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COVID-19 Pregnancy and Psycho-neurological Disturbance: Single Hospital Case Report

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Abstract – 31 years old pregnant woman at 38 1/7 week of gestation with fever has been admitted to the TSMU First University Clinic Emergency, with positive COVID-19 PCR test. With characteristic complains of COVID-19 infection. Family history not significant. Personal history reveals childhood seizure as a result of fever. Vital signs at the admission within normal ranges. All protocol based laboratory tests has been done and protocol based treatment initiated. On the seventh day of Covid-19 infection because of episodes of desaturation and termed gestation, pregnancy termination by induction has been done successfully. At the end of early puerperal period because of hypoxemia resistant to oxygen therapy and CT scan diagnosed severe viral induced pneumonia, with symptoms of encephalopathy has been documented. Later patient transferred to the mechanical ventilation, protocol based lab tests, diagnostic procedures and treatment initiated. After 1 month with improved condition patient has been transferred to the ob/gyn department for ongoing treatment and rehabilitation at this time severely expressed symptoms of encephalopathy were documented.
The underlying mechanisms of neurologic complications in patients with COVID-19 are diverse and, in some cases, multifactorial. Neurologic complications may arise from direct effects of the virus as well as systemic response to the infection or as a result of long lasting inadequate oxygenation of all tissues. Although mechanical ventilation is highly complicated by brain damage, covid-19 induced encephalopathies are as well documented and need more scientifically proved facts of the viral role in this complication.

Keywords – Severe Covid-19, Adult Respiratory Distress, Pregnancy, Psychiatric Disorder, Edinburgh Postnatal Depression Scale.

I. INTRODUCTION

Coronaviruses are important human and animal pathogens. At the end of 2019, a novel coronavirus was identified as the cause of a cluster of pneumonia cases in Wuhan. The World Health Organization designated the disease COVID-19 (coronavirus disease 2019) [1, 2].

Neurologic complications in patients with COVID-19 are common in hospitalized patients [5-12]. More than 80 percent of hospitalized patients may have neurologic symptoms at some point during their disease course [12 Myalgia, headache, encephalopathy, and dizziness may be most common, occurring in approximately one-third of patients in China, Europe, and the United States [5,8,12-14]. Stroke, movement disorders, motor and sensory deficits, ataxia, and seizures appear uncommon [12,13]. Critically ill patients have a higher proportion of neurologic complications than patients with less severe illness [5,12].

In a systematic review of 192 studies including over 64,000 pregnant and recently pregnant people with suspected or confirmed COVID-19 [45 46]. 3.3 percent were admitted to an intensive care unit (ICU), and the risk was higher in pregnant

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people compared with non pregnant females of reproductive age with COVID-19 (OR 2.13) and pregnant people without COVID-19 (OR 19).

- •1.6 percent received invasive ventilation
- •0.11 percent received extracorporeal membrane oxygenation (ECMO)
- •0.8 percent died

The most frequently reported neurologic disorders among pregnant people were – Headache, dizziness, myalgia, alteration of consciousness, disorders of smell and taste, weakness, strokes, seizures. several mechanisms of short and long lasted neurological disorders related to COVID-19 have been postulated - thrombophilia associated with the virus or the host immune response appears to be one important mechanism, as suggested by elevated markers of hypercoagulability and inflammation. Considerable evidence suggests that COVID-19 is associated with a hypercoagulable state. This is reflected in the extremely elevated D-dimer levels observed in many patients over the course of the first few weeks of disease, particularly those who are more severely affected [47]

II. CASE DESCRIPTION

31 years old pregnant woman at 38 1/7 week of gestation has been admitted to the TSMU First University Clinic Emergency department because of symptoms worsening, with positive COVID-19 PCR test done 5 days before. Complaints' at the admission: fever, general weakness, muscle, joint pain, head ache, sore throat, cough, anosmia, augenesia. Ob/gyn history: current pregnancy is 7-th, 2 vaginal deliveries and 4 artificial abortions. Menstrual cycle regular, menarche from 11 years. Family history not significant (Tab N1,2). Personal history reveals childhood seizure as a result of fever. Vital signs at the admission: RR-22, SpO2 98%, T/A 130/80 mmHg, P-107, T- 38,5. (Table N 3). All protocol based laboratory tests has been done and treatment initiated – corticosteroid inhalation, prophylactic anticoagulation treatment.

