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CASE REPORT

# Preeclampsia with posterior reversible encephalopathy syndrome and cerebral venous sinus thrombosis in a pregnant patient with COVID-19

Sevda Diker,[1] Ferda Selçuk,[2] Uğurcan Balyemez[3]

[1]Department of Neurology, Cyprus International University Faculty of Medicine, Nicosia, Cyprus
[2]Department of Neurology, Dr. Burhan Nalbantoğlu State Hospital, Nicosia, Cyprus
[3]Department of Radiology, Near East University Faculty of Medicine, Nicosia, Cyprus

**SUMMARY**

Since its discovery in December 2019, coronavirus disease 2019 (COVID-19) has been linked to a variety of systemic effects in addition to pulmonary involvement. Pregnancy increases the risk of severe COVID-19 symptoms. COVID-19 during pregnancy worsens maternal and fetal outcomes such as preterm delivery, preeclampsia, and vascular complications. Herein, we report the case of a pregnant woman with COVID-19 who developed preeclampsia, posterior reversible encephalopathy syndrome (PRES), and cerebral venous sinus thrombosis (CVST) in the peripartum period. We discussed the possible link between these neurological complications and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Headache can be observed in the natural course of SARS-CoV-2 infection; however, it can also result from numerous etiologies such as preeclampsia, PRES, and CVST in the peripartum period. An accurate diagnosis is crucial, as the treatment and prognosis of each differ.

**Keywords:** Cerebral venous sinus thrombosis; COVID-19; preeclampsia.

## Introduction

According to current evidence, pregnancy does not increase susceptibility to SARS-CoV-2 infection; however, it increases the risk of severe COVID-19 compared to non-pregnant women of the same age.[1] The odds of preeclampsia in both asymptomatic and symptomatic patients significantly increase during the infection.[2] Herein, we report a case of peripartum preeclampsia with posterior reversible encephalopathy syndrome (PRES) and CVST during a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.

## Case Report

A 25-year-old G5P2 female patient, at 35 weeks and 3 days of pregnancy, was admitted with a new-onset dry cough and hospitalized after being diagnosed with COVID-19 infection by real-time reverse transcriptase polymerase chain reaction (RT-PCR) assay in December 2021. The patient was not vaccinated against COVID-19. She had been previously evaluated for missed abortions and had been on daily prophylaxis with subcutaneous low-molecular-weight heparin (LMWH) since the early weeks of her current pregnancy.

During hospitalization due to COVID-19, a fetal heart rate decrement was detected on a non-stress test, and a caesarean section with spinal anesthesia was performed at 35 weeks and 5 days. Throughout the operation and in the early postoperative hours, her blood pressure increased to 200/120 mmHg and was gradually reduced by intravenous antihypertensives. She complained of a dull, gradual-onset headache and thereafter had a generalized tonic-clonic seizure. Brain magnetic resonance imaging (MRI) was compatible with PRES (Fig. 1).

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**Correspondence:** Dr. Sevda Diker. Uluslararası Kıbrıs Üniversitesi Tıp Fakültesi, Nöroloji Anabilim Dalı, Lefkoşa, Kıbrıs.
**Phone:** +90 - 392 - 680 80 80 **e-mail:** sevdaomrumdiker@gmail.com

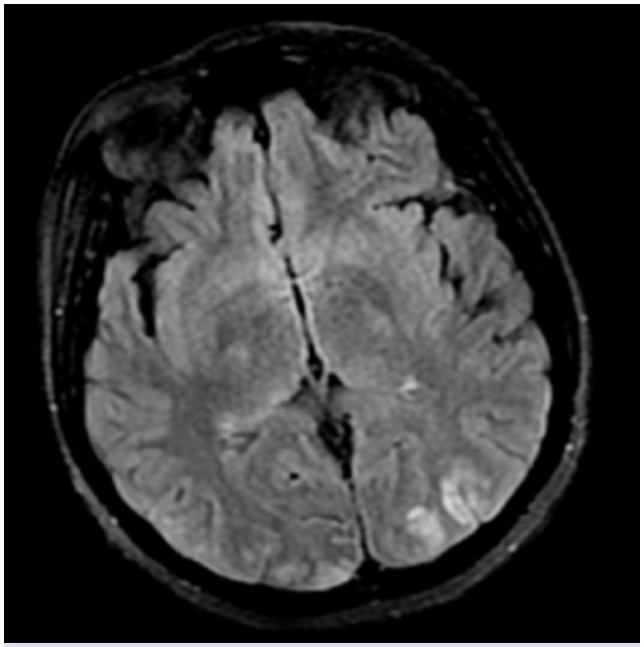

**Figure 1.** Axial FLAIR image showing focal hyperintensities affecting the cortical and subcortical areas of the bilateral occipital lobe, consistent with PRES. No diffusion restriction was observed (data not shown).

