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Peripartum cardiomyopathy in a COVID-19-infected woman: differential diagnosis with acute myocarditis—A case report from a Hub Institution during the COVID-19 outbreak

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Abstract

We report the case of a healthy 35-year-old woman who had experienced a flu-like syndrome during the week before childbirth and heart failure symptoms 10 days before the current hospitalization and presented to our emergency department with clinical signs of congestive heart failure, echocardiographic evidence of a severely dilated and hypokinetic heart, laboratory evidence of SARS-CoV-2 disease, and radiologic findings consistent with both virus-related pneumonia and heart failure. Early cardiac magnetic resonance was crucial for the diagnosis of postpartum cardiomyopathy and for the exclusion of virus-related myocarditis, allowing us to decide on a prudent and supportive clinical approach.

KEYWORDS

2D echocardiography, cardiac magnetic resonance imaging, cardiomyopathy, myopericarditis, thrombus, transthoracic echocardiography

1 | INTRODUCTION

Our Institution is one of two National Designed Hospitals for Infectious Diseases and the Milan Hub for Infectious Diseases. It has been directly and heavily involved in COVID-19 patient care since the beginning of the outbreak, taking care of patient no. 1 in Italy (and in Europe) and of his COVID-infected pregnant wife. Peripartum cardiomyopathy (PPCM) is a well-known cause of heart failure complicating pregnancy or the early postpartum period, presenting with heart failure symptoms secondary to left ventricular systolic dysfunction, where no other cause of heart failure is found. It is a diagnosis of exclusion.

The clinical course SARS-CoV-2 infection is dominated by pneumonia and respiratory tract symptoms, possibly culminating in the acute respiratory distress syndromes[1]; knowledge regarding the direct cardiovascular involvement by COVID-19 is sparse and the object of ongoing speculation.

COVID-19-related myocarditis has been described so far in reports from Hubei[2] and Northern Italy.[3-5]

The diagnosis of myocarditis is ideally made with the demonstration of the direct presence of the virus in the myocardium with an endomyocardial biopsy (EMB). However, in clinical practice it is currently achieved with cardiac magnetic resonance (CMR), given the potential complications and false negatives associated with the EMB. In particular, the presence of tissue edema in T2-weighed sequences and that of myocardial fibrosis in LGE in PSIR sequences, together with an increased T1 "native" value, are the hallmarks for the diagnosis of myocarditis at CMR.

We report on a postpartum woman with clinical signs of heart failure and hypokinetic heart; the differential diagnosis included

virus-induced cardiomyopathy versus PPCM. Early CMR was crucial for the diagnosis of PPCM and for the exclusion of virus-related myocarditis.

2 | CASE PRESENTATION

On April 22, 2020, an otherwise healthy 35-year-old primigravida with no personal or family history of cardiovascular disease, cardiomyopathy, or sudden cardiac death (SCD) presented to our emergency department (ED) coming from home with worsening fatigue, dyspnea on minimal exertion, and orthopnea in the previous week without fever.

The patient uneventfully gave birth on March 21, 2020. During the week before delivery, she had experienced influenza-like symptoms, with fever, cough, and altered sense of taste and smell. The symptoms gradually disappeared after childbirth. She breastfed her child in the following weeks in a well-being condition.

On arrival to our ED, her blood pressure was 110/70 mmHg, heart rate 120 b/m, respiratory rate 26/minute, and temperature 36.6°C.

A 12-lead EKG (Figure 1A) showed diffuse ST changes with negative T-waves in leads V3-V6. EKG obtained in another institute at the time of delivery was reported to be normal.

A chest CT scan (Figure 1B) showed interstitial and alveolar thickening in the right middle and both inferior lobes, bilateral pleural and pericardial effusion, cardiomegaly, and subsegmental pulmonary embolism.

Blood tests revealed elevated levels of NT-pro-BNP (6608 ng/L) and D-dimer (3328 μg/L) with mild increase in high-sensitivity troponin-T level (37 ng/L), C-reactive protein (9.7 mg/L), AST (74 U/L), ALT (101 U/L), and LDH (322 U/L).

