Postpartum cerebral venous thromboembolism in an asymptomatic COVID-19 patient

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ABSTRACT

Introduction: Cerebral venous thromboembolism is a serious condition whose diagnosis and management in the emergency department is vital. Although cerebral venous thromboembolism (CVT) is not as common as lower extremities venous thromboembolism (VTE) or pulmonary embolism (PE), several cases were reported in literature that linked it to both, COVID-19 and puerperium, as they are at the origin of hypercoagulable state.

Case Report: We report this case of a postpartum patient who presented in status epilepticus to the emergency department. She was diagnosed with CVT causing left temporal lobe infarction with hemorrhagic changes. Along this condition, she had a positive COVID-19 test. Anticoagulation was started and patient was discharged after 2 weeks having mild cognitive impairment as a sequela.

Conclusion: This case demonstrates the importance of considering CVT as one of the large differentials in a patient having neurological symptoms, and, highlights the need of starting antithrombotic therapy as prophylaxis in pregnant/puerperium women to avoid thromboembolic events in COVID-19 era.

Keywords: Cerebral venous thromboembolism, COVID-19, Postpartum, Status epilepticus

INTRODUCTION

Despite that venous thromboembolism (VTE) is the leading cause of maternal death in the United State, it remains an uncommon event that happens in 85/100,000 pregnancy, with a postpartum–anteprtum ratio of 2:0 [1]. However, as pregnancy is a hypercoagulable state, VTE events increase five folds during pregnancy compared to non-pregnant women [2]. In most of the cases, lower extremities are the main site of thrombosis [3, 4], while upper extremity DVT (UEDVT) occurs much lesser, as in ovarian hyperstimulation syndrome (OHSS) following an assisted reproductive technique (ART) [5]. But nowadays, in the COVID-19’s Era, the frequency of UEDVT cases has increased as new reported cases of CVT is being elucidated day after day [6]. What if a combination of two hypercoagulable states has occurred?

CASE REPORT

A 35-year-old lady, Gravida 1 Para 1, healthy, non-smoker, presented to our emergency department 25 days...
postpartum, mentioning four days history of recurrent episodes of seizures, which was exacerbating day after day. She started to have a unilateral headache two weeks postpartum with no other neurological symptoms. She did not seek any medical advice at that time.

A review of her previous hospitalization, 25 days ago, showed that she was admitted at 35+5w gestational age (GA) for high blood pressure readings reaching 150/100 mmHg, with mild fronto-occipital headache, denying nausea, vomiting, nor vision problems. She had 2+ proteinuria, but normal liver function test (LFTs), creatinine, uric acid, and lactate dehydrogenase (LDH) levels. Induction of labor was started, and magnesium course began. However, she ended up with primary cesarian section for non-improving headache and refractory blood pressure. She was discharged on day 2 post-cesarean, clinically and hemodynamically stable, with normal vitals and negative repeated preeclampsia workup.

When presenting to the emergency department (ED), she was in a status epilepticus picture, unconscious, desaturated (SpO₂ = 80%) on simple face mask (SFM) O₂ supply, febrile (39.1 °C) and tachycardic (heart rate, HR: 127). No signs of limb deep vein thrombosis (DVT). Her blood pressure, respiratory rate, and hemoglobin test (HGT) level were within normal range. Arterial blood gases (ABGs) revealed mild acidosis with a PO₂ level of 45, requiring urgent intubation. One shot of 4 g magnesium and she was given a loading dose of phenytoin intravenous (IV) and started on IV maintenance.

Laboratory tests showed leukocytosis (14*) with left neutrophil shift of 90.7%, without electrolyte disturbances, and a negative preeclampsia workup.

Brain computed tomography (CT) showed: left temporal hypodensity indicating left temporal lobe infarction with hemorrhagic changes, followed by computed tomography angiography (CTA) and computed tomography venography (CTV) that revealed: left internal jugular venous thrombosis, left sigmoid, and transverse sinuses thrombosis (Figures 1 and 2).

Meanwhile, polymerase chain reaction (PCR) result turned out to be positive, knowing that the patient wasn’t complaining from any COVID-19’s symptom all over the puerperium period prior to admission.

