Viral Myopericarditis and Viral Encephalitis as manifestations of COVID-19 infection: A Case Report

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Abstract

Introduction: Coronavirus disease (COVID-19) is currently a global health crisis and is caused by a new strain of coronavirus. However, emerging literature of case reports noted possible extrapulmonary manifestations of the disease. Because COVID 19 is a relatively new disease, at present, little existing literature tackles the diagnosis and therapeutic management of COVID-19-related conditions outside the pulmonary system.

Case: A 24-year-old male presented with sudden stiffening of all extremities but non-contrast computed tomography (CT) scan was unremarkable. Chest X-ray revealed interstitial pneumonia and SARS-CoV-2 RT-PCR (OPS/NPS) was positive. Electrocardiogram (ECG) findings showed supraventricular tachycardia and had elevated Troponin I levels. Pertinent physical findings noted were slurring of speech, dysmetria, and vertical nystagmus. The patient was initially treated as a case of Bacterial Abscess versus Viral encephalitis. Pericardial ultrasound revealed small pericardial effusion and was started on Colchicine. Repeat cranial CT scan noted unremarkable results but due to persistence of symptoms, the patient was started with Dexamethasone. On Day 16 of illness, the patient was noted to have full resolution of symptoms. Rapid antibody testing was done which revealed positive for both IgG and IgM hence the patient was discharged with the final diagnosis of Viral Myopericarditis resolved, Viral encephalitis resolved, COVID-19 pneumonia recovered.

Conclusion: Extrapulmonary manifestations have been reported increasingly as an atypical presentation of COVID 19 infection. Early recognition of viral myopericarditis and viral encephalitis as a manifestation of COVID 19 can lead to the initiation of proper treatment and management. More reports on these cases can aid future studies on diagnostics and therapeutic approaches during the COVID-19 pandemic.

Keywords: covid19, viral myocarditis, viral encephalitis, case report, COVID-19, SARS-COV-2, coronavirus infection

Introduction

The coronavirus disease (COVID-19) is currently a global health crisis and is caused by a new strain of coronavirus. None was known regarding this disease before the outbreak in Wuhan, China last December 2019.¹ Most of the patients infected with COVID-19 present with respiratory symptoms. According to the World Health Organization, the most common symptoms are dry cough, tiredness, and fever. However, emerging literature of case reports noted a possible extrapulmonary manifestation of the disease.

Because COVID-19 is a relatively new disease, at present, little existing literature tackles the diagnosis and therapeutic of COVID-19-related conditions outside the pulmonary system. The common systems associated with the deleterious effect of this virus studied are neurologic, cardiovascular, hematologic, renal, gastrointestinal, hepatobiliary, endocrinologic, and dermatologic. ² With these in mind of potential other organ involvement of this new disease, early recognition of these conditions is deemed important to implement individualized treatment approaches. Although the proposed pathogenesis of these occurrences has been discussed, case reports of such conditions were usually limited to one organ involvement. In this case report, we present a 24-year-old male with neurologic and concomitant cardiac manifestations of COVID-19.

Case Report

This is a case of Y.Z, a 24-year-old male who initially presented with a generalized tonic-clonic seizure. The patient's condition started six days prior to admission, he experienced involuntary stiffening of upper and lower extremities associated with upward rolling of eyeballs lasting for approximately 5 minutes in duration. There was also documented febrile episode of 40°C and was subsequently brought to another hospital where he had another episode of stiffening of all extremities, with the same character as before, hence admitted. There were no associated symptoms reported such as body weakness, postictal confusion, disorientation, headache,

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Gnilo, Amorado-Santos and Cruzat

or loss of consciousness. There were no aggravating factors or other symptoms reported like cough, chest pain, dyspnea, or vomiting. Chest X-ray revealed interstitial pneumonia hence, SARS-CoV-2 RT-PCR (OPS/NPS) test was done which yielded a positive result. Non-contrast Cranial CT scan was also requested, which was unremarkable. Initial ECG findings showed supraventricular tachycardia with elevated Troponin I and C-reactive protein. The patient was managed as bacterial meningitis, viral myocarditis, and COVID-19 pneumonia. He was treated with ceftriaxone 2gms intravenously (IV) once a day, azithromycin 500mg tablet once a day, trimetazidine 35 mg tablet twice daily as well as dexamethasone 6mg tablet once a day for COVID-19 pneumonia, severe. During his 3rd hospital day, the patient was noted to have slurring of speech and complained of rotatory dizziness. The patient had stable vital signs, and a repeat 12L ECG revealed anterolateral wall ischemia. The patient was transferred to our institution due to financial constraints. The patient has no known comorbidities and heredofamilial diseases. He was a military trainee who has recent travel history to Canlubang, Laguna for 24 days and to Calatagan, Batangas for 10 days before the onset of symptoms. He is a non-smoker, an occasional alcoholic beverage drinker (one to two bottles of beer twice per month), and denies illicit drug use. The patient denied exposure to any COVID-19 confirmed case or symptomatic patient.