General status at the admission

Table N1

Lang auscultation	Diminished lung sounds at lung basses
Abdominal palpation	Pregnancy induced enlargement, no labor contractions
Pasternatsky sign	Negative on both sides
Heart auscultation	Pregnancy related changes
ASA classification	15 score
Intestine function	Normal
Urinary system function	Normal
Presence of edema	Ankle edema resolving after rest
Varicose veins	Absent
Skeleton system	Normal
Vaginal discharge	Normal
Uterine fundal height	36.5 cm
Results of Leopold maneuvers	Fetal longitudinal lie, left occipital presentation
FHR auscultation	156 min
BMI	30 kg

Fetal assessment at the admission

Table N2

Ultrasound	Fetal data
Placenta	Normal location and structure
Amniotic fluid	Normal
FHR	157 min
Doppler (UA, MCV, a. uterine)	Normal
Fetal anatomy, presentation	Normal. Cephalic presentation
Fetal weight	3295±200 gr

Laboratory values at the admission

Table N3

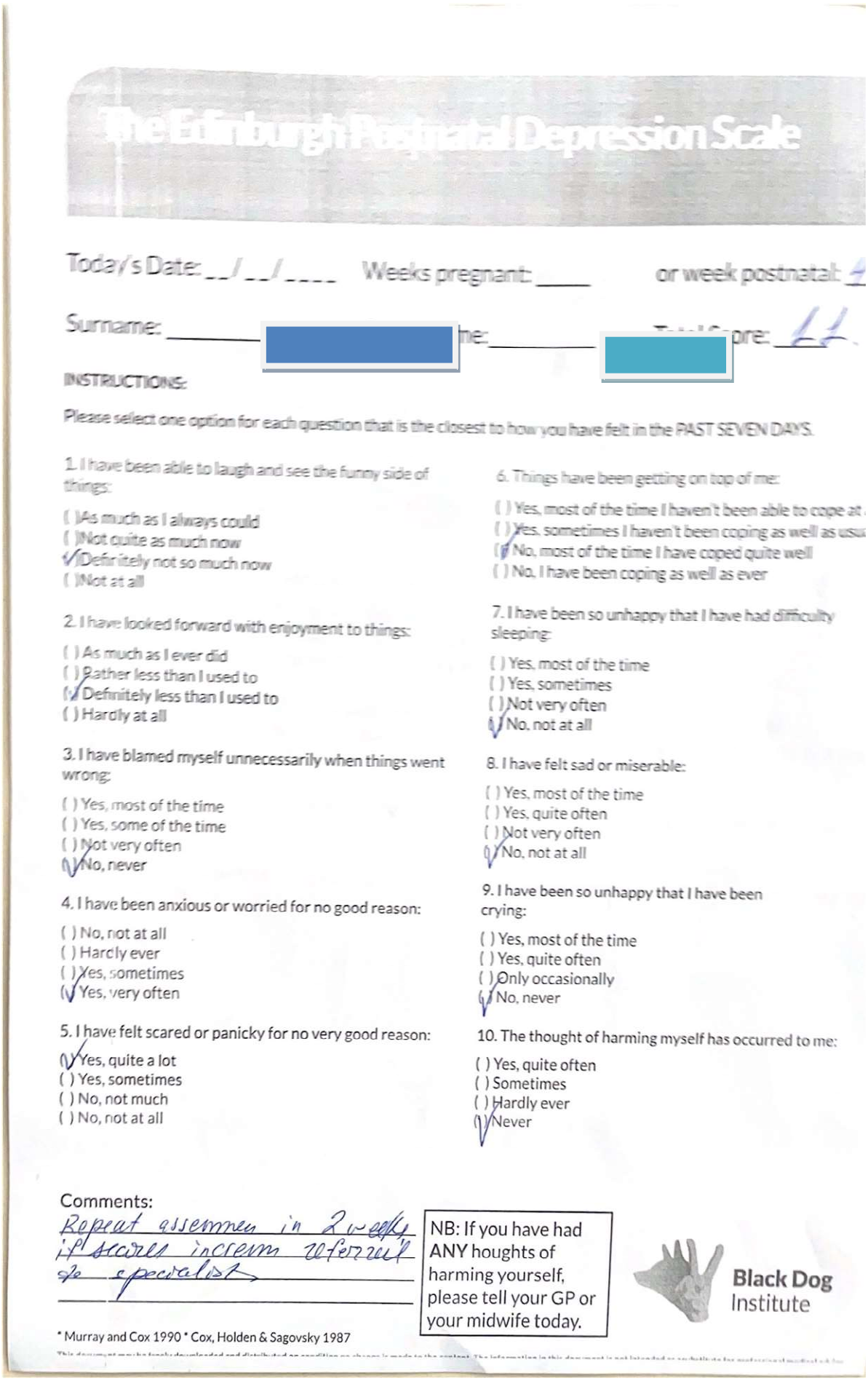
Blood type	O (I) Rh (+)
Lymphocyte	17.8 % - Decreased
WBC	4.03 10/9/L -Normal
Erythrocytes	3.77 10/12/L- Decreased
Hemoglobin	10.0 g/dl- Decreased
PLT	Normal
Fibrinogen	3.1- Normal
Prothrombin index	105% - Elevated
Prothrombin time	12.5% - Normal
APTT	49.7 sec - Prolonged
LDH	229 U/L - Increased
Urea, Creatinine	Normal
D-dimer	3.6 mg/L - Elevated
CRP	56 mg/L - Elevated
Ferritin	Normal
Iron	Normal
Troponin	Normal
HbsAg	Negative
Anti-Tp	Negative
Anti-HIV	Negative
Anti-HCV	Negative
Urine test	Protein (trace)