Computed tomography chest showed mild bi-basal alveolar condensation, with no major lung involvement (Figure 3).

This has put us in front of 2 main differential diagnoses (as puerperium preeclampsia was ruled out and vasculitis workup was negative)

- An uncommon postpartum internal jugular vein (IJV) thrombosis with cerebral sinus thrombosis versus
- post-COVID-19 hypercoagulable state
- or a combination of both.

Therefore, the patient was started on therapeutic anticoagulation (Lovenox 60 mg subcutaneous BID) transferred to intensive care unit (ICU) for a thorough monitoring. After improvement in ABGs and control brain CT scan, she was extubated and transferred to the regular floor, cooperative, with mild disorientation and a Glasgow Coma Scale of 14/15. Switched to sintrom 2 mg OD, dose adjusted according to daily international normalized ratio (INR) level, and discharged home one week later in a stable condition.

![Figure 1: CT scan showing left temporal lobe hypodensity indicating hemorrhage.](image1)

![Figure 2: CTV showing left IJV thrombosis.](image2)
microvascular thrombi of coagulation and fibrinolytic system resulting in viruses cause endothelial damage leading to impairment factors: infection and pro-coagulopathic state [9]. In fact, thromboembolism has been linked to two main risk cognitive impairment may result [11]. Cerebral venous rate compared with arterial stroke, a high incidence of postpartum [8]. Such as oral contraceptive pill (OCP) use, pregnancy ratio of 1:3, probably due to gender-specific risk factors approximately 0.5% of all strokes with a male to female stroke [10]. Cerebral venous thromboembolism is an uncommon cause of stroke, accounting for 0.5% of all strokes with a male to female ratio of 1:3, probably due to gender-specific risk factors such as oral contraceptive pill (OCP) use, pregnancy, and postpartum [8, 9, 11, 14]. Despite its overall low mortality rate compared with arterial stroke, a high incidence of cognitive impairment may result [11]. Cerebral venous thromboembolism has been linked to two main risk factors: infection and pro-coagulopathic state [9]. In fact, viruses cause endothelial damage leading to impairment of coagulation and fibrinolytic system resulting in microvascular thrombi, hence, a direct relation of COVID-19 and thromboembolic events. On the other hand, hypercoagulable state due to the use of OCP, pregnancy, and puerperium may predispose to CVT, which accounts for 2% of pregnancy associated stroke [9, 14]. The most common presenting symptom in CVT is headache—whose prevalence is 13% among COVID-19 patients—followed by seizures, then focal neurologic deficit [8, 10, 15, 16]. The puerperium is a window for many complications in women’s health including preeclampsia/eclampsia, reversible cerebral vasoconstriction syndrome, and venous thromboembolism [13, 16]. This is due to the physiological changes in her body during this period [17]. Headache is a common symptom in the postpartum period resulting from sleep deprivation, hormonal fluctuation, and irregular food intake [17]. Hence, diagnosis of CVT can be easily masked by other common causes of headache [13, 17, 18]. Marwah et al. described a case of CVT at day 7 postpartum, having headache and seizure as the main presenting symptoms and the patient was discharged home conscious and cooperative [17]. While Ghashimi et al. described a case of a patient during the postpartum period presenting to the emergency department in status epilepticus requiring endotracheal intubation, found to have simultaneous multiple thromboembolic events including pulmonary embolism and cerebral venous thrombosis who died because of tonsillar herniation [14], in contrast to our patient who had intellectual deficit and mild cognitive impairment upon discharge.

Treatment of CVT is mainly supportive and evidence suggests that anticoagulation therapy should be initiated as a secondary prevention of CVT in high risk factor patients for a duration of three months, while in idiopathic and thrombophilia cases the duration should be extended to 6–12 months [18, 19].

A growing body of literature has highlighted the association between thrombosis and COVID-19 infection, indicating the hypercoagulable state caused by COVID-19 itself, and the following provocation of venous thromboembolism including CVT [8, 11, 14]. A modest number of cases have discussed about CVT in puerperium. To our knowledge, this is the first case described in the literature concerning CVT in a COVID-19 infected patient in the postpartum period.

