Cardiac tamponade and massive pleural effusion in a young COVID-19-positive adult

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SUMMARY

COVID-19 has a broad spectrum of cardiac manifestations, and cardiac tamponade leading to cardiogenic shock is a rare presentation. A 30-year-old man with a history of COVID-19-positive, reverse transcription polymerase chain reaction (RT-PCR) done 1 week ago and who was home-quarantined, came to the emergency department with palpitations, breathlessness and orthopnoea. His ECG showed sinus tachycardia with low-voltage complexes, chest X-ray showed cardiomegaly and left pleural effusion and two-dimensional echocardiography showed large pericardial effusion with features suggestive of cardiac tamponade. He was taken up for emergency pericardiocentesis which showed haemorrhagic pericardial fluid. Intercostal drainage insertion was done for left-sided large pleural effusion. After ruling out all the other causes for haemorrhagic pericardial effusion, the patient was started on colchicine, steroids, ibuprofen and antibiotics to which he responded. Both pericardial and pleural effusions resolved completely on follow-up.

BACKGROUND

The COVID-19 pandemic is a challenge to healthcare systems and societies around the world. COVID-19 is a thromboinflammatory disease.[1] Most of the SARS-CoV-2 infection causes a mild disease, but in some cases, it can complicate a severe respiratory disease progressing to multiorgan failure and death.

The most frequently described cardiovascular manifestations of SARS-CoV-2 include acute coronary syndrome, cardiac arrhythmias, thromboembolism and myocarditis. Although pericardial involvement in patients with COVID-19 has been reported, its real frequency is not fully known. In a systemic review, 34 patients from 33 studies who presented with pericarditis, 76% of these patients had pericardial effusion and 35% had cardiac tamponade, 62% of patients were diagnosed as myopericarditis.[2] Pericarditis with pericardial effusion without myocardial involvement is rarely described.[3]

In this case, a rare cardiac manifestation of haemorrhagic pericardial effusion that led to cardiac tamponade which was life-threatening was noted.

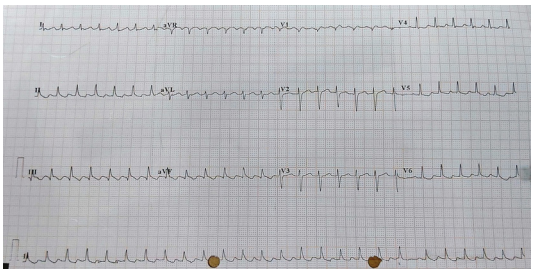

Figure 1 Low-voltage complexes on ECG.

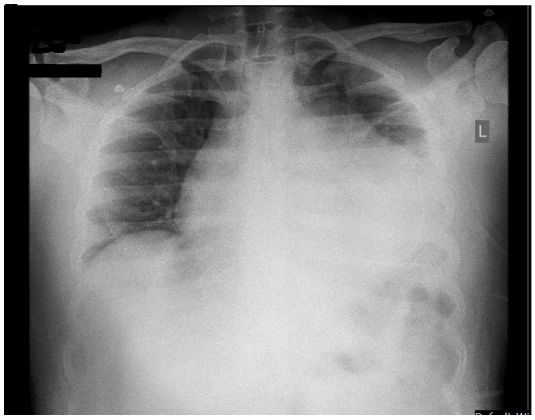

Figure 2 Enlarged cardiac silhouette and a large left pleural effusion on chest X-ray.

CASE PRESENTATION

A 30-year-old man, with a history of no cardiac illness who was diagnosed with COVID-19 1 week ago for which he was home-quarantined, presented with palpitations, progressive dyspnoea and orthopnoea. In the emergency department, he was afebrile and tachypnoeic. His heart rate was 140 beats/min, blood pressure was 100/60 mm Hg and SpO2 was 92% at room air. Dullness was present on percussion on the left infrascapular and infra-axillary areas. Breath sounds were decreased in the same area. Heart sounds were muffled on auscultation.