On the seventh day of Covid-19 infection because of episodes of desaturation and termed gestation, decision of pregnancy termination has been made. Under nasal oxygen cannula and epidural anesthesia induction of labor was successful. 3200 gr female neonate has been delivered with APGAR score 8/9. At the end of early puerperal period because of hypoxemia resistant to oxygen therapy and tachypnea patient has been transferred to CPAP regimen and chest CT has been performed revealing severe viral infection induced pneumonia. Patient has been transferred to intensive care unit with immediate initiation of protocol based management. On the 9-th day of COVID-19 - immune phase of the infection laboratory values of CRP was doubled, procalcitonine in a gray zone. First episode of alertness, confusion and agitation has been documented and sedation of

the patient been done. On the 14-th day of the viral infection because of sudden negative progression of the disease patient was transferred to the department of critical medicine and as a result of acute respiratory distress mechanical ventilation has been initiated. During the period of treatment in the department of critical medicine, symptoms of encephalopathy has been documented as a result of every episode of the decreasement of sedative medicines. After 1 month of treatment under mechanical ventilation patients general condition, laboratory values and CT results was improved and mechanical ventilation has been followed by oxygenation with tracheostomy cannula few days' later cannula has been removed and patient been transferred to the ob/gyn department. Starting from the moment of spontaneous respiration neurological symptoms became severely expressed: disorientation, agitation, phobias, inadequate reactions, sleep disturbance, motor irritation without any deficit. Patient is still oxygenation with nasal cannula with good hemodynamic and respiratory parameters. In the ob/gyn department condition of the woman has been assessed by postnatal Edinburgh scale (picture N1) and pregnancy induced psychogenic abnormalities been excluded. Patient was consulted by psychiatrics concluding presence of cognitive decreasement, intermittent disorientation, transient psychotic state. Antipsychotic and antidepressant medicines have been prescribed. Recommended psychiatric follow up.

