Case Report

A rare case of atrial and biventricular thrombi with dilated cardiomyopathy as a delayed presentation in a patient with COVID-19

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ARTICLE INFO	ABSTRACT
Keywords: DCM COVID-19 Nepal	*Introduction:* Coronavirus 2019 (COVID-19) can cause cardiovascular manifestations including myocardial injury and thromboembolic events. *Case presentation:* Here, we report a case of a 27-year-old female with dilated cardiomyopathy, right atrial and biventricular thrombi infected with COVID-19. *Discussion:* There are several complex coagulation abnormalities in COVID-19 patients that have been suggested to create a hypercoagulable state. Evidence have shown that endothelial injury potentially leading to thromboembolic events is caused by direct invasion of endothelial cell by SARS-CoV-2 and complement activation contributed by the virus spike protein. *Conclusion:* DCM can be complicated by atrial and biventricular thrombi due to coagulation abnormalities that are likely to persist after recovery from COVID-19. Thus, long-term careful monitoring of cardiac function is necessary after recovery of COVID-19.

1. Introduction

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection is the cause of ongoing global pandemic and is known to involve multiple organ systems. Patients with Coronavirus 2019 (COVID-19) typically present with signs and symptoms of the respiratory system but cardiovascular manifestations including myocardial injury and thromboembolic events are also reported [1]. Both ischemic and non-ischemic cardiomyopathies can be complicated by left ventricular (LV) thrombosis, which can result in arterial embolic consequences such as stroke [2,3]. Biventricular thrombi, on the other hand, are extremely uncommon, with only a few occurrences reported in the literature [4]. Here, we report the case of a 27-year-old female infected by COVID-19, presenting with dilated cardiomyopathy (DCM), who was diagnosed with right atrial, biventricular apical thrombi by transthoracic echocardiography (TTE). This case has been reported in line with SCARE 2020 criteria [5].

2. Case Presentation

A 27-year female presented to our center with shortness of breath for four months, cough for three weeks, and hemoptysis for three days. She had no joint pain, alopecia, oral ulcer or rashes. She had her last menstruation seven months ago with no history of spontaneous abortion. She doesn't smoke or consume alcohol and has no hypertension and diabetes mellitus.

She had COVID-19 one year ago for which she was hospitalized and managed conservatively. Three months after recovery from COVID-19 she was diagnosed to have peritoneal tuberculosis for which she was on anti-tubercular therapy (ATT). She was found to be non-compliant to ATT and two months later, she developed disseminated tuberculosis manifesting as peritoneal tuberculosis. She was managed conservatively in intensive care unit (ICU) and ATT was started on regular basis for tuberculosis peritonitis. She was managed with injectable (furosemide, tramadol, ondansetron, and hyoscine) and oral (digoxin, thiamine, ATT, spironolactone, isosorbide mononitrate, metoprolol, and potassium chloride).

Her blood pressure was 90/60 mm of Hg, pulse rate of 102 beats/minutes, respiratory rate of 23 breaths/min, body temperature of 98.2 °F, and oxygen saturation was 95% in room air. On general physical examination she had no pallor, icterus, clubbing, edema, or cyanosis. Peripheral blood smear showed the features of macrocytic anemia.

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Table 1
Lab values of the included patient.

Parameters	Values
Hemoglobin	9.25 gm%,
Packed cell volume	28.4%
Total red blood cell count	284000 cells/mm^3
Mean corpuscular volume	100fl
Monocytes	2%
Eosinophil	13%
Neutrophils	55%
Platelets	306000 cells/mm^3
Blood urea nitrogen	6 mg/dl
Creatinine	0.54 mg/dl
Sodium	133 mEq/L
Potassium	3.7 mEq/L
LDH	233 U/L
Amylase	67 IU/L
Free T$_3$	2.87 pg/ml
Free T$_4$	1.83 ng/dl
TSH	11.2 uIU/ml
Total protein	11.4 g/dl
Albumin	1.6 g/dl
Total bilirubin	0.8 mg/dl
Indirect bilirubin	0.5 mg/dl
Alanine aminotransferase (SGPT)	27 U/L
Aspartate aminotransferase (SGOT)	23 U/L
Alkaline phosphatase (ALP)	70 U/L
Gamma-glutamyl transferase (GGT)	28 U/L
Prothrombin time	16.7 seconds
International normalized ratio	1.2
Activated Partial Thromboplastin Time	30 seconds

Laboratory examination revealed triglyceride 59 mg/dl, cholesterol 85 mg/dl, HDL-cholesterol 24 mg/dl, and LDL-cholesterol 68 mg/dl. Her random blood glucose, calcium and phosphorus level was 70 mg/dl, 6.7 mg/dl, and 7.7 mg/dl respectively. The details of the lab values of the parameters are shown in Table 1.