The pertinent physical findings noted were slurring of speech, dysmetria, and vertical nystagmus. The patient was then managed as a case of Bacterial Abscess versus Viral encephalitis hence, antibiotics shifted to Cefepime 2gms IV q8 and metronidazole 500mg IV q6. Lumbar tap was not done due to the consideration of a probable bacterial abscess. Pericardial ultrasound revealed pericardial effusion at the posterior pericardial space with the greatest thickness of 0.9 cm and thus was started with Colchicine 0.5mg tablet once a day. Repeat cranial CT scan noted unremarkable results. Due to the persistence of slurring of speech, dysmetria, and vertical

Myocarditis and Encephalitis in COVID-19

nystagmus, the patient was restarted with Dexamethasone 6mg IV once a day. On the 8th hospital day (Day 16 of illness), the patient was fully awake, conversant, and had complete resolution of signs and symptoms. Rapid antibody testing was done which revealed positive for both IgG and IgM hence the patient was discharged and to complete isolation at home with the final diagnosis of Viral Myopericarditis resolved, Viral encephalitis resolved, COVID-19 pneumonia, recovered.

On follow-up after one month, the patient had stable vital signs and had no recurrence of seizures at home. He also denies dizziness, body weakness, or slurring of speech and denies any limitations of physical activity. 2D echocardiography was also done which showed normal left ventricular dimension with normal contractility and systolic function, mild mitral regurgitation, and tricuspid regurgitation. The patient was then advised for follow-up if with problems.

Figure 1 shows the course of hospitalization of the patient, which includes the diagnostics and management done from the onset of symptoms to his discharge and follow-up. Informed consent was provided by the patient.

Discussion

COVID-19 is a novel infection that recently affected the globe. The most common organ system affected by the virus is the pulmonary system.³ Although most cases of COVID-19 infection present with pulmonary symptoms, the extent of the disease has reached beyond the pulmonary system and has involved other systems as well. Several mechanisms have been studied to determine the cause of these manifestations in COVID-19. The pathophysiology of COVID-19 revolves around possible mechanisms: Renin-angiotensinthese aldosterone system (RAAS) dysregulation, direct cytotoxic effect, dysregulated immune response, and endothelial cell and thromboinflammation. These are also the possible mechanisms that may explain the pathophysiologic process of SARS-COV-2 infection

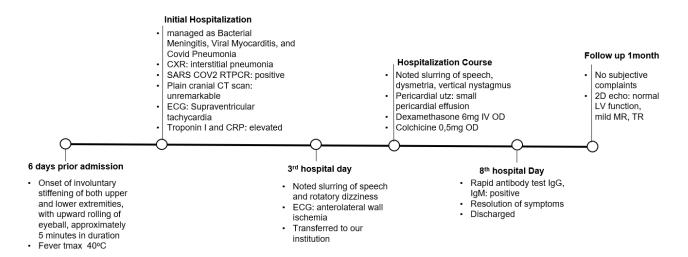


Figure 1. Timeline of the patient's course from onset of symptoms until follow-up

affecting multiple systems at once. However, these mechanisms are currently not fully understood.²

SARS-CoV-2 can affect the cardiovascular system causing direct and indirect sequelae such as cardiac arrhythmias, myocardial injury, myocarditis, heart failure, and even cardiac arrest.³ In this case, involvement of the myocardium due to possible viral myopericarditis was suspected due to the history of cardiac arrhythmia, supraventricular tachycardia, and pericardial effusion. Even though human coronavirus is a minor cause of viral myocarditis, it has been associated with patients with myocarditis, in varying age groups. Cardiotropism has also been observed since viral RNAs of both MERS-CoV-2 and SARS-CoV, which are closely linked to SARS-CoV-2 were seen in the heart tissues of diseased animals. One of the proposed mechanisms involves direct cardiac myocyte toxicity associated with direct viral injury because of binding affinity for the ACE-2 receptor in myocardial cells. Another possibility is cytokine storm or systemic inflammatory response syndrome as a setting for myocardial injury.6

