Cardiology in the Young

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Acute myocarditis in a paediatric patient with pre-existing dilated cardiomyopathy following SARS-COV-2 infection: a journey from decompensation to heart transplantation

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Brief Report

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Abstract

A 10-year-old child with stabilised idiopathic dilated cardiomyopathy was admitted to the hospital with sudden worsening of heart failure. Further analysis showed increased NT-proBNP and positive for COVID-19. Myocarditis secondary to COVID-19 was assumed. Recurrent hospitalizations with inotropic support were required due to the progressive worsening of cardiac function. Seven months after SARS-CoV-2 myocarditis, she underwent heart transplantation.

Introduction

The new coronavirus, severe acute respiratory syndrome coronaVirus 2, was identified in Wuhan, China, at the end of 2019 and was responsible for the coronavirus disease 2019.[1] The disease is often asymptomatic or characterised by mild upper respiratory or gastrointestinal symptoms. However, some children develop severe diseases, such as cardiac complications, myocarditis, and cardiomyopathy.[2–4]

Case report

A 10-year-old, 30 kg girl from Guinea-Bissau presented to the hospital emergency department in June 2020 with symptoms including nasal obstruction, rhinorrhoea, odynophagia, abdominal pain, vomiting, diarrhoea, and fatigue. Previously diagnosed with dilated cardiomyopathy of unexplained aetiology at the age 5, she had a history of heart failure. Her most recent echocardiogram in March 2020 revealed a left ventricle telediastolic dimension of 50, with a shortening fraction of 28 (Z-score −1.65). She had been in NYHA/Ross class 2 under optimised medication, and her echocardiographic findings remained stable for at least 3 years prior to her acute bout of COVID-19, without any hospital admissions. Her condition had been stabilised with carvedilol (12.5 mg twice daily), captopril (6.5 mg twice daily), and furosemide (20 mg daily).

Upon admission, her vitals were tachycardia (110 beats a minute), hypotension (81/52 mmHg), normal peripheral perfusion, blood oxygen saturation at 98%, respiratory rate of 18 breaths per minute, and no fever. Cardiac auscultation revealed a grade III/VI holosystolic murmur. She had jugular regurgitation at 35° and hepatomegaly extending 2 cm below the costal margins.

Initial laboratory tests showed elevated NT-proBNP levels to 1011 pg/mL (reference: < 317.1 pg/mL), while troponin I, using a high-sensitivity assay, was in normal range. No other blood anomalies were detected. The PCR tests for SARS-CoV-2 from nasal and oral swabs were positive.

Radiological examination revealed cardiomegaly and diffuse interstitial infiltrates on chest radiography (Figure 1a). Chest CT revealed diffuse ground-glass opacities in the lower lobes, predominantly in the left lower lobe, categorised as classic/probable COVID-19 infection (CVCT1) (Figure 1b).

Echocardiography indicated deteriorated cardiac function, with systolic dysfunction presenting an Ejection fraction (EF) of 14% and a significantly dilated left ventricle (67 mm). The left atrium was also dilated (PLAX 38 mm, LA/Ao ratio 2.5), with intact interatrial and interventricular septa. The tricuspid and mitral valves appeared normal, albeit with mild and moderate insufficiency, respectively. The right ventricle was neither dilated or hypertrophied and the tricuspid aortic valve functioned well. A thin layer of circumferential pericardial effusion was also observed.

