Fulminant myocarditis in a COVID-19 positive patient treated with mechanical circulatory support – a case report

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Background Coronavirus disease 2019 (COVID-19) spreading from Wuhan, Hubei province in China, is an expanding global pandemic with significant morbidity and mortality. Even though respiratory failure is the cardinal form of severe COVID-19, concomitant cardiac involvement is common. Myocarditis is a challenging diagnosis due to heterogeneity of clinical presentation, ranging from mild symptoms to fatal arrhythmia and cardiogenic shock (CS). The aetiology is often viral and endomyocardial biopsy (EMB) is the gold standard for definite myocarditis. However, the diagnosis is often made on medical history, clinical presentation, magnetic resonance imaging, and blood tests.

Case summary We present a 43-year-old man with mixed connective tissue disease treated with hydroxychloroquine who rapidly developed CS 4 days from symptom onset with fever and cough, showing positive polymerase chain reaction nasopharyngeal swab for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA. While computed tomography of the thorax was normal, high-sensitivity troponin T was elevated and electrocardiogram showed diffuse ST elevation and low voltage as signs of myocardial oedema. Echocardiography showed severe depression of left ventricular function. The myocardium recovered completely after a week with mechanical circulatory support (MCS). EMB was performed but could neither identify the virus in the cardiomyocytes, nor signs of inflammation. Still the most probable aetiology of CS in this case is myocarditis as a sole symptom of COVID-19.

Discussion COVID-19 patients in need of hospitalization present commonly with respiratory manifestations. We present the first case of fulminant myocarditis rapidly progressing to CS in a COVID-19 patient without respiratory failure, successfully treated with inotropes and MCS.

Keywords Case report • COVID-19 • Myocarditis • Cardiogenic shock • Mechanical circulatory support • Endomyocardial biopsy

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COVID-19 patient. Cardiogenic shock (CS) without pulmonary manifestations in a due to the host's immune response. The clinical course is characterized by fever, cough, fatigue, anosmia, and ageusia, sometimes complicated by acute respiratory distress syndrome (ARDS). Fulminant myocarditis is a rare critical clinical condition with poor in-hospital outcome, whose main characteristic is a rapidly progressive clinical course with the need for haemodynamic support. Aetiology includes a variety of triggers, often viral infections. Myocardial injury is common in patients with COVID-19, including myocarditis, myocardial infarction, and stress-induced cardiomyopathy. COVID-19-related myocarditis can be caused by a combination of direct viral injury and cardiac damage due to the host’s immune response.

We present a case of fulminant myocarditis rapidly progressing to cardiogenic shock (CS) without pulmonary manifestations in a COVID-19 patient.

Introduction

A large number of coronavirus disease (COVID-19) patients displaying cardiac involvement have been reported since the first cases of COVID-19 in Wuhan, China in December 2019. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pathogen is a positive-sense single-stranded RNA virus with transmission primarily via respiratory droplets. The clinical course is characterized by fever, cough, fatigue, anosmia, and ageusia, sometimes complicated by acute respiratory distress syndrome (ARDS). Fulminant myocarditis is a rare clinical condition with poor in-hospital outcome, whose main characteristic is a rapidly progressive clinical course with the need for haemodynamic support. Aetiology includes a variety of triggers, often viral infections. Myocardial injury is common in patients with COVID-19, including myocarditis, myocardial infarction, and stress-induced cardiomyopathy. COVID-19-related myocarditis can be caused by a combination of direct viral injury and cardiac damage due to the host’s immune response.

We present a case of fulminant myocarditis rapidly progressing to cardiogenic shock (CS) without pulmonary manifestations in a COVID-19 patient.

