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New Event NSTEMI in Severe-Critical COVID-19 Patient: Case Report

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Abstract: ***Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the causative agent for the ongoing pandemic of coronavirus disease 2019 (COVID-19). COVID-19 is associated with a lot of risk factors that affect its prognosis and outcomes. The interaction between the virus and ACE-2 receptors occur in multiple organs including the heart. Case Report: This article reports a 38 year old woman, diagnosed with Confirmed Pneumonia COVID-19 with NSTEMI, hypertension, type 2 diabetesmellitus and asthma bronchial. The patient was treated in the isolation room for approximately 23 days before being discharged. Conclusion: COVID-19 can impair cardiovascular functions causing myocardial disfunctions such as NSTEMI. However further investigations are needed to explain this further.***

Keywords: COVID-19, NSTEMI

1. Introduction

On February 11, 2020, the World Health Organization named the new virus SARS-CoV-2 and the disease name as Coronavirus Disease 2019 (COVID-19).[1]The most common comorbidities identified in COVID patients were hypertension (15.8%), cardiovascular and cerebrovascular conditions (11.7%), and diabetes (9.4%).The less common comorbidities were coexisting infection with HIV and hepatitis B (1.5%), malignancy (1.5%), respiratory illnesses (1.4%), renal disorders (0.8%), and immunodeficiencies (0.01%).[2,3]

COVID-19 symptoms can be categorized into asymptomatic, mild, moderate, severe and critical. Patients with mild symptoms are symptomatic patients without evidence of viral pneumonia or without hypoxia. Symptoms include fever, cough, fatigue, anorexia, shortness of breath, myalgia. Other non-specific symptoms such as sore throat, nasal congestion, headache, diarrhea, nausea and vomiting, loss of smell (anosmia) or loss of taste (ageusia) that appear before the onset of respiratory symptoms are also frequently reported. Patients with moderate symptoms are patients with clinical signs of pneumonia (fever, cough, shortness of breath, rapid breathing) but no signs of severe pneumonia. In patients with severe symptoms there are clinical signs of pneumonia (fever, cough, shortness of breath, rapid breathing) plus one of the following: respiratory rate> 30 bpm, severe respiratory distress, or SpO2 <93% in room air. Meanwhile, critical patients are patients with Acute Respiratory Distress Syndrome (ARDS), sepsis and septic shock.[1]

A metallopeptidase named angiotensin - converting enzyme 2 (ACE2) has been identified as the functional receptor for SARS-CoV. The most remarkable finding was the surface expression of ACE2 protein on lung alveolar epithelial cells and enterocytes of the small intestine.[4]Astudy published in European Heart Journal has investigated expression of ACE2 in human hearts.[5] They found ACE2 to be expressed in cardiomyocytes and pericytes, and at a lower level in fibroblasts, endothelial cells, and leucocytes.[6]

2. Case Illustration

A 38 year old female came to the Emergency Room (ER) with chief complain of shortness of breath since 1 day ago. Shortness of breath felt increasingly worse since 2 hours prior to arrival to the ER. This patient also complained of fever, nausea, loss of appetite and fatigue since 1 week prior to admission. Patient denied having history of diabetes mellitus hypertension and other heart diseases. Patient however had a history of asthma since 10 year old.Her last asthma attacked was a year ago. Patient had no history of medications taken for her asthma. Patient has previously taken Paracetamol for her fever but commented that there was no improvement. Patient works as a food stall seller in the market of local transmission area.

Physical examination revealed compost mental consciousness with blood pressure of 160/110 mmHg, pulse rate of 100 beats per minute, respiratory rate of 25 times per minute, axillary temperature of 38℃, and oxygen saturation 88% in room air. On physical examination, dyspnea was observed. Physical examination of the lungs revealed rhonchi in both lungs. Abdomen and extremities were within normal limits.

