartum exam was normal showing a uterine fundus below the umbilicus and little vaginal dark red bleeding.

Initial investigations showed 3+ proteinuria and normal serum creatinine (Scr) concentration. The diagnosis of preeclampsia was established. On the day of referral, her laboratory data were: white blood cell count 5600; hemoglobin, 12.3 g/dL; platelet count, 62,000/µL; serum creatinine, 86 mg/dL; and ASAT 482

As for Laboratory findings they revealed altered liver test results, normal hemoglobin level, and thrombocytopenia, HELLP syndrom was suspected.

An emergency Brain CT Scan was performed and showed sellar intracranial expansive process with suprasellar extension that can fit with a pituitary macroadenoma. She also had an abdominal ultrasound that was normal.

An ophthalmology exam concluded to a hypertensive retinopathy grade II (décollement séreux rétinien péripapillaire bilateral). The patient was put on IV Nicardipine and switched to oral Methyldopa.

The initial evolution was marked by a spontaneous recovery of sight as well as the stabilization of blood pressure. The liver enzymes lowered down gradually to normality (ASAT/ALAT=20/33) as well as her platelet count that gained normal rate 136 000. Her 24H proteinuria came back positive at 5g/24h and the diagnosis of severe Preeclampsia was retained.

At Day 5 post admission, she presented a sudden vaginal bleeding and a loss of consciousness.

The immediate exam showed a confused, agitated and pale patient, a right palpebral ptosis, temperature at 41°, blood pressure at 80/60 mmHg, heart rate at 100bpm, dark red minimal vaginal bleeding, and normal glycemia level, complaining of abdominal pain six days after

An urgent pelvic ultrasound did not show retained products of conception. Emergency lab results showed Hemoglobin at 7.3 g/DL and platelet count at 84 x103uL with serum creatinine measurement now on the rise at 125, 6 uml/Lthose results was appropriate for the diagnosis of pregnancy-associated TMA.

Considering the deterioration of her neurological state and the onset of a fever, a lumbar puncture was done and its result came back normal.

Upon interrogation the patient reported 3 episodes of diarrhea. HUS was suspected and the following laboratory exams demonstrated a Lactate dehydrogenase level at 8400 U//L,

*Corresponding Author: **MARWEN NADIA.**

Peripheral blood smears were performed for further evaluation of bicytopenia and showed fragmented red blood cells (the presence of schizocytes) . Natremia and Kaliemia levels were normal.

Meanwhile, two large IV catheters were inserted; high-volume fluid resuscitation were required,

Since profound anemia was detected at 4g/dl level, Transfusion was initiated immediately and the patient was administered fresh frozen plasma (FFP). after which her laboratory findings began to improve. Platelet counts improved without platelet transfusion and serum LDH levels gradually decreased. 4 units of red blood cells were given and 8 Fresh Frozen Plasma or FFP.

She was treated with Cefotaxim and Metronidazole for presumed shiga-toxin HUS. Nephrology was consulted and agreed with the diagnosis of HUS.

The platelet count decreases during After that, her kidney function worsened after the 8th day postpartum Her serum creatinine level started to increase approximately 8 days after delivery and continued to increase despite proper management. Microangiopathic anemia, thrombocytopenia and renal dysfunction were observed.

Together, these results were indicative of thrombotic microangiopathy. Despite The patient had a recent history of diarrhea, no enterohemorrhagic Escherichia coli was detected in her stool.

Platelet count started to regain normal level and hb post transfusion went up to 7g/dl

On day 15, she was stable with no biological abnormalities her clinical state improved significantly without additional treatments.

On her 1 week outpatient follow-up, at which her laboratory findings were serum creatinine level, 0.53 mg/dL; platelet count of 219,000/μL; and serum LDH level, 378 U/L.

On review after 2 months of onset, she remained stable and no kidney injury was detected furthermore proteinuria disappeared therefore a renal biopsy was not performed.

Figures 1, 2, and 3 summarize respectively the evolution of hemoglobin levels, platelets and renal function, liver enzymes.