Timeline

Laboratory measurements, circulatory and respiratory support

|                | Reference Day 0 | Day 1a | Day 1b | Day 4 | Day 5 | Day 6 | Day 7 | Day 9 | Day 11 | Day 12 |
|----------------|-----------------|--------|--------|-------|-------|-------|-------|-------|--------|--------|
| Haemoglobin, g/L | 137–170         | 161    | 159    | 154   | 131   | 125   | 107   | 96    | 97     | 97     |
| White blood cell count \(\times 10^9/L\) | 3.5–8.8         | 9.7    | 8.5    | 16.2  | 9.5   | 11.4  | 15    | 14.4  | 14.4   | 11.5   |
| Platelet count \(\times 10^9/L\) | 140–350         | 245    | 236    | 197   | 139   | 82    | 65    | 70    | 59     | 88     |
| Lymphocyte count \(\times 10^9/L\) | 1.1–4.8         | 1.8    | NA     | NA    | 0.7   | NA    | 0.5   | 1.2   | 1.6    | NA     |
| Sodium, mmol/L  | 137–145         | 136    | 129    | 134   | 134   | 136   | 135   | 142   | 155    | 154    |
| Potassium, mmol/L | 3.5–4.4        | 3.6    | 4.5    | 4.4   | 5     | 4.2   | 4.5   | 4     | 4      | 4.1    |
| Creatinine, µmol/L | 60–105         | 73     | 77     | 69    | 83    | 166   | 105   | 98    | 142    | 128    |
| C-reactive protein, mg/L | <10            | 4      | 6      | <5    | 9     | 88    | 134   | 44    | 25     | NA     |
| Procalcitonin, µg/L | <0.5           | 0.06   | 0.06   | 0.1   | 0.9   | 9     | 17    | 10    | 2.6    | 0.6    |
| Creatine kinase-MB, ng/mL | <5            | NA     | NA     | 111   | 37    | NA    | NA    | NA    | NA     | NA     |
| High-sensitivity troponin T, ng/L | <15           | 590    | 730    | 1620  | 1820  | NA    | NA    | NA    | NA     | NA     |
| N-terminal pro-brain natriuretic peptide, ng/L | <300         | NA     | 6100   | 10100 | 17300 | 28600 | NA    | 3400  | NA     | NA     |
| Interleukin-6, ng/L | <7            | NA     | NA     | 30    | 300   | 35    | 46    | NA    | NA     | NA     |
| D-dimer, mg/L | <0.20           | NA     | NA     | <0.5  | 0.56  | 0.67  | 0.19  | 0.28  | 0.24   | 0.54   |
| Lactate dehydrogenase, µkat/L | <3.5          | NA     | 5.1    | NA    | 6.4   | NA    | 2     | NA    | NA     | NA     |
| Ferritin, µg/L | 34–275          | NA     | 220    | NA    | 261   | NA    | 318   | NA    | NA     | NA     |
| Lactate, mmol/L | 0.5–2.2         | 3.4    | 5.1    | 4.7   | 4     | 5.8   | NA    | 0.9   | 0.9    | 0.6    |
| Impella          | x                | x      | x      | x     | x     | x     | x     | x     | x      | x      |
| VA-ECMO          | x                | x      | x      | x     | x     | x     | x     | x     | x      | x      |
| Intubated        | x                | x      | x      | x     | x     | x     | x     | x     | x      | x      |

Case presentation

A 43-year-old non-smoking male with a history of Mixed Connective Tissue Disease (MCTD) presented to the emergency room due to chest pain. His drug history was hydroxychloroquine 400 mg once daily (for the past 5 months), and he was otherwise healthy in excellent physical condition. The patient presented with a 4 day history of fever and cough. The patient’s wife was also suffering from similar symptoms. Physical examination revealed no murmurs or rales, systolic blood pressure (BP) of 100 mmHg, a heart rate of 130 b.p.m., and oxygen saturations of 90–100% on 10–15 L/min of oxygen. Electrocardiograms showed sinus tachycardia and diffuse ST-segment elevation. All electrocardiograms are presented in Figure 1A–C.

Thoracic computed tomography (CT) scan revealed no pathology. High sensitivity Troponin T (hsTnT) was 590 ng/L [upper limit of normal (ULN) 15 ng/L] and the patient was initially treated as non-ST-elevation myocardial infarction (NSTEMI) with aspirin, ticagrelor, and fondaparinux. Later, perimyocarditis was suspected and cefotaxime and colchicine were administered. Treatment with cefotaxime was not the hospitals’ policy, treatment was initiated to cover for a possible bacterial infection. The nasopharyngeal swab polymerase chain...
Figure 1  (A) Electrocardiogram 2019, normal sinus rhythm, left axis deviation. (B) Electrocardiogram at admission, sinus tachycardia, low voltage and diffuse ST-segment elevation in limb and precordial leads. (C) Electrocardiogram Day 24 at Coronary Care Unit during rehabilitation period.
infusions were started together with IV fluid. ScvO2 had dropped to 130 b.p.m., and BP 85/70 mmHg. Levosimendan and norepinephrine cant anxiety, and complained of chest and abdominal pain. He patient was referred to the local Coronary Care Unit (CCU). Upon culture. In total, the patient was positive for SARS-CoV-2 in three dif-