On admission, ECG (figure 1) showed low-voltage complexes. Chest radiography (figure 2) showed significant enlargement of the cardiac

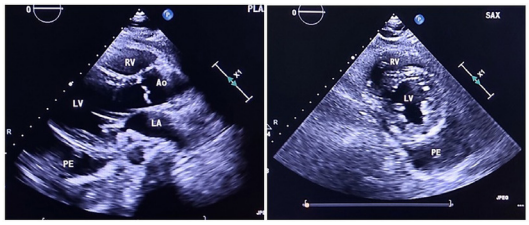

Figure 3 Two-dimensional echocardiography showing large PE with features suggestive of cardiac tamponade. PE, Pericardial effusion; RV,Right ventricle; LV,Left ventricle; LA,Left atrium; Ao,Aortic root.

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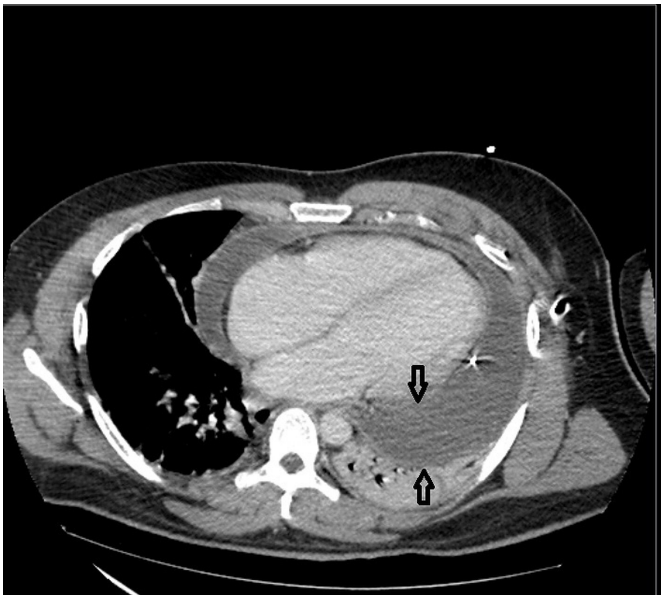

Figure 4 Large pericardial effusion (arrow mark) on CT-thorax.

silhouette and a large left pleural effusion was noted. Two-dimensional (2D) transthoracic echocardiography (figure 3) revealed a large pericardial effusion with right atrial collapse and early signs of right ventricular diastolic collapse, >25% and >40% reduction in mitral inflow and tricuspid inflow velocities, respectively, consistent with cardiac tamponade physiology.

He underwent pericardiocentesis. About 1500 mL of haemorrhagic fluid was aspirated under fluoroscopic guidance in the cath-lab and a pigtail catheter was placed in the pericardial cavity for continuous pericardial aspiration; another 2000 mL of pericardial fluid was aspirated in the next 72 hours. The patient continued to have dyspnoea. CT-thorax (figure 4) showed features of cardiomegaly with features of pulmonary hypertension and gross pericardial effusion causing compression of left hilum and collapse of the left lung. Patchy opacities with septal and fissural thickening of right lung suggestive of consolidation of infective aetiology and bilateral pleural effusion were also noted. An intercostal drainage was inserted by the pulmonologist in view of the large pleural effusion. About 1000 mL of straw-coloured pleural fluid was drained.