Abnormal biochemical test results were as follows: mildly elevated white blood cell count $10.8\times10^3$/microliter (neutrophil dominant with normal lymphocyte count), increased d-dimer (3.62, normal range 0–0.55 mg/l), increased C-reactive protein (6.3, normal range 0.0–0.5 mg/dl), low serum albumin (3.2 g/dl, normal range 3.5–5.2 g/dl) and total protein (5.5 g/dl, normal range 6.4–8.3 g/dl) with normal kidney function tests, mildly elevated hepatic enzymes (alanine aminotransferase=38, normal range 0–35 U/l; aspartate aminotransferase=44, normal range 0–33 U/l; gamma glutamyl transferase=47, normal range 0–40 U/l; alkaline phosphatase=96, normal range 35–130 U/l).

Magnesium and levetiracetam bolus infusions were administered intravenously. Methyldopa (1000 mg/day) and levetiracetam tablets (1000 mg/day) were started as maintenance therapy.

Four days after the delivery, she complained of headaches that were initially evaluated and managed as post-dural puncture headaches. Although her headache completely resolved after intravenous fluid infusions, her control brain MRI revealed hyperintensity of the right transverse and sigmoid sinuses on fluid-attenuated inversion recovery (FLAIR) images and near-complete resolution of PRES signs. MR venography revealed thrombosis in the right sigmoid and transverse sinuses and in the occipital region of the superior sagittal sinus (Fig. 2).

Prophylactic LMWH dosage was switched to therapeutic dosage. During follow-up, she did not complain of further headaches. The antiepileptic drug was tapered off, and she did not experience a new seizure during the six-month period afterwards.

A detailed evaluation of thrombophilia revealed low protein S activity, which was 36% (normal range: 55–160%), and heterozygotic mutations in factor V (H1299R), prothrombin (G20210A), and MTHFR (A1298C) genes. She was referred to the haematology department for further evaluation and management of the anticoagulation therapy.