In the laboratory's complete bloodresults of the patient, itwas found: Leukocytes 4.97 x 103 / µL; Erythrocytes 4.89 x 106 / µL; Hemoglobin 12.8 g / dL; Hematocrit 40%; Platelets 209 x 103 / µL; Monocyte 9.3%. Blood chemistry examination showed: SGOT 73 U / L; SGPT 76 U / L; Potassium 3.3 mmol. CRP 25 mg / L. Prothrombin time of 12.2 seconds. Random blood glucose 231 mg / dL. Reactive anti SARS CoV 2 IgM. Positive SARS CoV2 RT

PCR.Thorax X-rayshowed haziness in the right supra-perihilar and left and right perihilar-paracardial hence suggests Pneumonia [**Fig 1.**].ECG was within normal limits [**Fig 2.**]. The therapy addressed to this patient was an infusion of Normal Saline 20 drips per minute, 4 lpm nasal canule oxygenation,Favipiravir 1600 mg tablet every 12 hours for the first day, then 600 mg every 12 hours for the second until fifth day, Levofloxacin 750 mg injection every 24 hours,Azythromycin 500 mg tablet every 24 hours, Vitamin C 500 mg injection every 12 hours, Enoxaparin sodium 6000 IU injection every 12 hours, Paracetamol 500 mg tablet every 8 hours if axillary temperature more than 38℃, Omeprazole 40 mg injection every 24 hours, N-acetylcystein 200 mg tablet every 8 hours,Dexamethasone 0,5 mg tablet every 12 hours.

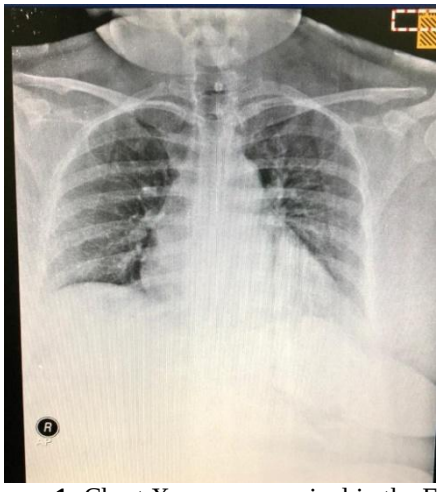

Figure 1: Chest X-ray upon arrival in the ER.

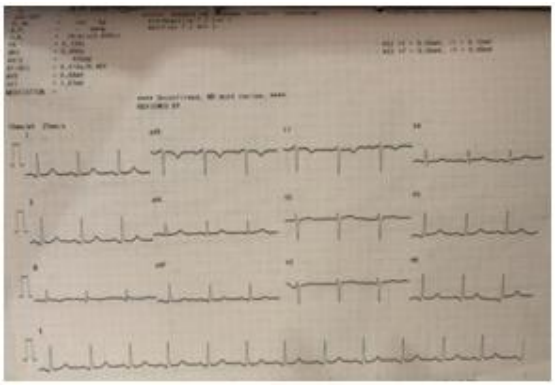

Figure 2: ECG upon arrival in the ER was within normal limit.

After 10 days, shortness of breath became worse. Blood Gas Analysis showed PaO2 of 73 mmHg with 10 lpm non-rebreathing mask oxygenation. Chest X-Ray showed infiltrate has greatly increased in both lungs**[Fig. 3]**. The patient complained of chest pain.ECG showed inferior and anterior NSTEMI **[Fig. 4]** and elevated Troponin I (0,21ng/ml) was found. The patient recieved additional therapies: Telmisartan 80 mg tablet every 24 hours, Hydrochlorothiazide 25 mg tablet every 24 hours, Furosemide 40 mg injection every 24 hours, Clopidogrel 75 mg tablet every 24 hours, Nitroglyceryn 2,5 mg tablet every 24 hours,Aspilet 80 mg tablet every 24 hours, Simvastatin 20 mg every 24 hours, Bisoprolol Fumarate 2,5 mg every 24 hours.

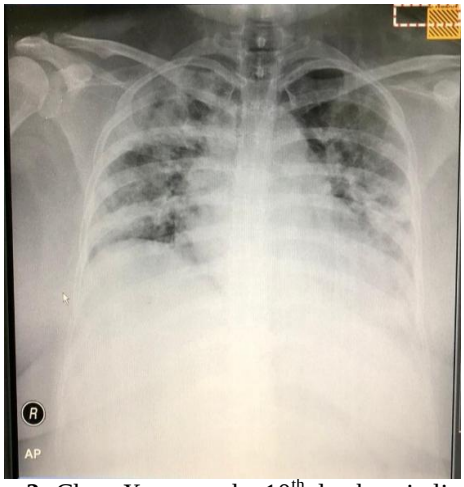

Figure 3: Chest X-ray on the 10th day hospitalization.

