

Thrombotic Microangiopathic in the ICU, postpartum hemolytic uremic syndrome: case report

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Abstract

Underlying injuries produced by Hemolytic Uremic Syndrome, a clinical entity defined by the triad, include: non-immune hemolytic anemia, thrombocytopenia, and organ involvement which are measured by the Thrombotic Systemic Microangiopathy (TSM) process. The atypical HUS (HUSa) is a subtype of HUS in which the phenomena of TSM are the result of the lack of regulation in alternative pathway of complements on cell surfaces, secondary to a genetic cause. The key role played by the deregulation of the complement system on the damaged endothelial layer in patients with HUSa has been established; this system measures by multiple mutations and polymorphisms in the genes that encode certain regulatory proteins of the add-in has been established. Taking into account the great complement activity of physiological way during gestation, each day more cases of HUSa related to pregnancy, are described. There is a monoclonal antibody, Eculizumab, which inhibits the terminal complement fraction (C5). Eculizumab blocks the formation of the attack complex of the membrane, with significant long-term improvement in morbidity and mortality associated with this disease, promoting long-term recovery of renal function and with a significant reduction in the need for dialysis or plasma therapy.

A case of 17 year in puerperium, who developed icteric syndrome considered as HELLP syndrome, whose atypical evolution made us think about alternative diagnosis of thrombotic microangiopathy in pregnant woman HUSa type. Discard diagnosis between sepsis, HELLP syndrome and disseminated intravascular coagulation was made. ADAMST13 measurement was taken, whose standard value allowed us to make the differential diagnosis with a Thrombotic Thrombocytopenic Purpura (TTP). In this way, we were able to achieve the clinical diagnosis of HUSa and begin treatment.

Key words: Hemolytic Uremic Syndrome atypical, Eculizumab, thrombotic microangiopathy, pregnancy. (MeSHsource).

Microangiopatías trombóticas en la UCI, síndrome hemolítico urémico atípico posparto: reporte de caso y revisión de la literatura

Resumen

El síndrome hemolítico urémico es una entidad clínica definida por la tríada: anemia hemolítica no inmune, trombocitopenia y compromiso de órgano, en la que las lesiones subyacentes están mediadas por un proceso de Microangiopatía Trombótica (MAT) sistémica. El SHU atípico (SHUa) es un subtipo de SHU en el que

los fenómenos de MAT son consecuencia de la pérdida de regulación de la vía alternativa del complemento sobre las superficies celulares, secundario a una causa genética. Se ha establecido el papel clave que desempeña la desregulación del sistema de complemento en la inducción de daño endotelial en los pacientes con SHUa, esto mediado por múltiples mutaciones y polimorfismos en los genes que codifican determinadas proteínas reguladoras del complemento. Cada día se describen más casos de SHUa relacionados al embarazo, teniendo en cuenta la gran actividad del complemento de manera fisiológica durante el estado de gestación. Eculizumab es un anticuerpo monoclonal que inhibe la fracción terminal del complemento (C5), bloqueando la formación del complejo de ataque de membrana, con mejoría significativa de la morbilidad asociada a esta enfermedad, logrando recuperación de la función renal a largo plazo y con una reducción importante en la necesidad de diálisis o terapia plasmática.

Se presenta un caso de una mujer de 17 años de edad en puerperio inmediato, quien presentó síndrome icterico considerado como síndrome de HELLP, cuya evolución atípica hizo pensar en diagnóstico alternativo de Microangiopatía Trombótica en mujer embarazada tipo SHUa. Se realizó diagnóstico de descarte entre sepsis, HELLP y coagulación intravascular diseminada. Se hizo medición de ADAMTS13, cuyo valor normal permitió hacer el diagnóstico diferencial con una Púrpura Trombocitopénica Trombótica (PTT). De esta manera, se logró realizar el diagnóstico clínico de SHUa e iniciar tratamiento dirigido con excelente respuesta clínica.

Palabras clave: Síndrome hemolítico urémico atípico, eculizumab, microangiopatía trombótica, embarazo (fuente DeCS).

Introduction

Much progress has been achieved in the understanding of the pathophysiology of HUSa since the initial description of two main categories of Hemolytic Uremic Syndrome. It is recognized as a genetic disease that is life threatening, characterized by the uncontrolled activation of the complement system, and its conditions the appearance of thrombotic microangiopathy by systemic (TMA) and severe damage of target organ.

