ESC HEART FAILURE
ESC Heart Failure 2021; **8**: 4307–4312
Published online 30 July 2021 in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/ehf2.13461

CASE REPORT

Presence of active myocarditis at the 6 month follow-up appointment for a severe form of COVID-19: a case report

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Abstract

Here, we present the case of an 81-year-old male patient, who was hospitalized for a severe form of COVID-19. Transthoracic echocardiogram (TTE) performed 1 month after symptom onset was normal. Respiratory evolution was favourable, and the patient was discharged at Day 78. At 6 months, despite a good functional recovery, he presented pulmonary sequelae, and the TTE revealed a clear reduction of left ventricular ejection fraction (LVEF) and mild LV dilatation without cardiac symptoms. The cardiac magnetic resonance (CMR) using Lake Louise Criteria (LLC), T1 and T2 mapping showed focal infero-basal LV wall oedema, elevated T1 and T2 myocardial relaxation times especially in basal inferior and infero-lateral LV walls, and sub-epicardial late gadolinium enhancement in those LV walls. The diagnosis of active myocarditis was raised especially based on TTE abnormalities and CMR LLC, T1 and T2 mapping. Currently, we are not aware of published reports of a 6 month post-COVID-19 active myocarditis.

Keywords COVID-19; SARS-CoV-2; Myocarditis; Myocardial injury; 6 month follow-up; Long-term sequelae

Received: 12 February 2021; Revised: 25 April 2021; Accepted: 23 May 2021
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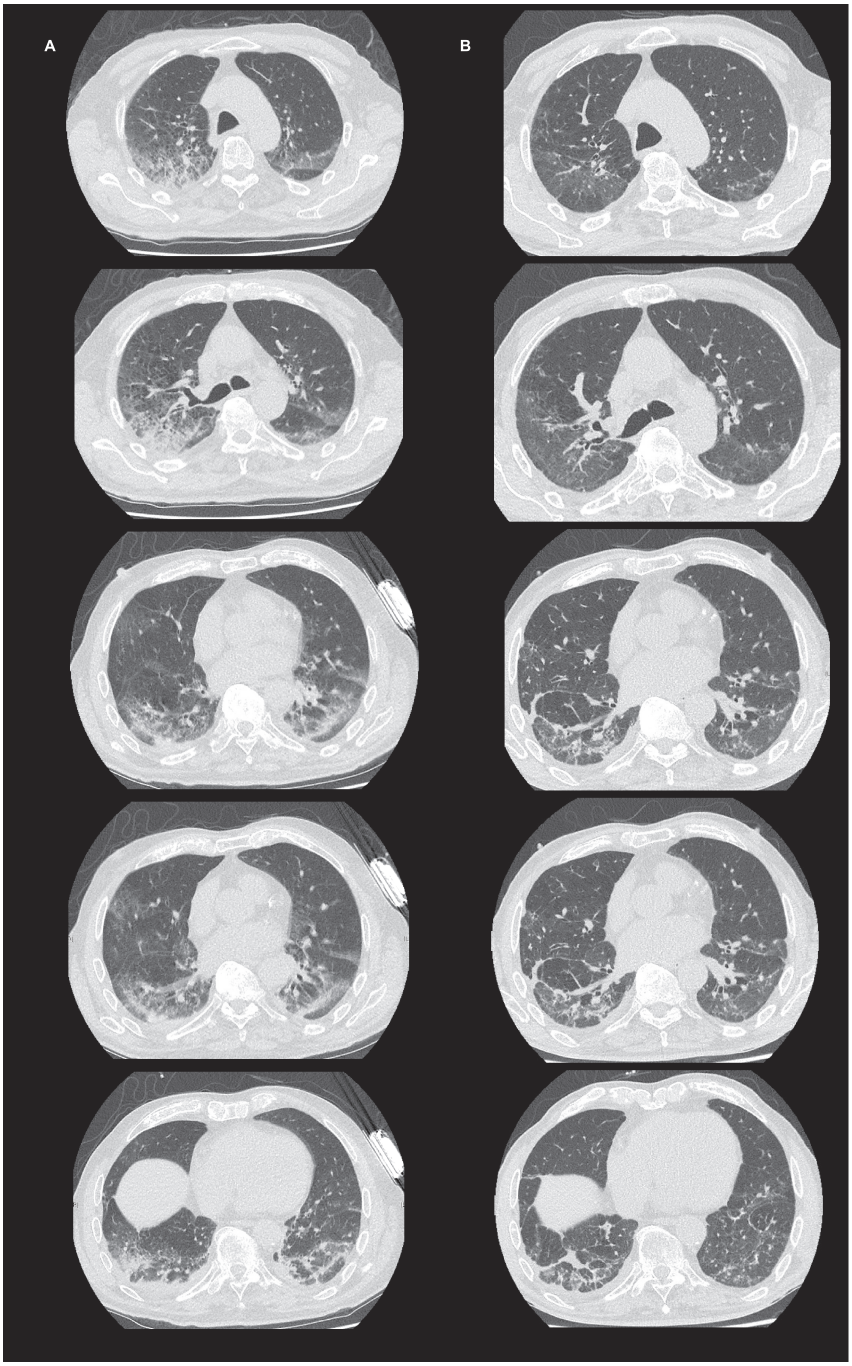
Introduction