Treatment and manipulations done in the Department of Critical Medicine

Tracheostomy
Pleural drainage
Tracheal sanitation
Chest CT. XR
Pleural, abdominal, urinary tract - USG
Bronchoscopy
Central (subclavian, jugular) and peripheral vessel catheterization
Urine bladder catheterization
Antibacterial treatment
Anticoagulation therapy
Oxygen therapy
Acid-base correction
Glycemic control
Infusion therapy
Treatment by anti agregants
Treatment of arrhythmia
Vaso - inotropic support
Analgesia
Stimulation of diuresis
Hormonotherapy
gastro protection
Continuous monitoring of vital signs
Observation by ob./gyn
Consultation of neurologist



The Edinburgh Postnatal Depression Scale

Today's Date: __/__/____ Weeks pregnant: ____ or week postnatal: 4

Surname: _____ [redacted] me: _____ [redacted] Total Score: 11

INSTRUCTIONS:

Please select one option for each question that is the closest to how you have felt in the PAST SEVEN DAYS.

1. I have been able to laugh and see the funny side of things:

( ) As much as I always could
( ) Not quite as much now
(✓) Definitely not so much now
( ) Not at all

2. I have looked forward with enjoyment to things:

( ) As much as I ever did
( ) Rather less than I used to
(✓) Definitely less than I used to
( ) Hardly at all

3. I have blamed myself unnecessarily when things went wrong:

( ) Yes, most of the time
( ) Yes, some of the time
( ) Not very often
(✓) No, never

4. I have been anxious or worried for no good reason:

( ) No, not at all
( ) Hardly ever
( ) Yes, sometimes
(✓) Yes, very often

5. I have felt scared or panicky for no very good reason:

(✓) Yes, quite a lot
( ) Yes, sometimes
( ) No, not much
( ) No, not at all

6. Things have been getting on top of me:

( ) Yes, most of the time I haven't been able to cope at
( ) Yes, sometimes I haven't been coping as well as usu
(✓) No, most of the time I have coped quite well
( ) No, I have been coping as well as ever

7. I have been so unhappy that I have had difficulty sleeping:

( ) Yes, most of the time
( ) Yes, sometimes
( ) Not very often
(✓) No, not at all

8. I have felt sad or miserable:

( ) Yes, most of the time
( ) Yes, quite often
( ) Not very often
(✓) No, not at all

9. I have been so unhappy that I have been crying:

( ) Yes, most of the time
( ) Yes, quite often
( ) Only occasionally
(✓) No, never

10. The thought of harming myself has occurred to me:

( ) Yes, quite often
( ) Sometimes
( ) Hardly ever
(✓) Never

Comments:

Repeat assessment in 2 weeks if scores increase refer back to specialist

NB: If you have had ANY houghts of harming yourself, please tell your GP or your midwife today.

Black Dog Institute

* Murray and Cox 1990 * Cox, Holden & Sagovsky 1987

III. Discussion

The underlying mechanisms of neurologic complications in patients with COVID-19 are diverse and, in some cases, multifactorial. Neurologic complications may arise from direct effects of the virus as well as systemic response to the infection [13]. Distinct mechanisms include: neurologic injury from systemic dysfunction – Hypoxemia, prevalent in patients with severe COVID-19, is likely to play a role in many patients with encephalopathy, as are metabolic derangements due to organ failure and medication effects. Neurochemical evidence of astrocytic and neuronal injury documented in plasma of patients with moderate and severe COVID-19 does not suggest a specific pathogenesis [16].

