COVID-19-induced silent myocarditis and newly developed hypertension in a 3-year-old boy

Elaheh Malakan Rad1* and Sara Momtazmanesh2

Abstract

Background: COVID-19 myocarditis occurs in 7–28% of patients admitted in the hospital with or without multisystem inflammatory syndrome. It may present as fulminant myocarditis. Dilated cardiomyopathy as a sequela of COVID-19 myocarditis has been reported in the pediatric population. However, to date, no case of silent COVID-19 myocarditis progressing to dilated cardiomyopathy has been reported in children. Furthermore, although newly developed hypertension as a sequela of COVID-19 infection has been reported in adults, there is no report of newly developed COVID-induced hypertension in children. We report a 3-year-old boy with silent COVID-19 myocarditis progressing to dilated cardiomyopathy and newly developed systemic hypertension.

Case presentation: A 3-year-old boy was referred to the emergency department because of respiratory distress. The parents gave a history of SARS-CoV-2 infection in the child 5 months ago that was manifested as fever and cough, for which he was treated as an outpatient. Echocardiographic examination revealed a severe decrease in left ventricular systolic function in favor of dilated cardiomyopathy. Cardiac magnetic resonance imaging established the diagnosis of myocarditis. The patient left ventricular systolic function did not improve after 2 weeks of intravenous inotropic support. Therefore, the child was transferred to another tertiary center with extracorporeal membrane oxygenation and pediatric cardiac transplantation facilities.

Conclusions: COVID-19 can induce silent myocarditis with progression to dilated cardiomyopathy and newly developed systemic hypertension. Thus, a thorough examination of the heart and measurement of blood pressure are mandatory in every child with COVID-19 infection. Cardiac MR is an indispensable tool in the diagnosis, follow-up, and prognostication of COVID-19 myocarditis. Moreover, four-chamber speckle tracking strain imaging showed apical rocking in all the four heart chambers in this child with opposite direction in the failed left ventricle compared with other cardiac chambers. Lastly, the presence of septal flash on M-mode echocardiography, apical rocking and prestretch–rebound stretch patterns on longitudinal strain imaging of the failed left ventricle in this child may be of predictive value for response to cardiac resynchronization therapy.

Keywords: COVID-19, Myocarditis, Dilated cardiomyopathy, Strain imaging, Speckle-tracking, Echocardiography, Magnetic resonance imaging, Hypertension, Case report

Background

COVID-19 myocarditis occurs in 7–28% of patients admitted in the hospital with or without multisystem inflammatory syndrome (MIS) [1]. It may present as fulminant myocarditis [2]. Dilated cardiomyopathy as a sequela of COVID-19 myocarditis has been reported in the pediatric population [3]. However, to date, no case
of silent COVID-19 myocarditis progressing to dilated cardiomyopathy has been reported in children. Furthermore, although newly developed hypertension as a sequela of COVID-19 infection has been reported in adults, there is no report of newly developed COVID-induced hypertension in children [4]. We report a 3-year-old boy with silent COVID-19 myocarditis progressing to dilated cardiomyopathy and newly developed systemic hypertension. We also present the findings on speckle-tracking strain imaging echocardiography of the four chambers of the heart in this patient.

**Case presentation**

A three-year-old was referred to the emergency department because of respiratory distress. He was a well-nourished boy with normal temperature and a respective heart rate and respiratory rate of 140 beats and 63 per minute on physical examination. His blood pressure was 135/110 mmHg. Cardiac auscultation revealed muffled heart sounds with a grade 2/6 regurgitant systolic murmur at the cardiac apex. The rest of the physical examination was unremarkable. The parents gave a history of SARS-CoV-2 infection in the child five months ago that was manifested as fever and cough, for which he was treated as an outpatient. Furthermore, he had a history of complete cardiac evaluation for a cardiac murmur, including a comprehensive echocardiographic examination by a pediatric cardiologist one year ago, which confirmed a normal structure and function and the innocent nature of the murmur. Family history was negative except a COVID-19 infection in five months ago in other family members.

Cardiomegaly, pulmonary edema, and blunted costophrenic angles were evident on the chest X-ray (Fig. 1). The electrocardiogram showed T wave inversion in left precordial leads (Fig. 2).

Comprehensive two-dimensional color Doppler echocardiography revealed a severe decrease in left ventricular systolic function in favor of dilated cardiomyopathy, significant left ventricular enlargement, mild to moderate holosystolic mitral regurgitation with eccentric posterolateral jet, trivial aortic regurgitation, and septal flash (Fig. 3). Left ventricular ejection fraction by Simpson’s method was 26%, and tricuspid annular plane systolic excursion (TAPSE) was 21.8 mm. There was no coarctation of the aorta.

Speckle-tracking longitudinal, circumferential, radial and transverse atrial and ventricular strain imaging was performed using velocity vector imaging (VVI) of Siemens Accuson SC 2000 (Siemens Medical Solutions USA, Inc.) (Figs. 4, 5, 6, 7, Additional files 1, 2, 3, 4, 5, 6, 7, 8, and 9: Movie clips 1–9). Compared with normal pediatric values, left ventricular longitudinal, transverse, circumferential, and radial strain were decreased [5–8]. Furthermore, there was a prestretch and rebound stretch pattern in the longitudinal strain of the left ventricle. Notably, apical rocking was detected in all four heart chambers with the direction of the apical movement in LV opposite to the rocking in the right ventricle, right atrium, and left atrium (Additional files 1, 2, 3, 4: Movie Clips 1 to 4). The results of the speckle-tracking strain imaging are depicted in Table 1.