CoV-2 RNA. Repeated PCR tests for SARS-CoV-2 were positive, due to MCTD. The biopsies showed no histopathological signs of myocarditis and myocardial samples tested negative for SARS-

did not result in histological evidence for myocarditis and preserva-

tion of the left ventricular function without any regional differences. In total, the patient was positive for SARS-CoV-2 in three differ-
tests. Despite massive inotropic and vasopressor support as well as Impella®, pre-shock signs remained. It was felt that this mandated an upgrade of MCS to include veno-arterial extracorporeal membrane oxygenation (VA-ECMO, Cardiohelp™ Maquet Cardiovascular, Bridgewater, NJ, USA) in combination with the Impella®. Within hours the circulation stabilized (initially blood flow of 3.7 L/min, sweep gas flow of 2.5 L/min at 100% oxygen) and inotropic support could gradually be decreased.

A new CT scan could not demonstrate any pulmonary infiltrates, and laboratory parameters improved. Within 24h after the VA-ECMO institution, renal function improved.

After 3 days, while weaning MCS, transthoracic echocardiography confirmed biventricular systolic improvement. After a multidisciplin-

ary meeting on Day 7, the patient was successfully weaned off MCS, the left ventricular function normalized (Figure 2B), and he was later moved to the CCU. At Day 25, he was referred to his local county hospital being treated for an infection of unclear focus.

Discussion

We describe a case of isolated fulminant SARS-CoV-2 associated myocarditis rapidly progressing to CS in need of and successfully treated with temporary MCS. Our main finding reflects that which has been previously reported by Inciardi et al.,4 that severe cardiac involvement may be the only clinical manifestation of SARS-CoV-2.

The first case report of myocarditis associated with COVID-19 was a 63-year-old male who after travelling to Wuhan, developed fever, shortness of breath and chest tightness. He was considered to have fulminant myocarditis (EF 32%) along with ARDS and needed respiratory support by veno-venous (VV) ECMO. Later, a similar case was reported from Lombardy, with SARS-CoV-2 associated myocarditis in a 69-year old man with ARDS requiring mechanical ventilation. Magnetic resonance imaging (MRI) showed regional sub-

epicardial late gadolinium enhancement suggestive of myocarditis. In addition, several mild cases of myocarditis without need of circula-
tory or respiratory support have been reported.6,7 EMB was not per-
duced firstly due to the MCS access site and received massive transfu-
sions with 48E erythrocytes, 22E fresh frozen plasma and 3E platelets. Hydroxychloroquine treatment was terminated upon his arrival to ICU.

The next day the patient was anaesthetized, intubated and surgical revision of the access site was performed as well as endomyocardial biopsy (EMB) via the right internal jugular vein. Milrinone was termi-

ated and vasopressin added because of vasodilatation. He showed signs of CS with cold extremities, oliguria, heart rate 120–

130 b.p.m., and BP 85/70 mmHg. Levosimendan and norepinephrine infusions were started together with IV fluid. ScvO2 had dropped to 36%. Immediate echocardiography confirmed the previous findings (Figure 2) and the patient was referred to the cardiothoracic intensive care unit (ICU). Inotropic support was enhanced with epinephrine and milrinone. He received a Swahn-Ganz pulmonary artery catheter as well as mechanical circular support (MCS) (Impella® CP Smart Assist, Abiomed, Aachen, Germany), initially at 3.8 L/min later increased to 4.2 L/min. Mixed venous gas saturation (SvO2) improved to 57%. However, cardiac index remained low between 1.8 and 2.5 L/m² and norepinephrine in high doses was needed to maintain mean arterial BP above 60 mmHg. During the night, he was bleeding profoundly from the MCS access site and received massive transfu-
sions with 48E erythrocytes, 22E fresh frozen plasma and 3E platelets. Hydroxychloroquine treatment was terminated upon his arrival to ICU.

Despite massive inotropic and vasopressor support as well as Impella®, pre-shock signs remained. It was felt that this mandated an

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lifesaving, in its ability to support the circulation, thereby preventing multi-organ failure, and allowing the myocardium, most often, to heal spontaneously.\textsuperscript{14} If other supportive or antiviral treatments should be offered to SARS-CoV-2 associated fulminant myocarditis is yet to be proven,\textsuperscript{15} and it is of importance to note that our patient recovered without antiviral treatments.

