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CEREBRAL VENOUS THROMBOSIS SECONDARY TO SARS-COV-2 INFECTION

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ABSTRACT

Cerebral venous thrombosis (CVT) is a relatively rare form of neurovascular emergency, and may present as headache, seizure, or focal neurological deficit. It typically has a higher occurrence in younger women. Recently, there are increasingly cases of CVT reported in association with COVID-19, which fall outside the typical demographics, suggesting a hyper-coagulable state attributable to COVID-19. Here, we present a case of CVT in a young gentleman with concomitant COVID-19, who presented with first-onset seizure.

Keywords: CVT; COVID-19; SARS-CoV-2

INTRODUCTION

COVID-19 is recognised as a multi-system disease, and neurological complications are also increasingly reported. Neurological manifestations of COVID-19 include anosmia, encephalopathy, stroke, Bell's palsy and CVT. A systematic review done in Singapore revealed an overall mortality rate of 45.5% in COVID-19 patients with CVT1. The staggering mortality rate warrants clinicians to have a high index of suspicion, and patients should be commenced on early anticoagulation therapy.

CASE STUDY

A previously healthy 34-year-old male prisoner with a history of methamphetamine abuse was witnessed to have 2 episodes of generalised tonic-clonic convulsions in the prison cell, that lasted for around 4 minutes each. He remained drowsy and had no recovery of consciousness in between these episodes. Upon arrival to the emergency department, he was found to be confused, with a Glasgow Coma Scale (GCS) of E2V2M5. Pupils were 3mm and reactive to light bilaterally. Kernig sign and Brudzinki sign were negative, and he had no documented neck stiffness. Neurological examination revealed hypertonia bilaterally with downgoing plantar responses. Muscle power assessment scored 3 over all four limbs according to the MRC scale, and the reflexes were normal. Fundoscopy was not able to be done due to the constraints of the personal protective equipment worn by the healthcare worker. There was otherwise no fever or abnormal respiratory signs, neither was there any symptoms suggestive of raised intracranial pressure. He had been incarcerated for 6 months and there was no methamphetamine abuse during this period. Chest radiograph was normal. As the initial laboratory tests (Table 1) showed raised white cell count of 18.55 x 109/L, C-reactive protein of 30.8 mg/L, creatinine of 132 μmol/L, a markedly raised creatinine kinase of 37, 654 U/L, lactate of 14.3 mmol/L, pH of 7.02 and glucose of 21.1 mmol/L, he was treated empirically as meningoencephalitis, in addition to intravenous phenytoin for seizures.

Table 1: Relevant investigations chart of the patient

Parameters	28/1/21	29/1/21	30/1/21	14/2/21	19/2/21	Unit	Normal range
White cell count	18.55				7.41	10^9/L	4 - 10
Haemoglobin	16.4				15.1	g/dL	13 - 18
Platelet	388				300	10^9/L	150 - 400
Haematocrit	48.1				44.7		40 - 54
Sodium	139	142			137	mmol/L	135 - 145
Potassium	4.6	5.3			4.2	mmol/L	3.5 - 5
Urea	6.3	5.3			4.2	mmol/L	2.8 - 7.8
Creatinine	132.3	97.6			72.0	µmol/L	90 - 110
Total bilirubin	7.6				4.7	µmol/L	0 - 17.1
Albumin	50				39	g/L	34 - 48
ALT	13				85	U/L	<40
AST	50				46	U/L	1 - 38
C-reactive protein	30.8	53.4	31.9	2.8		mg/L	<10
Lactate	14.3					mmol/L	0 - 2
Creatinine kinase	37654		15636	106		U/L	22 - 198
PT	10.3				23.5	seconds	10.7 - 13.8
aPTT	31.5					seconds	24.6 - 37.5
INR	1.01				2.40		1 - 1.5
Fibrinogen		522				mg/dL	200 - 400
D-dimer		0.57				µg/dL	<0.5
pH	7.02	7.32	7.41				7.35 - 7.45
pCO2	66	31	36				
pO2	37	90	48				
HCO3	9.6	18	22.8			mmol/L	22 - 28
BE	-20.9	-8.8	-1.8				
SO2	96%	96%	84%				
HIV serology			Non-reactive				