The first case, based on two main categories of systemic Thrombotic microangiopathy (TMA) and thrombotic thrombocytopenic purpura (TTP), was described in 1924 by Moschcowitz¹⁷, and was called Hemolytic Uremic Syndrome (HUS) by Gasser¹⁸ in 1955. Since then, there has been no more than a handful of critical advances in the diagnosis and treatment of TMA; however, each one of these discoveries has geometrically altered the course of HUSa.

The recognition of the plasma exchange therapy (PET) as the treatment of choice for the TTP; the isolation of *E. coli* producer of shiga toxin STEC as the etiologic agent of many cases of HUS associated with diarrhea, now known as HUS STEC; and, recently, the description of the activity in a speci-

fic protease (ADAMTS13) as the correct diagnostic method of the PTT, has allowed to improve the diagnostic and therapeutic possibilities of these patients. However, great advances in the description of the fundamental role of the complement system in the pathophysiology of HUSa, has made it possible to expand the knowledge and the possibilities of treatment directed to the latter entity in the last decade. This paper focuses on HUSa as a life threatening, rare systemic and chronic disease, with a very high degree of mortality and morbidity within the first year of diagnosis, unless be treated appropriately.

Normally there are two ways to define HUS. The most frequently used definition, which is presented in the 90 per cent of the cases, is HUS typical or classical and it is associated with diarrhea caused by the infection of *E. coli*, which is produced by Shiga toxin STEC. STEC is able to join the Gb3 receptors on the surfaces of the endothelial cells and cause their destruction, either directly or through the activation of the inflammatory and procoagulant cells. Most patients with SHU STEC evolve satisfactorily within 2 to 3 weeks while 10% of the cases may evolve into chronic kidney disease, only 25% of these develop permanent renal sequelae. Ten per cent of the remaining cases present as SHUa, multisystemic disease measured by the deregulation of the complement

system and a worse prognosis, because 40% of the patients die or they are on dialysis with the first manifestation and 63 per cent of the survivors progress to Terminal Chronic Renal Disease (CRD) or die in the course of the first year after diagnosis. The HUSa has an incidence of approximately 2 cases per million inhabitants/year and a reported prevalence of 4 to 6 per million inhabitants.

In the following I will describe the first case of HUSa related to pregnancy published in Colombia.

Clinical Case

17 years old female patient, without prior history, previously healthy, in immediate postoperative period of a cesarean section by diagnostic suspicion of HELLP syndrome. The patient characterized by three days - progressive jaundice condition, 36 weeks, of pregnancy without prenatal controls, previous physical examination after she was admitted then she was transferred to the Intensive Care Unit (ICU): the alertness of the patient, she was conscious with vital signs of TA: 123/93mmhg, FR: 18, FC:105, SCG: 15/15, SAT: 98% to air, jaundice of the skin and mucous generalized, rhythmic heart sounds tachycardia rhythms, breath sounds without additions, soft and palpable abdomen, below umbilical, surgical wound without bleeding, grade 1 edema of the lower limbs, hyperreflexia universal. Paraclinical data after admission: 15,900 leukocytes, Hb: 15, PT: 14 (13),PTT:30 (23), platelets: 88000, total bilirubin level was 12.5, direct bilirubin level was 10.8, indirect bilirubin level was 1.7, GPT: 44, GOT:10, creatinine level :2.3, BUN:27, LDH: 1143U/L, chest radiography with slight redistribution of fluids.

A pregnant patient with HELLP syndrome was considered, with icteric syndrome, bilirubin level was 11 , that is why cholestasis and/or choledocholithiasis has been discarded to be carried out through hepato-biliary echographies, reported as normal, at the same time, the cholangio-resonance, looks for extra liver duct obstruction. Multiple samples to search for infectious processes with a suspected intra-abdominal and treatment with cefepime and meropenem antibiotics start.

Patient evolves so torpid with systemic deterioration and, on the second day, she persisted with multiple organ dysfunction (renal, hepatic, hematological) coagulopathy with thrombocytopenia and consumption of fibrinogen, evidence of hydric overload in chest x-ray, HTA with intravenous nitroglycerin treatment and requirement of non-invasive mechanical ventilation. Likewise, she requires inodilator with dobutamine treatment. Patient persists with torpid evolution, signs of systemic inflammatory response without infection focus on persistence of metabolic acidosis, despite the revival and support inodilator, and good urine output. The third day, the patient becomes oligo-anuric with irregular response to medical treatment, so that she is evaluated by nephrology unit, which initiates infusion of 2 mg / hour furosemide . It was observed that HB fell to 8 without evidence of bleeding. The fourth day, the patient shows partial improvement of hemodynamic, best rates of perfusion and urine output; however, neurologically compromised given the delirious condition associated with cardiorespiratory failure, which requires initiation of conventional mechanical ventilation was evident. Paraclinical control: Hb: 10.1, Leukocytosis: 18500, platelets: 56000, Creatinine: 3, BUN: 65, TGO: 51.6, TGP: 23.1, increased uric acid, the ultrasound test shows a wall hematoma with hemo-peritoneum so she is taken to surgery for an exploratory laparotomy finding liquid sero-ascitic and wall hematoma, which does not explain the acute anemia evident in the patient.

