COVID-19 in pregnant women: description of a possible case of COVID-19-linked HELLP-like syndrome

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Abstract

New evidence suggests that Sars-CoV2 infection during pregnancy may result in complications such as hypertension, nephropathy, thrombocytopenia, and liver damage. A pre-eclampsia-like syndrome has also been proposed in pregnant women with severe SARS-CoV-2 infection, which meets the pre-eclampsia criteria but resolves without delivery, with improvement in respiratory symptoms. 31-year-old, second pregnancy, in Emergency Room for PROM (premature rupture of membranes), has Sars-CoV2 infection and has not been vaccinated. Normal examinations and mild hypertension were present upon admission, but no treatment was administered. Vaginal Leukocytic Delivery 12 hours after admission, newborn Apgar score 9/10, weight 3.250 kg. At 20 hours after delivery, epigastric pain VAS 8-9 for 20 minutes, systolic/diastolic hypertension peak, increase in transaminases, LDH, ALP, Bilirubin, Dimer, platelet and fibrinogen drop. Neurological and respiratory objectivity were negative, and renal indices were within normal limits, so nifedipine 30mgx2/day + methyldopa 500 mgx2/day was started. Abdominal ultrasound revealed a thin perihepatic fluid stratum. A prophilaxis of dexamethasone 12mg twice a day and magnesium sulfate was introduced. At 32 hours after delivery, the laboratory detected an increase in transaminases, LDH, and worsening of thrombocytopenia. The patient is always eupnoic, and the diuresis is adequate. Blood tests improved gradually after 56 hours postpartum. Methyldopa and steroids are escalating. On day 7, discharge with normalized platelet and bilirubin counts and a decreasing trend in transaminases, LDH, and PAL. At the one-week follow-up, liver enzymes and coagulation were completely normal, and blood pressure was well controlled with methyldopa. We conclude that the simultaneous presence of the two diseases could have had a synergistic or opportunistic effect, resulting in severe clinical manifestations via interaction with the Renin-Angiotensin-Aldosterone system.

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Key words: pregnancy, COVID-19, HELLP-like syndrome.

Conflict of interest: the authors declare no potential conflict of interest, and all authors confirm accuracy.

Ethics approval and consent to participate: the authors have obtained consent from the patient and from the Hospital's Health Management to the processing of personal and sensitive data and the publication of this paper. The authors of this paper have not disclosed any details or information that could be used to identify the patient, nor have they used references to names, as well as pictures or videos. There was no use of compassionate or experimental therapies.

Availability of data and materials: the data used to support the findings of this study are available from the corresponding author upon request.

Acknowledgments: thanks to the hospital staff and the hospital management.

Received: 18 December 2023.
Accepted: 1 March 2024.

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Licensee PAGEPress, Italy
Advances in Anesthesia and Pain Medicine 2024; 2:39
doi:10.4081/aapm.39

Introduction

Preeclampsia is a multisystem, multifactorial hypertensive disorder of pregnancy, mediated by the placenta. It has an incidence of about 5%, and it is considered a clinical manifestation of maternal endothelial dysfunction.[1] Clinically, preeclampsia presents with hypertension (BP ≥ 140/90 mmHg) associated with proteinuria and/or alterations in renal or hepatic function, neurological signs, hemolysis or thrombocytopenia, and/or fetal hypodevelopment. As gestation progresses, preeclampsia can evolve into more serious conditions, such as eclampsia, hemorrhagic stroke, and HELLP (Hemolysis, Elevated liver enzymes and low platelets) Syndrome.[2]

The pandemic of COVID-19 due to the SARS-CoV-2 coronavirus resulted in a high number of critical patients and deaths.[3] Emerging data on the maternal impact of COVID-19 suggest that the clinical course is similar regardless of pregnancy.[4,5]

However, it has been shown that SARS-CoV-2 infection in pregnant women significantly increases the risk of going through serious complications.[5] A meta-analysis published in 2023 involving 13,136 pregnant women found out that in the case of SARS-CoV-2 infection, the risk of death during pregnancy or delivery increases 7-fold.

In addition, the risk of intensive care unit admission is three times higher and the risk of mechanical ventilation is 15 times higher. Finally, the chance of thrombotic complications is 5-fold higher than in pregnant women who have never contracted the virus.[6]

In pregnant and postpartum women with severe inflammatory forms of COVID-19, an increased prevalence of preeclampsia has been proved, and many of these cases have evolved into HELLP syndrome.[7] A new clinical-laboratory entity termed "COVID-19-Linked HELLP-Like Syndrome" (CLHLS) has been described.[8]

Case Report

We present the clinical case of a 31-year-old woman, second pregnancy, 38th week of gestation, who arrived at the emergency department of our hospital for Premature Rupture of Membranes (PROM) and the onset of labor.

At admission, we found nasopharyngeal swab positivity for SARS-CoV-2 (qRT-PCR).

The medical history was silent; the patient was not taking medications, and she had not had vaccination for SARS-CoV-2 and COVID-19 infections in the past.

On objective examination, there was apyrexia (body temperature 36.8°C), eupnea with RR of 16 acts/min, saturation of 99% in Ambient Air, and HR of 86 beats/min but mild hypertension emerged (NIBP 140/85 mmHg). The patient's BMI was 22 kg/m2.

Laboratory tests were normal.

The patient began antibiotic prophylaxis with Cefazolin (first dose of 2 g intravenous, then 1 g every 8 hours) and antithrombotic prophylaxis with subcutaneous enoxaparin 4000 UIx2/day.

About 12 hours after admission, the woman delivered by vaginal delivery without any complications: a female fetus with a birth weight of 3.250 kg, Apgar 9-10.