The incidence, underlying mechanisms, and risk factors of SARS-CoV-2-associated myocarditis are currently unclear.[1] The mechanism of myocarditis could be due to the combination of direct cell injury and T-lymphocyte-mediated cytotoxicity. The SARS-CoV-2 enter into the human cells by binding its spike protein to the membrane protein angiotensin-converting enzyme 2 (ACE2), which could be founded on the cardiomyocytes.[2] According to the European Society of Cardiology (ESC),[1] myocarditis should be suspected in COVID-19 patients with acute-onset chest pain, ST segment changes, cardiac arrhythmia, and haemodynamic instability. In addition, in the presence of left ventricular (LV) dilatation, global and/or LV wall motion abnormalities on transthoracic echocardiogram (TTE), and a significant increase in cardiac troponin and BNP/N-terminal pro-brain natriuretic peptide (NT-pro-BNP) levels, without significant coronary artery disease (CAD), the suspicion of myocarditis should be raised in COVID-19 patients, and if cardiac magnetic resonance (CMR) is available, it may be used for further diagnostic assessment.

Whilst the literature is abundant with case descriptions of COVID-19 cardiac manifestations and post-COVID-19 myocarditis cases, there are limited data regarding the follow-up and evolution over time of cardiac manifestations in COVID-19 patients.[3–9]

We present here the case of the very first and so far only COVID-19 patient hospitalized in our Geriatric Department during the first local wave of COVID-19 who received a systematic follow-up at 6 months. At 6 months, despite a good functional recovery, the patient presented pulmonary sequelae and an active myocarditis with evidence of a clear reduction of his left ventricular ejection fraction (LVEF) and mild LV dilatation. These cardiac conditions were not present on the TTE performed 1 month after the COVID-19 diagnosis.

Figure 1 Thoracic CT scan of an 81-year-old male with severe COVID-19 at admission and 6 months after.