The fifth day, the patient evolves with progressive clinical deterioration, with acute renal failure established with HB at 8 with multiple organ dysfunction that evolves dependent on pressure vessel support, without showing site of infection, kidney failure with nitrogenous increased (creatinine 3.4, BUN:76) and volume overload. Prolonged coagulation times, lipemic serum and it is decided to perform staging to meropenem on suspicion of sepsis. High transfusion requirements (6 UGRE, 24 U platelets and 8U of plasma). Taking into account the severity of the disease and non-clinical evolution and improvement, five days after finishing pregnancy, HELLP syndrome is considered differential possi-

ble diagnoses and, because there is no presence of infectious agents, it is physicians consider to study possible and different causes of TMA. Haptoglobin is recommended ADAMTS13, complement tests and spread of peripheral blood and take other para-clinical tests in order to complete studies and the results were: Profile of autoimmunity: negative, HIV negative, direct and indirect Coombs: negative, Leptospira: negative.

The sixth day, multiple organ dysfunction with severe compromises to renal activity, oligúric, metabolic acidosis and water load continues. Coagulopathy is controlled, but persists with clear signs of intravascular hemolysis, given by LDH in persistent increase despite the medical management established and thrombocytopenia in progression. A TAC scan of the chest (Figure 1), finds bilateral pleural effusion and the presence of severe ascites. Upper endoscopy performed has not demonstrated digestive bleeding despite persistent anemia. Para-clinical control: Platelets: 67000/mm, creatinine: 2.5, BUN: 96, TGO: 103, TGP: 33, BT: 12, triglycerides: 1354, HB: 8.

The patient is still with evident anemia, THROMBOCYTOPENIC, with increased renal failure, hyper-bilirubinemia and elevated liver enzymes without finding infectious agent or bleeding and with neurological affection given by delirium. Negative cultures, without achieving clinical response despite being more than a week under medical management, which is not common in preeclampsia, HELLP, and makes preponderant consider HUA as her postpartum diagnostic.

By the twelfth day, the patient continues with MAT active and severe neurological involvement, encephalopathy and presenting, in addition, episode of seizure by what is done CT of the skull (Figure 2), evidencing: ischemic zone left temporal. Again it is evaluated by the gynecology department, which performs medical board discarding infectious processes related and continues to expectant treatment in ICU. Paraclinical additional for differential approaches of systemic MAT with activity report of ADAMTS13:64%; complement test : C3: 73.4mg/dl (90-180mg/dl); C4: 8.6 mg/dl (10-40 mg/dl), bo-