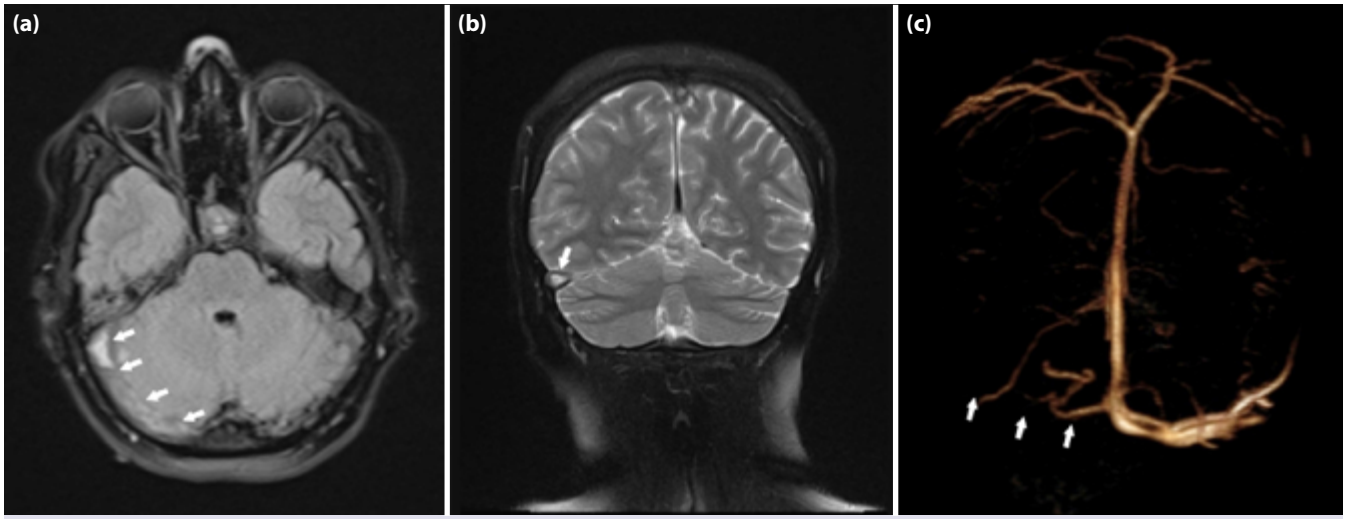


**Figure 2.** Axial FLAIR image **(a)** and coronal T2 weighted image **(b)** showing signal void loss in the right transverse sinus (arrows). **(c)** Loss of right transverse sinus flow on the volume-rendered Time-of-flight (TOF) MR venography image (arrows).

## Discussion

COVID-19 during pregnancy has been shown to be independently associated with preeclampsia.[2] Downregulation of the RAS system following virus binding to ACE2 receptors has been proposed as an underlying mechanism, resulting in unopposed vasoconstrictive and proinflammatory effects of angiotensin II. COVID-19 severity does not appear to be a factor in this association. SARS-CoV-2 also increases the risk of developing preeclampsia with severe features and eclampsia.[2]

Our patient had mild symptoms of COVID-19 but developed preeclampsia with radiological features of PRES and CSVT. The diagnosis of eclampsia could also be discussed based on the coexistence of headache, hypertension, and a grand mal seizure. On the other hand, the patient's symptoms can already be attributed to PRES, a clinical–neuroradiological syndrome. PRES is often associated with preeclampsia and eclampsia,[3] and eclampsia has been considered as obstetric PRES. The International Society for the Study of Hypertension in Pregnancy (ISSHP) does not define eclampsia as a separate condition and considers it a neurological complication of preeclampsia.[3] Therefore, we preferred to define our patient's condition as preeclampsia with severe features.

In terms of CSVT, many etiological factors overlap in the present case. First of all, puerperium is a major acquired risk factor for CSVT. Secondly, the patient already had inherited risk factors for thrombophilia, as shown by genetic tests. Also, CSVT could be a neurological complication of preeclampsia.[3] Finally, COVID-19 has been shown to increase the risk of venous thrombosis, particularly in hospitalized patients.[4]

Studies and meta-analyses on venous thromboembolism during COVID-19 have mostly focused on pulmonary thromboembolism or deep vein thrombosis.[4] A recent meta-analysis found that COVID-19 was complicated by deep vein thrombosis or pulmonary embolism in approximately 30% of cases, regardless of whether the majority of patients had received thromboprophylaxis.[4] The underlying mechanisms are thought to be elevated pro-inflammatory cytokines, increased systemic inflammation, endothelial injury by the virus through angiotensin 2 receptors, and platelet activation.[5,6]

CVST has rarely been reported in pregnant women with COVID-19. One of these reports was a case of CVST in a SARS-CoV-2-infected pregnant woman with twins in the first trimester, with negative acquired or inherited thrombophilia assessments.[7] Another case was a 35-week pregnant woman with a heterozygous prothrombin mutation who developed CVST during SARS-CoV-2 infection.[8]

Our case demonstrates the neurological complications of pregnancy during COVID-19. Our patient had mild COVID-19 symptoms, which did not worsen during follow-up. At the time of the patient's admission, PCR positivity for SARS-CoV-2 was an indication for hospitalization, irrespective of the disease severity. Unfortunately, the patient's status deteriorated due to preeclampsia, PRES, and CSVT during follow-up, but clinical stabilization was achieved within a short period. The role of COVID-19 in these complications is still doubtful. As mentioned, both acquired and genetic risk factors existed in our patient. However, we cannot totally deny or accept reciprocal interactions between COVID-19 and these factors.

Irrespective of COVID-19, both preeclampsia and CSVT can complicate pregnancy, and early diagnosis is critical to prevent morbidity and mortality. Notably, in the alarming course of preeclampsia and PRES, CSVT can be clinically and radiologically overlooked. However, these can coexist, as in our case. The answer to whether this coexistence is increased during COVID-19 needs further research.

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