

Cerebral Venous Sinus Thrombosis (CVST) in COVID 19 Pandemic

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We present a case of CVST complicating COVID19 infection in a 58 year-old female with first ever generalized tonic clonic convulsions. The patient has a past medical history of bilateral frontal lobes tumor excision, COVID 19 previous infection and recent history of COVID19 adenovirus vaccination. The first presentation and the CT Brain finding of residual encephalomalacia did not prompt further workup. However; fever with new positive PCR-SARS-COV-2, unimproved patient's conscious level and upcoming neurologic sign of lateralization mandate further brain imaging revealing cerebral venous sinuses thrombosis, cortical and subarachnoid venous haemorrhages. The evidenced hypercoagulable state associated with COVID19 infection together with the reported thrombotic-thrombocytopenic complication of adenovirus COVID19 vaccines were two important key players. Therapeutic anticoagulation was the main line of treatment.

Keywords: Cerebral Venous Sinus Thrombosis (CVST); COVID 19 Pandemic**Introduction**

Our patient meets case definition criteria for para infectious syndrome of SARS-CoV-2 infection, with evidence indicating neurologic manifestations occurring during acute infection.

Case Presentation

This is a 58 years old female with past history of bilateral frontal lobes tumors excision four years ago and residual abulia major (Akinetic mute syndrome); COVID 19 infection four months ago and COVID 19 adenovirus vaccine two weeks before presentation. Hospitalized with sudden onset of first ever generalized tonic clonic convulsions (GTCs) that lasts more than ten minutes (status epilepticus). Few hours before presentation; patient was examined by internist in the emergency room (ER) because of four days history of fever ; flu symptoms; abdominal pain and vomiting. New swab Nasopharyngeal real-time polymerase chain reaction (RT-PCR) severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was ordered with home isolation till swab result. At that time neurolog-

ical examination revealed no signs of lateralization or meningeal irritation with spontaneous eyes opening and response to painful stimuli by localization. Neurologic examination at time of admission revealed post ictal sleepiness with flaccid extremities and no response to painful stimuli without lateralization.

Uncontrasted CT brain at admission revealed bilateral residual frontal encephalomalacia of the past surgical insult. At intensive care unit (ICU); Patient received loading phenytoin 750 mg and maintenance 300 mg per day. Full blood tests profile and cultures for high fever (blood-urine and stool). Despite treatment; the patient didn't regain consciousness. On the second day of admission the PCR swab for COVID 19 was positive. This raises the suspicion of further underlying cerebral pathologies with differential diagnosis of non Convulsive Status Epilepticus (NCSE); CNS Infections; cerebral complications of COVID 19 infection like strokes (cerebral ischemia; Haemorrhage; Dural Cerebral venous sinus thrombosis (CVST); viral meningoencephalitis and acute necrotizing haemorrhagic encephalitis. Due to patient isolation; CSF tap, EEG and MRI

Brain were postponed. Blood results revealed elevated markers of infection (WBCs; LDH; ESR; CRP; Ferritin and D-Dimer). Fundus examination was normal and chest X-Ray was free of lesions. Patient received antiviral treatment favipiravir 800 mg twice daily and acyclovir 500 mg three times daily for two weeks. Empirical antibiotics of vancomycin 2 gm; cephalosporins 2 gm and dexamethasone 24 mg daily. Maintenance anti epileptics of phenytoin 300 mg and levetiracetam 2000 mg daily and prophylactic low molecular weight heparin (LMWH) enoxaparin 40 units daily. The patient conscious level was not improved with GCS 5/15 with mechanical ventilation. On the fourth day of admission; patient showed lateralizing left lower limb weakness. New uncontrasted CT Brain revealed right parietal haematoma and right sub arachnoid haemorrhage (SAH). The cortical site of the haematoma with the adjacent SAH raises the suspicion of venous haemorrhages; particularly with the rising titre of D-Dimer above 5000 and the unimproved conscious level. MRI Brain and MRV Cerebral veins were done on the fifth day and revealed bilateral cortical and subcortical infarctions on the distribution of bilateral transverse sinuses; together with the right parietal cortical haemorrhage and right SAH and bilateral attenuated transverse sinuses and left IJV decreased signal flow.

The decision at that time was to increase the dose of (LMWH) to subtherapeutic dose of enoxaparin 40 units twice daily to treat these extensive cerebral venous sinuses thrombosis (CVST). Patient received good hydration therapy with electrolytes correction for hypernatremia (Sodium level 170). In the second week the patient conscious level started to improve with GCS 8 and quadriplegia with hypotonia.

Daily blood tests revealed decreased platelets count 90.000. This raises the possibility of COVID 19 adenovirus vaccine induced thrombosis and thrombocytopenia. Despite of the current recommendation of using other LMWH than enoxaparin in such reported cases. The decision was to continue on it considering the clinical improvement of the patient and the rising sequential platelets count.

At the third week of hospital admission PCR COVID 19 swab was negative and the inflammatory markers improved with decreased D-Dimer titer.

