Emergency Cesarean Section in a Patient with Delayed Diagnosis of Hemolytic Uremic Syndrome: A Case Report

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Abstract

Hemolytic uremic syndrome (HUS) is a thrombotic microangiopathy defined by thrombocytopenia, non-immune microangiopathic hemolytic anemia, and acute renal failure. The disease is frequently associated with infections by Shiga-like toxin-producing bacteria (STEC-HUS), and other bacteria. Clinical findings vary, including abdominal pain, diarrhea, vomiting, neurological impairment and hematuria.

When the patient presents at surgery, an unrecognized HUS may add a greater risk, due to crucial physiologic changes. We report a case where the patient presented to an emergency cesarean section, and in the intensive care unit, few hours later; we confirmed the diagnosis of HUS.

Keywords: *Hemolytic Uremic Syndrome; Anemia; hematuria; Thrombocytopenic Purpura; Thrombotic microangiopathy*

Introduction

Microangiopathic disorders in pregnancy present a challenge for both the Obstetrician and the Anesthesiology, concerning diagnosis and therapeutics. They include Thrombotic Thrombocytopenic Purpura (TTP), Hemolytic Uremic Syndrome (HUS) and HELLP Syndrome; disorders that can result in thrombocytopenia, hemolytic anemia, and systemic injury. Although these conditions are not common, they can promote severe multiorgan damage; therefore, leading to devastating maternal and fetal outcome if neglected or misdiagnosed.

Case Report

A twenty-one year-old-primigravid (37 weeks) came to our emergency ward complaining of non-productive cough, throat pain, intense myalgia, shivering, dysuria and fatigue. She had also a progressive dyspnoea, vomiting and diarrhea. The symptoms started two days earlier. She had also a history of renal lithiasis, and she denied symptoms of abnormal bleeding. Clinical exam showed regular general state, peripheral cyanosis and 28 breaths per minute. She was hydrated, anicteric and afebrile (36.7°C, axillary measure). Oxygen saturation was 88% in the room air, increased to 93% with supplementary oxygen, through a nasal catheter 4 L/min. Cardiac and pulmonary auscultations were normal. She had an edema of the lower limbs, with no signal of deep-vein thrombosis. Arterial pressure was 100/60 mmHg; heart rate was 120 beats per minute. Urinalysis showed macroscopic hematuria (40-50 red blood cells per high power field) and leukocyturia (white blood cells > 100 per high power field); EKG showed sinus tachycardia. The cardiotocography did not evidence non-reassuring fetal status; however, due to the maternal conditions, obstetricians indicated an emergency cesarean section.

We decided to perform general anesthesia, because of the poor clinical conditions of the mother. The patient was fasting for 20 hours, and intubation seemed easy. We provided pulse oximeter, non-invasive blood pressure, cardioscope with five leads, capnography, and two 18 gauge intravenous catheters. The patient was maintained temporarily in reverse Trendelenburg position.

We started the anesthesia induction, with Fentanyl (200 mcg), Etomidate (18 mg) and succinylcholine (80 mg). After applying Cricoid pressure, we easily intubated the patient (Cormack-Lehane 1). Airway pressures were normal. Anesthesia maintenance was provided with oxygen and air (FiO$_2$ = 0.5), and 3% sevoflurane. After the removal of the fetus (Apgar scores 10/10/10; in 1, 5 and 10 minutes), we gave cisatracurium (6 mg), propofol in continuous infusion (50 mcg/kg/min) and sevoflurane was then reduced to 1%. Estimated blood loss was about 800 mL.

Ten units of oxytocin were ineffective to cause uterine contraction. We repeated the same procedure, after 5 minutes, without success. The uterus finally contracted satisfactorily with metylergometrin (0.2 mg).

We maintained levels of the blood pressure between 100/50 and 110/60 mmHg during the 60-minute-procedure. At the end of the surgery, we administered supporting drugs for pain and nausea. The total amount of fluids was 1.5L of Lactated Ringer's solution and 500 mL of Hydroxyethyl Starch; we observed 100 mL of urinary output.