Pleural fluid showed exudative pleural effusion but acid-fast bacilli were not detected. HbsAg, HIV-1 and HIV-2 antibody, anti-HCV antibody, and rapid plasma reagin (RPR) were non-reactive. Serum protein electrophoresis revealed hypoalbuminemia with peak and abnormal shape in gamma region while serum protein immunotyping did not show monoclonal bands. Anti-smooth muscle antibody (ASMA), anti-mitochondrial antibody (AMA), anti-nuclear antibody (ANA), anti-phospholipid antibody (APLA), SS-A, SS-B, SCL-70 IgG, and JO-1 antibodies were negative. *Mycobacterium tuberculosis* was not detected via

XPERT test. Urinalysis was unremarkable except for dark yellow colored urine with 2–3 pus cells per high power field and 4–6 calcium oxalate crystals. Bence jones protein was not found in urine. Stool examination did not show ova of *Paragonimus westermani* and *Entamoeba histolytica.*

Electrocardiogram showed poor regression of R-wave (Fig. 1). Chest X-ray showed cardiomegaly, right sided pleural effusion and bilateral opacities (Fig. 2). Echocardiography showed global hypokinesia of left ventricular wall with left ventricular ejection fraction of 20%, right ventricular dysfunction, thrombus of 15 * 16 mm in the lateral wall of right ventricle, and spontaneous echo contrast in inferior venacava (Fig. 3). Under ultrasound guidance and aseptic precaution 12Fr pigtail catheter was inserted in right pleural cavity, which showed brownish colored viscous fluid in drain tube. Ultrasonography of abdomen and pelvis showed right sided moderate pleural effusion. Computed tomography (CT) of chest and abdomen showed cardiothoracic ratio of
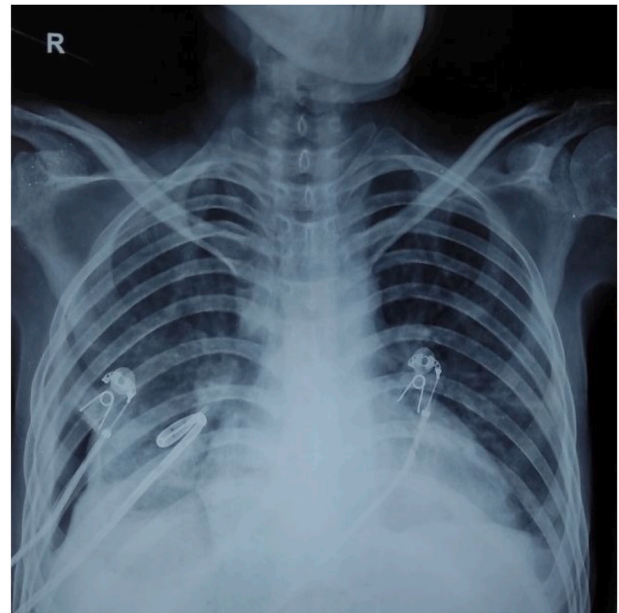