We reported this case to reveal the seriousness of well receiving and analyzing even the milder neurological complaints in postpartum patients in the COVID-19’s era. Findings could range from a simple primary headache or secondary one to seizures. These symptoms can be caused by viral illnesses including COVID-19, preeclampsia/eclampsia or cerebral venous thromboembolism. The latter can be the result of any etiology increasing hypercoagulability, including COVID-19 and puerperium. Through this case, we wanted to point out the importance of anticoagulation prophylaxis during pregnancy and puerperium especially in COVID-19 infected patients to avoid venous thromboembolism and their possible complications.

DISCUSSION

This case of COVID-19 associated CVT in a young lady in the postpartum period, whose pregnancy was complicated by pre-eclampsia, and presenting solely with neurological symptoms, adds to the current and ongoing body of literature on CVT, as being a complication of both COVID-19 infection, and, pregnancy or puerperium, that predispose the patient to a hypercoagulable state.

The COVID-19 pandemic is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [7]. It has been linked to acute respiratory distress syndrome, acute cardiac and renal injuries, but also to thromboembolic events, via direct viral invasion to endothelial cells found in brain through angiotensin-converting enzyme (ACE) receptor, or via activation of mechanisms related to systemic inflammatory cascade [8–11]. Hypercoagulability induced by COVID-19 has been implicated in pulmonary embolisms (PEs), venous thromboembolisms (VTEs), disseminated intravascular coagulation (DIC), acute limb ischemia and recently in stroke [10, 12, 13]. Cerebral venous thromboembolism is an uncommon cause of stroke, accounting for approximately 0.5% of all strokes with a male to female ratio of 1:3, probably due to gender-specific risk factors such as oral contraceptive pill (OCP) use, pregnancy, and postpartum [8, 9, 11, 14]. Despite its overall low mortality rate compared with arterial stroke, a high incidence of cognitive impairment may result [11]. Cerebral venous thromboembolism has been linked to two main risk factors: infection and pro-coagulopathic state [9]. In fact, viruses cause endothelial damage leading to impairment of coagulation and fibrinolytic system resulting in microvascular thrombi, hence, a direct relation of COVID-19 and thromboembolic events. On the other hand, hypercoagulable state due to the use of OCP, pregnancy, and puerperium may predispose to CVT, which accounts for 2% of pregnancy associated stroke [9, 14]. The most common presenting symptom in CVT is headache—whose prevalence is 13% among COVID-19 patients—followed by seizures, then focal neurologic deficit [8, 10, 15, 16]. The puerperium is a window for many complications in women’s health including preeclampsia/eclampsia, reversible cerebral vasoconstriction syndrome, and venous thromboembolism [13, 16]. This is due to the physiological changes in her body during this period [17]. Headache is a common symptom in the postpartum period resulting from sleep deprivation, hormonal fluctuation, and irregular food intake [17]. Hence, diagnosis of CVT can be easily masked by other common causes of headache [13, 17, 18]. Marwah et al. described a case of CVT at day 7 postpartum, having headache and seizure as the main presenting symptoms and the patient was discharged home conscious and cooperative [17]. While Ghashimi et al. described a case of a patient during the postpartum period presenting to the emergency department in status epilepticus requiring endotracheal intubation, found to have simultaneous multiple thromboembolic events including pulmonary embolism and cerebral venous thrombosis who died because of tonsillar herniation [14], in contrast to our patient who had intellectual deficit and mild cognitive impairment upon discharge.

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CONCLUSION

Symptoms such as headache and/or seizure in the postpartum period of a patient, whose pregnancy was complicated by preeclampsia, should not be presumed as eclampsia. Cerebral venous thromboembolism may occur in young COVID-19 patients in the puerperium period mimicking eclampsia. As CVT is commonly missed in the emergency department, clinicians need from now on to carefully evaluate any neurological symptom whether headache and/or seizure and to consider CVT as one of the extended differential diagnoses in a patient where her postpartum period in these circumstances of enlarging COVID-19 cases throughout the world. This might reduce morbidity and mortality by allowing early initiation of treatment.

REFERENCES


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Author Contributions

Mayssaloun Ibrahim Khairallah – Conception of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Eva Koulaymi – Design of the work, Interpretation of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Authors declare no conflict of interest.

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All relevant data are within the paper and its Supporting Information files.

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