DOI: 10.1002/ehf2.13461

Case report

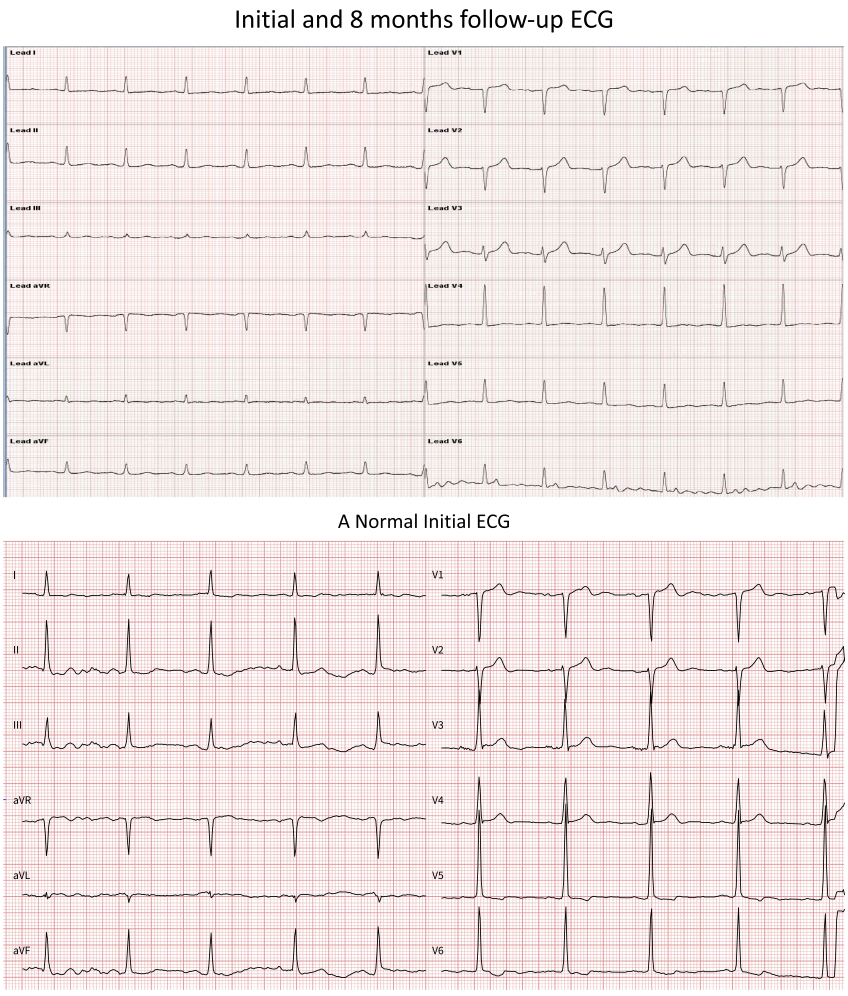
Hospitalization

In March 2020, an 81-year-old male patient was hospitalized in our geriatric unit for a severe form of COVID-19. Past medical history included hypertension and prostate adenocarcinoma treated with radiotherapy 2 years prior. The patient recalled a 7 day history of flu-like symptoms prior to admission including cough and dyspnoea. He was admitted for worsening dyspnoea 7 days after the date of first symptom onset (dso). On admission, his temperature was 38.2°C, blood pressure 166/77 mmHg, heart rate 69 b.p.m., and oxygen saturation 95% on supplemental oxygen through a non-rebreather mask at a rate of 7 L/min.

Pertinent features of the blood, biochemical, and virological results on admission included a low lymphocyte count 0.60 G/L [normal range (NR): 1.00–4.00], C-reactive protein (CRP) of 122 mg/L (NR $<$ 4), BNP of 46 ng/L (NR $<$ 100), and a positive RT-PCR for SARS-CoV-2 with a cycle threshold (Ct) value of 22. Thoracic computed tomography (CT) scan on admission showed ground glass opacities with a peripheral subpleural topographical distribution with extensive involvement (25–50%) and associated reticulations (*Figure 1A*).

Empirical treatment with amoxicillin-clavulanic acid IV, 3 g/day, was initiated, and enoxaparin sodium SC 4000 UI once a day. After 7 days, amoxicillin-clavulanic acid was switched to ceftriaxone IV, 1 g daily, in view of poor clinical response. Despite preventive anticoagulation, deep vein thrombosis and pulmonary embolism occurred on Day 14 dso, treated with apixaban 5 mg twice daily. Electrocardiogram (ECG) was normal (*Figure 2A*). TTE performed 1 month after dso showed a normal LVEF of 59%, normal LV volume, and no wall kinetic disorder.

Figure 2 Initial and 8 months of follow-up ECG. (A) Normal initial ECG. (B) ECG at 8 months, that is, 2 months after CMR, with inverted T waves on lateral leads.