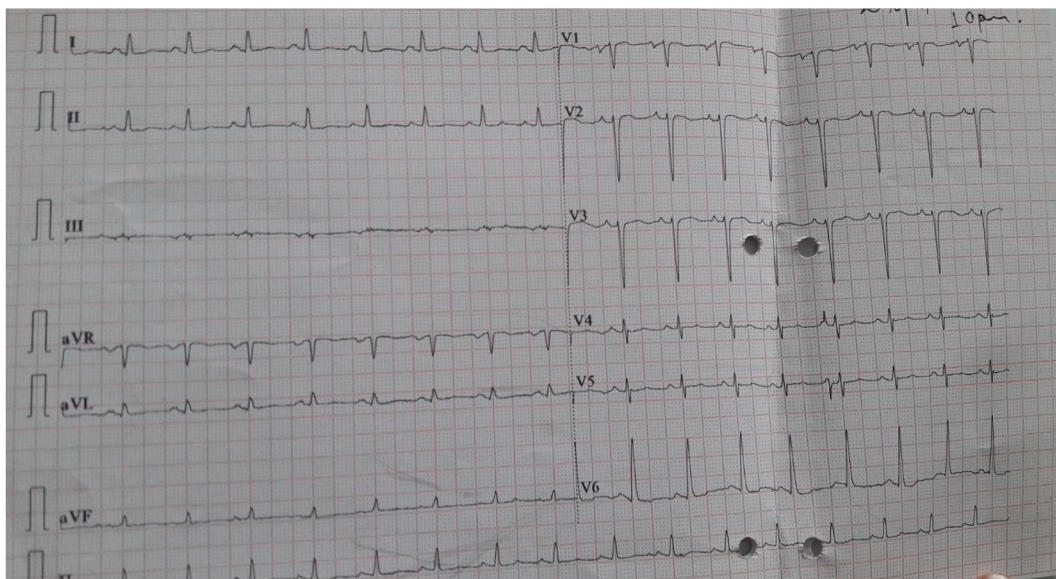**Fig. 2.** Chest X-ray showing cardiomegaly, right sided pleural effusion, and bilateral opacities.

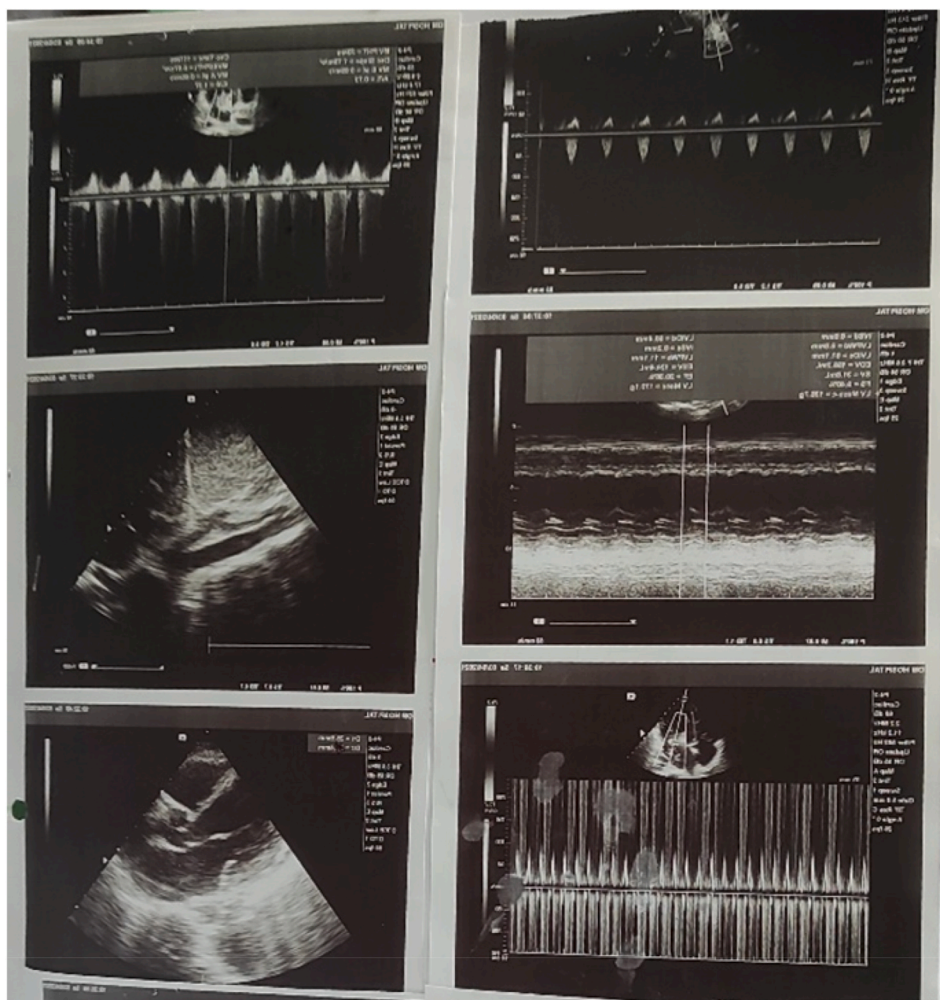**Fig. 1.** ECG showing poor progression of R wave.

