

COVID-19 Mimicking Hemolysis, Elevated Liver Enzymes and Low Platelets (HELLP) Syndrome: A Case Report

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ARTICLE INFO	ABSTRACT
<i>Article type:</i> Case report	Background & aim: Hemolysis, elevated liver enzymes, and low platelets syndrome (HELLP) was mimicked by several infectious conditions. It is critically important to distinguish these two, since their management and course differs, substantially.
<i>Article History:</i> Received: 03-Sep-2021 Accepted: 25-Sep-2021	Case report: The case was a 27-year-old gravid patient with gestational age of 30 weeks who initially presented with headache and lower limb pain as well as leukopenia (and lymphopenia), normochromic normocytic anemia, thrombocytopenia, abnormal liver enzymes, increased lactate dehydrogenase enzyme and C-reactive protein. The patient was initially managed for HELLP syndrome, but due to the atypical presentation (low blood pressure and an episode of delirium when admitted), the novel coronavirus disease 2019 (COVID-19), real-time reverse transcription polymerase chain reaction (rRT-PCR) was requested for the patient that was positive. The spiral lung high-resolution computed tomography scan revealed changes compatible with COVID-19 diagnosis. Finally, the patient underwent uncomplicated normal vaginal delivery at 39 th gestational week.
<i>Key words:</i> COVID-19 HELLP Syndrom Overlapping Conditions Pregnancy	Conclusion: It is important to consider the COVID-19 in differential diagnosis of patients suspected to HELLP syndrome, as the isolation and treatment of the patient is different and time-sensitive.

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Introduction

Since infection with the novel coronavirus disease 2019 (COVID-19) can result in highly variable clinical presentations, healthcare professionals with different specialties are encountering COVID-19 patients mimicking a previously well-established condition in their field; therefore imposing a unique challenge. For example, COVID-19 as a mimicker of ST elevation myocardial infarction has been previously reported (1). Hemolysis, elevated liver enzymes, and low platelets syndrome (HELLP) has been mimicked by several

infectious conditions (2, 3); it is important to distinguish these two since their management and course differs substantially. Recently, there have been few reports of COVID-19 in gravid cases mimicking HELLP syndrome (4). The diagnostic criteria of HELLP syndrome consists of microangiopathic hemolysis, elevated liver enzymes and thrombocytopenia (5). HELLP is also frequently associated with hypertension and proteinuria; however, the cases of HELLP lacking these two features have also been reported (6, 7); therefore, making the

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distinction more challenging for the clinician. Apart from COVID-19 as a mimicker of HELLP syndrome, some argue that concomitant to COVID-19 infection may superimpose an initiating HELLP syndrome and exacerbate the patient's condition. For example, in a report by Ronnje et al., the authors described a 26-year-old patient with shortness of breath, myalgia and fever and a positive nasopharyngeal swab for COVID-19. The patient's condition rapidly deteriorated and she developed severe hepatic failure and coagulopathy. She underwent an emergency Caesarean section at 32 week +6 day, after which her condition rapidly improved (8). However, it is unclear if the COVID-19 exaggerated the course of an atypical HELLP syndrome or that the course of COVID-19

infection was worsened by a concomitant pregnancy, making pregnant patients a vulnerable group to the complications of COVID-19 infection.

Here, we reported a case of COVID-19 gravid patient presenting with headache and abnormal laboratory tests mimicking HELLP syndrome.

Case report

The case was a 27-year-old gravid patient G2P1 with gestational age of 30 weeks with complaints of headache and lower limbs pain who presented to a secondary-care center. The patient was transferred to our center since she had a low platelet count and abnormal liver function tests.