INVESTIGATIONS

Investigations	Observed value	Reference range	Units
Total leucocyte count	12 300	400–11 000	cells/mm^3
Differential count (DC)	Neutrophils: 78	40–75	%
	Lymphocytes: 21	20–40	
	Eosinophils: 1	1–6	
Platelet count	483 000	1 50 000–4 00 000	cells/mm^3
Random blood sugar	161	<140	mg/dL
Glycated haemoglobin	6.5	4.8–5.9	%
Potassium	4.32	3.5–5.1	mmol/L
Sodium	136	136–145	mmol/L
Chloride	100.3	98–107	mmol/L
Calcium	8.1	8.6–10	mg/dL
Total protein	5.9	6.6–8.7	g/dL
Serum albumin	2.76	3.5–5.2	g/dL
Serum globulin	3.14	2.3–3.5	g/dL
Albumin/globulin ratio	0.88	1.5–2.5	
Total bilirubin	0.60	Upto 1.2	mg/dL
Direct bilirubin	0.31	<0.2	
Indirect bilirubin	0.29	0–0.75	
Serum glutamic oxaloacetic transaminase	20.4	0–32	U/L
Serum glutamic pyruvic transaminase	42.8	0–33	U/L
Alkaline phosphatase	108	60–170	U/L
Urea	31.5	16.6–48.5	mg/dL
Creatinine	0.84	0.7–1.4	mg/dL
COVID-19 swab test (reverse transcriptase-PCR)	Positive		
Thyroid-stimulating hormone	3.44	0.27–4.2	uIU/mL
Free T4	1.68	0.93–1.7	ng/dL
Activated partial thromboplastin time	Test: 37.3		s
	Control: 34.3	26–40	
Prothrombin time	Test: 16.3		s
	Control: 4.4	11–16	
	International normalized ratio (INR): 15		
Bleeding time	2′00″	2–7	min
Clotting time	6′30″	4–9	min
C reactive protein	73.72	≤6	mg/L
D-dimer	7.53	<0.5	µg FEU/mL
Alpha-fetoprotein	1.31	≤7	ng/mL
Serum beta Human chorionic gonadotropin (HCG)	<0.100	<2	mIU/mL
Carcinoembryonic antigen	1.47	≤4.7	ng/mL

Pericardial fluid analysis

Pericardial fluid protein	5.0 g/dL
Pericardial fluid sugar	116 mg/dL
Pericardial fluid lactate dehydrogenase (LDH)	2209 U/L
Pericardial fluid adenosine deaminase (ADA)	19.1 U/L (normal <40)

Pericardial fluid cytology:
Cell count: 85 cells /mm^3.
DC: neutrophils 81% and lymphocytes 19%.
Smears studied are moderately cellular and show predominantly neutrophils and few lymphocytes against haemorrhagic background.
Impression:
Indian Academy of Cytologists (IAC) system of reporting fluid cytology—category II—benign.[4]

Pleural fluid analysis

Pleural fluid protein	3.5 g/dL
Pleural fluid sugar	152 mg/dL
Pleural fluid ADA	7.1 U/L (normal <24)
Pleural fluid LDH	486 U/L

Pleural fluid cytology:
Cell count: 212 cells/mm^3.
DC: lymphocytes 65%, reactive mesothelial cells 32% and neutrophils 3%.
Smears studied are highly cellular and show predominantly lymphocytes, few reactive mesothelial cells and occasional neutrophils against haemorrhagic background.
Few atypical cells having multinucleation, high N:C ratio, coarse chromatin and prominent nucleoli and irregular nuclear margins are also seen.
Impression :
IAC system of reporting fluid cytology—category III—atypical (most probably secondary to viral infection).[4]

Ultrasound scan of the abdomen—mild hepatosplenomegaly; bilateral pleural effusion (left>right).

CT-thorax (figure 4)—gross pericardial effusion noted measuring maximum thickness of 6.5 cm. Drain tube noted;

cardiomegaly with features of pulmonary arterial hypertension and gross pericardial effusion causing compression of left hilum and collapse of left lung. Enhancement of pericardium with no significant thickening. Advised evaluation for tubercular aetiology; patchy opacities with septal and fissural thickening of right lung suggestive of consolidation of infective aetiology; bilateral pleural effusion (left>right).