The significantly raised creatinine kinase level, coupled with the severe lactic acidosis, were attributed to the convulsive episodes. In view of the COVID-19 outbreak situation in the prison, SARS-CoV-2 nasopharyngeal swab RT-PCR was done, where it was initially negative. An urgent computed tomography (CT) brain done was reported as normal. Cerebrospinal fluid (CSF) analysis demonstrated xanthochromia, low opening pressure, a raised protein of >2 g/L, a normal glucose ratio of 0.9, negative culture and acid-fast bacilli (AFB). CSF differential cell count was unable to be tested due to the suspected COVID-19 status, in accordance to local hospital policy. The CSF was subsequently negative for SARS-CoV-2 on RT-PCR test. Antibiotic was subsequently discontinued after blood and CSF cultures came back as negative.

Based on abnormal CSF analysis with xanthochromia, a contrasted CT brain was done on day 6 of admission, and CT venogram revealed an extensive superior sagittal sinus thrombosis (Figure 1). He was fully anticoagulated with subcutaneous enoxaparin and warfarin. He responded clinically as he regained full GCS with seizure resolution since day 7 of admission.

He was subsequently kept inpatient for optimisation of anticoagulation. A repeated SARS-CoV-2 nasopharyngeal swab RT-PCR via the Allplex 2019-nCoV Assay on day 12 was then found to be positive, with a cycle threshold (CT) values of E gene 38.90, Rdrp 33.52, and N gene 31.29. His neurological examination returned to normal at the time of discharge on day 23. He was discharged well, and we anticipate continuing anticoagulation for 6 months due to its extensive nature. His thrombophilia panel was not screened during this admission and was planned to be done once anticoagulation therapy is completed.

DISCUSSION

Despite previously thought to be a rare clinical entity, CVT has been increasingly reported. The clinical presentation of CVT can vary from mild acute headache to severe status epilepticus and death. The diagnosis can be difficult as the symptoms may mimic other neurological syndromes; hence, CT venogram should be done in any patient with suspicion of CVT.

As the COVID-19 pandemic develops, several studies have reported significant risks of arterial and venous thrombosis;[2] however, the reports on CVT in the context of COVID-19 are still sparse. The mechanism behind it is now beginning to come to light as it is currently thought that the expression of ACE2 receptors on the endothelial cells in multiple organ systems facilitates virus uptake into cells, 3 leading to endotheliitis. The cytokine abnormalities further lead to inflammation and hyper-coagulopathy.4

Neurological manifestations are thought to revolve around inflammatory processes, as although SARS-CoV-2 can be detected in the brain via RT-PCR, its rarity implied immune-mediated processes, rather than directly infecting neurons.5

In most of the case reports found in current literature, the COVID-19 infection preceded the symptoms of CVT. However, it was the direct opposite from what we demonstrated in this case. This implies that the hyper-coagulopathy effect may possibly occur even prior to the overt symptoms of the disease, although more studies are necessary to support this observation. In addition, the case presented here did not display any respiratory symptoms related to COVID-19, thus indicating that the hyper-coagulable state may be present even in mild or asymptomatic infection, highlighting the occurrence of CVT in COVID-19 infection across the spectrum of severity.1

Management of CVT include anticoagulation, thrombolysis or percutaneous venous mechanical thrombectomy. However, the optimal choice of anticoagulant and duration of treatment for COVID-19 related CVT remains uncertain, as the data to make definite recommendations remains limited currently.

CONCLUSION

COVID-19 is associated with a hyper-coagulable state. CVT in the context of COVID-19 can be potentially life-threatening and our case highlighted the importance of having a high index of suspicion in patients presenting with headache, encephalopathy, or seizures, since starting early anticoagulation therapy is lifesaving. At present, there is insufficient evidence to support optimal treatment and more studies are needed to address this.

Conflicts of interest

The authors have no potential conflicts of interest to disclose.

Ethical approval

The authors have obtained the informed written consent for writing and publishing this article from the patient.

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