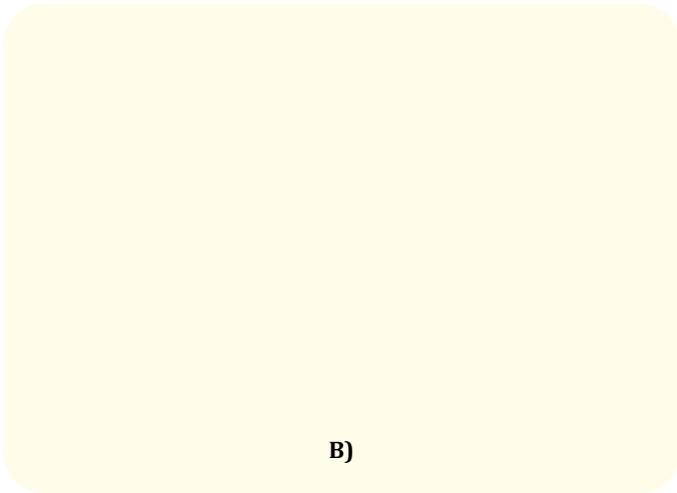
Patient clinical condition stabilized with spontaneous eye opening and flexion to pain on the right lower limb. During the next 6

weeks patient received long term care and maintained on therapeutic LMWH. New uncontrasted CT Brain showed resolved parietal haematoma and SAH. Follow up MRV cerebral veins with contrast revealed recanalization of sinuses.

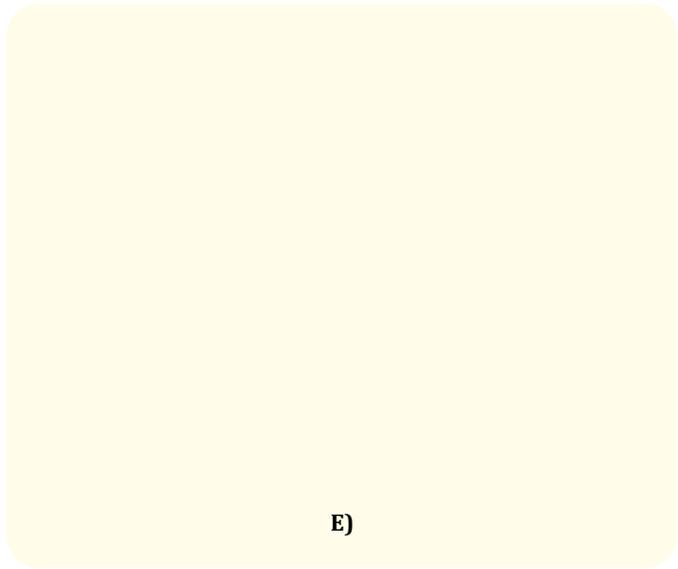
Figure 1: CT brain at admission: Residual encephalomalacia.

Figure 2: CT brain after 4 days: Right cortical haematoma and Right SAH.