\textbf{Figure 2} (A and B) Longitudinal strain at admission and after 15 Days.
Dr Joanna-Maria Papageorgiou graduated from Sofia Medical University, Bulgaria in 2005. Her clinical carrier began as a Resident Doctor in Internal Medicine at Höglandssjukhuset, Eksjö, Sweden. She completed her Cardiology residency programme in University Hospital of Linköping, Sweden in 2016. With a keen interest in Heart Failure, Pulmonary Arterial Hypertension, and Heart Transplantation, she is currently a clinical fellow of Cardiology at University Hospital of Linköping, Her current research focuses on Heart Failure and Pulmonary Arterial Hypertension.

Supplementary material

Supplementary material is available at European Heart Journal - Case Reports online.

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Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: H.v.d.W. has previously received personal fee from Orion Pharma and J-M.P. has previously received personal fee from Orion Pharma as well as Novartis. None of the other authors had any competing interests.

References

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J et al. A novel coronavirus from patients with pneumonia in China. 2019. N Engl J Med 2020;382:727–733.
2. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382:1708–1720.
3. Inciardi RM, Lupi L, Zaccone G, Italia L, Raffo M, Tomasini D et al. Cardiac involvement in a patient with coronavirus disease 2019 (COVID-19). JAMA Cardiol 2020;5:819.
4. Zeng JH, Liu YX, Yuan J, Wang FX, Wu WB, Li JX et al. First case of COVID-19 complicated with fulminant myocarditis: a case report and insights. Infection 2020;48:773–777.
5. Doyen D, Moceri P, Ducrues D, Dellamonica J et al. Myocarditis in a patient with COVID-19: a cause of raised troponin and ECG changes. Lancet 2020;395:1516.
6. Paul JF, Charles P, Richaud C, Causin C, Diakov C et al. Myocarditis revealing COVID-19 infection in a young patient. Eur Heart J Cardiovasc Imaging 2020;21:776.
7. Kim IC, Kim JY, Kim HA, Han S et al. COVID-19-related myocarditis in a 21-year-old female patient. Eur Heart J 2020;41:1859.
8. Joyce F, Fabre A, Mahon N. Hydroxychloroquine cardiotoxicity presenting as a rapidly evolving biventricular cardiomyopathy: key diagnostic features and literature review. Eur Heart J Acute Cardiovasc Care 2013;2:77–83.
9. Ungprasert P, Wannarang T, Panichhullakit T, Cheungpasitporn W, Thongprayoon C, Ahmed S et al. Cardiac involvement in mixed connective tissue disease: a systematic review. Int J Cardiol 2014;171:326–330.
10. Sala S, Peretto G, Gramigna M, Palmisano A, Villatore A, Vignale D et al. Acute myocarditis presenting as a reverse Tako-Tsubo syndrome in a patient with SARS-CoV-2 respiratory infection. Eur Heart J 2020;41:1861–1862.
11. Bentzgen X, Kruger K, Supady A, Durschmied D, Schibisky D, Bamberg F et al. First successful treatment of COVID-19 induced refractory cardiogenic shock and oxygenation failure by combination of pVAD and ECMO—a case report. ASAIO J 2020;66:607–609.
12. Jacobs JP, Stammers AH, St Louis J, Hayanga JW, Firstenberg MS, Mongoero LB et al. Extracorporeal membrane oxygenation in the treatment of severe pulmonary and cardiac compromise in COVID-19: experience with 32 patients. ASAIO J 2020;66:722–730.
13. Sultan I, Habenteuer A, Ulman AA, Klic A, Gnall E, Frisica ME et al. The role of extracorporeal life support for patients with COVID-19: Preliminary results from a statewide experience. J Card Surg 2020;35:1410–1413.
14. Caforio AL, Pancuweit S, Arbustini E, Basso C, Gimeno-Blanes J, Felix SB et al. 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. Eur Heart J 2013;34:2636–2648. 2648a–2648d.
15. Siripanthong B, Nazarian S, Muser D, Deo R, Santangeli P, Khanji MY et al. Recognizing COVID-19-related myocarditis: the possible pathophysiology and proposed guideline for diagnosis and management. Heart Rhythm 2020;17:1463–1471.