Case report

Fulminant myocarditis as an early presentation of SARS-CoV-2

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SUMMARY

Myocarditis is well known to be caused by viral infections such as Coxsackie virus group B, human herpes virus 6 and parvovirus B19. However, during the current emerging outbreak of SARS-CoV-2, there have been few case reports describing myocarditis as a possible presentation. In our case report we describe, early cardiac manifestations of SARS-CoV-2 in a UK District General Hospital. A 44-year-old Caucasian woman without any comorbidities presented with SARS-CoV-2 related fulminant myocarditis without initial respiratory symptoms. Patient underwent treatment with milrinone and methylprednisolone that showed reduction in myocardial inflammation and significantly improved myocardial contractility. This was then followed by a second phase of SARS-CoV-2 associated pneumonia and renal failure requiring ventilatory support and haemofiltration. Although, not described in the literature, we have found conjunctive use of milrinone and methylprednisolone effective in patient with SARS-CoV-2 fulminant myocarditis.

BACKGROUND

Myocarditis is well known to be caused by viral infections such as Coxsackie virus group B, human herpes virus 6 and parvovirus B19. However, during the current emerging outbreak of SARS-CoV-2, there have been few case reports describing myocarditis as a possible presentation.1,2 In our case report we describe, early cardiac manifestations of SARS-CoV-2 in a UK District General Hospital.

CASE PRESENTATION

A 44-year-old Caucasian woman without any previous co-morbidities, presented to the emergency department, with a 3-day history of febrile illness, lethargy, muscle aches and two episodes of syncope. These were not preceded by any warning symptoms and there was no family history of cardiovascular diseases.

She was care provider for a patient suffering from SARS-CoV-2 and had a nasopharyngeal swab specimen for SARS-CoV-2 taken a day before admission and the results were awaited. Despite being in close contact with a SARS-CoV-2 positive individual, she did not have chest pain throughout this illness and serial ECGs never identified myocardial ischaemia. Fluid resuscitation was commenced and the intensive care team was involved in the patient’s care.

While she was in the emergency department, patient developed a presyncopal episode with hypotension (BP 85/40 mm Hg). A 12-lead ECG demonstrated atrial fibrillation with a ventricular rate of 177 bpm (figure 1) requiring DC cardioversion. This then reverted to sinus rhythm with no features to suggest myocardial ischaemia. The patient did not have chest pain throughout this illness and serial ECGs never identified myocardial ischaemia.

Laboratory investigations on admission revealed elevated high-sensitivity troponin I (639 ng/L), CK (1403 U/L), D-dimer (579 ng/mL), mild leukocytosis (15.8×10^9/L), lymphocytes (2.0×10^9/L), CRP (47 mg/L), creatinine (149 µmol/L), eGFR (33 mL/min/1.73 m²) and lactate of 7.1 mmol/L. CT of chest–abdomen–pelvis (figure 2) revealed 1 cm rim of pericardial fluid and minimal bi-basal lung inflammatory changes.

Bedside echocardiography (figure 3) demonstrated moderate concentric biventricular hypertrophy, diffused left ventricular hypokinesia with moderate to severe left-ventricular systolic dysfunction (estimated Ejection Fraction (EF) 37% by Simpsons) and pericardial effusion with no signs of tamponade. PCR for SARS-CoV-2 was positive in both nasopharyngeal swabs taken in the community and at the time of admission. Screening for enteroviruses and parvovirus B19 came back negative.

Serial cardiac biomarkers showed steady decline in high-sensitivity troponin I from initial value of 639-309 ng/L on day 5 and 90 ng/L on day 18.

Moderate increase in inflammatory markers was observed by day 5 (CRP 126 mg/L, WCC 29.2×10^9/L) with subsequent decline over the course of treatment (CRP 84 mg/L, WCC 7.4×10^9/L).

INVESTIGATIONS

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of overwhelming sepsis that could have lead to sepsis-related cardiomyopathy.

Type 2 myocardial infarction (MI) based on oxygen demand–supply mismatch can be one of the reasons for the elevated cardiac biomarkers. According to the Universal Definition of MI, the diagnosis of MI requires the rise and/or fall of cardiac biomarkers with clinical evidence of ischaemia, defined by symptoms, electrocardiographic changes, or new regional wall motion abnormalities. However, in this case there were no ECG changes consistent with ischaemia and echocardiography demonstrated global myocardial dysfunction rather than regional wall motion abnormalities. Coronary angiography was not performed due to low suspicion of acute coronary syndrome and patient’s haemodynamic instability.