Myocarditis, recognized as one of the possible extrapulmonary manifestations of COVID-19, may often lead to complications such as arrhythmia. The possible mechanism of supraventricular tachycardia is due to cardiomyocyte injury when SARS-CoV-2 gains entry into cardiomyocyte via ACE2 receptor, disrupting the electrical conduction in the heart, re-entrant arrhythmias due to myocardial fibrosis or scars, and also arrhythmogenicity due to cytokines. Further infection of the pericardium leads to pericardial inflammation which could also explain the pericardial effusion while ischemic changes in ECG may result from microvascular ischemia due to damage of SARS-CoV-2 to pericytes around the cardiac microvasculature. Despite these, the prevalence of COVID-19 related myocarditis remains unclear.⁶ In one systematic review of patients with COVID-19 related myocarditis, the majority of patients survived to discharge and most of them have received steroid therapy along with other treatment strategies such as immunoglobulin therapy and colchicine. Others were given tocilizumab and interferon for cytokine storm.⁷

The neurologic complications in COVID-19 have been increasingly reported. Clinical manifestations include dizziness, headache, hypogeusia, and hyposmia, more serious disorders are cerebrovascular disease, polyneuropathy, and rarely encephalitis.⁸ The neurologic involvement may be due to the direct access of SARS-CoV-2 to the central nervous system via viral invasion of neural parenchyma through entry to the nasal mucosa, and olfactory bulb.² Diagnosis is often pathological but clinical evaluation may be used in terms of CSF findings, imaging changes, or electroencephalogram abnormalities. However, it is important to note that the presence of the virus in cerebrospinal fluid does not provide a diagnosis of encephalitis especially if no brain inflammation is detected.9

Various case reports on the neurologic manifestation of COVID-19 have also been published. Similar to this case,

one report noted complete resolution of symptoms after supportive management after 11 days hence a possible self-limited course was entertained.¹⁰ Another report noted symptoms of tremor, gait instability, and dysmetria in which was associated with a possibility of mild encephalopathy with a reversible splenial lesion in which the patient was treated with favipiravir, steroid, meropenem, and ciclesonide.¹¹ In an ENCOVID Multicenter study, 25 cases out of 45 screened of encephalitis were positive for SARS-CoV-2 infection. Based on data collated in this study, they have estimated an incidence of at least 58/100,000 COVID-19 related encephalitis cases.¹² Treatment of COVID - 19 related encephalitis is mainly supportive. Some patients experience persistence of neurological dysfunction despite resolution of acute illness while others may have complete resolution of symptoms.^{10,13}

Our patient, a 24-year-old male, presented with stiffening of both extremities. Other salient features present are dizziness, cardiac arrhythmia, vertical nystagmus, and cerebellar ataxia. The patient was diagnosed with a COVID-19 infection. Myocarditis was suspected in this case as it fulfilled the criteria for clinically suspected myocarditis which are unexplained arrhythmia symptoms as well as supraventricular tachycardia.⁴ New onset of pericardial effusion, ECG abnormalities, and the absence of any other cause also led to a diagnosis of possible pericarditis.⁵ On the other hand, the presence of seizure, dizziness, and nystagmus in a COVID-19 confirmed patient indicates neurologic involvement in the form of possible viral encephalitis. Encephalitis was considered in this case due to generalized seizure not fully relatable to a preexisting seizure disorder as well as new onset of neurologic findings.¹⁴ Likewise, focal probable encephalitis in a COVID-19 patient was considered because of the detection of SARS-CoV-2 in the respiratory sample and because no other explanatory pathogen or cause was found. The presence of these signs and symptoms without any other possible cause and in the background of a confirmed COVID-19 signifies involvement of the cardiovascular and nervous system secondary to COVID-19 infection. The treatment was supportive including colchicine mainly and dexamethasone. Interestingly, there was complete resolution of neurologic symptoms on Day 16 of illness which may lead to an assumption of a self-limited course of the disease.

