Case Report

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Dilated Cardiomyopathy with Congestive Hepatopathy Post COVID-19: A Case Report

Internal Medicine Section

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ABSTRACT

In the current situation of pandemic, Coronavirus Disease 2019 (COVID-19), main organ involvement is of respiratory system ranging from mild symptoms to acute severe respiratory distress syndrome. Some studies are showing an increasing number of patients being hospitalised for COVID-19 with acute heart failure and multi-system inflammatory state. A 17-year-old male, with no known co-morbidities, presented with breathlessness and jaundice. He was diagnosed as a case of Dilated Cardiomyopathy (DCM) with congestive hepatopathy. He was treated with diuretics and supportive medications for which he showed symptomatic improvement, and there was a significant improvement in his ejection fraction during the course of treatment. The patient had Coronavirus Disease 2019 (COVID-19) infection 15 days prior to the onset of the above symptoms. The progression of COVID-19 complications seems potentially life-threatening, if associated with cardiac and hepatic manifestations. The present case illustrates the probable course of the ailment that has led to DCM. There was liver involvement too which was monitored and treated meticulously. These patients have high chances of deterioration even in simple situations of fever or pain, due to an increase in metabolic demands. It is a unique case which shows a strong association between COVID-19, acute heart failure, and congestive hepatopathy.

Keywords: Acute heart failure, Acute severe respiratory distress syndrome, Coronavirus disease 2019, Jaundice

CASE REPORT

A 17-year-old male, with no known co-morbidities, came to causality in August 2021 with complaints of breathlessness on exertion for the past 45 days, yellowish discolouration of the sclera for 25 days, abdominal pain, vomiting, and swelling of both legs for three days. He was on medication from a native healer for jaundice 25 days back. In the month of June 2021, he was exposed to Coronavirus Disease 2019 (COVID-19) infection, treated as mild COVID-19, and advised supportive care and home quarantine.

At presentation, the patient's pulse rate was 110 per minute, regular, no radio-radial delay with all peripheral pulses were felt equally, and his blood pressure was 100/70 mmHg. Patient's room air saturation was 96% with a respiratory rate of 22 breaths per minute, and his body temperature was normal. General examination was suggestive of icterus, elevated jugular venous pressure, and bilateral pitting pedal oedema. The extremities were warm and well perfused with no pallor, cyanosis, clubbing. The abdomen was soft and distended. He had tenderness over the right hypochondrium, which on palpation showed tender hepatomegaly (liver span: 15 cm) also with shifting dullness on percussion. Cardiovascular examination showed soft S1 and a pansystolic murmur over the mitral area radiating to the back and entire precordium and axilla, apex beat was shifted out, downward and was hyperdynamic in character. Central nervous system examination and the respiratory system revealed bilateral basal crepitations.

Baseline investigation on Day 1 showed- thrombocytopenia (81,000/cumm), hyponatremia (126 mg/dL), Hyperbilirubemia (3.9 mg/dL) with elevated indirect bilirubin (2.8 mg/dL) and elevated enzymes (Aspartate aminotransferase: 584 U/L, Alanine transaminase: 462 U/L, Alkaline phosphatase: 95 U/L). The patient also had mild coagulopathy (prothrombin time: 23 sec, International normalised ratio: 1.8). The renal parameters were normal (urea: 31 mg/dL, creatinine: 1.15 mg/dL) [Table/Fig-1].

Electrocardiogram (ECG) was suggestive of borderline right axis deviation (100°) with decreased amplitude in QRS complex in the frontal plane lead, poor R wave progression in the precordial leads (V1-V4), and incomplete Right Bundle Branch Block (RBBB). Chest x-ray was suggestive of cardiomegaly [Table/Fig-2]. A 2D Echocardiography (Echo) showed enlargement of all four chambers, global hypokinesia of the left ventricle with severe Left Ventricle (LV) systolic dysfunction (Ejection Fraction: 23%). Mild to moderate mitral regurgitation and severe tricuspid regurgitation with (Pulmonary artery systolic pressure: 52 mmHg) and right ventricle dysfunction [Table/Fig-3]. Ultrasonography (USG) abdomen showed hepatomegaly, mild to moderate ascites, mild right-sided pleural effusion. N-Terminal Pro-B-Type Natriuretic Peptide (NT-proBNP) was elevated (4894 pg/mL). Cardiac enzymes {Creatine phosphokinase (CPK) NAC :507 U/L, CPK MB: 25 U/L, troponin-I: 5.7 ng/L) were normal. Thyroid function test and lipid profile were normal. Immunoglobulin G (IgG) and Immunoglobulin M (IgM) for Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) was positive [Table/Fig-4].