Antinuclear antibody (ANA) /Extractable nuclear antigen antibodies (ENA) qualitative profile

nRNP (Ribonucleoprotein)/Sm (Smith antibody)	Negative
Sm (Smith antibody)	Negative
SS-A (Sjogren syndrome A)	Negative
SS-B (Sjogren syndrome B)	Negative
Ro-52	Negative
Scl-70 (Scleroderma)	Negative
PM-Scl (Polymyositis-Scleroderma)	Negative
Jo-1 (Histidyl transfer RNA synthase)	Negative
CENP-B (Centromere protein-B)	Negative
PCNA (Proliferating cell nuclear antigen)	Negative
dsDNA (Double stranded deoxyribonucleic acid)	Negative
Nucleosomes	Negative
Histones	Negative
Ribosomal-P protein	Negative
AMA-M2 (Antimitochondrial antibody-M2)	Negative
Control	Valid

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for haemorrhagic pericardial effusion in this patient included tuberculous pericarditis, connective tissue disorders, malignancy and idiopathic pericarditis. The patient was investigated to rule out each of the differential diagnosis.

TREATMENT

Based on the positive COVID-19 RT-PCR report, the patient was started on oral vitamin C 500 mg, three times per day, and zinc 50 mg, two times per day, as per the hospital protocol. Antivirals were not given after consultation with the pulmonologist as the patient presented after 10 days of the onset of symptoms. Emergency pericardiocentesis was done and the patient's condition started improving after removal of about 3500 mL of haemorrhagic pericardial fluid over the next 3 days. About 1000 mL of straw-coloured pleural fluid was aspirated after insertion of the intercostal drainage. PCR test on pericardial and pleural fluid for COVID-19 couldn't be done as it is not done in the hospital. The serum LDH and troponin levels were normal. The possible aetiologies of haemorrhagic pericardial effusion including connective tissue disorders, tuberculosis, metastatic and occult malignancies were excluded by appropriate tests. Based on the clinical symptoms, signs, findings on chest-CT and epidemiological data, the causes of pericardial and pleural effusions were thought to be due to COVID-19. Colchicine 0.5 mg, two times per day, oral steroid prednisolone 40 mg once daily and intravenous antibiotics were given. Colchicine is a non-selective inhibitor of nucleotide-binding oligomerization domain, Leucine rich Repeat and Pyrin domain 3 (NLRP3) inflammasome and was effective in suppressing interleukin (IL)-1b, IL-18 and IL-6, which was attributed to inflammasome inhibition in a Greek study.[5] Ibuprofen 400 mg, three times a day, was given for 1 week. His condition improved over the next few days. His chest X-ray showed fully expanded lungs (figure 5) and

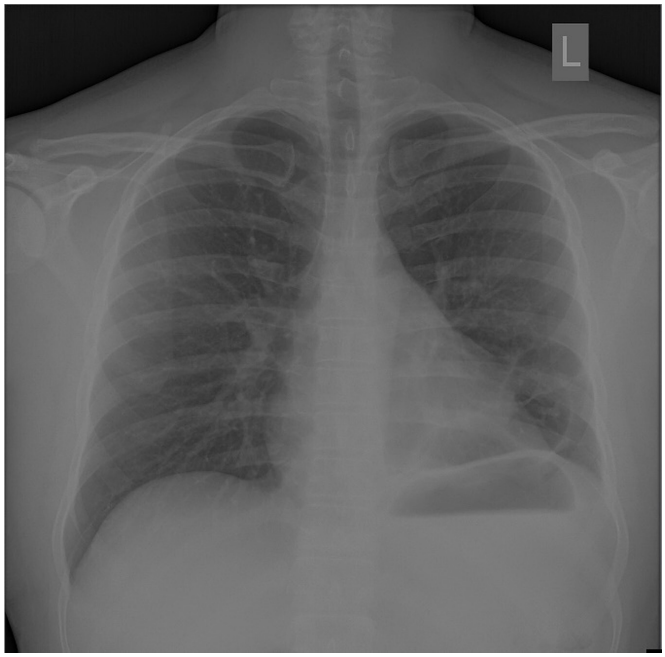

Figure 5 Completely resolved pericardial and pleural effusion on follow-up chest X-ray.

2D echocardiography showed significant resolution of pericardial effusion. He was discharged after 5 days from the hospital. Steroids were tapered and stopped in the next 2 weeks.

