Severe Headache, Seizures and Supraventricular Tachycardia in a 33-year-old Filipino Male with Confirmed COVID-19: A Case Report

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ABSTRACT

COVID-19 primarily presents as a pulmonary problem, ranging from mild respiratory illness to fatal acute respiratory distress syndrome. Most common manifestations are fever (89%) and cough (72%), while headache and arrhythmia are found in 28% and 17%, respectively. We aim to present a confirmed COVID-19 case presenting with both neurologic and cardiac manifestations.

A 33-year-old Filipino male nurse initially consulted at the emergency room due to progressive diffuse headache, with associated localized seizures progressing to generalized tonic clonic seizure and arrhythmia. He had no coryza, cough, sore throat, and diarrhea. He was previously well and had no known co-morbidities or direct exposure to confirmed COVID-19 patients. Physical examination showed elevated blood pressure, tachycardia, and sensory and motor deficits in the left upper and lower extremities.

Pertinent diagnostic test results included the detection of SARS-CoV-2 viral RNA via RT-PCR. Imaging studies demonstrated cortical venous thrombosis with hemorrhagic venous infarction in the right parietal lobe. Ground glass appearance on the middle lobe of the left lung was also evident. ECG showed supraventricular tachycardia. Prothrombin time, activated partial thromboplastin time, and D-dimer were all within the normal limits. Carotid massage was done. He was treated with anti-epileptics, anticoagulants, antiarrhythmics, antivirals, antibiotics, and supportive management. During the hospital stay, his symptoms resolved; he was discharged after 21 days. Follow-up done after 3 weeks revealed no recurrence of severe headache, seizure, or tachycardia.

It is theorized that an interplay exists between ACE-2 tropism, systemic inflammation, cytokine storm, and hypoxemia in the background of COVID-19 infection. These mechanisms may lead to thrombosis and arrhythmia resulting to neurologic derangements and myocardial injury.

Underlying mechanisms make the cerebro-cardiovascular systems vulnerable to the coronavirus disease 2019 infection. COVID-19 should therefore be part of the differential diagnoses in patients presenting with headache, seizures, and arrhythmias.

Keywords: COVID-19, headache, seizure, supraventricular tachycardia

INTRODUCTION

Coronavirus disease 2019 (COVID-19) has emerged as an overwhelming illness due to its rapid spread and its propensity to cause serious complications and mortality. With severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as its causative agent, its clinical presentation is primarily pulmonary, ranging from a mild respiratory illness to a fatal acute respiratory distress syndrome. In a meta-analysis comprised of ten studies from China, the most common recorded initial manifestations are fever

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(89.1%) and cough (72.2%).[1] Nevertheless, there are recent reports on COVID-19 patients exhibiting extrapulmonary manifestations.

A study done in Wuhan, China involving 214 COVID-19 patients showed neurologic symptoms in 36.4%. Among these symptoms, dizziness (36%) ranked first, followed by headache (28%).[2] Noted complications include encephalopathy, acute cerebrovascular diseases, and impaired consciousness.[3]

On the other hand, cardiovascular involvement has been recorded in the setting of COVID-19. Arrhythmia is recognized as one of the manifestations observed in 16.7% among 138 patients.[4] In addition, Wang reported arrhythmia as a cause of ICU transfer in 44.4% of COVID-19 patients.[5] Proposed mechanisms of both neurologic and cardiovascular involvement include direct injury to target organs, hypoxia leading to ischemia, immune injury resulting from cytokine storm, and the role of angiotensin-converting enzyme 2 present in the brain and the heart.[6]

There is increasing literature regarding COVID-19's cardiovascular and neurologic manifestations as separate entities. However, cases affecting both organ systems simultaneously are not adequately reported. This paper aims to present a confirmed COVID-19 case presenting with both neurologic and cardiac manifestations.