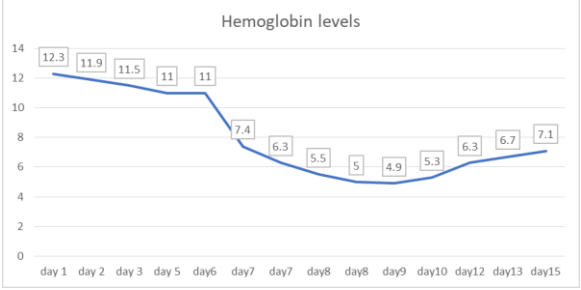

Figure 1: Evolution of hemoglobin levels

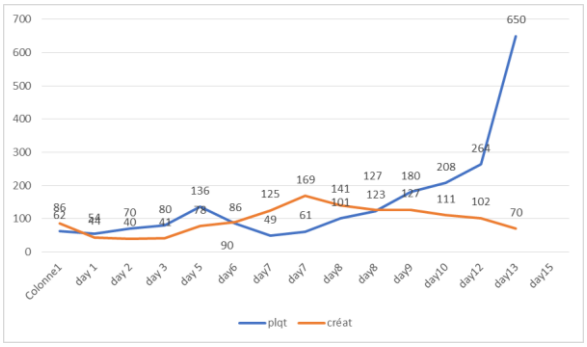

Figure 2:Evolution of palalets count and renal function

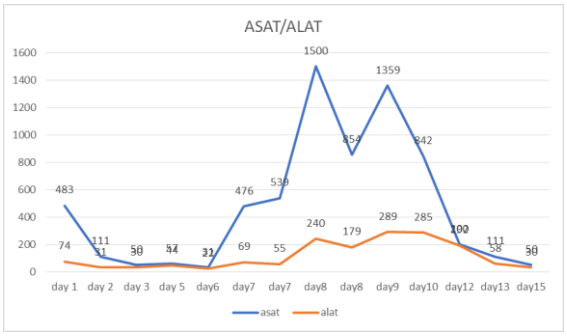

Figure 3: Evolution of liver enzymes

DISCUSSION:

1. Eidemiology:

TMA occurs in approximately 1 per 25,000 pregnancies [7]. The incidence of aHUS is estimated at 0.23 per year per million people,1 but varies by population. aHUS constitutes 5-10% of all cases of adult HUS [4], [6] Approximately 10–20% of aHUS diagnoses occur in the setting of pregnancy [7]. After analyzing clinical and biologic features in several reviews of pregnancy-associated HUS, the Mean age was 29 to 31 years [5], [15] around 16% of patients had history family of TMA and only 8% experienced one or many (four in one patient) episodes of atypical HUS related or not to pregnancy before presenting with pregnancy-associated HUS. Bruel and al [5] also concluded that the risk for HUS occurrence was similar for the first pregnancy (48 out of 82, 58%) and for subsequent (second or subsequent) pregnancies (42%), regardless of the rank of pregnancy [5]. Authors [7], [15] retained that HUS occurred predominantly in the postpartum period with 76%up to 96% of the patients, at median post-partum day ranging from 4 to 7 days post-partum, after cesarean delivery mainly in 70% of cases , [5], [7], [15]. Therefore, 77% of the presented patients with HUS during pregnancy are mostly in the third trimester [5]. Only third of pAHUS with AKI didn't recuire (29%) dialysis at presentation. In contrast, thrombocytopenia was mild (mean platelet count 97+/-99 10^3 /ml) and even absent in 15% patients [5]. Extrarenal manifestations such as neurological atteinte were noted in 14% of patients [5]. Kidney biopsy performed in less than 10% of patients disclosing typical features of thrombotic microangiopathy [5][15]. In a large cohort[8] of 214 aHUS subjects in France assessed the disease presentation and outcome Fremeaux and al found that 81% of

*Corresponding Author: **MARWEN NADIA.**

adults presenting with first episode aHUS required dialysis and 46% progressed to end-stage renal disease (ESRD) and renal prognosis was worse in adults than children.But, Gupta and al found 19% of PHUS progresses to end-stage kidney disease[9].Also blood transfusion were required in with 68% [7] and 41% received plasma infusions at first line therapy[5]