Conclusion

Despite the serious pulmonary complications of COVID-19, extrapulmonary manifestations have been reported increasingly throughout the world. Early recognition of viral myopericarditis and viral encephalitis as a manifestation of COVID-19 can lead to the initiation of proper treatment and management. More reports on these cases can aid future studies on diagnostics and therapeutic approaches during the COVID-19 pandemic.

Conflict of Interest: None

Gnilo, Amorado-Santos and Cruzat

Myocarditis and Encephalitis in COVID-19

References

- 1. Mackenzie JS, Smith DW. COVID-19: a novel zoonotic disease caused by a coronavirus from China: what we know and what we don't. Microbiology Australia. 2020;41(1):45.
- Gupta A, Madhavan MV, Sehgal K, Nair N, Mahajan S, Sehrawat TS, Bikdeli B, Ahluwalia N, Ausiello JC, Wan EY, Freedberg DE, Kirtane AJ, Parikh SA, Maurer MS, Nordvig AS, Accili D, Bathon JM, Mohan S, Bauer KA, Leon MB, Krumholz HM, Uriel N, Mehra MR, Elkind MSV, Stone GW, Schwartz A, Ho DD, Bilezikian JP, Landry DW. Extrapulmonary manifestations of COVID-19. Nature Medicine. 2020;26(7):1017–32.
- Johnson KD, Harris C, Cain JK, Hummer C, Goyal H, Perisetti A. Pulmonary and Extra-Pulmonary Clinical Manifestations of COVID-19. Frontiers in Medicine. 2020;7.
- 4. Caforio AL, Pankuweit S, Arbustini E, Basso C, Gimeno-Blanes J, Felix SB, Fu M, Heliö T, Heymans S, Jahns R, Klingel K, Linhart A, Maisch B, McKenna W, Mogensen J, Pinto YM, Ristic A, Schultheiss HP, Seggewiss H, Tavazzi L, Thiene G, Yilmaz A, Charron P, Elliott PM.Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. European Heart Journal. 2013;34(33):2636–48.
- Imazio M, Trinchero R. Triage and management of acute pericarditis. International Journal of Cardiology. 2007;118(3):286–94.
- Siripanthong B, Nazarian S, Muser D, Deo R, Santangeli P, Khanji MY, Cooper LT Jr, Chahal CAA. Recognizing COVID-19– related myocarditis: The possible pathophysiology and proposed guideline for diagnosis and management. Heart Rhythm. 2020;17(9):1463–71.

- Sawalha K, Abozenah M, Kadado AJ, Battisha A, Al-Akchar M, Salerno C, et al. Systematic Review of COVID-19 Related Myocarditis: Insights on Management and Outcome. Cardiovascular Revascularization Medicine. 2021; 23:107–13.
- Tsivgoulis G, Palaiodimou L, Katsanos A, Caso V, Köhrmann M, Molina C, Cordonnier C, Fischer U, Kelly P, Sharma V, Chan A, Zand R, Sarraj A, Schellinger P, Voumvourakis K, Grigoriadis N, Alexandrov A, Tsiodras S. Neurological manifestations and implications of COVID-19 pandemic. Therapeutic Advances in Neurological Disorders. 2020; 13:175628642093203.
- 9. Ellul, M., Benjamin, L., Singh, B., Lant, S., Michael, B., Kneen, R., Solomon, T. Neurological Associations of COVID-19. SSRN Electronic Journal. 2020;
- Ye M, Ren Y, Lv T. Encephalitis as a clinical manifestation of COVID-19. Brain, Behavior, and Immunity. 2020; 88:945–6.
- Hayashi M, Sahashi Y, Baba Y, Okura H, Shimohata T. COVID-19-associated mild encephalitis/encephalopathy with a reversible splenial lesion. Journal of the Neurological Sciences. 2020; 415:116941.
- Pilotto, A., Masciocchi, S., Volonghi, I., Zotto, E. D., Magni, E., Giuli, V. D., Padovani, A. The clinical spectrum of encephalitis in COVID-19 disease: the ENCOVID multicentre study. 2020;
- Haider A, Siddiqa A, Ali N, Dhallu M. COVID-19 and the Brain: Acute Encephalitis as a Clinical Manifestation. Cureus. 2020;
- Venkatesan A, Geocadin RG. Diagnosis and management of acute encephalitis: A practical approach. Neurology: Clinical Practice. 2014;4(3):206–15.