CASE PRESENTATION

A 33-year-old male, nurse, from Baguio City, presented at the emergency room with an 8-day history of progressive occipital headache, not relieved by non-steroidal anti-inflammatory drugs, and associated with focal seizures of the left upper and lower extremities, progressing to a 1-minute generalized tonic clonic seizure. Coryza, cough, sore throat, or diarrhea were absent. He had no previous seizure episodes and had no known co-morbidities. Direct exposure to confirmed COVID-19 patients was absent. He was a regular alcoholic beverage drinker and a previous smoker for 5 pack years, who stopped 2 years ago.

Upon examination post-ictal, he was tachycardic at 167 beats per minute, with elevated blood pressure of 160/100 mmHg, but was afebrile. Examination of the left extremities demonstrated 4/5 muscle strength and sensation of 70%. The patient also had neck rigidity. The rest of the general and neurologic findings were unremarkable.

Investigations

Results of the pertinent diagnostic tests are shown in Table 1. SARS-CoV-2 Viral RNA via real time polymerase chain reaction was detected on admission. C-reactive protein was elevated and arterial blood gas showed uncompensated metabolic acidosis with more than adequate oxygenation. The rest were within normal limits.

Cranial CT scan conveyed hemorrhagic venous infarction in the right parietal lobe (Figure 1A). CT venogram showed cortical venous thrombosis on the right parietal area (Figure 1B). Chest radiograph suggested a pneumonic process on the left lower lobe, while chest CT scan was evident of ground glass opacity in the medial segment of the middle lobe (Figure 1C). ECG displayed supraventricular tachycardia at 167 beats per minute (Figure 1D). Two-dimensional echo-cardiography done prior to discharge showed normal results.

Treatment

Seizures were controlled with levetiracetam and diazepam as needed. For anticoagulation, enoxaparin was started, which was bridged to warfarin, and eventually shifted to dabigatran. Probable concomitant bacterial CNS and pulmonary infections were covered with vancomycin, ceftriaxone, and azithromycin.

Supraventricular tachycardia was managed with carotid massage initially, then adenosine was loaded which controlled the heart rate. The patient was later maintained on metoprolol.

The following COVID investigational drugs were also administered: hydroxychloroquine, oseltamivir, lopinavir + ritonavir, and melatonin. Supportive management was provided through correction of acidosis, pain relief, immune support, and adequate hydration. Oxygen inhalation via nasal cannula was given and weaned off as tolerated.

Outcome and Follow-up

There was no recurrence of seizure or tachycardia, but the patient had episodes of tolerable headache. He regained normal muscle strength and sensation of affected limbs and there was resolution of neck rigidity. He was discharged after 21 days. Follow-up after 3 weeks revealed no recurrence of severe headache, seizure, or tachycardia. Figure 2 depicts the timeline of the patient's disease course.

DISCUSSION

Our patient exhibited a progressive diffuse headache, associated with focal and generalized tonic clonic seizures, early in the disease progression. A study done in Wuhan, China stated that out of 214 patients, 13.1% had headaches, while 0.5% had seizures.[2] Unfortunately, these studies did not expound on the specific characteristics of the said manifestations. COVID-19 can be linked with anaerobic metabolism in the neuronal mitochondria due to impairment in gas exchange. Acid accumulation can therefore lead to cerebral vasodilation, causing headache.[6] Seizures, on the other hand, are proposed to be due to the neuro-invasive propensity of SARS-CoV-2 to enter glial cells and neurons which express angiotensin-converting enzyme 2 (ACE-2).[7] The medical community is still attempting to fully understand the neurologic syndromic complexity of COVID-19.[8] It is therefore recommended for future studies to look into other possible mechanisms for neurologic involvement in order to unravel more definite targets for treatment.