Figure 1

A CT scan of the chest with bilateral pleural effusion

Source: Zulma Urbina, Rayza Soledad

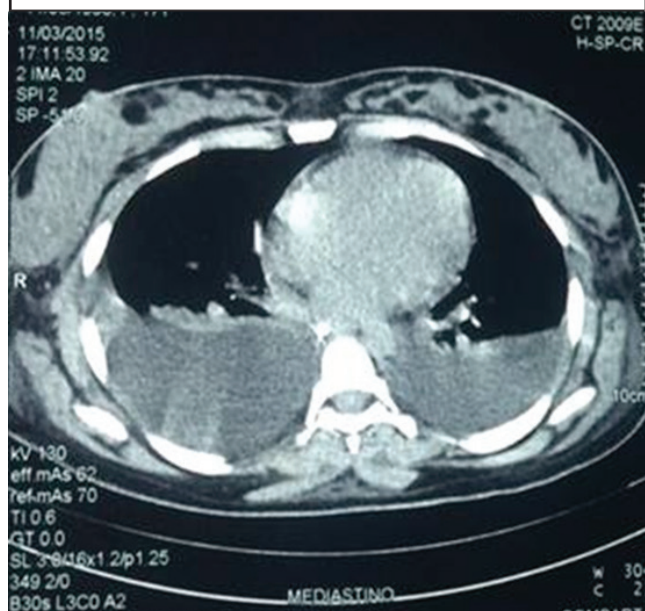
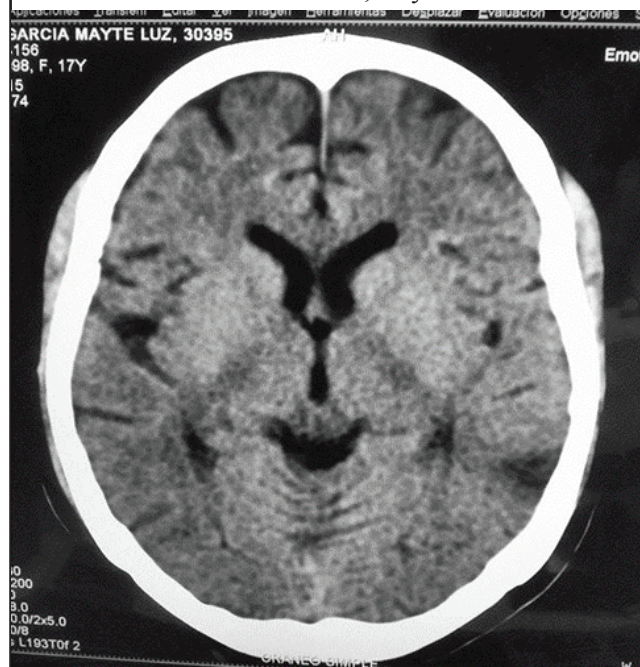


Figure 2

Simple brain CT. Ischaemic zone left temporal

Source: Zulma Urbina, Rayza Soledad



th diminished, without evidence of concomitant autoimmune disease. It is MAT status associated with pregnancy, with torpid evolution despite treatment of HELLP syndrome as a first diagnostic approximation, with a result of ADAMTS13 that discards the presence of PTT associated with pregnancy and it is considered HUSa as definitive diagnosis, which explains the persistence of severe systemic commitment, MAT persistent, the HTA of difficult management that requires polypharmacy and the current multisystem involvement, by which it decided to launch plasmapheresis, pending availability of treatment directed to lock the snap-in. Sorts previous vaccination against meningococcus was applied. The patient continues encephalitic, convulsive status, managed with valproic acid, sedation with benzodiazepines and propofol, spontaneous bleeding by tracheal tube.

The thirteenth day hematology dpt. decides to start Eculizumab because of HUSa. The following day, hemodynamic response it is observed, diminishing the TMA and extubation of the patient on a program-

med manner. RMN control is performed (Figure 3) of control. It continues Eculizumab infusion according to the weekly schedule. After three weeks of handling treatment by blocking the complement, the patient improved very appropriately in relation with tensional figures, liver dysfunction and normalization of the renal function.