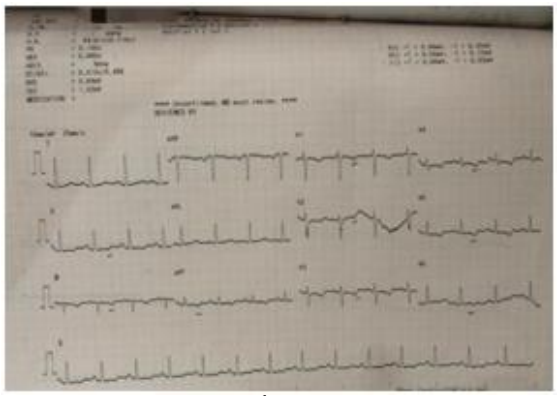

Figure 4: ECG on the 10th day hospitalization showed inferior and anterior NSTEMI.

After 23 days of care in the isolation ward, shortness of breath and chest pain resolved eventually. Patient was reevaluated and her ECG showed to be within normal limits [**Fig 5**]. Patient was finally discharged after negative SARS CoV-2 RT PCR result.

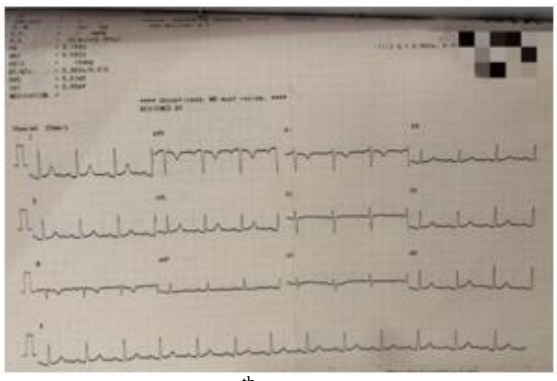

Figure 5: ECG on the 23th day hospitalization was within normal limit.

3. Discussion

We report a case of a 38 year old woman with severe to critical COVID-19 symptoms. Comorbidities noted in this patient are asthma, hypertension and diabetes mellitus.Asthmatic patients are thought to have increased susceptibility and severity of COVID-19 due to decreased anti-viral immune response and increased risk of viral

induced exacerbation.[7,8,9] It has been proposed that asthma associated type II inflammatory response decreases host anti-viral immunity. In addition, asthma induced mucus plugging in the lower respiratory tract, limits airflow which could worsen the hypoxemia from diffuse alveolar damage caused by COVID-19 infection.[10]

The specific pathogenesis of hypertension that may lead to more severe COVID-19 remains to be studied. The imbalance of cytokine may be considered an explanation for the correlation between hypertension and severe COVID-19. Clinical data have shown a relationship between the deterioration of COVID-19 and cytokine stormssuch as elevated levels of IL-6, IL-7, granulocyte-macrophage colony-stimulating factor, and tumor necrosis factor α. Clinical studies have found that the increase in these cytokines is also associated with the hypertension.[12]

As discussed, diabetes is associated with poorer outcomes in COVID-19.[13] Diabetic mice have been found to have increased expression of ACE-2 in the renal cortex, liver and pancreas.[14]Diabetes is also associated with an increase of furin, which might facilitate viral replication.[15]Furthermore IL-6 is increased in diabetes and may play a more deleterious role in Covid-19 infection.[16]

COVID-19 patients with severe symptoms must present signs of pneumonia (fever, cough and shortness of breath) with a respiration rate of more than 30x/minute or severe respiratory distress or oxygen saturation of less than 93% in room air.[1]This patient came to the ER with shortness of breath with an SpO2 of 88% in room air.

Critically ill COVID-19 patients are those with Acute Respiratory Distress Syndrome (ARDS), sepsis dan septic shock.[1] ARDS is defined as a new onset or worsening of respiratory symptoms within 1 week of recognition. The severity of ARDS is based on hypoxemic conditions. Hypoxemia is defined as arterial oxygen pressure (PaO_2) divided by inspired oxygen fraction (FIO_2) less than <300 mmHg. Important investigations are chest imaging such as chest X-ray, chest CT scan or lung ultrasound. Imaging findings may reveal bilateral opacity, unexplained due to effusion, lobar or pulmonary collapse or nodules. The source of the edema cannot be fully explained by heart failure or fluid overload, so other objective investigations such as echocardiography are needed to exclude the hydrostatic cause of edema in the absence of risk factors. It is important to perform blood gas analysis to see blood oxygen pressure in determining the severity of ARDS and therapy.[8]BGA was performed after 10 days of care in the isolation ward and revealed PaO2 of 73 (O2 10 lpm using NRM). From this result, the PF ratio is 73.74. A follow up chest X-ray on the same day showed an increase in infiltrates in both lungs. Thus, this patient can be classified as an ARDS patient, meeting the criteria for a critically ill COVID-19 patient.