Table 1. Summary of diagnostic test results

Parameter	Result	Reference Range	Unit
ESR	12 (HIGH)	0-10	mm/hr
Procalcitonin	0.09	0.5-2.0	ng/ml
Ferritin	604.8 (HIGH)	4-341.2	ng/ml
CRP	63.58 (HIGH)	<1	mg/L
Blood Culture *(2 sites)*	No microorganism		
Complete Blood Count			
Hemoglobin	167	140-180	g/L
Hematocrit	26	0.40-0.54	L/L
WBC	9.67	5.0-10.0	10^9/L
Neutrophils	66	50-70	%
Lymphocytes	26	20-40	%
Monocytes	5	0-10	%
Eosinophils	3	0-7	%
Basophils	0	0-1	%
Platelet	238	150-400	10^9/L
Coagulation Studies			
PT	11.5	11-14	sec
INR	1		
%Act	95		
APTT	27.7	24.8-34.4	sec
D-dimer	<0.50	0.19	ug/mL
Transaminases			
AST	23.58	<50	U/L
ALT	36.66	<50	U/L
Serum Electrolytes			
Sodium	140.67	135-145	mmol/L
Potassium	3.64	3.5-5.1	mmol/L
Ionized calcium	1.56	1.1-1.4	mmol/L
Magnesium	0.93	0.73-1.06	mmol/L
Creatinine	104.37	64-104	Umol/L
Thyroid Stimulating Hormone	2.261	0.3-3.6	mIU/mL
Arterial Blood Gas			
pH	7.29 (LOW)	7.35-7.45	
pCO_2	17.3 (LOW)	35-45	mmHg
pO_2	154.1 (HIGH)	80-100	mmHg
HCO_3	8.3 (LOW)	22-26	mmol/L
SO_2	98.9		%
FiO_2	60		

Although CT venogram performed in our patient revealed an underlying cortical venous thrombosis, we are uncertain if the COVID-19 infection preceded this thrombosis. Similarly, Hughes reported a case of cerebral venous sinus thrombosis, as a presentation of COVID-19 in a 59-year-old male in Wales.[9] Many studies demonstrate that the behavior of clotting variables and platelet count in COVID-19 is suggestive of a hypercoagulation state. A case series performed by Cavalcanti et al. described cerebral venous thrombosis in relation to COVID-19. The authors associated coagulopathy with endothelial cell dysfunction leading to thrombin generation and inhibition of fibrinolysis. Also, they attributed thrombotic events to hypoxemia resulting in blood viscosity elevation and activation of genes mediating coagulation and fibrinolysis.[10] Moreover, the viral infection itself results to a severe inflammatory response resulting in a cytokine storm inducing a pro-coagulable state.[11] NoX2, the most important enzyme generating reactive oxidant species (ROS) elicited by several RNA viruses, is implicated in both clotting and platelet aggregation. However, data regarding NoX2 in SARS-CoV-2 is still lacking.[12] It is therefore recommended for further investigation on the possible role of NoX2 in SARS-CoV-2 infection.

Viral myocarditis was considered as a cause of the patient's supraventricular tachycardia, although histological evidence associated with positive viral polymerase chain reaction