Based on the epidemiologic setting, COVID-19 myocarditis was suspected. A nasopharyngeal swab was performed, yielding a positive result for SARS-CoV-2 on real-time PCR. A rapid antibody test detected IgG antibodies and a "weak" presence of IgM.

Echocardiography revealed dilated left ventricle (LV) (end-diastolic indexed biplane LV volume = 105 mL/m^2—Figure 2C), diffuse marked hypokinesis of LV walls with severe reduction in systolic function (biplane LV ejection fraction = 20%), impairment of LV diastolic function, moderate mitral regurgitation (Figure 2D), mild right ventricular dilation and dysfunction, and pericardial effusion (10 mm). A 10-mm thrombus was seen attached to the inferior portion of the LV apex (Figure 2A,B).

The patient was treated with low-molecular-weight heparin (enoxaparin 6000 IU) and furosemide and admitted to the ICU with a diagnosis of cardiac dysfunction causing congestive heart failure in a patient with COVID-19 pneumonia.

The day after admission CMR was performed (Figure 3, Movies S1 and S2) showing an oval-shaped, enlarged left ventricle (EDV = 240 mL, EDV/BSA = 134 mL/m^2, TD diameter = 67 mm) with normal thickness; diffuse hypokinesis of LV walls with reduced systolic function (LVEF = 17%). LV apical thrombus was confirmed (Figure 3D,E and Movie S2). The right ventricle was enlarged (EDV = 150.6 mL, EDV/BSA = 84.6 mL/m^2, TD diameter = 47.7 mm) with diffuse hypokinesis and reduced contractile function (RVEF = 19%).

Crucially, no evidence was shown of tissue edema indicative of acute inflammation in STIR sequences (Figure 3A,B) nor of myocardial fibrosis in late gadolinium enhancement sequences (no LGE in PSIR sequences—Figure 3C). Pleural and pericardial effusion was confirmed, with no evidence of LGE in the pericardium (Movies S1 and S2).

Cardiac magnetic resonance findings were consistent with the diagnosis of peripartum cardiomyopathy without evidence of either acute inflammation or fibrosis.

The patient remained afebrile. She was treated with IV ethacrynic acid 25 mg, enoxaparin 8000 + 6000 IU sc, spironolactone