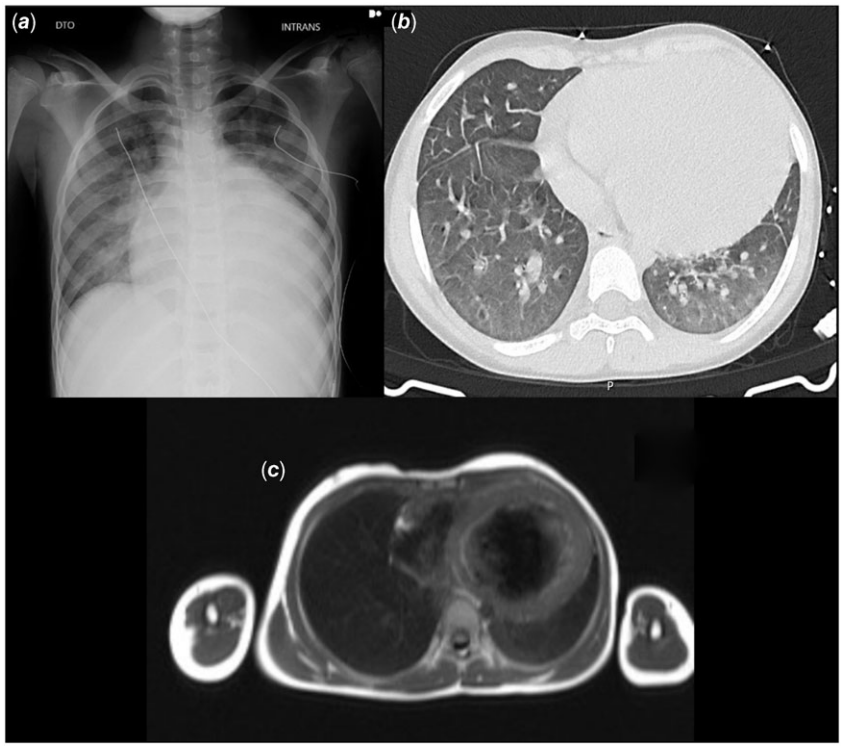

Figure 1. (***a***) Chest radiograph. Cardiomegaly and diffuse interstitial infiltrate. (***b***) Chest CT. Diffuse ground glass alterations in the lower lobes, with predominance in the left lower lobe. (***c***) Cardiac MRI. Left ventricle markedly dilated (VTD 239 ml/m^2), not hypertrophied, with severe dysfunction (EF 24%) due to global hypokinesia.

Additionally, a cardiac MRI revealed a markedly dilated left ventricle (VTD 239 ml/m^2) with severe dysfunction (EF 24%) due to global hypokinesia, more pronounced in the mid segments of the interventricular septum and the anterior and inferior walls. The right ventricle was not dilated or hypertrophied, and systolic function was preserved (EF 55%). Notably, there was evidence of myocardial oedema, with elevated native T2 mapping, particularly in the mid segments of the SIV and the anterior and inferior walls, consistent with acute myocarditis. Late gadolinium enhancement was observed in a non-ischaemic pattern in the mid-interventricular septum and basal anterior septum, indicating a myocardial injury. The native global T1 mapping was elevated at 1070 (above the upper limit of normal for the equipment values), further supporting the presence of myocardial inflammation. Mild mitral regurgitation was also observed (Figure 1c).

Based on these findings, myocarditis secondary to SARS-CoV-2 was diagnosed. Treatment commenced with aminergic support using dopamine at 5 mcg/kg/min and captopril at 6.25 mg thrice daily. In addition, she was treated with remdesivir at a dose of 75 mg/day for 5 days to address the COVID-19 infection. However, due to the worsening heart failure and severe systolic dysfunction, milrinone at 0.3 mcg/kg/min was introduced. The patient showed a progressive clinical improvement. The final ultrasound assessment displayed systolic dysfunction with an EF of 29% and left ventricle at 62 mm. The remaining examinations did not reveal any significant changes. After 13 days of hospitalisation, the patient was discharged on carvedilol (12.5 mg twice daily), furosemide (20 mg daily), and captopril (12.5 mg twice daily).

Over the subsequent 6 months, the patient was readmitted multiple times due to deteriorating heart failure, presenting with symptomatic hypotension requiring inotropic support with dopamine and levosimendan. Frequent and complex ventricular extrasystoles, including episodes of bigeminy and polymorphic pairs and triplets, prompted the placement of an implantable cardioverter defibrillator in line with the guidelines for high-risk paediatric patients awaiting transplantation. In December 2020, she was readmitted due to further clinical decline marked by anuria, pronounced anorexia, and difficulty in daily activities. Laboratory tests revealed elevated NT-proBNP levels, rising from 4603 pg/mL to 13440 pg/mL (reference: <317.1 pg/mL), HsTroponin I at 2207 pg/mL (reference: <15.6 pg/mL), acute kidney injury, and elevated transaminases with aspartate aminotransferase at 1443 U/L (reference: 21–44 U/L) and alanine aminotransferase at 427 U/L (reference:9–25 U/L).

The patient required high-flow oxygen and inotropic support, with milrinone and levosimendan. Echocardiography revealed further deterioration, with an inferior vena cava measuring 15 mm without respiratory variability, a dilated left ventricle (end-diastolic volume (EDV) 220 ml, left ventricle 68 mm), without hypertrophy, and severe global systolic function depression (EF 13%, VTI Ao = 8.5 cm, previously 11 cm). Consequently, she was prioritised on the heart transplant list and successfully underwent transplantation 7 months post-SARS-CoV-2 infection.

Discussion

There is evidence of a link between SARS-CoV-2 infection and increased morbidity and mortality from cardiovascular diseases, especially in children with previous heart disease.[2] Clinical presentation ranges from mild symptoms to heart failure and cardiogenic shock.[2,3,5] The temporal association between SARS-CoV-2 infection (the only identified pathogenic agent) and

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myocarditis in our patient strongly supports the hypothesis that this virus is the cause of cardiac morbidity and poor outcomes.