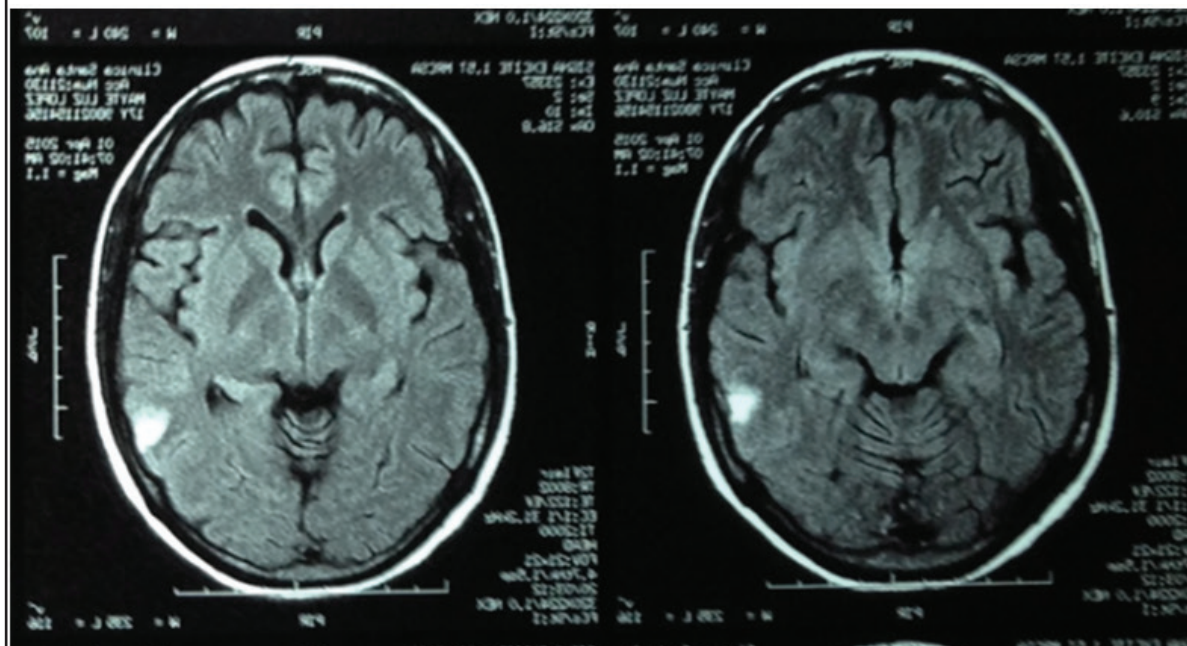
Discussion

HUSa is a chronic genetic pathology, that threatens the life, where deregulation of the complement alternate routing causes multisystem involvement. Different entities amplify the complement system, either physiological, such as pregnancy, or pathologic, such as infections, surgeries among others, exposes the underlying HUSa have been described. As previously mentioned in this paper, the HUSa makes part of the systemic TMA where the diagnosis is made in a clinical way, back to rule out other causes of TMA (which are mentioned below). In this opportunity, we describe a case of HUSa related to pregnancy.

Figure 3

MRI of the brain. Ischemic zone left temporal, shows cerebral infarction small temporary cortical later left ++ focal HSA discrete perilesional edema

Source: Zulma Urbina, Rayza Soledad



HUSa is caused by TMA during the third trimester of pregnancy or in the postpartum period. Pregnancy is associated with a systemic activation of the complement system to protect both the mother and the fetus from possible infections. It has been shown that the levels of the anaphylatoxins C3a, C4a and C5a are higher in pregnant women than in non-pregnant, around three times more¹. Among every 100 cases of women with HUSa, 21 per cent were related to pregnancy². HUSa related to pregnancy has been reported in the international register SHUa/PTT and are abnormalities of the complement system in 86% of these patients³. The case reported in this paper is considered to be the first one published in Colombia.

Pathogenesis

The complement system is responsible for the defense against microorganisms; its objective is the lysis of these microorganisms through the activation of three tracks: the classical pathway, the lectin pathway and the alternative pathway. Clarifying that the disorder is in the regulation of one of these three routes, of the alternative pathway, which conduct to HUA the clinical manifestations, it should be observed that this track is active continuously with the spontaneous activation of C3 and it is amplified quickly thanks to the action of proteins such as endotoxins and immunoglobulins, among other. La C3 convertase is formed by C3B/Bb; C3b covers cell surfaces and works as an opsonin on the walls of the microorganisms. When you join the C3 convertase, to create the C5 convertase, this cleaved or divided aC5 in c5a and C5b, releasing C3a and C5a that are chemo-tactical of leukocytes and platelets, which activate the path of coagulation and participate in the endothelial activation, C5a being highly proinflammatory.

All this mechanism is controlled by inhibitory proteins or regulatory mechanisms as are the Factor I (IFC), the factor H (FCF), the protein of the cofactor of the Membrane (PCM), the Trombomodulina (THBD), the Factor of accelerating deterioration (DAF/CD55), Protectina or CD59, responsible for stopping the immune response, thus avoiding damage to own guest⁴.

Patients with HUSa lack, intrinsically, the regulators of the complement system, allowing an overactive response; inducing endothelial damage and microvascular thrombosis secondary to inflammation and a continuous activation of the complements, which allows different clinical manifestations and complications and high morbimortality.

The term MAT (thrombotic microangiopathy) means histologic damage of the arterioles and capillaries, characterized by thickening and inflammation of the vessel wall, detachment of endothelial cells; the sub-endothelial elongation, caused by the deposits of protein and the material of the cellular lysis; and the presence of platelet thrombi that occlude the vascular spaces, which can be suspected by the decrease in the platelet count, hemolysis, and even of systemic form with multiple injuries to different bodies⁴.

There are two clinical entities concerned on injuries of primary thrombotic microangiopathy, which both differ in its physiopathologic basic cause: the thrombotic thrombocytopenic purpura (PTT) and the SHU⁶.