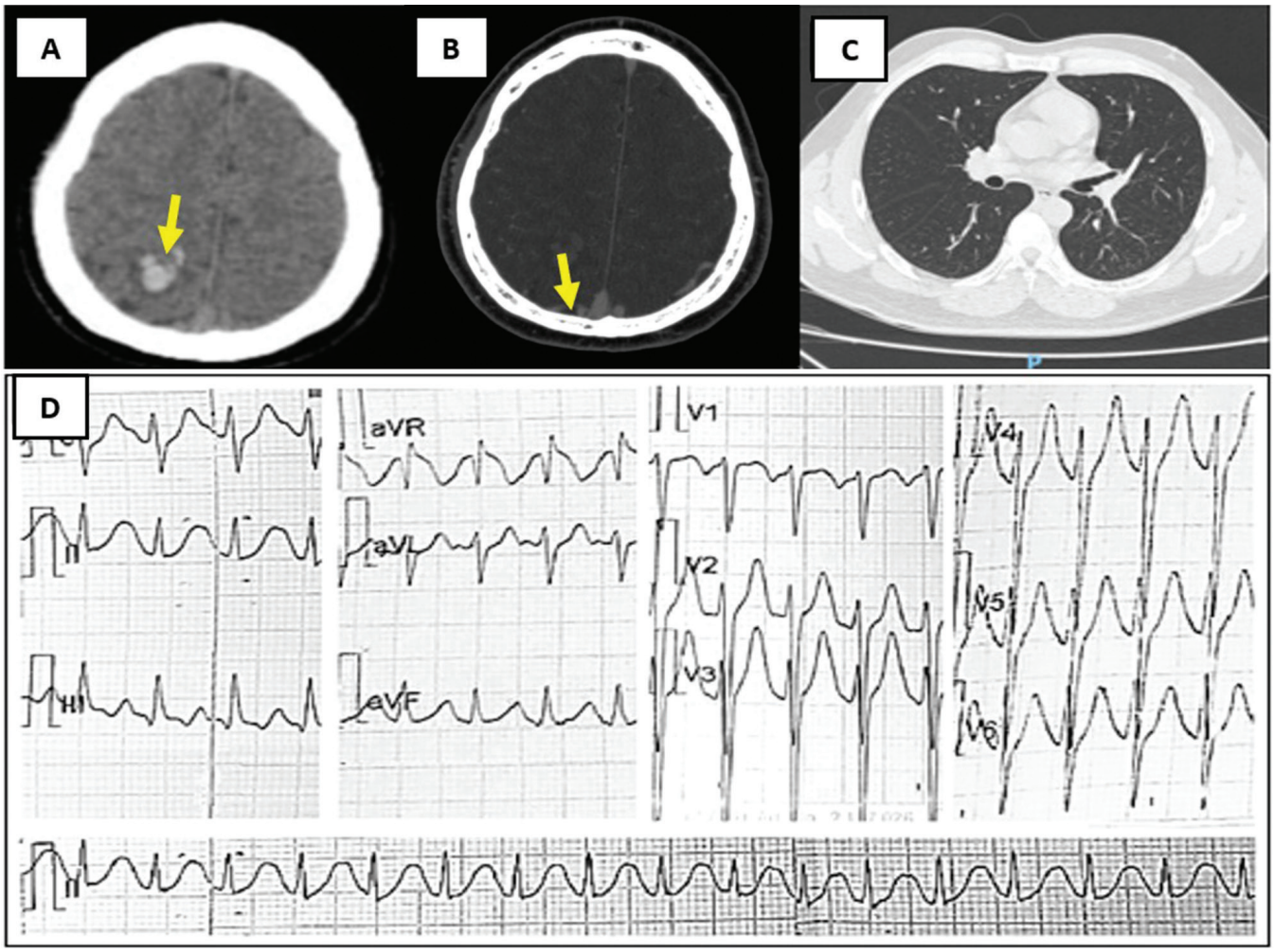

Figure 1. **(A)** CT image of acute blood attenuation in the right parietal lobe, approximately ±3 cc. **(B)** CT venogram image of a filling defect in a superficial vein in the right parietal region. **(C)** HRCT showing ground glass opacity in the middle lobe of the right lung. **(D)** ECG showing supraventricular tachycardia at 167 beats per minute.

was not obtained. The actual prevalence of arrhythmia in COVID-19 patients remains unknown. However, a study in Hubei, China reported a 7.3% incidence of palpitations among 137 patients.[13] Studies show that the nature of arrhythmias could be secondary to an underlying electrolyte imbalance or in the context of myocarditis. Possible pathophysiologic explanations include direct injury to cardiomyocytes disrupting electrical conduction, infection of the pericardium causing massive edema, ischemia from microvascular disease due to infection, re-entrant arrhythmia due to myocardial fibrosis, and pro-inflammatory cytokines predisposing to arrhythmogenicity.[5] Although additional investigations are on-going, many authors recommend adequate assessment of the cardiovascular system through serial ECG and cardiac biomarkers in patients with COVID-19.