Guidelines and literature underscore endomyocardial biopsy as the gold standard for diagnosing myocarditis, providing definitive histological evidence by identifying inflammatory infiltrates and potential specific aetiologies. Despite its diagnostic value, the invasive nature of endomyocardial biopsy carries inherent risks, such as cardiac perforation and arrhythmias, which are particularly pronounced in paediatric populations. Furthermore, the patchy nature of myocarditis introduces a significant risk of sampling error, potentially yielding false-negative results if the biopsy does not capture the affected tissue. The necessity for specialised pathology expertise further complicates the universal application of endomyocardial biopsy, highlighting its limitations in specific clinical settings.[6,7]

Cardiac MRI is a mandatory imaging exam in the context of a clinical suspicion of myocarditis, as it allows us to detect the presence of oedema and/or myocardial fibrosis, with the typical pattern being subepicardial/intramural involvement (as opposed to the ischaemic pattern of fibrosis with subendocardial involvement). Absolute contraindications include a patient with chronic kidney disease on haemodialysis (except if they have a dialysis session scheduled within less than 24 h after the exam) and the presence of devices incompatible with the MRI field (such as older implantable cardioverter defibrillators or pacemaker. Most current implantable cardioverter defibrillators/PMs are MRI compatible, with their only limitation being the ferromagnetic artifacts they produce, a situation that can potentially be overcome with specific strategies in the acquisition of certain image sequences. The ability of Cardiac Magnetic Resonance Imaging (CMR) to provide a comprehensive view of the myocardium, detect signs of inflammation and tissue injury characteristic of myocarditis, and mitigate the risks associated with EMB underscores CMR's diagnostic robustness, offering a safer diagnostic alternative that avoids the procedural risks associated with endomyocardial biopsy.[8,9]

In the context of the COVID-19 pandemic, the diagnostic and therapeutic approaches to myocarditis, particularly in paediatric populations, have necessitated careful consideration. Paediatric reviews during this period have indicated a noticeable incidence of clinically suspected myocarditis in children presenting with multisystem inflammatory syndrome, where CMR findings have played a pivotal role in diagnosis, complementing, or, in fewer instances, supplanting confirmation by biopsy or autopsy. The challenge of detecting SARS-CoV-2 via PCR in EMB or myocardial autopsy samples, with about a third of affected patients showing positive results, underscores the diagnostic complexities of COVID-19.[10,11]

Despite the high levels of viral replication observed in autopsy samples, instances of lymphocytic infiltration were uncommon, and myocarditis meeting the Dallas criteria was confirmed in only a fraction of the cases. Predominant pathological changes identified in autopsy samples, such as cardiac dilatation, ischaemia, intracardiac thrombi, and pericardial effusion, lead to a cardiac injury model stemming mainly from respiratory overload or multiorgan damage due to hypoperfusion and hypercoagulability. This pattern of cardiac damage is especially evident in patients with pre-existing conditions, such as myocardial hypertrophy or fibrosis. [6,7]

Given the clinical presentation, CMR findings indicative of acute myocarditis, and the goal of minimising harm while effectively managing the patient's condition, we opted for a non-invasive diagnostic approach. This decision was further reinforced by healthcare resource constraints and the imperatives imposed by the COVID-19 pandemic, necessitating the judicious use of healthcare interventions. The specific clinical context further influenced the decision not to perform an EMB. The patient's acute presentation, along with a positive SARS-CoV-2 infection amidst a global pandemic, provided a plausible aetiological basis for myocarditis, supported by the diagnostic capabilities of CMR.

Data on children are limited, and the incidence of myocarditis varies with age, season, and geography. In a 2021 study, only 0.133% of children with COVID-19 were diagnosed with myocarditis.[4,12] A systematic review of cardiac manifestations in children infected with SARS-CoV-2 found that myocarditis, arrhythmias, and heart failure are notable complications, emphasising the importance of early recognition and treatment in children presenting with potential cardiac symptoms.[3] The use of levosimendan has limited evidence of its effectiveness, but during the pandemic, it proved to be a useful drug in heart failure when used in combination with other amines. It improves both the systolic function of the left and right ventricles, as well as the diastolic function of the left ventricle.[13]

Physicians should be vigilant of mildly symptomatic COVID-19 patients, especially those with pre-existing cardiac conditions. Diagnosis is vital for adequate treatment and better management with the aim of reducing SARS-CoV-2 mortality. The long-term cardiac consequences of COVID-19 in children remain an area of active research and concern.[14]

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Competing interests. The authors declare that there is no conflict of interest.

Ethical standards. This case does not involve human and/or animal experimentation.

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