A Normal Initial ECG

B ECG at 8 months, i.e. 2 months after CMR, with inverted T waves on lateral leads

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High-sensitivity troponin I was tested on one occasion during admission, the day of the TTE, detectable at 11.9 ng/L ($N < 57$, Centaur, SIEMENS). BNP was regularly tested and stayed <100 ng/L. Oxygen supplementation through a nasal cannula withdrawal was not possible until Day 50 after dso and only after the use of systemic corticosteroid therapy: prednisolone 60 mg/day for 7 days followed by progressive weaning over 12 days. Evolution was then slowly favourable, and the patient was discharged on Day 78 dso. Serology was positive at 36 dso for IgA (22.7), IgM, and IgG (13.7).

Follow-up

Due to overload of services and mass cancellations of routine follow-ups and appointments caused by COVID-19 at the time, scheduling a systematic follow-up with a cardiologist and a respiratory physician was difficult. This case is therefore the only patient in our geriatric cohort[10,11] who had routine follow-up appointment scheduled at 6 months.

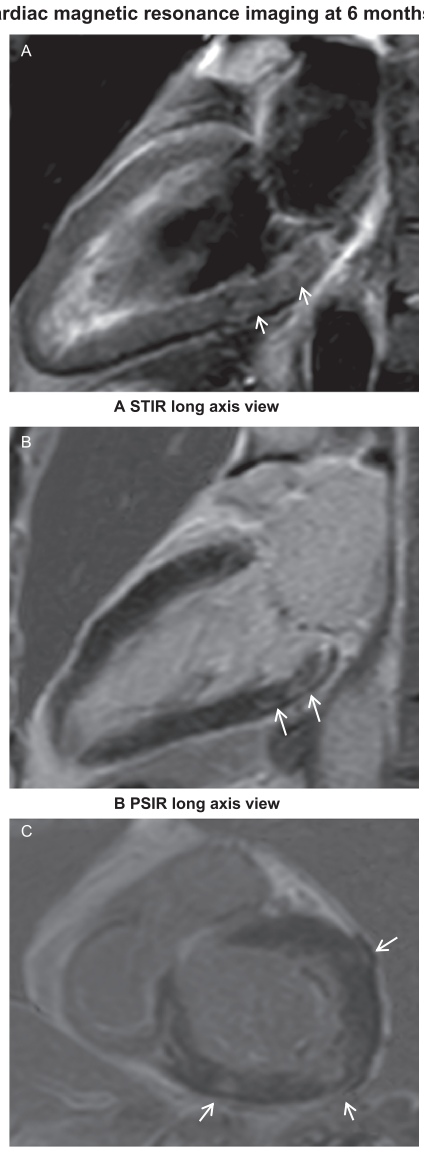
At 6 months, the clinical evolution was favourable; he was not dyspnoeic anymore and had resumed his usual physical and even sports activities. However, the TTE revealed a reduced LVEF of 39%, due to global mild hypokinesia and severe inferior wall hypokinesia.

Cardiac magnetic resonance imaging (CMR 3T Philips) performed at 6 months using short inversion time inversion recovery sequences (STIR) showed focal infero-basal LV wall oedema; T1 and T2 maps showed elevated T1 and T2 myocardial relaxation times (T1 = 1400 ms and T2 = 60 ms, respectively) especially in basal inferior and infero-lateral LV walls. Cine sequences showed LV basal inferior, and anterior wall hypokinesia, decreased LVEF up to 41% and increased LV volume (105 mL/m^2, $N < 95$ mL/m^2). The post-contrast sequences showed sub-epicardial and mid-wall late gadolinium enhancement (LGE) in the basal inferior, basal infero-lateral, and anterior LV walls (*Figure 3*). The ECG at 8 months, that is, 2 months after CMR, showed inverted T waves on lateral leads (*Figure 2B*), and myocardial perfusion myocardial single-photon emission computed tomography (SPECT) was normal. The diagnosis of myocarditis was established based especially on the TTE abnormalities and CMR Lake Louise Criteria (LLC), T1 and T2 mapping.

Chest CT scan at 6 months showed a regression of alveolar condensations but overall stability of the ground glass opacities and subpleural reticulations (25–50%) and a mild fibrosis pattern (*Figure 1B*).