SARS-CoV-2 can elicit intense release of cytokines and chemokines, possibly leading not only to vascular inflammation and atherosclerotic plaque instability but also to myocardial inflammation. Therefore, possible mechanisms for elevated troponin levels in this patient include demand ischaemia, stress cardiomyopathy, microvascular thrombosis, and secondary effects of systemic inflammation. Direct viral infection of the myocardium is another possible causal pathway of myocardial damage. The unique affinity of SARS-CoV-2 and ACE-2 receptors raises the possibility of direct viral infection of vascular endothelium and myocardium, such that in some patients, COVID-19-associated myocardial injury could represent viral myocarditis.[21]It has been observed that there are high levels of myocardial macrophages in COVID-19 patients and they may largely result from the elevated systemic levels of proinflammatory cytokines. Patients with severe COVID-19 have been shown to have systemic elevations of the proinflammatory cytokines interleukin-6 (IL-6) and tumour necrosis factor-a (TNF-a).[20,21]

ACE2 are expressed in a number of tissues, including the heart, lung, gut smooth muscle, liver, kidney, and immune cells.In an autopsy study of patients who died of severe acute respiratory syndrome (SARS), 7 (35%) of 20 hearts were shown to harbor the related coronavirus SARS-CoV. [17]Given the extensive homology of SARS-CoV-1 and SARS-CoV-2, and the intensity of SARS-CoV-2 binding to ACE2, it is reasonable to presume that SARS-CoV-2 directly invades human myocardium.[18] In a report of 104 patients with COVID-19 infection who developed acute heart failure and underwent endomyocardial biopsy, 5 were positive for the SARS-CoV-2 genome in the myocardial tissue and associated with typical features of myocarditis, including pronounced intramyocardial inflammation, microvascular thrombosis, and myocardial necrosis. More recently, in a larger autopsy series of consecutive patients, SARS-CoV-2 positivity in cardiac tissues could be documented in 24 (61.5%) of 39 patients.[20]

Myocardial infarct resulting from an imbalance between myocardial oxygen supply and demand is classified as NSTEMI.[21] In particular, 4 specific mechanisms in the context of COVID-19 seem relevant: 1) fixed coronary atherosclerosis limiting myocardial perfusion; 2) endothelial dysfunction within the coronary microcirculation; 3) severe systemic hypertension resulting from elevated circulating Ang II levels and intense arteriolar vasoconstriction; and 4) hypoxemia resulting from acute respiratory distress syndrome (ARDS) or from in situ pulmonary vascular thrombosis. In the setting of sepsis, lung injury, and respiratory failure, severe physiological stress can be associated with elevations in biomarkers of myocardial strain and injury.[21,22]It is very likely that multiple concurrent mechanisms of myocardial injury overlap within individual patients.[20,21]

4. Conclusion

As the lung is the prime site of pathology in patients with COVID-19, the heart scores second as a target organ of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The reason may be an abundance of ACE-2 receptor in the heart, which helps the virus get easily internalised into the cells.MI has been observed in 6–7% cases of patients with COVID-19.[21,22] MI type 1 and type 2 have been proposed in patients with COVID-19 owing to inflammed coronaries vulnerable to plaque ruptureleading to thrombosis or spontaneous coronary artery dissection and a

demand–supply mismatchin coronaries resulting from hypoxia, increased core body temperature, decreased cardiac contractility and increased heart rate, respectively.[20] However, further study is needed.