OUTCOME AND FOLLOW-UP

The patient had significant improvement with anti-inflammatory medications. In the first month follow-up, he remained asymptomatic and 2D echocardiogram showed trace pericardial effusion (figure 6). The pleural effusion and collapse consolidation on chest X-ray had resolved.

DISCUSSION

COVID-19 is caused by a novel coronavirus (SARS-CoV-2). It was first reported from Wuhan, China in late December 2019, and rapidly led to a global pandemic.[6]

Symptoms usually include headache, fever, dry cough and shortness of breath. Lungs are the most affected organs.[7] However, there have been reports of extrapulmonary involvement such as cardiovascular complications from around the world.[8]

Patients with pre-existing cardiovascular diseases are more likely to develop severe illness and higher mortality rate.[9] COVID-19 causes a number of cardiovascular complications including acute myocardial injury, myocarditis, arrhythmia, thromboembolism and cardiogenic shock, however, there have been rare reports of pericardial involvement also.[10 11]

The pathophysiological mechanisms causing cardiovascular involvement by SARS-CoV-2 infection include direct damage (figure 7) mediated through downregulation of ACE-2 receptors by the S-protein of SARS-CoV-2 producing vascular endothelial cell dysfunction, microvascular dysfunction, pericyte injury and hypoxemia. This can result in myocarditis, heart failure and arrhythmias. The indirect damage may be mediated by cytokine release syndrome where the release of inflammatory cytokines and chemokines, such as tumour necrosis factor alpha, IL-6, IL-1β and monocyte chemoattractant protein-1 causes myopericarditis, cardiac tamponade, thromboembolism and acute coronary syndrome.[12]

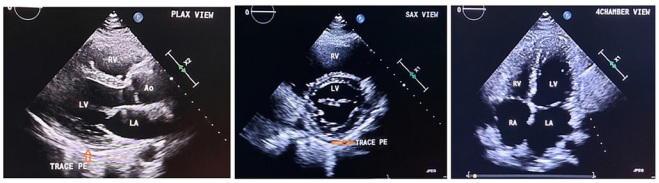

Figure 6 Completely resolved pericardial effusion on two-dimensional echocardiography. Ao, Aortic root; LV, Left ventricle; LA, Left atrium; PE,Pericardial effusion; RV, Right ventricle.

Pericardial and pleural effusions often coexist as it was seen in this case and it has been shown that bilateral pleural effusions (not left-sided or right-sided only pleural effusion) are associated with increased risk of in-hospital cardiac tamponade, but do not affect the long-term risk of pericarditis recurrence.[13] From awareness of such data, stems the speculation that pericardial diseases may be considered either as isolated diseases or as part of complex systemic conditions due to activation of both innate and adaptive immunity (with autoinflammatory and autoimmune mechanisms, respectively), with continuous dynamic interaction with environmental factors.[14]

Evaluation of chest CT scan findings in patients with COVID-19 in a study revealed approximately 5% of patients had pericardial effusion, which 'may indicate the occurrence of severe inflammation'.[15]

Haemorrhagic pericardial effusion has been described in pericarditis due to malignancy, tuberculous pericarditis, collagen-vascular diseases, uraemia, trauma, irradiation, post-myocardial infarction syndrome, streptococcal infection and idiopathic pericarditis.[16] The association of haemorrhagic pericardial effusion with viral infections is less known but it has been reported in coxsackie virus.[17]

This young man who presented with palpitations and progressive shortness of breath underwent pericardiocentesis due to massive pericardial effusion and signs of cardiac tamponade. The interesting finding, in this case, was a haemorrhagic pericardial effusion and non-haemorrhagic straw-coloured pleural effusion, where 3500 mL of pericardial fluid and 1000 mL of pleural fluid were aspirated. His general condition improved following pericardiocentesis.

The SARS-CoV-2 RT-PCR was the only remarkable positive test result among the complete work-up which was done for the evaluation of possible causes of exudative haemorrhagic pericardial effusion. Complementary investigations for tuberculosis, malignancy, HIV, hypothyroidism and connective tissue diseases were proven negative.