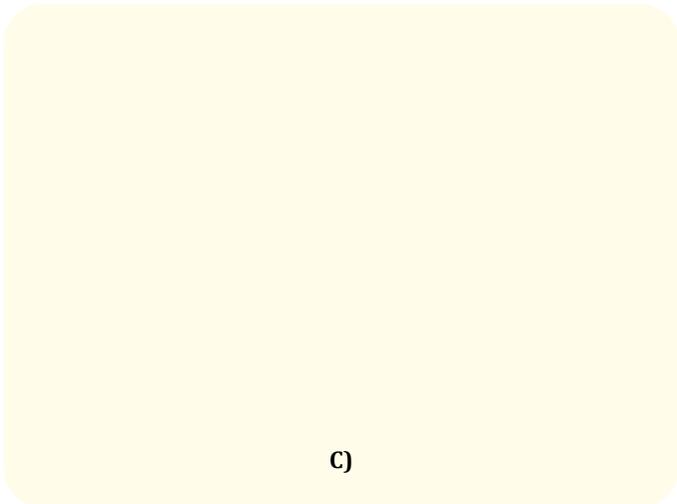
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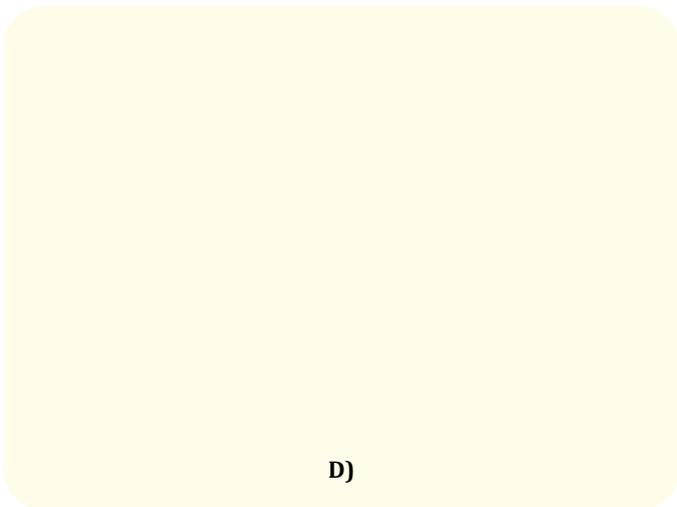
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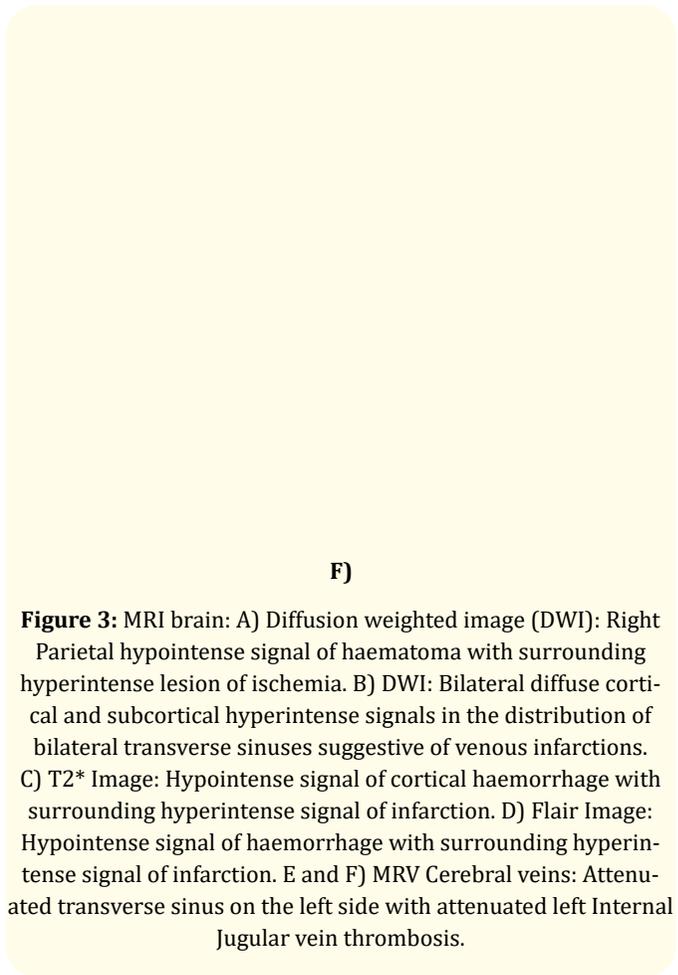
E)



C)



D)



F)

Figure 3: MRI brain: A) Diffusion weighted image (DWI): Right Parietal hypointense signal of haematoma with surrounding hyperintense lesion of ischemia. B) DWI: Bilateral diffuse cortical and subcortical hyperintense signals in the distribution of bilateral transverse sinuses suggestive of venous infarctions. C) T2* Image: Hypointense signal of cortical haemorrhage with surrounding hyperintense signal of infarction. D) Flair Image: Hypointense signal of haemorrhage with surrounding hyperintense signal of infarction. E and F) MRV Cerebral veins: Attenuated transverse sinus on the left side with attenuated left Internal Jugular vein thrombosis.

Figure 4: MRA CAs: Normal vasculature.

Figure 5: FUP CT brain after 3 weeks: Resolved right parietal haematoma.

Figure 6: Chest X-Ray and CT: No pneumonic lesions.

Figure 7: MRV Cerebral veins with contrast: Improved signal flow in the transverse sinus and IJV.

Discussion

Our patient meets case definition criteria for para infectious syndrome of SARS-CoV-2 infection, with evidence indicating neurologic manifestations occurring during acute infection. Detection of SARS-CoV-2 in nasopharyngeal swab with systemic prodromal symptoms even with the absence of pneumonic lesions are reported in the literature; 13.5% of hospitalized COVID 19 patients have neurologic manifestations [1-3].

Cerebrovascular complications of COVID-19 are likely due to altered coagulation pathways, as demonstrated by observations of elevated D-dimer and disseminated intravascular coagulation [4]. Strokes may also occur in individuals who have no risk factor other than COVID-19. Potential causes include interaction between the virus and Angiotensin converting enzyme 2 (ACE2) receptor on endothelial cells, including the cerebral vasculature and antiphospholipid antibodies [5]. In a single-center case study recruiting 219 hospitalized patients, 4.6% had ischemic stroke and 0.5% had intracerebral hemorrhage [6]. Ischemic stroke, hemorrhagic stroke, and CVST have all been reported [7,8]. Some patients may develop microhemorrhages and have other signs of microvascular injury [9-12].

Several cases of CVST and splanchnic vein thrombosis have been reported with the two vaccines that use the adeno-associated viral vector for delivery. These patients have a vaccine induced throm-

botic thrombocytopenia with antibodies to platelet factor 4. These patients should not be treated with heparin because heparin can induce such immune phenomena. Intravenous immunoglobulins (IVIg) and non heparin anti coagulation should be used [13-17].

Conclusion

Neurologic complications of COVID 19 patients can occur during the acute phase of the illness. A prothrombotic state develop and can result in occlusion of multiple arteries and the venous system simultaneously. This can be further complicated with hemorrhagic lesions. Early recognition and treatment are key to effective management of these patients.

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