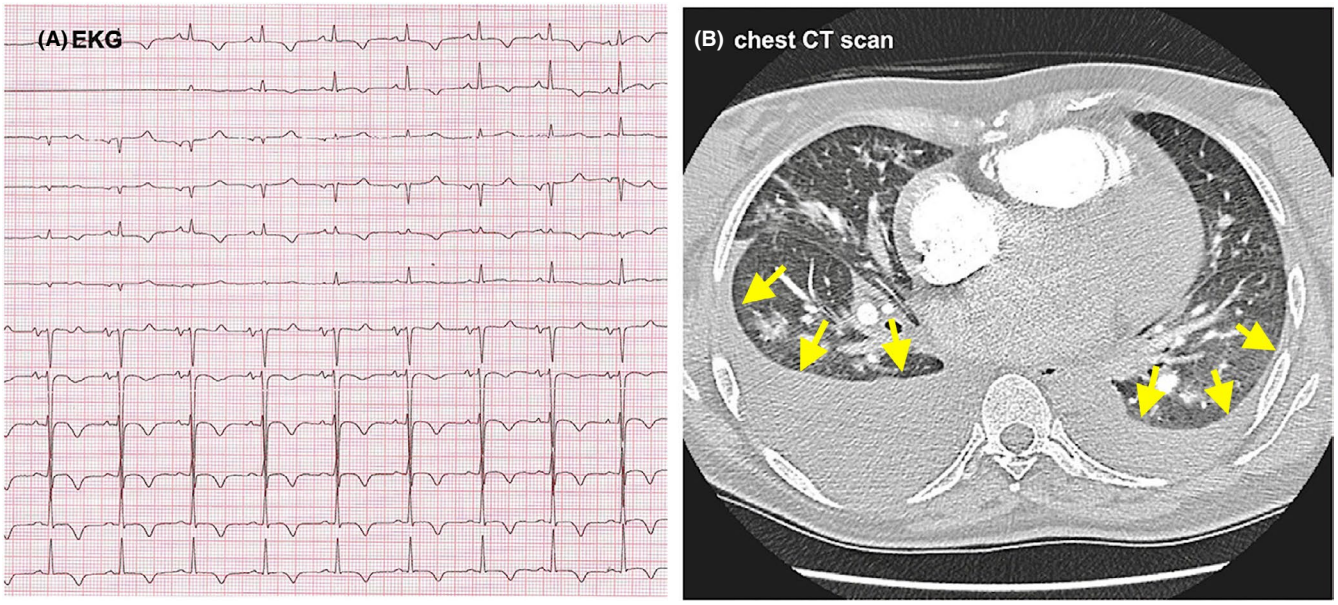

FIGURE 1 EKG and chest CT scan. A, 12 leads EKG. B, chest CT scan

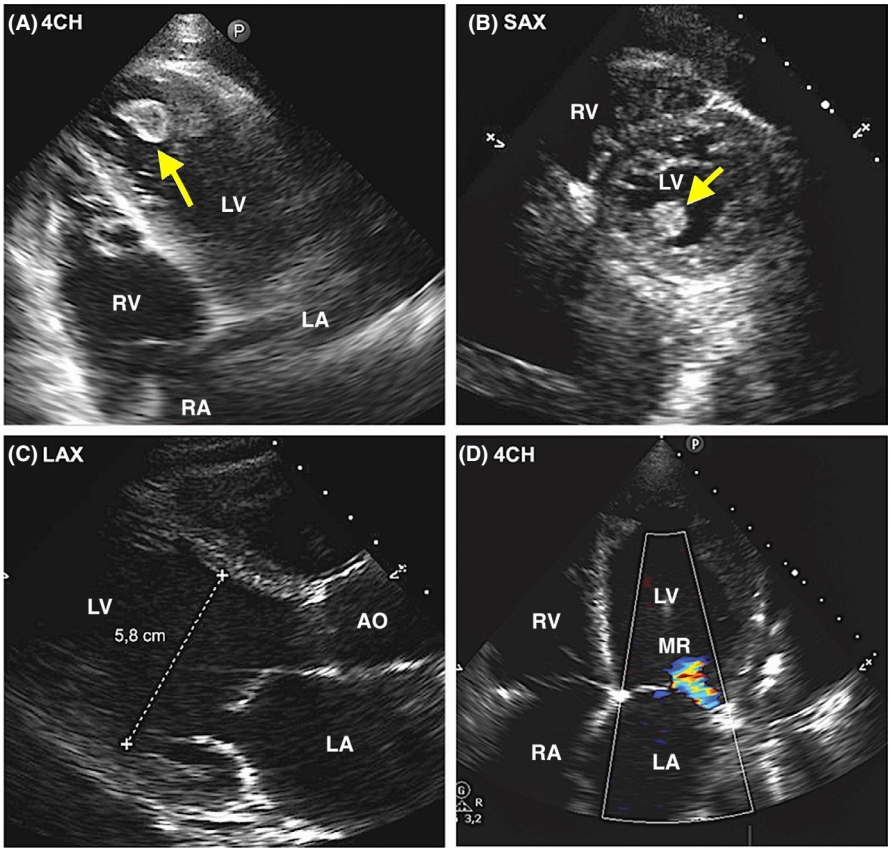

FIGURE 2 Echocardiographic findings. A, "Modified" apical 4-chamber view. B, Parasternal short-axis view. C, Parasternal long-axis view. D, Apical 4-chamber view

25 mg, bisoprolol 2.5 mg, and ramipril 2.5 mg PO QD. No antiviral or anti-inflammatory medications were administered.

Repeat echocardiography on day 4 was stable with reduction in the severity of mitral regurgitation, decrease in pericardial effusion, and recovery of right ventricular function. Unchanged apical thrombus was confirmed.

No arrhythmias were noted during continuous EKG monitoring.