Neuropathologic case series of patients who succumbed to COVID-19 revealed acute hypoxic ischemic damage in nearly all patients, as well as the presence of hemorrhagic and bland infarcts, microglial activation with microglial nodules [17,18]. In other series, neuroimaging findings appeared consistent with a leukoencephalopathy and are similar to those described in patients with acute respiratory distress syndrome (ARDS) unrelated to COVID-19 [19-21]. Maladaptive activity of the renin-angiotensin system (RAS) may be another relevant path mechanism of COVID-19 infection. SARS-CoV-2 utilizes angiotensin converting enzyme 2 (ACE2), a membrane-bound protein, as its point of entry into cells [22,23]. By binding to ACE2, the SARS-CoV-2 virus may damage vascular endothelial cells by inhibiting mitochondrial function and endothelial nitric oxide synthetase activity resulting in secondary cardio- and cerebrovascular effects [24].

A dysregulated systemic immune response to SARS-CoV-2 has also been implicated [25,26]. Critically ill patients with COVID-19 often develop signs of severe systemic inflammation consistent with a cytokine release syndrome-like presentation that manifests with persistent fever, elevated inflammatory markers (eg, D-dimer, ferritin), and elevated pro-inflammatory cytokines [27,28]. Markers of inflammation - TNF-alpha, and interleukin 6 [IL-6]) are elevated in patients with severe COVID-19 [29,30]. High levels of circulating pro-inflammatory cytokines can cause confusion and alteration of consciousness [9,31]. A single case series described five patients with delayed awakening after ventilation for COVID-19-related ARDS who underwent brain vessel wall magnetic resonance imaging, which revealed abnormal contrast enhancement in the vascular wall of the basal skull arteries, a finding interpreted as possible endotheliitis [32]. However, evidence of resolution of these imaging abnormalities after corticosteroid treatment was not presented nor was there pathological confirmation of inflammation. [33, 34]. Cytokine release may also lead to brain injury by microglial activation and a systemic inflammatory response [18,35 ,36].

Some reports provide evidence for direct viral invasion of the nervous system [37-39]. In postmortem case series, SARS-CoV-2 was detected in most brain specimens, but these findings were unrelated to the severity of neuropathological findings [18,37,38]. It is uncertain if SARS-CoV-2 directly infects the cerebral vessels. Autopsy studies have reported potential evidence of direct endothelial invasion by the SARS-CoV-2 [40,41,42,43, 44,45].

Reported case describes psycho-neurological disturbance revealed in a postpartum period after severe COVID-19 infection. Instead of known facts of viral induced brain damage and big amount of clinical cases presented with short and long lasting psycho-neurological disturbances the problem still need accurate clinical and scientific assessment [46,47,48]

References

[1] World Health Organization. Director-General's remarks at the media briefing on 2019-nCoV on 11 February 2020. http://www.who.int/dg/speeches/detail/who-director-general-s-remarks-at-the-media-briefing-on-2019-ncov-on-11-february-2020 (Accessed on February 12,2020).

[2] World Health Organization. Novel Coronavirus (2019-nCoV) technical guidance. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance (Accessed on February 14, 2020).

[3] Centers for Disease Control and Prevention. 2019 Novel coronavirus, Wuhan, China. Information for Healthcare Professionals. https://www.cdc.gov/coronavirus/2019-nCoV/hcp/index.html (Accessed on February 14, 2020).

[4] National Institutes of Health. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. https://covid19treatmentguidelines.nih.gov/ (Accessed on May 27, 2021)

[5] Mao L, Jin H, Wang M, et al. Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China. JAMA Neurol 2020; 77:683.

[6] Helms J, Kremer S, Merdji H, et al. Neurologic Features in Severe SARS-CoV-2 Infection. N Engl J Med 2020; 382:2268.

[7] Montalvan V, Lee J, Bueso T, et al. Neurological manifestations of COVID-19 and other coronavirus infections: A systematic review. Clin Neurol Neurosurg 2020; 194:105921.