Table 1. Patient's laboratory tests' results

Laboratory test	Result
White cell count (WBC)	3600 mcl
Hemoglobin	10.7 g/dL
Platelet	22000mcl
Ferritin	1360 ng/mL
Reticulocyte count	1
Erythrocyte sedimentation rate (ESR)	17 mm
C- reactive protein (CRP)	114 mg/L
D- dimer	10192 ng/mL
Fibrinogen	<484 mg/dL
Fibrin degradation product (FDP)	<20000
Creatinine	0.8 mg/dL
Urine protein	negative
Aspartate transaminase (AST)	126 u/L
Alanine transaminase (ALT)	89 u/L
Bilirubin (total)	2.3 mg/dL
Lactate dehydrogenase (LDH)	1036 u/L
Wright test	negative
2-mercaptoethanol Brucella agglutination test	negative
Indirect coombs test	negative
Hepatitis B surface antigen (HBsAg)	negative
Hepatitis C virus antibody	negative
Antinuclear antibody (ANA)	negative
dsDNA IgM	negative
dsDNA IgG	negative
Anticardiolipin IgM	negative
Anticardiolipin IgG	negative
Antiphospholipid IgM	negative
Antiphospholipid IgG	negative
C3 level	negative
C4 level	negative
B2 glycoprotein IgM	positive
B2 glycoprotein IgG	negative
COVID-19 real-time reverse transcription polymerase chain reaction (rRT-PCR)	1 st test negative, 2 nd test positive

At admission, the patient had blood pressure of 100/70 mm Hg, pulse rate of 90 to 100 pulse per minute, fetal heart rate (FHR) of 95 pulse per minute, a reactive non-stress test (NST) and no signs of contraction or vaginal hemorrhage on examination.

In addition, the patient did not have any severe signs. Since HELLP syndrome was suspected, a single dose of dexamethasone was administered for the patient and was started on magnesium sulfate.

The first laboratory test revealed leukopenia of 2600 per microliters, neutrophilia of 85.5 percent and lymphopenia of 13.1 percent, normochromic normocytic anemia, and hemoglobin of 10.1. The lactate dehydrogenase (LDH) and C-reactive protein (CRP) increased to 1036 U/L and 114 mg/L, respectively (Table1). The fetal ultrasound was performed to evaluate the fetal health that was unremarkable.

The brain magnetic resonance imaging (MRI) was performed to address the cause of patient's delay in responding to verbal commands with a suspected brain hemorrhage considering low platelet count, although the patient's neurological examination was unremarkable. The brain MRI was normal. The patient developed delirium in the course of admission and haloperidol was started to alleviate the symptoms.

The multidisciplinary panel consisting of gynecologists, rheumatologists, hematologists and infectious diseases specialists was promptly

formed and discussed the case. Differential diagnoses including HELLP syndrome, hematological pathologies, systematic lupus erythematosus (SLE) and COVID-19 were considered for the patient.

On peripheral blood smear which was performed for the patient, giant platelet, atypical lymphocytes and granular neutrophils were detected and schistocyte count of less than 1 percent was reported. Furthermore, morphological changes compatible with infectious stress (viral or bacterial) was evident. Bone marrow aspiration (BMA) was performed to rule out the possibility of hematological pathologies or severe sepsis that the result was normal. Also, a flow-cytometry was performed for acute myeloid leukemia subtype M3 that was negative. Additionally, SLE was ruled out since the corresponding markers were negative.

Considering that the patient developed tachycardia during admission and also ferritin level was 1360 mg/Dl, lung computed tomography angiography (CTA) was done to rule out COVID-19 and pulmonary emboli. The CTA did not show any signs of emboli in main, lobar and segmental pulmonary arteries, but revealed several foci with patchy ground glass appearance in both lungs accompanied with scattered small patchy consolidations and also consolidation in posterior-inferior segments of lower lobe of both lungs and cardiomegaly (Figure 1).