90% of cases of SHU are caused by an enteric infection by STEC, derived from contaminated food (SHU typical/STEC)⁷. In the U.S., it is estimated that HUSa has an annual incidence rate of 1-2 cases per million inhabitants⁵ and, in Europe, a Multicenter international study reported an incidence of 0.11 cases per million inhabitants between the ages of 0 and 18 years old^{6,9}. The distribution men: women is equitable in childhood, but tended to predominate in women in adult life. The clinical manifestations can be multiple and varied in each patient. The completion of a relevant interview and physical exam will allow for a complete medical history. Generally SHU manifests as an abrupt start⁹, but in 20% of patients manifestation can be progressive with subclinical anemia, thrombocytopenia fluctuating and renal function preservation. The table is characterized by the triad of microangiopathic hemolytic anemia not immune, thrombocytopenia—or 25% consumption—and commitment of organ, such as the acute renal failure¹⁰. High levels of lactic dehydrogenase, the undetectable levels of haptoglobin and/or the presence of esquistocitos confirms the existence of intravascular hemolysis¹¹. The presence of

HTA because of volume overload or vascular lesion is frequent, like the oligoanuria in the acute renal failure. HUSa injury predominantly affects the renal vessels; the diffuse nature of the TMA leads to the affection of the microvasculature of organs (brain, heart, intestines, pancreas and lungs), which explains the emergence of the extrarenal^{9,12} sign-symptomatology. The most frequent are the neurological (48%), including irritability, drowsiness, confusion, seizures, encephalopathy, stroke, hemiparesis, or a hemiplegia coma¹²⁻¹⁴, as happened with this patient. The acute myocardial infarction has been reported in up to 3 per cent of the patients with HUSa, being able to relate with sudden death^{12,15}. The variability of the symptomatology hinders the differential diagnosis with other causes of TMA.

The relationship of HUSa and pregnancy has been exposed previously by other authors, in the same way the relationship of MAT and pregnancy, reported by Fakhouri, et al.², with an approximate incidence of 1 in 25000 pregnancies. The dysfunction of the complement system has been related, recently, with pathologies such as HELLP. This increase in the snap-in during the state of gestation is controlled in normal women through regulatory proteins, like DAF, MCP and CD59, which are located on the cell surface of the trophoblast. On the contrary, in women with alterations in the regulation of the plug-in, as occurs in the HUSa, could explain the unmasking of HUSa associated with pregnancy. Further, as it was described by Fakhouriet al.², after childbirth, which could increase, per se, the activation of the complement system and explain the greater number of cases of HUSa diagnosed after childbirth.

Diagnosis

HUSa is a pathology of clinical diagnosis. Within the multiple parameters studied, the most accurate method for the diagnosis is based on the exclusion of TMA, and keep in mind the common symptoms of commitment of organs by the microangiopathy: laboratory values compatible with the presence of intravascular hemolysis not immunological, as is the elevation of the LDH secondary to fragmentation of red blood cells, presence of schistocytes in the ex-

tended peripheral blood, Coombs negative, hemoglobin values low or undetectable levels of haptoglobin; mention must be made of the classical triad characterized by: 1) hemolysis microangiopática, 2) thrombocytopenia, and 3) organ damage, with the greatest frequency of acute kidney injury (hematuria, proteinuria or reduced kidney function). This is a condition that is potentially fatal and requires immediate treatment to prevent the irreversible damage of the organs or death.

The most common causes of TMA are the thrombotic thrombocytopenic purpura (TTP), the Hemolytic Uremic Syndrome (HUS), which in turn is divided into SHU STEC (caused by the Shiga toxin of *E. coli* invasive integer) and HUSa (chronic disease, genetics by deregulation of the complement system). Unlike the HUS as described previously, the intravascular thrombosis in the TTP is the result of a severe deficiency of the activity of the metalloprotease ADAMST¹³, a plasma enzyme in charge of fragmenting Von Willebrand¹⁵. factor multimers. Currently, a severe deficiency acquired or congenital of ADAMTS¹³ (<5-10%) confirms the diagnosis of thrombotic thrombocytopenic purpura (TTP). This blood sample should be taken before the beginning of the plasmapheresis or plasma infusion, not to alter their outcome¹². On the other hand, the HUS-STEC is caused by the Shiga toxin produced by the *Escherichia coli* invasive integer, which is detected by PCR techniques in stool or in a positive culture for this germ.

The TMA can occur in other contexts, formerly recognized as secondary mat by its association with other pathologies; however, it is worth emphasizing that there exist conditions amplifiers of the add-in that can expose the diagnosis of HUSa of base. Among these, the most frequent are: Malignant arterial hypertension, HELLP syndrome, autoimmune diseases (LES), HIV, pneumococcus infection, glomerulopathies, neoplasms and medication, among others. In these conditions, these events or pathologies are considered the triggering factor of HUSa, exposing the patient to suffer all clinical manifestations of this pathology.