Patients with massive haemorrhagic pericardial effusion may be at risk of recurrence and constrictive pericarditis, if not treated intensively.[18] Therefore, intensive treatment must be started immediately to prevent recurrence and constrictive pericarditis.

Usually, a 2D echocardiography is not routinely done in patients with COVID-19. It can give invaluable information in patients with severe symptoms. Haemorrhagic cardiac tamponade can be a life-threatening complication or presenting feature of COVID-19, which can be treated effectively if diagnosed early.

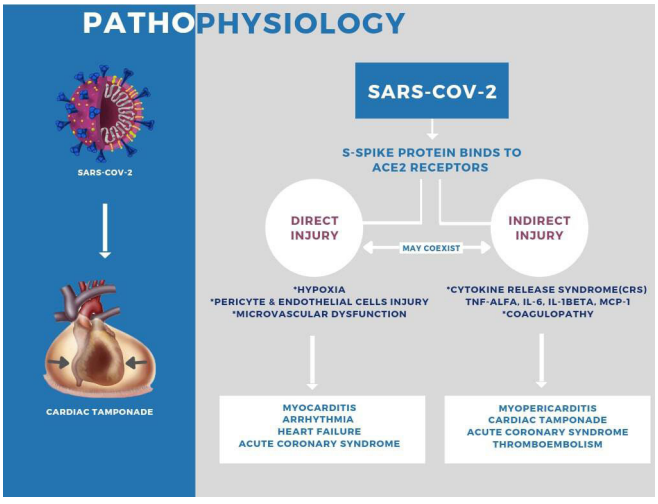

Figure 7 Pathophysiology of the development of cardiovascular complications in COVID-19. TNF, tumour necrosis factor; IL, interleukin; MCP, monocyte chemoattractant protein.

Patient's perspective

When I came to the hospital for the first time with fever, myalgia and sore throat, I was investigated with certain blood tests along with a reverse transcriptase-PCR test for COVID-19. The result was positive and I preferred to quarantine myself at home as I was told to have milder disease.

After 1 week, I started having uneasiness, palpitations and breathing difficulty even at rest. Hence, I visited the hospital again and underwent ECG, chest X-ray and echocardiography. I was told that there was a substantial amount of fluid accumulation around my heart and lungs. Immediately, the medical team admitted me into the intensive care unit (ICU) and a thin tube was inserted into the lower central part of my chest which collected a lot of blood-stained fluid. Later, they also inserted a larger tube into the left side of my chest to drain fluid from my lungs.

I felt better after the fluids were drained out of my chest. The doctors initiated certain medications for me after all the investigations were done. I was closely monitored in the ICU for the next 5 days and was shifted to the ward once I was fully stable.

I was told that the fluid accumulation had fully subsided and that it was a rare complication due to COVID-19. The early detection and subsequent treatment had saved my life. I felt better and was discharged on tapering doses of steroids. After a month, during my follow-up consultation, I was told that the fluid accumulation around my heart had been fully resolved and the doctor said that I would not require any further medications. All my symptoms have subsided, and I am once again able to resume all my normal activities.

Learning points

- To recognise that COVID-19 can have extra-pulmonary manifestations, which can be readily identified with physical examination and diagnostic tests like ECG, chest X-ray and two-dimensional echocardiography.
- Haemorrhagic pericardial effusion producing cardiac tamponade is a rare manifestation of COVID-19.
- Pericardial and pleural effusions often coexist and bilateral pleural effusions are associated with an increased risk of cardiac tamponade.
- Gaining a better understanding regarding the systemic effects of COVID-19 will lead to an improved management of such complications.

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Contributors DJ: concepts, design, literature search, data acquisition, manuscript editing, management of the patient and supervision of the case. SK: overall management of the patient and life-saving pericardiocentesis, concepts, design, manuscript editing and supervision of the case. NB and GBH: clinical management and intercostal chest tube drainage insertion.

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