[8] Romero-Sánchez CM, Díaz-Maroto I, Fernández-Díaz E, et al. Neurologic manifestations in hospitalized patients with COVID-19: The ALBACOVID registry. Neurology 2020; 95:e1060.

[9] Koralnik IJ, Tyler KL. COVID-19: A Global Threat to the Nervous System. Ann Neurol 2020; 88:1.

[10] Xiong W, Mu J, Guo J, et al. New onset neurologic events in people with COVID-19 in 3 regions in China. Neurology 2020; 95:e1479.

[11] Herman C, Mayer K, Sarwal A. Scoping review of prevalence of neurologic comorbidities in patients hospitalized for COVID-19. Neurology 2020; 95:77.

[12] Liotta EM, Batra A, Clark JR, et al. Frequent neurologic manifestations and encephalopathy-associated morbidity in Covid-19 patients. Ann Clin Transl Neurol 2020; 7:2221.

[13] Pezzini A, Padovani A. Lifting the mask on neurological manifestations of COVID-19. Nat Rev Neurol 2020; 16:636.

[14] Chou SH, Beghi E, Helbok R, et al. Global Incidence of Neurological Manifestations Among Patients Hospitalized With COVID-19-A Report for the GCS-NeuroCOVID Consortium and the ENERGY Consortium. JAMA Netw Open 2021; 4:e2112131.

[15] Graham EL, Clark JR, Orban ZS, et al. Persistent neurologic symptoms and cognitive dysfunction in non-hospitalized Covid-19 "long haulers". Ann Clin Transl Neurol 2021; 8:1073.

[16] Kanberg N, Ashton NJ, Andersson LM, et al. Neurochemical evidence of astrocytic and neuronal injury commonly found in COVID-19. Neurology 2020; 95:e1754.

[17] Solomon IH, Normandin E, Bhattacharyya S, et al. Neuropathological Features of Covid-19. N Engl J Med 2020; 383:989.

[18] Thakur KT, Miller EH, Glendinning MD, et al. COVID-19 neuropathology at Columbia University Irving Medical Center/New York Presbyterian Hospital. Brain 2021; 144:2696.

[19] Kandemirli SG, Dogan L, Sarikaya ZT, et al. Brain MRI Findings in Patients in the Intensive Care Unit with COVID-19 Infection. Radiology 2020; 297:E232.

[20] Radmanesh A, Derman A, Lui YW, et al. COVID-19-associated Diffuse Leukoencephalopathy and Microhemorrhages. Radiology 2020; 297:E223.

[21] Agarwal S, Jain R, Dogra S, et al. Cerebral Microbleeds and Leukoencephalopathy in Critically Ill Patients With COVID-19. Stroke 2020; 51:2649.

[22] Strawn WB, Ferrario CM, Tallant EA. Angiotensin-(1-7) reduces smooth muscle growth after vascular injury. Hypertension 1999; 33:207.

[23] Ye M, Wysocki J, William J, et al. Glomerular localization and expression of Angiotensin-converting enzyme 2 and Angiotensin-converting enzyme: implications for albuminuria in diabetes. J Am Soc Nephrol 2006; 17:3067.

[24] Lei Y, Zhang J, Schiavon CR, et al. SARS-CoV-2 Spike Protein Impairs Endothelial Function via Downregulation of ACE 2. Circ Res 2021; 128:1323.

[25] Pilotto A, Padovani A, ENCOVID-BIO Network. Reply to the Letter "COVID-19-Associated Encephalopathy and Cytokine-Mediated Neuroinflammation". Ann Neurol 2020; 88:861.

[26] Muccioli L, Pensato U, Cani I, et al. COVID-19-Associated Encephalopathy and Cytokine-Mediated Neuroinflammation. Ann Neurol 2020; 88:860.