Recent studies have shown that 40-60 % of patients with HUSa are carriers of specific mutations in the

genes of the plug-in, causing deregulation¹⁵ of the alternative pathway of the complement in the more common are Factor H(CHF) (20-30%), MCP (5-15%), Factor I (4-10%), C3 (2-10%), factor B (1-4%) and THBP (3-5%)¹².

Given the wide variety of mutations and the incomplete penetration of the same, in addition to that, in approximately 50 per cent of the cases it is not possible to identify the mutation, genetic tests are not a diagnostic criterion⁴. In all patients with clinical suspicion of HUSa, it is recommended to measure the levels of C3 and C4 in serum, which can help to clarify the diagnosis without being this a fundamental factor.

Treatment

Plasmapheresis: recent evidence suggests that the therapy of plasma exchange / plasma infusion (PF/IPes) is ineffective to adequately control the systemic and permanent activation of the complement in patients with HUSa. Plasma therapy is reasonably effective in the normalization of the hematological parameters of thrombotic microangiopathy, but is not uniformly effective in preventing the progression of kidney disease¹⁶.

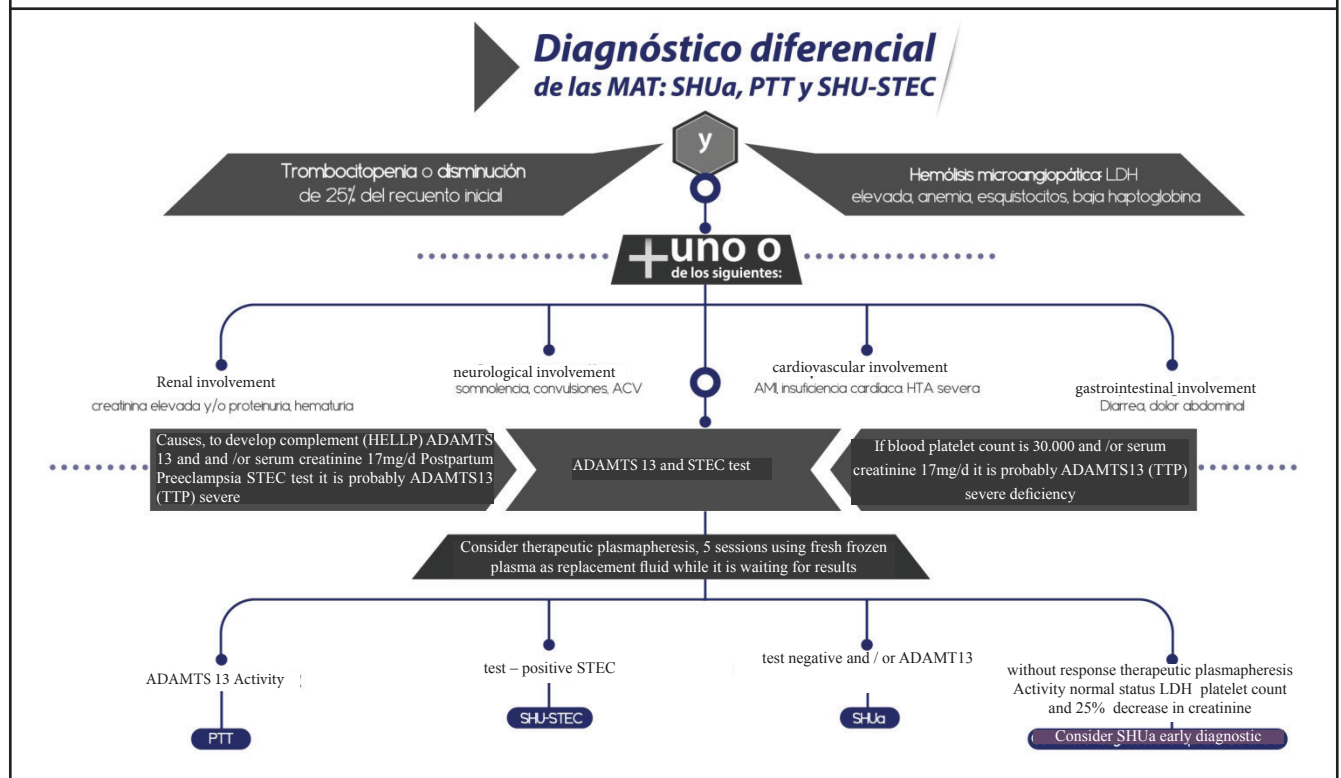
Noris and collaborators' study¹² shows that 70% of the patients with diagnosis of HUSa commutations CFH, CFI, C3 or THBD, or anti-body anti-FCF died

Figure 4

Graph1.algorithm for differential diagnosis of thrombotic microangiopathy document of Colombian consensus¹.