Troponin values remained stable (37-29 U/L). Chest radiography showed decrease of pleural effusion and regression of pulmonary congestion.

3 | DISCUSSION

Peripartum cardiomyopathy (PPCM) is a rare form of pregnancy-associated cardiac dysfunction.

Currently, the ESC defines PPCM as "an idiopathic form of cardiomyopathy presenting with heart failure secondary to left ventricular systolic dysfunction towards the end of pregnancy or in the months following delivery, where no other cause of heart failure is found".[6] To substantiate the diagnosis, the left ventricle does not need to be dilated, but the ejection fraction needs to be <45%.

Several pathophysiological mechanisms have been proposed in the development of PPCM, such as auto-immunity, myocarditis, maladaptation to the hyperdynamic state of pregnancy, prolonged tocolysis, secretion of antiangiogenetic factors by the placenta, and oxidative stress in combination with high levels of prolactin, which in turn can impair endothelial function resulting in cardiac inflammation.[7] PPCM is a diagnosis of exclusion, with considerable overlap with other conditions.

Given the epidemiological setting, in the case we describe, the vitally important differential diagnosis was with acute myocarditis, possibly COVID-19-related.

The pathogenesis of any SARS-CoV-2 cardiac involvement and of pathological findings possibly involves several mechanisms, such as non-specific ventricular dysfunction due to hypoxemia, direct COVID-19 heart damage due to replication and dissemination, small-vessel cardiac vasculitis in the context of a multisystem inflammatory syndrome similar to Kawasaki disease,[8] or triggering of an exaggerated inflammatory response causing myocardial injury, possibly explaining the beneficial effects of corticosteroids reported in critically ill COVID-19 patients.[3]

Notably, mononuclear inflammatory infiltration in heart tissue but no viral inclusion bodies was observed in COVID-19 autopsy studies.[9]

Myocardial injury, as defined by an increased troponin level, is known to occur in 35% of myocarditis cases. In the setting of ARDS and hypoxia due to COVID-19, many patients may be expected to develop such injury.

Elevated troponin levels are described in many patients infected with COVID-19, with significant differences between patients who died and those who survived.[10]

Reports have also suggested that acute cardiac injury is frequent in patients with COVID-19 and is associated worse prognosis.[9]

Prior studies in other coronavirus species (MERS-CoV) have demonstrated evidence of acute myocarditis using CMR.[11]