2. Clinical presentation and differential diagnosis

We present a case of a typical SHU, although the patient developed the triad in the postpartum context. The difficult part in this particular case was to distinguish the HUS from a pregnancy complication (especially pre-eclampsia), indeed, since both pathologies have numerous similarities and thus can lead to a false diagnosis. Historically, the presence or absence of bloody diarrhea, classified HUS in two different entity typical HUS, or atypical HUS (aHUS). But this classification is limited actually because few cases of aHUS presented gastrointestinal symptoms such as nausea, vomiting, and diarrhea[8], [10]. The involvement of extrarenal vascular beds in PHUS has been less reported. HUS is due to Shiga toxin producing Escherichia coli (E. coli) and the condition is termed STEC-HUS. So the presence of Shiga toxin confirm diagnosis. However, no matter how difficult the diagnosis is immunoassay polymerase chain reaction (PCR) stool testing, or stool culture confirm the presence of Shiga toxin[11], [12]. Atypical HUS is known to be triggered by factors that induce the activation of complement cascades, including infection, pregnancy, organ transplantation, malignancy, autoimmune disease, and drugs [11]. Cases of pregnancy-associated atypical HUS are known to occur during the postpartum period[7] Gupta and al noticed that Patients' Characteristics and Outcome Depended on the Timing of HUS (during Pregnancy or in the Postpartum Period) such as dialysis in the acute phase Compared with patients with HUS in the postpartum period, patients presenting with HUS during pregnancy tended to require less frequently dialysis in the acute phase (56% versus 76%, P=0.08), even though this difference was not statistically significant[7] . p- aHUS Patients generally present with facial puffiness, edema, and high blood pressure, oliguria ultimately leading to anuria and kidney failure. In some cases, patients might have flu like prodromal phase. PHUS is basically an inflammatory disorder that s why symptoms, such as neurologic symptoms (headache, confusion, seizures) or gastrointestinal symptoms (abdominal pain, diarrhea) are often present[8], [10]. Anyway, this case suggests PHUS could also involve multiple organ dysfunctions and result in bad outcomes even if the appropriate treatments have been given wihout delay. Zhou and al reported for the first time in 2012 a severe case of PHUS complicated by pancreatic necrosis[13], bilateral visual loss due to central retinal artery occlusion (CRAO) and disseminated intravascular coagulation (DIC) the patient is a 20-year-old primigravid was admittted for severe preeclampsia when she was 34 weeks pregnant[13]. apHUS typically following a normal delivery after a symptom-free interval. The prevalence of pre-existing diabetes, hypertension, and obesity was higher in Women with AHUS during pregnancy compared with uncomplicated pregnancies [9], [14] .There is currently no exact definition or a precise presentation of neurological manifestations in the literature and this explains the wide variation between 10% and 25% of the reported rate of brain involvement in patients with HUS.[15]. aHUS may play a role in pregnancy complications of the fetus like increased risk for preterm birth, intrauterine growth restriction, and stillbirth [14]. Diagnosis was predominantly retained based on clinical presentation 44% only renal biopsy showed typical features of thrombotic microangiopathies[16]. [7].Since Atypical hemolytic uremic syndrome (aHUS) is caused by the dysregulation of the complement pathway, the Consensus of the establishment of diagnosis of (aHUS) relays on the Current advances in molecular analysis and pathogenesis. But only 60% of patients with aHUS have mutations in genes involving the complement and coagulation systems. However, based on recent published consensus [17]in Taiwan wich is the presence of TMA with normal ADAMTS13 activity without known secondary causes we could provide suggestions regarding the diagnosis and management of aHUS. Complementary gene mutation testing could be considered to confirm suspected aHUS. But diagnosis remain guided by clinical features until better guidelines are available. According to some authors Genetic testing was performed to identify the cause of the atypical HUS, By Sequencing 17 genes known to be associated with atypical HUS (i.e., *C3*, *C4BPA*, *CD46*, *CFB*, *CFH*, *CFHR1*, *CFHR2*, *CFHR 3*, *CFHR4*, *CFHR5*, *CFI*, *DGKE*, *THBD*, *PLG*, etc.) as well as of *ADAMTS13* and *C5* was performed[18]. According to recent data, he molecular analysis is suggestive for guiding the treatment decision-making, predicting the prognosis, and deciding renal transplantation[17]. The diagnosis was facilitated by using multiple advanced techniques such as multiplex ligation-dependent probe amplification (MLPA) and new generation sequencing (NGS). HUS, especially aHUS, is a life-threatening condition that requires intensive care once diagnosed[19], [20]. In effect , it is due to severe outcomes that complicates those pregnancies such as, , preeclampsia, eclampsia, , placental abruptio, disseminated intravascular coagulation, , venous thromboembolism, , sepsis, myocardial infarction, post-partum hemorrhage, in effect it could lead even to maternal death[14]. Therefore, revealing the origin of TMA is a high priority and any delay can lead to multiple complications for the mother such as renal failure, seizures, stroke, pulmonary edema and disseminated intravascular coagulation (DIC)[14], [19], [20].Clinically pregnancy associated HUS has symptoms similar to other pregnancy TMA and associated conditions like Pre eclampsia, AFLP, TTP making the diagnosis very tricky.[4] Atypical HUS is often hard to distinguish from TTP in the acute care setting. In pregnancy, the most common TMA disorder is HELLP syndrome it occurs in the setting of preeclampsia, where it contributes disproportionately to maternal morbidity and mortality.Usually HELLP syndrome in most women recover within 3 to 4 days postpartum. However, experiencing severe TMA that worsens after delivery, the diagnosis of atypical hemolytic uremic syndrome (aHUS) must be considered.The differential Diagnosis may be