Pulmonary function testing revealed a restrictive ventilatory disorder with 76% forced vital capacity (FVC) (2910 mL), FEV1 (forced exhaled volume at first second) 78% (2190 mL), FEV1/FVC 75%, 75% total lung capacity (TLC), and decreased diffusion capacity for carbon monoxide (DLCO) at 44%. The 6 min walking test achieved a distance of 444 m walked, with oxygen saturations of 97% at the beginning and 92% at the end.

Figure 3 Cardiac magnetic resonance imaging at 6 months. CMR STIR sequence showed myocardial oedema of the left ventricular (LV) infero-basal wall (A, STIR long-axis view). T1 and T2 maps showed elevated T1 and T2 myocardial relaxation times (T1 = 1400 ms, *N* = 1200 ms and T2 = 60 ms, *N* = 50 ms) especially in basa-inferior and infero-lateral LV walls. The post-contrast sequences showed sub-epicardial and mid-wall late gadolinium enhancement in the LV basal inferior, infero-lateral, and anterior walls (B and C, PSIR long-axis and short-axis views). The diagnosis of myocarditis was made based on CMR LLC, T1 and T2 mapping.



The first biological assessment after the diagnosis of myocarditis was carried out in the seventh month post-COVID-19, that is, 1 month after the diagnosis of myocarditis on CMR. Biochemical and virological analyses at 7 months included a

normal lymphocyte count 1.26 g/L (NR 1.10–4.00), CRP < 5 mg/L, NT-pro-BNP of 250 pg/mL (<1800), high-sensitivity troponin I < 10 ng/L (*N* < 34.2, CMIA, Abbott), a negative RT-PCR for SARS-CoV-2, and a positive serology for COVID-19 IgA (7.6) and IgG (26.8). The SARS-CoV-2 RT-PCR was not repeated further.

A beta-blocker treatment was introduced with bisoprolol 1.25 mg, and his usual ACE inhibitor ramipril increased to 10 mg daily.

Discussion

In summary, at the 6 month follow-up, despite a good functional recovery, the COVID-19 patient presented pulmonary sequelae, LVEF reduction, and LV dilatation on TTE without clinical signs of heart failure. The myocardial perfusion SPECT did not reveal myocardial ischaemia. The CMR LLC, T1 and T2 mapping revealed signs suggestive of active myocarditis. Cardiac biomarker levels and blood inflammation parameters at follow-up were normal perhaps because there were available 1 month after the CMR. The diagnosis of myocarditis was raised especially based on TTE and CMR LLC, T1 and T2 mapping. The LGE was of sub-epicardial and mid-wall topography that was suggestive of myocarditis rather than ischaemic myocardial lesion. P. Lurz *et al*. reported that the diagnostic performance of CMR in acute myocarditis using especially the native T1 and T2 mapping was superior to the LLC.[12] The use of T1 mapping combined LLC improved diagnostic accuracy up to 96%. Although the endomyocardial biopsy (EMB) was reported to be the gold standard in a diagnostic workup of inflammatory heart disease to identify viral pathogen specifically, the EMB was not performed in our case as it was recently reported that EMB is not recommended in COVID-19 patients with suspected myocarditis.[1]

Because the cardiac abnormalities were not present at initial presentation and at 1 month follow-up after the COVID-19 diagnosis, this could attest to the delayed onset, the persistence of an infectious or auto-immune/inflammatory disorder at 6 months following COVID-19 infection. This result is pertinent as he is the only patient in our cohort of 76 patients who benefited from systematic follow-up. Therefore, the incidence of this complication in our cohort is not known, and his case may not be an exception, highlighting the importance of a systematic cardiac and respiratory follow-up in severe COVID-19 patients.

The mechanism of myocarditis in the present case is not well established as SARS-CoV-2 PCR was negative at the 7 month follow-up and cardiac autoantibodies were not assessed.

The treatment of the patient at 6 months of follow-up was only based the introduction of beta-blockers and increased posology of ACE2 inhibitor as there is no yet clear ESC recommendation for SARS-CoV-2-associated myocarditis treatment.[1]

Currently, we are not aware of any published reports showing post-COVID-19 active myocarditis after such a period of 6 months.

Conflict of interest

The authors declare no conflict of interest.

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