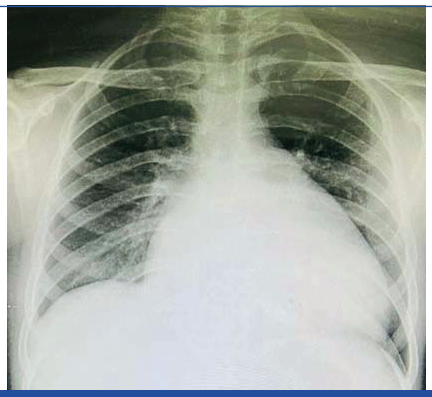
In view of elevated indirect bilirubin, the patient was further worked up for haemolysis which showed- Lactate Dehydrogenase (LDH): 988 U/L, peripheral smear suggestive of moderate thrombocytopenia with an elevated reticulocyte count (3). The haptoglobin was low (22 mg/dL). Antinuclear Antibodies (ANA) was weakly positive. Direct and indirect Coomb's tests were negative. Bile salts, bile pigments, and urobilinogen were negative. Erythrocyte Sedimentation Rate (ESR) and C-Reactive Protein (CRP) were negative. The hepatitis panel was negative [Table/Fig-4].

Day 10 investigations showed, thrombocytopenia (1,38,000/cumm), liver function showed hyperbilirubemia (2.4 mg/dL) direct bilirubin (1 mg/dL), and indirect bilirubin (1.4 mg/dL) with reducing enzymes (AST: 43 U/L, ALT: 101 U/L, ALP: 86 U/L) and (Prothrombin time: 18.3, INR: 1.4) [Table/Fig-1].

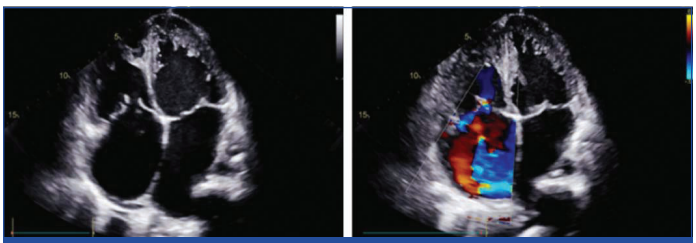
Following the investigative findings, the diagnosis was established as DCM with congestive hepatopathy probably due to post COVID-19. On day 1, patient was decongested using frusemide (40 mg BD), and spironolactone (25 mg OD), while ensuring that his blood pressure was normal. Inj. Vitamin K (10 mg OD) was also started in view of coagulopathy. Prothrombin time-INR was monitored on daily basis.

Parameters	Day 1: Admission	Day 4: Follow-up	Day 10: On discharge	7th Day: After discharge	3 month follow-up
Complete blood count					
Total Count (/cumm)	7300	9100	4800	6500	6800
Haemoglobin (gm/dL)	14.7	15.8	12.7	13.7	12.9
Platelet Count (/cumm)	81,000	78,000	1,38,000	1,64,000	2,73,000
Renal function test					
Urea (mg/dL)	31	60	23	25	19
Creatinine (mg/dL)	1.15	1.41	0.82	0.79	0.89
Sodium (mg/dL)	126	124	138	141	137
Potassium (mg/dL)	4.3	4.6	4.0	5.0	4.6
Chloride (mg/dL)	95	96	105	99	95
Liver function test					
Total protein (gm/dL)	5.9	6.2	5.2	7.2	6.5
Albumin (gm/dL)	3.2	3.7	2.7	3.9	3.7
Globulin (gm/dL)	2.7	2.5	2.5	3.3	2.8
Total bilirubin (mg/dL)	3.9	3.7	2.4	2.3	0.6
Direct bilirubin (mg/dL)	1.1	1.4	1.0	1.0	0.3
Indirect bilirubin (mg/dL)	2.8	2.3	1.4	1.3	0.3
Aspartate aminotransferase (U/L)	584	420	43	30	13
Alanine transaminase (U/L)	462	265	101	60	12
Alkaline phosphatase (U/L)	95	94	86	98	71
International normalised ratio	1.80	1.70	1.40	1.38	1.1
Prothrombin time (sec)	23	22.1	18.3	18.1	14.2
Peripheral smear report	Red blood cell: Normocytic Normochromic; White blood count: Normal count and distribution; Platelets: Moderate thrombocytopenia Reticulocyte count: 3				

[Table/Fig-1]: Investigation chart.