Fig. 3. Echocardiography showing global hypokinesia of left ventricular wall and right ventricular dysfunction.

13:23 and non-enhancing hypodense thrombus in right atrium, right ventricle (20* 11.7 mm), left ventricle, left renal vein, infra-renal portion of inferior venacava, right common iliac vein, internal iliac vein and common femoral vein. Furthermore, it showed minimal free fluid and free air in the right and the left pleural cavity giving air fluid level, patchy peripheral based consolidation with surrounding ground glass opacities scattered in bilateral lung fields. Homogenously enhancing lymph nodes were seen in pretracheal, paratracheal, pre-carinal region (measuring 1.2*1.1 cm in precarinal region), mesenteric, aortocaval, and bilateral pelvic nodes (12.5mm) (Fig. 4). Minimal as-cites and multiple small collections in the abdominal wall were also seen. Bone marrow aspiration from posterior superior iliac spine showed normocellular bone marrow with 13% plasma cells. However, bone marrow biopsy findings were not suggestive of multiple myeloma. However, she was tested negative for SARS-CoV-2 by reverse tran-scriptase polymerase chain reaction (RT-PCR) method.

Following this, she was diagnosed with DCM, thrombi in right atrium, both ventricles, and in multiple veins as a sequela of COVID-19. Following this, she was managed with isosorbide mononitrate (5 mg OD), IV furosemide (40 mg BD), spironolactone (25 mg OD), thyroxine (12.5 mg OD), IV clindamycin (600 mg TDS), and digoxin (0.125 mg OD).

3. Discussion

COVID-19 causes several complications like acute respiratory distress syndrome (ARDS), arrhythmias, myocardial injury, heart failure and shock, venous thromboembolism (VTE), including extensive deep vein thrombosis (DVT) and pulmonary embolism (PE), arterial throm-botic events, including acute stroke and limb ischemia, encephalopathy, stroke, movement disorders, motor and sensory deficits, ataxia, seizures, and other inflammatory complications. There are reported cases of cardiac emboli in COVID-19 patients [6,7]. Our patient was in her apparent state of her health prior to SARS-CoV-2 infection and was never diagnosed with any heart conditions. She presented to our center with the features of heart failure and was diagnosed with DCM following five months of COVID-19 recovery. She developed thrombi in atria, both the ventricle, and multiple veins. We believe she developed DCM and thromboembolic features most likely due to COVID-19.

We screened and ruled out the potential underlying etiologies of DCM in our patient including infectious (viral, bacterial, spirochetal, and parasitic), autoimmune, endocrine, medications, toxins, deposition disease, and electrolyte abnormalities on the basis of lab parameters. Since the patient was young and had no chest pain hence, ischemic heart disease as a probable cause was ruled out. We suspected anti-phospholipid antibody syndrome since there were multiple thrombi with abscess. However, APLA turned out to be negative. Tuberculosis causing DCM was ruled out since the patient was on ATT for five months for peritoneal TB. She had no family history for DCM thus familial cause of DCM was excluded. Multiple myeloma was ruled out based on criteria proposed by international myeloma working group [8]. After ruling out all the possible causes causing DCM and biventricular thrombus, COVID-19 was only the potential cause left.