On the second day after delivery, the patient presented with an episode of epigastric pain (VAS 8-9) lasting about 20 minutes and NIBP 160/100 mmHg finding. She started antihypertensive therapy with nifedipine 30 mgx2/day + methyldopa 500 mgx2/day orally.

Blood tests showed increased values of transaminases aspartate aminotransferase (AST) and alanine aminotransferase (ALT), lactate dehydrogenase (LDH), alkaline phosphatase (ALP), bilirubin, White Blood Cells, D-Dimer and decreased values of platelets and fibrinogen. An abdominal ultrasound was performed that showed a perihepatic fluid of about 7 mm.

Due to the increasing trend of liver enzymes, worsening thrombocytopenia (Plt 84,000 u/µL), and suspected HELLP syndrome, dexamethasone 12mg x 2/day was added in therapy, and prophylaxis with magnesium sulfate was started.

On the third day after delivery, blood tests recorded a further increase in AST, ALT, and LDH values and a worsening of thrombocytopenia (Plt 75,000 u/µL), with no change in the clinical picture.

From the fourth postpartum day on, there was a progressive decrease in AST, ALT, LDH, ALP, Bilirubin, D-dimer, and Fibrinogen values and a progressive increase in platelet count. Initiated descalation of antihypertensive therapy obtaining good control of blood pressure values with methyldopa 500 mg/day. Declaration of corticosteroid therapy was implemented based on platelet count.

The patient was discharged on day 8 based on the normalization of platelet count and bilirubin and the decreasing trend of AST, ALT, LDH, and alkaline phosphatase.

The patient was checked in the outpatient clinic one week after discharge and showed complete resolution of liver function and coagulation profile. Her blood pressure was well controlled with oral methyldopa 500 mg/day.

Discussion

We described the case of a pregnant patient with a mild form of COVID-19 in late pregnancy and preeclampsia who developed "COVID-19-Linked HELLP-Like Syndrome" CLHLS. This case adds to the growing body of evidence that there is considerable overlap in the clinical and laboratory presentations of the two etiologies, which may complicate the timely diagnosis of HELLP syndrome in the context of SARS-CoV-2 infection.

Both preeclampsia and COVID-19 infection are examples of microvascular disease causing endothelial damage. Both cause a high prothrombotic tendency leading to multi-organ failure. The presence of both diseases probably has a synergistic or opportunistic effect, which could lead to severe clinical manifestations through the interaction of the renin-angiotensin-aldosterone system in their pathogenesis.

Indeed, although the pathology of COVID-19 appears to be multifactorial, it has been shown that angiotensin-converting enzyme 2 (ACE 2) mediates the entry of SARS-CoV-2 into target cells through binding to the spike protein of SARS-CoV-2 itself.[9]

ACE 2 is found not only in the pulmonary epithelium, but also in the heart, intestines, kidneys, and blood vessels.[10] It is one of the central enzymes in the renin-angiotensin system (RAS) that regulates blood pressure, fluid, electrolyte balance, and systemic vascular resistance, but it is also involved in mechanisms of platelet activation, thrombosis, and endothelial dysfunction.

ACE 2 is highly expressed in placental tissue, including the trophoblast syncytium, endothelium, cytotrophoblast, and vascular villus musculature.[11] Infection caused by COVID-19 can alter ACE2 expression, promoting a preeclamptic state.

Mendoza, in his case series, postulates a preeclamptic-like syndrome in patients with severe SARS-CoV-2 infection, who meet the criteria for preeclampsia but recover without delivery, only after improvement in respiratory status.[12] Recent reports on pregnant patients with COVID-19 show evidence of maternal vascular malperfusion, vascular injury, and thrombi.[13,14]

The strong association between the severe form of COVID-19 and CLHLS was demonstrated in a Spanish study,[15] with a prevalence of 28.6% (10/35 cases) of severe cases admitted to the ICU and no cases of CLHLS in mild cases of COVID-19 in pregnancy (0/34). These data would lead to the hypothesis that CLHLS is related to the severity of COVID-19.

However, recent literature reports several cases of mild COVID-19 infection and CLHLS.[16-19]

Because of the close similarity between CLHLS and classic HELLP syndrome in pregnant women with COVID-19, it is difficult to establish a differential diagnosis. Some authors are beginning to suggest laboratory parameters (such as LDH >600 UI/L) and imaging test results (such as uterine artery Doppler UtAPI >p95) to diagnose pre-eclampsia/HELLP syndrome.[14] Angiogenic markers, including maternal sFlt-1/PlGF levels, have also shown clinical utility as they can help rule out suspicion of preeclampsia.[15]

The differential diagnosis between CLHLS and HELLP syndrome is important because the treatment approach is different.

For CLHLS, conservative treatment is recommended, and the viral infection and inflammatory condition should be allowed to resolve spontaneously and gestation continues, thus preventing the mother's condition from worsening and avoiding iatrogenic preterm birth.

Differently, in classic HELLP syndrome, increased blood pressure, alterations in blood tests, organ dysfunction, and alterations in placental function persist even after the viral infection has regressed, indicating the need for delivery.[8]

Conclusions

The pandemic of COVID-19 has introduced additional challenges in the diagnosis of HELLP as COVID-19 infection can cause other systemic complications including elevated blood pressure, hemolysis, thrombocytopenia, renal impairment, and hypertransaminasemia that mimic preeclampsia and features of HELLP-Syndrome.

Early diagnosis of HELLP syndrome is essential to avoid maternal and fetal complications. Physicians should be aware of the similarities in presentation between HELLP syndrome and COVID-19 for timely diagnosis and treatment.

Although our understanding of COVID-19 maternal-fetal health is incomplete, pregnant patients with concomitant COVID-19 may have an increased risk of complications. Therefore, a careful screening for SARS-CoV-2 infection in pregnant patients is advisable for appropriate treatment.

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