The patient was transferred to the Intensive Care Unit (ICU). She was hemodynamically stable, in the mechanical ventilation, with oxygen saturation of 97% and FiO$_2$ = 0.5, without the need of vasoactive drugs. Since the precise diagnosis was still unclear, we decided to maintain her in mechanical ventilation. At that point, a respiratory failure after extubation was a matter of concern. We gave her Midazolam (15 mg) and Cisatracurium (4 mg) for the duration of ICU stay. When she was uncovered, we spotted a huge circular hematoma in the left arm, with about ten-cm - diameter; in the place we gave the intramuscular injection of metylergometrin. That hematoma gave us a sign of an impaired coagulation status. Table 1 shows laboratory findings. The urine specimen grew *Escherichia coli*, more than 100,000 colony-forming units per mL. The physicians at ICU confirmed the diagnosis of HUS, and started Ceftriaxone and platelet transfusion, according to the rise in the platelet count. The patient was extubated in the next day, and progressively recovered until the discharge, 10 days later. The renal function was almost fully recovered.

Day of Admission	1st	2nd	4th	5th
White bloodcell (x 10^3/mm^3)	17.9	15.0	11.1	10.8
SerumCreatinine (mg/dL)	5.11	4.3	2.3	1.23
SerumUrea (mg/dL)	135	141	114	75
Plateletcount (Units/mm^3)	12.800	12.400	29.600	87.400
Hemoglobincount (g/dL)	10.4	9.1	8.2	8.9
Hematocrit (%)	0.31	0.27	0.24	0.26
SerumSodium (mmol/L)	138	136	142	141
SerumPotassium (mmol/L)	4.3	3.3	3.6	3.9
Serum C-reactiveprotein (mg/L)	280	78	31	45
Total plasma bilirrubin (mg/dL)	2,21	0,43	0,32	
Directbilirrubin (mg/dL)	0,49	0,08	0,09	
IndirectBilirrubin (mg/dL)	1,76	0,35	0,23	

Table 1: Laboratorial Findings of the Patient in the Intensive Care Unit.

Discussion

Knowledge of clinical conditions in obstetric anesthesia is of paramount importance, because of the physiologic changes related to the pregnancy, and the risk that some specific diseases may add to the pregnant patients and to the fetus. Sometimes, there is limited time available to make a complete evaluation and to reach the best decision when facing a complex scenario.

The purpose of this report is to show that sometimes we have to deal with patients suffering from complex diseases, insufficient current medical history and different anesthetic techniques to settle on. In this report, a wrong technique could lead to devastating results, for example, a spinal hematoma, if the choice were subdural or epidural anesthesia. The patient could also end up with a severe

hemodynamic instability, if the physiologic changes of a spinal block were superimposed to a highly probable septic profile she seemed to have in the admission.

We had four hypotheses when the cesarean was indicated. First, severe urinary tract infection resulting in hemodynamic profile of septic shock (previous renal lithiasis, dysuria, shivering, urinalysis). Second, the H1N1 flu virus, also known as the swine flu, as we had seen few cases in the local community (myalgia, throat pain, cough, fatigue). Third, HELLP syndrome without hypertension (nauseas, vomiting, myalgia, malaise). Finally, the possibility of HUS (vomiting, previous diarrhea, fatigue). We decided for general anesthesia for two reasons: we could not guarantee the coagulation status, and the hemodynamic profile seemed to be unstable.

Hemolytic Uremic Syndrome (HUS) is a thrombotic microangiopathy that presents with thrombocytopenia, non-immune microangiopathic hemolytic anemia, and acute renal failure. There are frequent associations with previous infection by Shiga-like toxin-producing bacteria (STEC-HUS), like Eschericha coli and Shigella dysenteriae.

It has recently been demonstrated that an involvement of the complement system in the pathogenesis of the disease occurs [1].

The difference between TTP and HUS has long been difficult. The occurrence of central nervous system abnormalities, thrombocytopenia, microangiopathic hemolytic anemia, fever, and kidney dysfunction can be present in both contexts. Renal dysfunction in HUS is often more severe than that in TTP, whereas neurologic abnormalities are more prevalent in TTP [2]. HUS is more frequently observed in children who have had a preceding gastrointestinal infection; however, this condition has also been reported in adults and pregnant women [1]. Finally, preeclampsia may present without hypertension, and show clinical features that can overlap those signs and symptoms, making it difficult to differentiate among the three comorbidities [3].