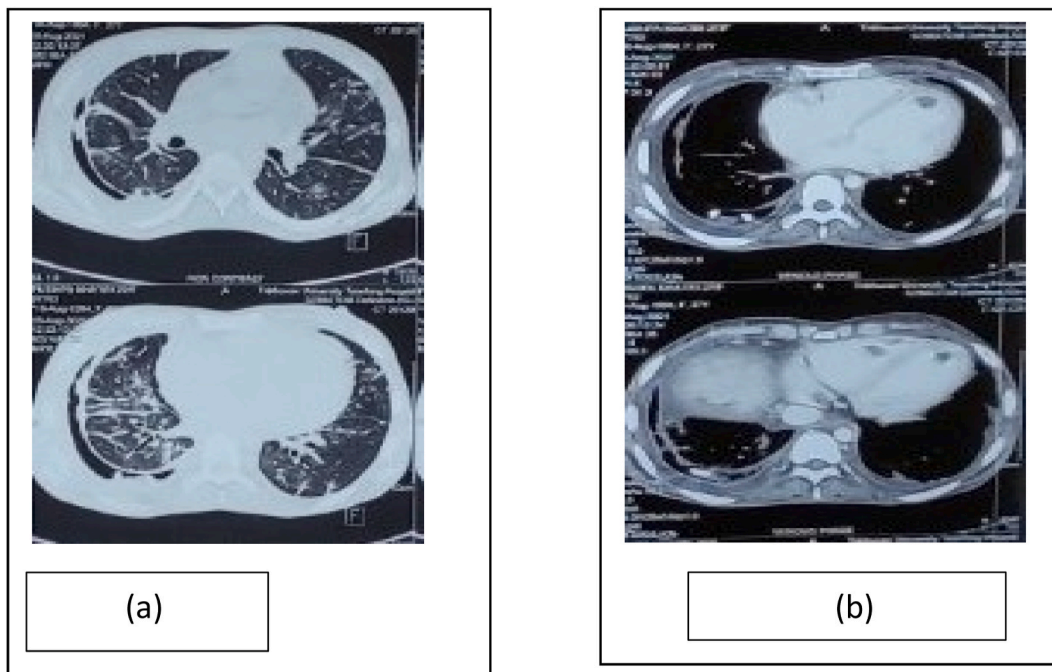Angiotensin-converting enzyme-2 (ACE-2) enzyme that is attached

Fig. 4. (a) CT of chest showing patchy peripheral based consolidation with surrounding ground glass opacities scattered in bilateral lung fields (b) non-enhancing hypodense thrombus in right atrium, right ventricle (20* 11.7 mm), left ventricle.

on the membrane of cells found in kidney, heart, lungs, intestines, sheds into the vascular compartment. The ACE-2 enzyme inhibits the renin–angiotensin aldosterone system (RAAS) by degrading angiotensin-II and thus prevents the development of heart failure, hypertension, and diabetes [9]. ACE-2 also act as a receptor through which SARS-CoV-2 enter the host cells. Binding of SARS-CoV-2 spike protein to ACE-2 receptor causes disruption of RAAS leading to multiple organ system failure. Therefore, SARS-CoV-2 could have potentially caused direct myocardial and endothelial injury leading to DCM and thromboembolic events in our patient.

COVID-19 predisposes the patient to arterial and venous thromboembolism but the mechanism is not clear. However, there are several complex coagulation abnormalities in COVID-19 patients that have been suggested to create a hypercoagulable state. Evidence have shown that endothelial injury potentially leading to thromboembolic events is caused by direct invasion of endothelial cell by SARS-CoV-2 and complement activation contributed by the virus spike protein [10,11]. Other factors facilitating the thromboembolic events in COVID-19 patient includes stasis of blood caused by immobilization in hospitalized patients and changes in circulating prothrombotic factors (elevated factor VIII, elevated fibrinogen, circulating prothrombotic micro particles, neutrophil extracellular traps (NETs) and hyper-viscosity [12,13]. It is speculated that anticoagulation prophylaxis may improve overall outcome in patients with COVID-19.

Left and right ventricular thrombi may lead to systemic and pulmonary embolization respectively. Biventricular thrombi are rare and very serious condition. There are only few case reports describing thrombi in both ventricles [14–16]. Our patient had thrombus in right atrium, right ventricle, left ventricle, left renal vein and infrarenal portion of inferior venacava. Progressive and persistent state of hypercoagulability caused by SARS-CoV-2 infection, blood stasis due to ventricular and vascular dilatation, and myocardial contractile dysfunction have been suggested to form thrombi in atria, ventricles, and large veins [17]. Biventricular thrombi were previously reported in patients with severe ventricular dysfunction, autoimmune disease, HIV infection, nephrotic syndrome, hypereosinophilic syndrome, heparin-induced thrombocytopenia, and antiphospholipid syndrome [4].