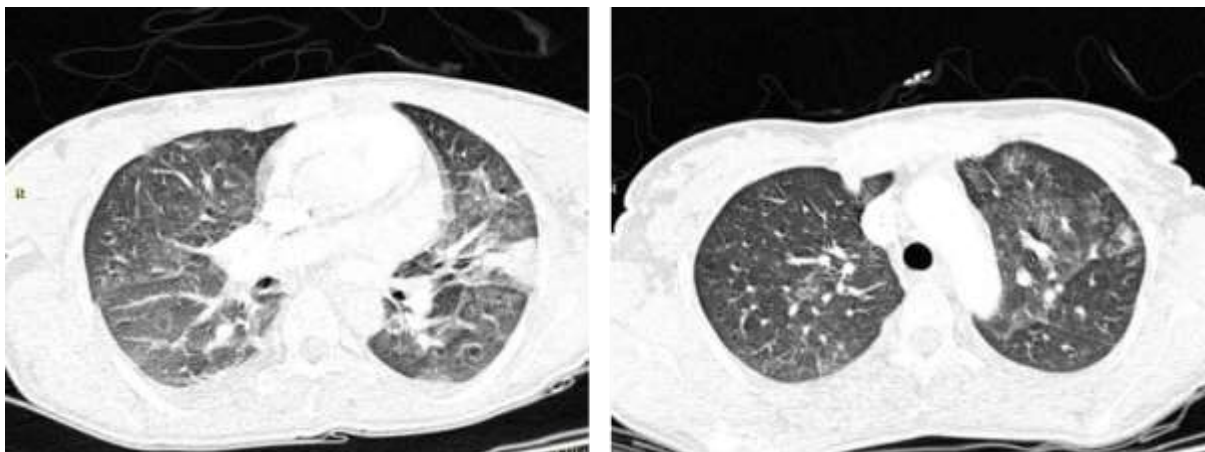


Figure 1. CTA; Peripheral ground glass opacity (GGO) mostly seen at left and right upper lobe of lungs and consolidation with subsegmental collapse at anterior segment of the left lower lobe suggestive of COVID-19 infection

During admission, the patient received 40 units of enoxaparin every 12 hours, as well as, azithromycin and ceftriaxone. Real-time reverse transcription polymerase chain reaction (rRT-PCR) was requested that was performed from the nasopharyngeal mucosa, but it was negative. Since malignancy, systematic lupus erythematosus (SLE) and HELLP were ruled out, and she did not develop and the liver function tests didn't improve, the second COVID-19 PCR was performed due to high suspicion for COVID-19 and it was positive. After confirming the diagnosis of COVID-19, stabilization of patient's condition and improvement in laboratory findings, she was discharged at gestational age of 33 weeks.

Finally, the patient underwent uncomplicated normal vaginal delivery at 39th gestational week. The neonate had an Apgar score of 9-10 and did not show any signs of distress. An informed consent was obtained from the patient to publish this case and attached figures.

Discussion

The present report highlights a case of COVID-19 mimicking HELLP syndrome and indicates the importance of considering this differential diagnosis during the pandemic because the management of these two conditions varies significantly. However, this should not be confused with the fact that these two can coexist in a patient. Futterman *et al.* described the two cases of gravid patients at 22 and 29 weeks admitted due to a suspected COVID-19 infection and subsequently developed laboratory parameters were consistent with HELLP syndrome (elevated liver enzymes, thrombocytopenia and hemolysis)⁽⁴⁾. Researchers emphasize that although similarities between these two conditions are evident, there are criteria which can help differentiating the two conditions. The first feature, unlike COVID-19 cases, is the presence of hypertension which occurs in up to 20% of HELLP syndrome cases. Another differentiating feature is the course of the disease after delivery. HELLP syndrome will resolve 24 to 72 hours after delivery, but in COVID-19, delivery does not necessarily affect its course.

A systematic review by Juan *et al.* showed that although quite uncommon, but fetal complications of maternal COVID-19 can occur and range from spontaneous miscarriage to fetal asphyxia and death (9). Therefore, differentiating COVID-19 from other conditions, such as HELLP syndrome and early treatment is critically important to minimize fetal complications.

It should also be noted that if the clinical suspicion for COVID-19 is high enough, a negative PCR test does not rule out COVID-19 as a differential diagnosis. In a retrospective study by Miller *et al.*, the researchers reported that the sensitivity of PCR decreased from 90% to approximately 70% after 9 days post symptoms (10). Since in the present case, we are not aware when exactly did the patient's symptoms start, it might have affected the diagnostic value of PCR. Additionally, the quality of sample taking in the first PCR test may have been suboptimal. It is recommended that in the case of high suspicion for COVID-19, a single negative PCR test should not hinder clinicians from considering the possibility of COVID-19 in a pregnant patient, especially during COVID-19 pandemic.

Conclusion

The close similarities in terms of laboratory abnormalities between HELLP syndrome and COVID-19 should be taken into account by primary care physicians, gynecologists and emergency medicine specialists to make the correct early diagnosis and prevent the possible fetal and maternal complications of these two conditions.

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Conflicts of Interest

The authors declare no conflicts of interest.

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