At present, there are no existing local guidelines in the management of seizure or arrhythmia among COVID-19 patients. Nevertheless, guidelines on anticoagulation have been stated for oxygen requiring COVID-19 patients.[1] As evidence of neurologic and cardiovascular affection in the setting of COVID-19 may increase, it is imperative for the Philippines to derive a set of guidelines pertaining to this, adapting the demands and resources of the locality.

Similar to the case reported by Hughes, our patient did not have a complicated course in the ward and was discharged improved. Data on the clinical outcomes of COVID-19 patients presenting with concomitant neurologic and cardiac manifestations are scarce. Nonetheless, poor outcome is related to elevated D-dimer, prothrombin time prolongation, and low platelet count.[12] Definite conclusions for appropriate prognostication in these types of patients cannot be derived, necessitating further studies on the matter.

To our knowledge, this is the first case of COVID-19 infection presenting primarily as headache and seizure with concomitant supraventricular tachycardia in the Philippines.

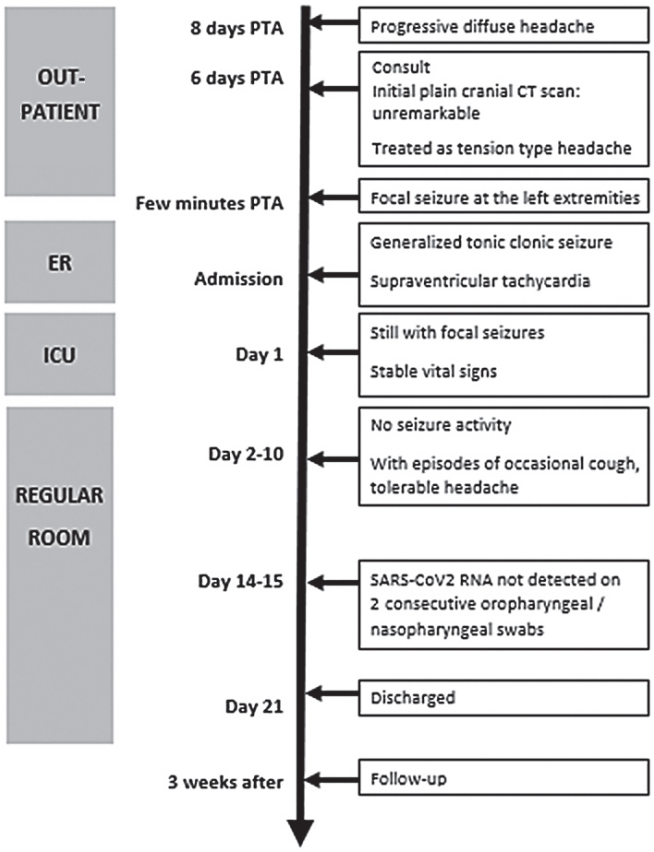

Figure 2. Timeline of progress of patient's condition.

CONCLUSION AND RECOMMENDATION

This case demonstrates an uncommon presentation of the coronavirus 2019 infection. COVID-19, which was known to be primarily a respiratory disease, can initially present with atypical manifestations. A high index of clinical suspicion for COVID-19 is therefore necessary in the evaluation of patients with neurologic and concomitant cardiac complaints in order to avoid delay in diagnosis, treatment, and prevention of further transmission of this viral infection.

As this report contain information that need further verification, additional studies and researches are highly recommended.

Statement of Authorship

All authors contributed to the conceptualization of work, acquisition and analysis of data, drafting and revising, and approval of the final version submitted.

Author Disclosure

All authors declared no conflicts of interest.

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