References

[1] PENYUSUN T. PEDOMAN TATALAKSANA COVID-19.
[2] Paudel SS. A meta-analysis of 2019 novel coronavirus patient clinicalcharacteristics and comorbidities. Research Square. 2020.
[3] Zhou F, Yu T, Du R, Fan G, Liu F, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395(10229): 1054–62.
[4] Hamming I, Timens W, Bulthuis ML, Lely AT, Navis GV, van Goor H. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. The Journal of Pathology: A Journal of the Pathological Society of Great Britain and Ireland. 2004 Jun;203(2):631-7.
[5] Nici L, Abplanalp, WT, Mellentin H, Kattih, B, Tombor L, John D, Schmitto JD, Heineke J, Emrich F, Arsalan M, Holubec T, Walther T, Zeiher AM, Dimmeler S. Cell type-specific expression of the putative SARS-CoV-2 receptor ACE2 in human hearts. Eur Heart J 2020;41:1804–1806.
[6] Ferrario CM, Jessup J, Chappell MC, Averill DB, Brosnihan KB, Tallant EA, Diz DI, Gallagher PE. Effect of angiotensin-converting enzyme inhibition and angiotensin II receptor blockers on cardiac angiotensin-converting enzyme 2. Circulation 2005;111:2605–2610.
[7] Jackson DJ, Busse WW, Bacharier LB, et al. Association of respiratory allergy,asthma, and expression of the SARS-CoV-2 receptor ACE2. J Allergy ClinImmunol. 2020;146:203-206.e3.
[8] Liu S, Zhi Y, Ying S. COVID-19 and asthma: reflection during the pandemic.Clin Rev Allergy Immunol. 2020;59:78-88.
[9] Sajuthi SP, DeFord P, Jackson ND, et al. Type 2 and interferon inflammation stronglyregulate SARS-CoV-2 related gene expression in the airway epithelium. Biorxiv. 2020.
[10] Konopka KE, Wilson A, Myers JL. Postmortem lung findings in a patient with asthma and coronavirus disease 2019. Chest. 2020;158:e99-e101.
[11] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinicalfeatures of patients infected with 2019 novel coronavirus inWuhan, China. Lancet. 2020;395:497–506
[12] Drummond GR, Vinh A, Guzik TJ, Sobey CG. Immunemechanisms of hypertension. Nat Rev Immunol. 2019;19:517–32.
[13] Chen X, Hu W, Ling J, Mo P, et al. Hypertension and Diabetes Delay the Viral Clearance in COVID-19 Patients. medRxiv: 2020.2003.2022.20040774, 2020.
[14] Singh AK, Gupta R, Ghosh A, Misra A. Diabetes in COVID-19: Prevalence, pathophysiology, prognosis and practical considerations. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2020 Apr 9.
[15] Fernandez C, Rysa J, Almgren P, Nilsson J, Engstrom G, Orho-Melander M, Ruskoaho H, Melander O. Plasma levels of the proprotein convertase furin and incidence of diabetes and mortality. J Intern Med 284: 377-387, 2018
[16] Chinese Clinical Trial Registry, A multicenter, randomized controlled trial for the efficacy and safety of tocilizumab in the treatment of new coronaviruspneumonia (COVID-19), (2020). http://www.chictr.org.cn/%0Dshowprojen.aspx?proj=49409 (accessed March 6, 2020)
[17] Liu PP, Blet A, Smyth D, Li H. The science underlying COVID-19: implications for the cardiovascular system. Circulation 2020;142:68–78.
[18] Oudit GY, Kassiri Z, Jiang C, et al. SARS-coronavirus modulation of myocardial ACE2 expression and inflammation in patients with SARS. Eur J Clin Invest 2009;39:618–25.
[19] Kim IC, Kim JY, Kim HA, Han S. COVID-19- related myocarditis in a 21-year-old female patient. Eur Heart J 2020;41:1859.
[20] Lindner D, Fitzek A, Brauninger H, et al. Association of cardiac infection with SARS-CoV-2 in confirmed COVID-19 autopsy cases. JAMA Cardiol 2020 Jul 27 [E-pub ahead of print].
[21] Giustino G, Pinney SP, Lala A, Reddy VY, Johnston-Cox HA, Mechanick JI, Halperin JL, Fuster V. Coronavirus and cardiovascular disease, myocardial injury, and arrhythmia: JACC Focus seminar. Journal of the American College of Cardiology. 2020 Oct 27;76(17):2011-23.
[22] Thygesen K, Alpert JS, Jaffe AS, et al. Fourth universal definition of myocardial infarction (2018). J Am Coll Cardiol 2018;72:2231–64.