ADAMTS13: a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13; LDH: lactate dehydrogenase; MAT: thrombotic microangiopathy; PTT: thrombotic thrombocytopenic purpura; SHU: called hemolytic uremic syndrome;

SHUa: called hemolytic uremic syndrome atypical; STEC: Shiga toxin-producing Escherichia coli. LES: Systemic Lupus Erythematosus. HELLP: síndrome HELLP. Tomado de Córdoba et al.⁴



or came to end-stage renal disease during the first three years of the diagnosis, even in the course of plasmapheresis as standard operation.

Eculizumab: is a humanized monoclonal antibody that blocks the excision of terminal complement C5 protein in the inflammatory protein C5a and C5b, preventing the generation of complex C5B-9 terminal complement¹. Taking into account the pathophysiology of the disease, in relation to the deregulation of the complement system, Eculizumab blocks the terminal complement action, preventing the injury and chronic damage of the body, thus protecting the patient from the devastating consequences of the hyperactivity of the complement system. Multiple clinical studies have demonstrated the benefits of this therapy to change the natural history of this devastating disease and ultra-orphan⁴.

The recommended dose of Eculizumab for patients under the age of eighteen years of age is done according to the body weight, taking into account the following table:

It is advisable to consider Eculizumab as a therapeutic strategy in patients with TMA in those who do not observe the therapeutic response of the plasma exchange or there is¹⁶ dependency of this therapy. The inhibition of the TMA, mediated by the complement with Eculizumab, led to rapid hematologic improvements, significant improvements in the re-

nal results and the disruption of plasma exchange/infusion of plasma (PE/PI) and dialysis in the majority of patients, as well as in the case of this article.

According to Roxanne and collaborators¹⁵, in patients with HUSa, with and without complement mutations identified, the terminal complement locks with Eculizumab and interrupts the progression of inflammation to the renal injury and prevents dysfunction of the organs, despite the evidence of persistent AP and the activation of endothelial cells.

Conclusion

HUSa is an ultra-orphan disease, characterized by the presence of TMA, which is defined by the triad: non-immune hemolytic anemia, thrombocytopenia and compromised organ activity. In the pathophysiology of HUSa, the phenomena of TMA are a result of the lack of regulation of the alternative pathway of complement on the cell surfaces, secondary to a genetic cause, which led to the endothelial damage and multi organ involvement. Each day more pregnancy related cases of HUSa are described, taking into account the great physiological complement activity during gestation. The case reported is considered to be the first of its kind in our country. Eculizumab is a monoclonal antibody that inhibits the terminal complement fraction (C5), blocking the formation

Table 1

Dose of Eculizumab for patients under the age of 18 years
Taken from Cordoba et al.⁴

| Patient weight | Inducement | Treatment |
|---------------------------|---------------------------|---|
| 40kg and more | 900 mg per week x 4 doses | 1200 per week 5 ; later 1200 mg e/week |
| 30 kg and less than 40 kg | 600 mg per week x 2 doses | 900 mg per week 3; later 900 mg e/2 weeks |
| 20 kg and less than 30 kg | 600 mg per week x 2 doses | 600 mg per week 3; later 600 mg e/2 weeks |
| 10 kg and less than 20 kg | 600 mg per week x 1 doses | 300 mg per week 2; later 300 mg e/2 weeks |
| 5 kg and less than 20 kg | 300 mg per week x doses | 300 mg per week 2; later 300 mg e/2 weeks |

For patients under 18 years of age, therapy with Eculizumab consists of:

- 900 mg weekly during the first 4 weeks, followed by
- 1200 mg in the fifth week and then
- 1200 mg every 2 weeks.

of the attack complex of the cell membrane, with significant improvement in morbidity and mortality associated with this disease, allowing long term recovery of renal function and significant reduction in the need for dialysis or plasma therapy. Proper understanding and timely diagnosis of this entity and its relation with the pregnancy will allow these patients to be treated in a timely manner, avoiding the severe sequels of morbidity associated with ERC V and/or premature mortality.

Financing

There are no sources of financing.

Conflicts of Interest

Dr. Juan Pablo Cordoba is the medical director of Alexion Pharma Colombia. The rest of the authors did not report any conflict of interest.

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