*Corresponding Author: **MARWEN NADIA.**

difficult because of similarities of clinical signs, such as fatigue, headache, nausea, and vomiting, between P-aHUS and more common pregnancy complications such as preeclampsia and HELLP[14]. For the obstetrician , this is a highly nuanced differentiation and unlikely reached in the immediat diagnosis (in the Emergency , urgent situations). The history and physical examination findings of HUS are not similar to HELLP syndrome. Differences include the common findings of bloody diarrhea, anuria, oliguria, and hypertension in HUS-predominant variants.In case of laboratory abnormalities persist above 72h after delivery we should raise suspicion for aHUS[21]. Also When hemolysis and kidney injury remain, or worsen after delivery without other explanation, we should suspect aHUS[21]. Dramatic acute kidney injury with rapid increasing in serum creatinine(> 3–4 mg/dl), is most likely characteristic of aHUS [21].Martin Jr and al proposed a useful screening tool for clinicians to Correctly distinguish between HELLP syndrome and an imitator disorder such as aHUS[22] .Their findings after studying the data of Fifty-eight pregnant/postpartum women presented with a diagnosis of presumptive HELLP syndrome supported the concept of the LDH:AST ratio[22].In effect, they demonstrated constant total LDH to AST ratio greatly exceeding 22:1 with TTP/aHUS (mean = 32:1)comparing to HELLP syndrome 2:1[22]. Despite the lack of genetic and complement dosage evidence and on Based on clinical characteristics and biological feature of , we retained in our case the diagnosis of aHUS. In fact 49% of the established diagnosis were based on clinical presentation. Gupta and al also didn't include such testing in their algorithm. Most authors [21] considered diagnosis short term management should
be guided by clinical picture

3. **Physiopathology(role of complement system):**

The elucidation of the pathophysiology and mechanisms underlying the two main forms of HUS, in the past decade , has transformed our understanding of aHUS and paHUS threw developed concepts of the phenotypes, genotypes and therapies for these life-threatening disorders.Several authors reconsider since few years the pathogenesis of post-partum HUS wether result from 2 distinct pathogenic mechanisms: verotoxin-induced endothelial cell activation and apoptosis by Shiga toxin of E. Coli , or constitutional complement alternative pathway dysregulation leading to complement-induced endothelial cell damage[23]. An imbalance in its regulation can result in inflammation and thrombosis. Pregnancy is a condition that itself amplify complement activity and can unmask TMA [5], [24], [25].

Recent studies revealed alternative complement convertase dysregulation were detected in most PHUS patients suggesting PHUS was probably associated with complement gene mutation[23], [26]. Most likely Atypical HUS is caused by inborn or acquired genetic defects of genes that are associated with regulation of the complement pathway. Complement gene mutations are often found in women with aHUS[10], [27], [28], and in rare cases severe forms of PE or HELLP[29]. more than 60% of PHUS cases have loss-of-function mutations in complement regulators or gain-of function mutations in complement activators wich induce Uncontrolled complement activation[28]. Bruel A. and al [5], after analyzing the frequency of complement alternative pathway gene variants in a larger international (France, United Kingdom, Italy) cohort of 87 patients with Pregnancy-associated hemolytic uremic syndrome and atypical hemolytic uremic syndrome non-related to pregnancy concluded that both groups have the same frequency of complement gene variants. Mutations in several genes regulating the complement system has been reported in more than half of thrombotic microangiopathies associated with pregnancy. Atypical HUS can also be due to various, more or less well-defined patterns of endothelial cell lesions in the heterogeneous group of secondary HUS associated with autoimmune diseases, drugs and infections. But, according to the "multiple-hit" hypothesis , PHUS is a consequence of both genetic predisposition to alternative complement dysregulation as well as the occurrence of events or conditions that may precipitate TMA by activating complement and/or damaging the endothelium[24] such as HELLP or severe PE . The complement pathway may be activated postpartum due to maternal circulation of fetal cells, infections, and hemorrhage wich is a Complement-amplifying conditions (CACs), can comorbid with HUS and unmask a previously undiagnosed case [24].A study conducted by Di Song and al. [16] concluded that overactivation pathway of complement induced by genetic deficiencies and autoantibodies of CFH may participated in the pathogenesis of postpartum aHUS. Kandari and all detected also a high proportion of deletions of exons of *CFHR1* & *CFHR3* genes in al large multicentral study of Indian P-aHUS patients studied [23] .The deficiency of ADAMTS-13, a metalloprotease that cleaves ultra-large von Willebrand factor (VWF) multimers observed in PHUS[30] suggest that PHUS may be also associated with ADAMTS-13 deficiency. However, regnancies should be monitored closely, because rare genetic variants cannot predict the risk of a given pregnancy[9].Since our patient presented neurological symptoms such as seizure and headache we reviwed the pathogenesis of those clinical features. In effect, the physiopathology involved in central nervous system is thought to be attributed to endothelial damage, affecting the small vessels of the brain, which results in hemorrhages and infarcts . However, given the rarity of CNS involvement in HUS compared to renal involvement, other reported data suggested a combined effect of simultaneously inflammation vascular injury, endothelial dysfunction, and nephropathy induced-hypertension and electrolyte derangements[15]