There are several case reports that histologically confirmed myocarditis in COVID-19 patients. Similar to Middle East Respiratory Syndrome coronavirus (MERS-CoV), SARS-CoV-2 can also cause myocardial damage, acute or fulminant myocarditis. Evidence of high ACE-2 expression in the heart strongly suggests that SARS-CoV-2 can cause myocarditis leading to DCM. Viruses are the well-known causative agent of myocarditis and have been implicated in the development of DCM. Persistent immune mechanism activation after viral infections is presumed to transit myocarditis to DCM [18]. There are reports of viral genomes in myocardium from DCM diagnosed patients [19]. Moreover, there can be persistent infection of the heart by the virus, but it cannot be ruled out after testing negative for SARS-CoV-2 from the nasopharyngeal mucosa sample. Thus, routine echocardiographic screening should be warranted in all hospitalized COVID-19 patients who have recovered. Several studies have suggested the worse outcomes in the hospitalized COVID-19 patients with elevated troponin levels [20]. Routine assessment of troponin level in patients recovered from COVID-19 can potentially help diagnose the cardiac sequelae (myocarditis, DCM, and thromboembolic events) that can occur after COVID-19 recovery or during the acute illness.

4. Conclusion

This is a rare case depicting the potential of SARS-CoV-2 causing DCM as cardiac sequelae after recovery from COVID-19. DCM can be complicated by atrial and biventricular thrombi due to coagulation abnormalities that are likely to persist after recovery from COVID-19. Thus, long-term careful monitoring of cardiac function is necessary after recovery of COVID-19. The monitoring should be more intense in patients whose blood troponin levels are elevated after SARS-CoV-2 infection.

Data availability statement

All the required information is within the manuscript itself.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Ethics statement

None.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Authors' contribution

RY and SS prepared the original manuscript, reviewed, and edited the manuscript. SY, RK, and CMP reviewed and edited the manuscript. RY, SS, SY, RK, and CMP reviewed and edited the manuscript and were in charge of the case.

Declaration of competing interest

None.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.amsu.2022.104057.

References

[1] A.A. Rabaan, S.H. Al-Ahmed, M.A. Garout, A.M. Al-Qaaneh, A.A. Sule, R. Tirupathi, et al., in: Diverse Immunological Factors Influencing Pathogenesis in Patients with COVID-19: A Review on Viral Dissemination, Immunotherapeutic Options to Counter Cytokine Storm and Inflammatory Responses, Pathog, Basel, Switzerland), 2021 May 1 [cited 2022 Jun 19];10(5). Available from: https://pubmed.ncbi.nlm.nih.gov/34066983/.

[2] S.V. F H, Challenges in management of left ventricular thrombus, Ther Adv Cardiovasc Dis (2017 Aug 1) [cited 2021 Aug 31];11(8):203–13. Available from: https://pubmed.ncbi.nlm.nih.gov/28589748/.

[3] L. Jm, P. Jj, J. Hw, C. Ys, O. Iy, Y. Ch, et al., Left ventricular thrombus and subsequent thromboembolism, comparison of anticoagulation, surgical removal, and antiplatelet agents, J. Atherosclerosis Thromb. (2013) [cited 2021 Aug 31];20 (1):73–93. Available from: https://pubmed.ncbi.nlm.nih.gov/22986555/.

[4] L. Missault, A. Koch, F. Colardyn, D. Clement, Biventricular thrombi in dilated cardiomyopathy: massive simultaneous pulmonary and systemic embolisation, Eur. Heart J. 15 (5) (1994 May) 713–714.

[5] R.A. Agha, T. Franchi, C. Sohrabi, G. Mathew, A. Kerwan, A. Thoma, et al., The SCARE 2020 guideline: updating consensus surgical CAse REport (SCARE) guidelines, Int. J. Surg. (2020 Dec 1) [cited 2022 Apr 13];84:226–30. Available from: https://pubmed.ncbi.nlm.nih.gov/33181358/.