[27] Channappanavar R, Perlman S. Pathogenic human coronavirus infections: causes and consequences of cytokine storm and immunopathology. Semin Immunopathol 2017; 39:529.

[28] Huang KJ, Su IJ, Theron M, et al. An interferon-gamma-related cytokine storm in SARS patients. J Med Virol 2005; 75:185.

[29] Chen G, Wu D, Guo W, et al. Clinical and immunological features of severe and moderate coronavirus disease 2019. J Clin Invest 2020; 130:2620.

[30] Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020; 395:497.

[31] Fotuhi M, Mian A, Meysami S, Raji CA. Neurobiology of COVID-19. J Alzheimers Dis 2020; 76:3.

[32] Pugin D, Vargas MI, Thieffry C, et al. COVID-19-related encephalopathy responsive to high-dose glucocorticoids. Neurology 2020; 95:543.

[33] Connors JM, Levy JH. Thromboinflammation and the hypercoagulability of COVID-19. J Thromb Haemost 2020; 18:1559.

[34] Magro C, Mulvey JJ, Berlin D, et al. Complement associated microvascular injury and thrombosis in the pathogenesis of severe COVID-19 infection: A report of five cases. Transl Res 2020; 220:1.

[35] Al-Dalahmah O, Thakur KT, Nordvig AS, et al. Neuronophagia and microglial nodules in a SARS-CoV-2 patient with cerebellar hemorrhage. Acta Neuropathol Commun 2020; 8:147.

[36] Zhao H, Shen D, Zhou H, et al. Guillain-Barré syndrome associated with SARS-CoV-2 infection: causality or coincidence? Lancet Neurol 2020; 19:383.

[37] Matschke J, Lütgehetmann M, Hagel C, et al. Neuropathology of patients with COVID-19 in Germany: a post-mortem case series. Lancet Neurol 2020; 19:919.

[38] Meinhardt J, Radke J, Dittmayer C, et al. Olfactory transmucosal SARS-CoV-2 invasion as a port of central nervous system entry in individuals with COVID-19. Nat Neurosci 2021; 24:168.

[39] Song E, Zhang C, Israelow B, et al. Neuroinvasion of SARS-CoV-2 in human and mouse brain. bioRxiv 2020.

[40] Varga Z, Flammer AJ, Steiger P, et al. Endothelial cell infection and endotheliitis in COVID-19. Lancet 2020; 395:1417.

[41] Ackermann M, Verleden SE, Kuehnel M, et al. Pulmonary Vascular Endothelialitis, Thrombosis, and Angiogenesis in Covid-19. N Engl J Med 2020; 383:120.

[42] Goldsmith CS, Miller SE, Martines RB, et al. Electron microscopy of SARS-CoV-2: a challenging task. Lancet 2020; 395:e99.

[43] Varga Z, Flammer AJ, Steiger P, et al. Electron microscopy of SARS-CoV-2: a challenging task - Authors' reply. Lancet 2020; 395:e100.

[44] Hanafi R, Roger PA, Perin B, et al. COVID-19 Neurologic Complication with CNS Vasculitis-Like Pattern. AJNR Am J Neuroradiol 2020; 41:1384.

[45] Keller E, Brandi G, Winklhofer S, et al. Large and Small Cerebral Vessel Involvement in Severe COVID-19: Detailed Clinical Workup of a Case Series. Stroke 2020; 51:3719.

[46] Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. BMJ 2020; 370:m3320.

[47] Martinez-Portilla RJ, Sotiriadis A, Chatzakis C, et al. Pregnant women with SARS-CoV-2 infection are at higher risk of death and pneumonia: propensity score matched analysis of a nationwide prospective cohort (COV19Mx). Ultrasound Obstet Gynecol 2021; 57:224.

[48] Connors JM, Levy JH. Thromboinflammation and the hypercoagulability of COVID-19. J Thromb Haemost 2020; 18:1559.