TREATMENT

Treatment was started with methylprednisolone 1000 mg on the first day and 250 mg/day for the subsequent 2 days with the aim of reducing myocardial inflammation. Antiviral treatments like remdesivir and inflammation modulating immunosuppressive monoclonal antibodies such as tocilizumab were not employed in her care.

In the intensive care unit, patient developed cardiogenic shock with a BP of 60/40 mm Hg despite being on optimally titrated dobutamine infusion. ECG revealed atrial fibrillation with ventricular rate of 140 bpm and patient had signs of peripheral hypoperfusion despite being on inotropic support and amiodarone infusion. She had anuria with significant metabolic acidosis. The pH was 7.192 and had a base excess of −17.5 with partial respiratory compensation (PCO₂ 3.17; PO₂ 16.41 on 15 L via non-rebreather mask). Cardiac output monitoring was initiated and the cardiac index was calculated using a pulse contour cardiac output (PICCO) line and the Stewart-Hamilton equation. Patient was commenced on milrinone infusion at 0.375 µg/kg/min and norepinephrine infusion at 0.10–0.20 µg/kg/min was used as an adjunct in order to counteract the vasodilatory effect of milrinone. A loading dose of milrinone was avoided due to high risk of cardio-vascular systemic collapse. The milrinone dose was up-titrated according to clinical response to the maximal dose of 0.6 µg/kg/min. Acid–base balance improved (pH 7.375 with base excess of −9.4, PCO₂ 3.24; PO₂ 9.37 on 40% FiO₂), though anuria persisted which prompted the initiation of haemofiltration.

Interval echocardiography done on the third day of admission showed normalisation of left ventricular systolic function with biventricular hypertrophy and a small pericardial effusion. By the end of the fourth day, cardiac index had improved from 1.8 to 4. Inotropic support was discontinued, and the patient remained in sinus rhythm. The patient’s oxygen requirement increased on the fifth day and was eventually intubated. Chest X-ray (figure 4) demonstrated bilateral patchy air space shadowing consistent with SARS-CoV-2 pneumonia. Antibiotics were commenced for superadded bacterial infection.

OUTCOME AND FOLLOW-UP

Interval echocardiography at 2 weeks (figure 5) demonstrated mild residual left ventricular posterior wall hypertrophy with complete resolution of right ventricular hypertrophy and preserved biventricular function. Improvement in respiratory support was observed by day 15 and tracheostomy was performed. Patient continued to improve and was finally discharged on day 41 after closure of her tracheostomy. Patient continues to recover at home.
Due to full recovery of left ventricular (LV) systolic function, drugs which are used to prevent cardiac remodelling like ACE inhibitors and beta-blockers were not started.

Outpatient cardiac MRI has been arranged and cardiology follow-up appointment is booked at 1 month.

DISCUSSION
Clinical presentation of SARS-CoV-2 mainly constitutes of respiratory symptoms. Presentation is, however, very heterogeneous. In our case we describe a predominant cardiac presentation of SARS-CoV-2 in the absence of respiratory symptoms at baseline. This emphasises the importance of having a low index of suspicion for this novel virus as being the underlying aetiology of acute fulminant myocarditis.

While uncommon, fulminant myocarditis is a malignant condition requiring rapid recognition and treatment due to high morbidity and mortality. Our patient had a clinical picture consistent with acute myocarditis with rapid deterioration leading to cardiogenic shock and need for inotropic support. This was followed by a second phase of typical SARS-CoV-2 pneumonia and renal failure. Normal biventricular function was regained within few days on milrinone and methylprednisolone treatment. Milrinone, a phosphodiesterase inhibitor that is selective for cAMP-specific cardiac receptors, is known to be used for acute heart failure resulting from systolic dysfunction secondary to infectious or toxic myocarditis. However, at present there is not enough literature of its use in SARS-CoV-2 myocarditis. Individual cases have been reported which show success of methylprednisolone in patients with SARS-CoV-2 myocarditis. Though, the use of methylprednisolone in conjunction with milrinone has not been described so far.

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Learning points
- SARS-CoV-2 can present as fulminant myocarditis in absence of respiratory symptoms.
- Echocardiography can play a crucial role in the diagnosis and Cardiac MRI (CMR) can be useful in confirmation of diagnosis.
- Milrinone and methylprednisolone combination is a viable treatment option for SARS-CoV-2 myocarditis.
New disease

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