Apart from renal impairment, HUS may also involve the liver as well as cardiovascular, pulmonary and central nervous system. The anesthetic implications of HUS are countless. We decided for general anesthesia because we had in mind the four possible diagnoses we described earlier, and the mother's poor condition on arrival. A case report, describing a 28-month-old girl with HUS who presented for arteriovenous shunt for hemodialysis, recommended inhaled anesthesia, with the use of isoflurane and atracurium [4]. That was our approach, except we used cisatracurium instead of atracurium, and sevoflurane instead of isoflurane. After the delivery, we lowered sevoflurane concentration, to help uterine contraction. The Apgar scores were a maximum score of 10 in the three moments, indicating that we provided satisfactory uteroplacental flow and oxygen, despite the alveolar-arterial gradient the patient presented.

Thrombocytopenia in pregnant women may result from a number of diverse etiologies, and sometimes it may be difficult to discern from one another, mainly TTP, HUS and HELLP syndrome. Gestational thrombocytopenia is the most frequent cause of thrombocytopenia in pregnancy, affecting 5% of all pregnant women and accounting for more than 75% of cases of pregnancy-associated thrombocytopenia [4]. The patient in the present report presented low platelets count, hemolytic anemia, renal failure without hypertension and signs of central nervous system disease. Table 2 shows the main differences of pregnancy-associated Microangiopathies, regarding clinical and laboratorial data.

The present patient had an uneventful recovery; however, it is advisable that patients with signs of recent E. coli infection should be followed postoperatively for signs of HUS. Anesthesiologists must be aware that HUS is an uncommon differential diagnosis in patients with post-operative seizures and coma [5]. Even though it is a rare illness, a meta-analysis describing the long-term prognosis of patients who survived an episode of STEC-HUS reported death or permanent end-stage renal disease in 12% of patients and glomerular filtration rate below 80 ml/min/1.73 m^2 in 25 % [6].

Prior therapies to HUS included plasma therapy, and supportive interventions, including blood transfusions, dialysis if indicated, and blood pressure control. The challenge of management is to maintain renal perfusion while avoiding deleterious fluid overload. Some authors discourage platelet transfusion (unless hemorrhage occurs) because platelet infusion could exacerbate thrombosis [7].

	MAHA	Thrombocytopenia	Coagulopathy	Hypertension	Renal Disease	CNS Disease	Peak Time
Preeclampsia	+	+	±	+++	+	+	3rd trimester
HELLP	++	+++	+	±	+	±	3rd trimester
HUS	++	++	±	±	+++	±	Postpartum
TTP	+++	+++	±	±	+/±	+++	2nd trimester, term
SLE	+	+	±	±	+/++	+	Anytime
APS	±	+	±	±	±	+	Anytime
AFLP	+	+/±	+++	±	±	+	3rd trimester

Table 2: Differentiation of Pregnancy-associated Microangiopathies.

Abbreviations: MAHA, microangiopathic hemolytic anemia; HUS, Hemolytic Uremic Syndrome; TTP, Thrombotic Thrombocytopenic Purpura; SLE, Systemic Lupus Erithemathosus; APS, Antiphospholipid Syndrome; AFLP-Acute Fatty Liver of Pregnancy; ±, variably present; +, mild; ++, moderate; +++, severe.

Eculizumab, a monoclonal antibody that blocks the proinflammatory and cytolytic effects of terminal complement activation, is now recognized as the treatment of choice for atypical HUS (aHUS). The term aHUS should now be used for the 10% of HUS cases not caused by inborn errors of metabolism, Shiga toxin *Escherichia Coli* (STEC) or *S. pneumoniae*. Even though Eculizumab was first indicated in aHUS, it has been recognized that patients with STEC-HUS (which includes this present case) may benefit from Eculizumab [8]. Unfortunately, the cost of the drug is still prohibitive; and we have not been able to get hold of this drug. This therapeutic discussion is beyond the scope of this case report.

Conclusion

In conclusion, our approach of the case included brief preoperative assessment, good intravenous line, fluid expansion, and rapid sequence of intubation, inhalational-relaxant technique with sevoflurane and cisatracurium, and postoperative recovery in ICU. It seemed to be the most appropriate we could offer in spite of limited information we had from the admission to the onset of the surgery. We initially considered the four possible diagnoses as we had discussed earlier; and HUS was confirmed in the ICU. Anesthesiologists must be aware of these uncommon, but life-threatening diseases when they treat patients with little information in an emergency setting.

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