

SUPPLEMENTAL MATERIAL

Cerebral Venous Sinus Thrombosis Associated with COVID-19: A Case Series and Literature Review

Supplementary Clinical Vignettes of the Case No.2-6.

Case no. 2

A 68-year-old woman presented with a gradual loss of consciousness within the last 2 weeks before the admission. Meanwhile, she progressively lost her ability to communicate with the surroundings and perform daily activities. Her PMH was significant for chronic progressive dementia. On arrival at the hospital, she was stuporous with a GCS of 9 out of 15. Her vital signs were stable and she was afebrile. Neurological examination revealed localizing with bilateral upper limbs symmetrically and producing incomprehensible sounds, in response to the painful stimuli. Otherwise, the neurological examination was unremarkable. The initial laboratory tests showed leukocytosis ($16.4 \times 10^3/\mu\text{l}$, normal: $4-10 \times 10^3/\mu\text{l}$), thrombocytopenia ($89 \times 10^3/\text{mm}^3$, normal: $150-450 \times 10^3/\text{mm}^3$), increased CRP (97mg/l , normal: 0-6 mg/l), and elevated LDH (702 u/l, normal: <480 u/l). Due to the COVID-19 pandemic, thrombocytopenia, elevated CRP and LDH, RT-PCR for SARS-CoV-2 using oropharyngeal/nasopharyngeal swabs and lung HRCT were performed. RT-PCR was positive and Lung HRCT raised suspicion of pulmonary thromboembolism (PTE); therefore, the patient underwent spiral chest CT-angiography with PTE protocol which confirmed the diagnosis of PTE. Brain CT scan demonstrated hyperdensity within the superior sagittal, straight, and bilateral transverse sinuses. Brain MRI revealed widespread filling defects (in the sinuses which were hyperdense on brain CT scan) in T1-weighted with gadolinium sequence, suggestive for thrombosis. Brain MRV was consistent with extensive venous sinuses thromboses. Consequently, UFH 1000 units/hour IV infusion was immediately started. Despite the relative improvement in the clinical and laboratory findings and removal of the clot in the follow-up brain CT scans, the patient died on the 21st day of admission due to sudden bradycardia and cardiac arrest.

Case no. 3

A 40-year-old male presented with headache, fluctuating level of consciousness, and weakness of both lower extremities for 3 weeks before the admission. On the day of admission, he developed a profound loss of consciousness; therefore, the patient was brought to the hospital. His PMH was consistent with chronic hepatitis C and opium addiction; however, he had not taken any antiviral medication. Upon arrival, he was unconscious (GCS: 3 out of 15) and vital signs were as follows: Temperature of 38.5 °c, blood pressure of 90/50 mmHg, pulse rate of 130 beats/min, and respiratory rate of 25 breaths/min with oxygen saturation (SpO₂) of 95% on room air. He underwent intubation.

Brain CT scan showed bilateral thalamic hypodensities as well as hyperdensities in the bilateral internal cerebral veins, the vein of Galen, straight sinus, superior sagittal sinus, cortical veins, and right transverse sinus suggestive of extensive thromboses. Due to the COVID-19 pandemic and fever, RT-PCR for SARS-CoV-2 using oropharyngeal/nasopharyngeal swabs and lung HRCT was performed. RT-PCR was positive and lung HRCT was suggestive for SARS-CoV-2 infection. Because of the bilateral swollen legs, a color doppler ultrasound of both lower extremities was performed which revealed extensive thrombosis of both lower extremities' veins. As a result, UFH 1000 units/hour IV infusion, meropenem 1 gram every 8 hours, vancomycin 1 gram every 12 hours, and levophed 10 mcg/min IV infusion were administered. Nevertheless, he passed away on the same day of admission.

Case no. 4

A 46-year-old male was admitted to the emergency department complaining of fever, cough, shortness of breath, and thoracic pain. Due to the COVID-19 pandemic and history of flulike symptoms, lung HRCT and RT-PCR for SARS-CoV-2 using oropharyngeal/nasopharyngeal swabs were performed which proved positive for SARS-CoV-2 infection. He received treatment with lopinavir/ritonavir and dexamethasone. On the 14th day of admission, his clinical condition was relatively improved and he was discharged from the hospital.

One day later, he developed a severe progressive headache; hence, he was admitted back into the hospital. On arrival at the hospital, he was awake and oriented, and his vital signs were stable. Neurological examination was unremarkable except for right-sided hemianopia. A brain CT scan showed a hemorrhagic venous infarct in the left parieto-occipital area. Consequently, low-molecular-weight heparin (LMWH) 60 mg subcutaneously twice per day was immediately started. However, he abruptly developed a decreased level of consciousness and was deceased on the same day.

Case no. 5

A 32-year-old woman in the 9th week of pregnancy presented to our emergency department complaining of fever and decreased level of consciousness. She had a history of progressive headache, nausea/vomiting, and fever for three days before admission. After two days, she developed a progressively decreased level of consciousness and muteness. Her PMH was unremarkable. On arrival at the hospital, she was drowsy and mute and her temperature was 38.5 °C. Neurological examination revealed a stuporous state and flexion of the right upper limb in response to the painful stimulation. Plantar reflexes were extensor bilaterally. Otherwise, the neurological examination was unremarkable. Brain MRI showed bilateral thalamus and basal ganglia hyperintensities and hypointensities in the T2-weighted and gradient echo (GRE) sequences, respectively, associated with hyperintensities and blooming artifact of the bilateral internal cerebral veins, the basal vein of Rosenthal, and straight sinus in the T1-weighted and GRE sequences, respectively. These findings were suggestive for deep veins thrombosis in association with hemorrhagic infarct. Due to the COVID-19 pandemic and a history of fever, RT-PCR for SARS-CoV-2 was performed using an oropharyngeal/nasopharyngeal swab which was positive. UFH 1000 units/hour IV infusion was immediately started. After 10 days of anticoagulant initiation, the level of consciousness was significantly improved and neurological deficits were completely subsided except for mild right-sided weakness. She was discharged from the hospital with LMWH 60 mg subcutaneously twice per day.

Case no. 6

A 31-year-old woman presented to our emergency department, complaining of headache and seizure. She had a history of progressive headache, sore throat, generalized body pain, and fever for four days before admission. On the day of admission, she developed four episodes of focal clonic movements in the left upper limb which progressed to a generalized tonic-clonic seizure. Her PMH was consistent with provoked CVST (following oral contraceptive usage) 2 years ago and hence she had been on warfarin for one year and then discontinued it according to the physician's recommendation. On arrival at the hospital, she was drowsy and her temperature was 39 °C. Neurological examination in the postictal phase revealed an obtunded state and bilateral dilated pupil with sluggish response to the light reflex. Plantar reflexes were extensor bilaterally. Otherwise, the neurological examination was unremarkable. Brain MRI showed right perisylvian area hyperintensity in the T1 and FLAIR sequences associated with hyperintensity and filling defect in the adjacent cortical vein in the FLAIR and T1-weighted with

gadolinium sequences, respectively, suggestive for right sphenoparietal sinus and superficial middle cerebral vein thrombosis associated with hemorrhagic venous infarct. Due to a history of flu-like symptoms, Lung HRCT and RT-PCR for SARS-CoV-2 using an oropharyngeal/nasopharyngeal swab were performed which were positive. Anticonvulsants, LMWH, dexamethasone, antiviral, and antibiotics were promptly initiated. After 14 days of treatment initiation, fever and headache were completely subsided and she had no new episode of seizure.