[6] S. Berrichi, Z. Bouayed, K. Benbouchta, A. Kossir, H. Bkiyar, N. Ismaili, et al., Incidental diagnosis of a large cardiac thrombus swinging through an interatrial communication in a COVID-19 patient: case report and literature review, Ann Med Surg (2021 Nov 1) [cited 2022 Jun 19];71. Available, from:/pmc/articles/PMC8524807/.

[7] Post COVID-19 large atrial thrombus found incidentally, PubMed [Internet]. [cited 2022 Jun 19]. Available from: https://pubmed.ncbi.nlm.nih.gov/35704866/.

[8] S.V. Rajkumar, M.A. Dimopoulos, A. Palumbo, J. Blade, G. Merlini, M.V. Mateos, et al., International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma, Lancet Oncol [Internet] 15 (12) (2014) e538–e548, https://doi.org/10.1016/S1470-2045(14)70442-5. Available from:.

[9] S. Lukassen, R.L. Chua, T. Trefzer, N.C. Kahn, M.A. Schneider, T. Muley, et al., SARS-CoV-2 receptor ACE2 and TMPRSS2 are primarily expressed in bronchial transient secretory cells, EMBO J. 39 (10) (2020 May).

[10] M. C, M. Jj, B. D, N. G, S. S, H. J, et al., Complement associated microvascular injury and thrombosis in the pathogenesis of severe COVID-19 infection: a report of five cases, Transl. Res. 220 (2020 Jun) 1–13.

[11] J. Yu, X. Yuan, H. Chen, S. Chaturvedi, E.M. Braunstein, R.A. Brodsky, Direct activation of the alternative complement pathway by SARS-CoV-2 spike proteins is blocked by factor D Inhibition, Blood 136 (18) (2020 Oct) 2080–2089.

[12] M. Panigada, N. Bottino, P. Tagliabue, G. Grasselli, C. Novembrino, V. Chantarangkul, et al., Hypercoagulability of COVID-19 patients in intensive care unit: a report of thromboelastography findings and other parameters of hemostasis, J. Thromb. Haemostasis 18 (7) (2020 Jul) 1738–1742.

[13] R. M, B. A, D.D. U, B. E, D.P. M, R. M, et al., The procoagulant pattern of patients with COVID-19 acute respiratory distress syndrome, J. Thromb. Haemostasis 18 (7) (2020 Jul) 1747–1751.

[14] S.M. M S, Biventricular thrombi associated with myocardial infarction in a patient with COVID-19, Can. J. Cardiol. (2020 Aug 1) [cited 2021 Sep 1];36(8):1326.e9-1326.e11. Available from: https://pubmed.ncbi.nlm.nih.gov/32599017/.

[15] K. Ferguson, N. Quail, P. Kewin, K.G. Blyth, COVID-19 associated with extensive pulmonary arterial, intracardiac and peripheral arterial thrombosis Findings that shed new light on the possible pathogenesis of a disease or an adverse effect, BMJ Case Rep. (2020) [cited 2021 Sep 1];13:237460. Available from: http://casereports.bmj.com/.

[16] O. M, A. F, M. M, G. Sy, S. E, Massive biventricular thrombi complicating new-onset heart failure in a patient with suspected COVID-19, J Cardiol Cases (2021 Mar 14) [cited 2021 Sep 1];24(3):144–7. Available from: https://europepmc.org/articles/PMC7955911.

[17] J.L. Mehta, G. Calcaterra, P.P. Bassareo, COVID-19, thromboembolic risk, and Virchow's triad: lesson from the past, Clin. Cardiol. 43 (12) (2020 Dec) 1362.

[18] C. Kawai, A. Matsumori, Dilated cardiomyopathy update: infectious-immune theory revisited, Heart Fail. Rev. 18 (6) (2013) 703–714, 186. 2013 Jul.

[19] U. Kühl, M. Pauschinger, M. Noutsias, B. Seeberg, T. Bock, D. Lassner, et al., High prevalence of viral genomes and multiple viral infections in the myocardium of adults with "idiopathic" left ventricular dysfunction, Circulation 111 (7) (2005 Feb) 887–893.

[20] S. Shi, M. Qin, B. Shen, Y. Cai, T. Liu, F. Yang, et al., Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China, JAMA Cardiol 5 (7) (2020 Jul) 802–810.