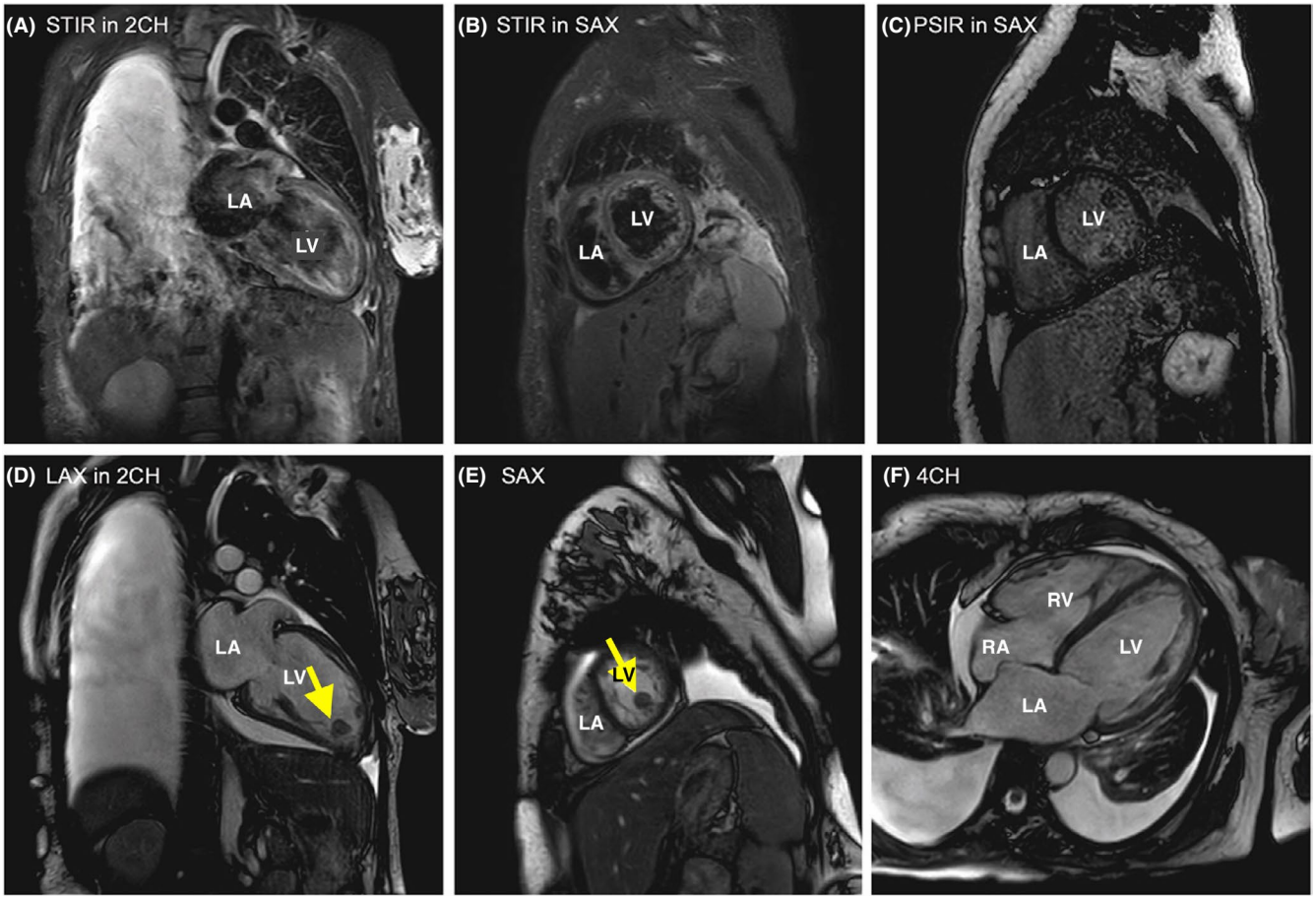

FIGURE 3 CMR findings. A, STIR sequence in 2-chamber view. B, STIR sequence in short-axis view. C, PSIR sequence with LGE in short-axis view. D, Long-axis cine sequence in 2-chamber view. E, Short-axis cine sequence

Published studies regarding presumed COVID-related myocarditis[3] do not show evidence of virus in the cardiac muscle cells; in the two COVID-19-positive patients reported from Italy who underwent endomyocardial biopsy,[4,5] no viral particles in cardiac cells were observed; Tavazzi et al[5] report viral particles in cytopathic macrophages and their surroundings.

In our patient, although the initial findings and the epidemiologic setting raised the possibility of COVID-19 myocarditis, early performance of CMR prompted the diagnosis of peripartum cardiomyopathy by excluding myocarditis.

4 | STUDY LIMITATIONS

A limitation of our study is the unavailability of T1 mapping at CMR in our Institution.

5 | CONCLUSIONS

We believe this one of the first reported cases of peripartum cardiomyopathy during the COVID-19 outbreak.[12] Early CMR avoided the unnecessary exposure of our patient to as yet unproven antiviral regimens.

We maintain that this case underscores the need to keep in mind non-COVID-19-related disorders, even in the setting of the COVID-19 epidemic and in a patient with COVID-19 disease.

Furthermore, it is to be noted that our patient showed evidence of thrombosis both in the apical left ventricle and in a branch of the pulmonary artery, adding strength to reports of a thrombotic state in patients with COVID-19. In fact, although pregnancy itself may represent a pro-thrombotic state, overt manifestations of thrombosis in healthy women are infrequent.

Finally, the lack of demonstration of viral particles in cardiac myocytes on EMB in published literature so far leaves open the question of whether COVID-19 is actually capable of directly causing cardiac disease.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

Movie S1. Cine 4CH.

Movie S2. Cine balance volume in SAX.

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