4. **Treatement**

The multidisciplinary involvement is of essential importance. All patients need inpatient admission, likely to a high-acuity unit for close monitoring. If the institution does not have the resources to provide proper care, then transfer to a tertiary care facility with those capabilities is warranted The primary approach to treatment with PHUS is supportive care, which includes blood transfusions when needed, FFP infusion,

*Corresponding Author: **MARWEN NADIA.**

judicious control of hypertension (preferably with nifedipine or nicardipine), careful maintenance of fluids and electrolytes, and hemodialysis when clinically indicated[31], [32]. Other treatment modalities should be suggested also in first-line therapy ; dialysis plasma exchange, corticosteroids, and Complement blockade with anti-C5 monoclonal antibody[17]. Plasma therapy should be considered for removing autoantibody in patients with atypical HUS caused by anti-CFH or if complement inhibitor is unavailable[17] [23]. More recent case studies also documented the efficacy of eculizumab in the treatment of P-aHUS, Emerging evidence shows the safety of eculizumab during pregnancy despite potential placental transfer to the fetus and there were no adverse effects on the newborns noted. Eculizumab, as a novel treatment has been approved for aHUS treatment, but it may be feasible also in selected HELLP cases with the clear evidence of the complement activation[33]. The demonstration of eculizumab efficacy in aHUS renewed interest in a potential role of complement activation also in STEC-HUS. Indeed, while a decrease (generally slight) of C3 plasma levels is observed in only 20%-25% of patients at the acute phase of postdiarrheal or STEC-HUS[34]. The treatment of aHUS arising from a secondary cause, is aimed at the underlying etiology[28]. But When the primary etiology cannot be treated easily, or when aHUS is refractory, complement blockade with eculizumab could be useful. Accumulating evidence,showed that Eculizumab improves long-term disease prognosis [35] [26], [28]. In fact our patient needed only supportive care with Improvements of clinical conditions, resolution of headache, visual symptoms, abdominal pain, increasing platelet counts. Therefore, Gupta and al also found that resolution occurred in almost half of diagnosed PHUS after supportive care but only 57% of patients regained normal kidney function and normal laboratory data[7]

Conclusion and perspective

Thrombotic Microangiopathies during pregnancy and puerperium are very rare and tricky diagnostical challenge , if left undiagnosed , they could be lifethreating. Therefore, obstetricians are usually the first to observe clinical symptoms and laboratory abnormalities suggestive of Thrombotic Microangiopathies. Complement gene mutation testing may be considered in those with suspected or confirmed aHUS, to guide long-term management, including length of treatment, frequency of follow up, prognosis, and future pregnancy[21].

Nonstandard Abbreviations and Acronyms

aHUS atypical hemolytic uremic syndrome ALT alanine transaminase AST aspartate transaminase HELLP hemolysis, elevated liver enzymes, and low platelet count LDH lactate dehydrogenase PlGF placental growth factor SFLT1 soluble fms-like tyrosine kinase 1 TMA thrombotic microangiopathy TTP thrombotic thrombocytopenic purpura

AFLP, TTP

ADAMTS13, a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13; ALT, alanine transaminase; AST, aspartate transaminase; HELLP, hemolysis, elevated liver enzymes, low platelet count syndrome; HUS, hemolytic uremic syndrome; RBC, red blood cells; MAHA, microangiopathic hemolytic anemia; PCR, polymerase chain reaction; ULN, upper limit of normal.

Conflicts of Interest The authors declare no conflicts of interest.

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Data availability

No data is associated with this article.

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*Corresponding Author: **MARWEN NADIA.**

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*Corresponding Author: **MARWEN NADIA.**