[Table/Fig-2]: Chest radiograph showing cardiomegaly.



[Table/Fig-3]: A 2D Echo four chamber view showing all chambers to be dilated and non coapting tricuspid valve, and tricuspid regurgitation.

Laboratory parameters on day 2 and day 3 (following admission)	Results
Immunoglobulin G (IgG), Immunoglobulin M (IgM) for COVID-19	Positive
Hepatitis panels:	Negative
Human immunodeficiency virus	
Hepatitis B surface antigen	
Hepatitis C virus	
Hepatitis A	
Hepatitis E	
Dengue	

Bacterial infection screening	
Scrub	Negative
Leptospira	
Blood culture	
Urine culture	
Cardiac biomarkers	
CPK NAC (U/L)	507
CPK MB (U/L)	25
Troponin I (ng/L)	5.7
N-Terminal Pro-B-Type Natriuretic Peptide (pg/mL)	4894
Serum lactate dehydrogenase (U/L)	988
Haptoglobin	22
Coombs TEST	Negative
Bile salt	
Bile pigment	
Urobilinogen	
Thyroid function test	Normal
Lipid profile	Normal
Antinuclear Antibodies (ANA)	Weakly positive
Erythrocyte Sedimentation Rate (ESR)	Normal
C-Reactive Protein (CRP)	Negative

[Table/Fig-4]: Other investigation findings.

On the third day of hospitalisation, the patient went into hypotension following the decongestion probably due to the diuretic effect (2,400 mL urine output compared to 750 mL of oral fluid intake). Hence, the diuretic was withheld, and he was started on inotropic support (dopamine) along with causation usage of intravenous (i.v.) fluid which was slowly tapered and stopped (36 hours).

Following haemodynamic stability of 48 hours, on 7th day patient was initiated on Angiotensin-Converting Enzyme 2 (ACE 2) inhibitors (Enalapril 2.5 mg BD), low diuretics (Spironolactone 25 mg OD,

Furosemide 20 mg OD) and Digoxin 0.25 mg OD. On the 10th day of admission patient showed improvement clinically, his leg swelling, breathlessness and jaundice decreased, laboratory parameters liver function test, coagulopathy (INR: 1.40 and echocardiogram (ejection fraction 30%) showed an improving trend. Hence, the patient was discharged from the hospital on the 10th day of admission and was followed up on an Outpatient Department (OPD) basis.

After one week, the patient was reviewed in OPD. The leg swelling had resolved and breathlessness reduced. His platelets had improved (164000/cumm), and liver function showed hyperbilirubemia (2.3 mg/dL) direct bilirubin (1.0 mg/dL), and indirect bilirubin (1.3 mg/dL) with reducing enzymes (AST: 30 U/L, ALT: 60 U/L, ALP: 98 U/L) and (Prothrombin time: 18.1, INR: 1.38). His repeat ECHO showed ejection fraction of: 40%. So, he was advised to continue his ACE inhibitors, diuretics, digoxin and suggested regular monthly follow-up.

Following a three month review, the patient was asymptomatic and on regular medication for heart failure, and his laboratory parameters such as liver function test and thrombocytopenia resolved completely.

DISCUSSION

Post COVID-19 Dilated Cardiomyopathy (DCM): In this pandemic of COVID-19, the hallmark of COVID-19 is respiratory involvement ranging from mild symptoms to acute severe respiratory distress syndrome. But some studies are showing an increasing number of patients being hospitalised for COVID with acute heart failure and multisystem inflammatory state [1,2]. Post COVID-19 cardiovascular sequelae are considered to be an involvement of the direct viral injury to the cardiac cells and host immune response against the virus [3]. Cardiovascular sequelae associated with COVID-19 are myocardial injury, myocarditis, acute coronary syndrome, cardiac arrhythmias, cardiac arrest, cardiomyopathy, heart failure, and cardiogenic shock [4]. Cardiomyopathies are the main cause of heart failure and sudden death in adolescents [5].

Though the aetiology of non hereditary DCM has not yet been elucidated, several viral genomes have been detected in myocardial tissue samples from patients diagnosed with DCM, even when infiltrating inflammatory cells are undetectable [6]. A prolonged immune mechanism gets activated following a viral infection which causes a transition to DCM [7]. COVID-19 infects the human heart especially, in case of heart failure as ACE 2 is upregulated because COVID-19 enters into human cells by binding its spike protein to the membrane protein Angiotensin-Converting Enzyme 2 (ACE 2) [8].

In the index case, the patient presented with DCM with elevated levels of NTPro-BNP (4894 pg/mL), which was similar to the case-series by Guo T et al., that analysed patients with COVID-19. Among 187 patients, 66 (35.3%) had cardiomyopathy out of which 27.8% of patients had myocardial injury. This study also reported that 8 (4.3%) of the study populace had cardiomyopathy with significant rise in troponin levels (p-value <0.001) [9]. but there was no significant rise in troponin levels in the present case probably due to late presentation.

Similarly, a study of 416 hospitalised COVID-19 patients, showed evidence of myocardial injury which manifested with elevated high-sensitivity troponin-I levels. It was found that severe systemic inflammation was associated with greater leucocyte counts, C-reactive protein and procalcitonin. Other biomarkers such as creatine kinase, myoglin and NT-proBNP were elevated as well [1].

The patient's 2D Echo was suggestive of enlargement of all four chambers, global hypokinesia of the left ventricle with severe LV systolic dysfunction (EF: 23%). This was similar to a study conducted by Inciardi RM et al., in which a 53-year-old female presented with elevated NT-proBNP levels and cardiac MRI showed increased wall thickness with diffuse biventricular hypokinesis in the apical segments, and severe left ventricular dysfunction (left ventricular ejection fraction of 35%) [10].

In all the cases reported so far, the troponin levels were elevated but in the index case, the troponin levels were within normal limits. This emphasises better prognosis for the patient compared to patients with cardiovascular disease with elevated troponin levels that leads to significant morbidity and mortality rates. Though the patient had chief complaints of breathlessness and jaundice; bedside clinical examination revealed congestive heart failure, and the echocardiography, suggestive of DCM. The patient was not vaccinated and had a COVID-19 infection (COVID-19 IgG and IgM: positive) 15 days prior to onset of the above symptoms. The patient would have still been having a persistent immune mediated activation due to the COVID-19, which could have led to haemolytic pictures as well as the DCM.

Dilated Cardiomyopathy (DCM) with congestive hepatopathy: Any cause of elevated central venous pressure such as right-side heart failure, biventricular dysfunction, severe pulmonary hypertension or cor-pulmonale, constrictive pericarditis leads to the development of hepatic congestion, which is also referred to as congestive hepatopathy [11].

Ascites is also clinically present in up to 20% of patients with congestive hepatopathy [12], while cases presenting with pleural effusion and pericardial effusion were also reported [11]. Congestive heart failure shows a broad range of liver abnormalities, a hepatocellular pattern with predominantly elevated transaminases is seen in hypoxic hepatitis. In cardiac hepatopathy, hyperbilirubinemia is reported with a mild increase in unconjugated bilirubin (<3 mg/dL) in 70% of patients [13].

In congestive hepatopathy, the common laboratory abnormalities are hyperbilirubinemia, which is reported with a mild increase in unconjugated bilirubin (<4.5 mg/dL); out of which 50-60% are unconjugated because of mild haemolysis, reduced uptake, and decreased conjugation by hepatocytes. INR derangement in acute congestion may rise up to twice the normal and it is not responsive for the vitamin K, and may return normal after successful decongestion. Aminotransferases are elevated 3-4 times the UNL, and AST >ALT as the AST is rich in cardiac myocytes. And these enzymes return to normal in 3-7 days after improving cardiac function. Albumin is decreased to 30-50%, it takes more than a month to improve following the resolution of the heart failure [14].

In the present case, patient had the characteristic laboratory abnormalities congestive hepatopathy of such as predominant unconjugated hyperbilirubinemia and elevation of aminotransferases with which became normal after successful treatment with the ACE inhibitors (enalapril), low diuretics (spironolactone, furosemide), and digoxin. And also features of mild haemolysis such as mild coagulopathy, with low haptoglobin level, elevated LDH, and a weakly positive ANA report which may probably be due to the immune-mediated effect of the COVID-19 or because of the native medication which the patient had during the event of jaundice.

CONCLUSION(S)

Many studies have been reported on coronavirus-related DCM, but due to a rapid deterioration in such patients it is difficult to extend the process of research among these patients. This patient was asymptomatic without any cardiac symptoms until the event of COVID-19 illnesses. However, immediately 15 days post COVID-19 infection, he started to have acute symptoms of breathlessness, pedal oedema, and abdominal pain. Further evaluation confirmed presence of DCM with congestive hepatopathy. These symptoms might have shown due to the persistent immune mediated activation, seen in post COVID-19 infection. Still future research is needed to determine the cause of myocardial injury and adverse cardiac outcome after this viral infection.

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