According to the classification of Singh et al. for categorization of LV diastolic function based on the left atrial strain imaging, the patient had grade 3 LV diastolic dysfunction [9].

Given the past medical history of confirmed COVID-19 infection in the past months and normal echocardiogram in the last year, the clinical diagnosis of silent
Fig. 3  Septal flash on M-mode echocardiography of the patient

Fig. 4  Left ventricular transverse and longitudinal strain imaging of the patient
and undiagnosed COVID-19 myocarditis was suspected. COVID-19 reverse transcription-polymerase chain reaction (RT-PCR) and SARS-CoV-2 IgG and IgM antibodies were negative. Similarly, the polymerase chain reaction for other viruses, including adenovirus, enterovirus, Coxsackievirus, Epstein-Barr virus, Influenza virus, Cytomegalovirus, Human Immunodeficiency Virus, Hepatitis B and C virus, Herpes viruses were negative. The level of troponin I was normal, but NT-proBNP was elevated.

To look for Lake Louise criteria of myocarditis, cardiac magnetic resonance (CMR) imaging was performed with gadolinium study and Short Tau Inversion Recovery (STIR)/T2 weighted-sequences [10]. This evaluation revealed mild pericardial effusion, severely enlarged left ventricle without left ventricular hypertrophy, evidence of diffuse myocardial edema, and severely reduced systolic function. Left ventricular and right ventricular ejection fractions were 13% and 45%, respectively, on cardiac MRI. Late-gadolinium enhancement was observed in the left ventricle’s basal and mid-posterolateral segments in favor of post-myocarditis scarring (Fig. 8).

Complete workup including endocrinologic, nephrologic, neurologic, and rheumatologic causes of hypertension was performed. The only abnormal finding was significantly elevated renin (> 550 micro IU/mL, normal levels at supine position: 4.2–59.7 micro IU/mL). Measurement of aldosterone and angiotensin II was not available. Kidney function and Doppler ultrasound of renal arteries and veins were normal. Cortisol and ACTH were normal. The absence of left ventricular hypertrophy on CMR and echocardiography, absence of hypertension in the past medical history of the patient, and negative workup for other causes of hypertension were in favor of COVID-19-induced newly developed systemic hypertension.

Intravenous infusion of Dopamine (7.5 µg/kg/min), dobutamine (7.5 µg/kg/min), and milrinone (0.6 µg/kg/min), in conjunction with aspirin at a dose of 5 mg/kg/day, were administered for the patient. The patient’s hypertension was controlled by the administration
Fig. 6  Bull's eye plot of left ventricular longitudinal strain and time to peak longitudinal strain

Fig. 7  Bull’s eye plot of left ventricular circumferential strain and time to peak circumferential strain
of captopril (6 mg/kg/day every 6 h) and hydralazine (0.2 mg/kg/dose every 4 h). The patient left ventricular systolic function did not improve after 2 weeks of intravenous inotropic support. Therefore, the child was transferred to another tertiary center with extracorporeal membrane oxygenation and pediatric cardiac transplantation facilities.

**Discussion**

This is the first report of silent myocarditis and newly developed systemic hypertension after SARS-CoV-2 infection in a child.

Silent myocarditis has been reported in several diseases such as Takayasu arteritis, myasthenia gravis, and systemic sclerosis [11–13]. However, there is no report of silent myocarditis following viral infections, let alone COVID-19 disease, to the best of our knowledge.

COVID-19 infection in children is often milder than in adults [14]. Fever and cough are the most common manifestations in children aged 0–19 years [15]. In the meta-analysis of 9335 COVID-19 patients ≤19 years, 13% (as mean proportion) of children were asymptomatic [15]. The risk for the development of myocarditis during SARS-CoV-2 infection has been reported to be 0.146% [16].

Furthermore, the similarity of pulmonary and cardiac involvement manifestations makes distinguishing the cardiac from the pulmonary causes challenging. The associated fever and cough in this child and the child's young age that prevents communication of symptoms further distract the primary care physician of attention to the cardiac problem.

Moreover, while Chen et al. [4] reported newly developed hypertension as a consequence of SARS-CoV-2 infection in about 8% of the 190 patients, aged 40–86 years, this sequelae has not been reported in children before. The absence of left ventricular hypertrophy, the patient's past medical history, and the completely negative workup for cardiologic, endocrinologic, nephrologic, and neurologic causes of systemic hypertension and the significantly elevated renin level were in favor of COVID-19-induced systemic hypertension (CISH). Similar to this study, renin was elevated in our patient. This newly developed hypertension may be due to increased

### Table 1 Results of speckle-tracking strain imaging of the atria and ventricles

| Parameters                                      | Right atrium | Left atrium | Right ventricle | Left ventricle |
|-------------------------------------------------|--------------|-------------|-----------------|---------------|
| Ejection fraction %                             | 49%          | 65%         | –               | 20%           |
| End-diastolic volume (mL)                       | 13           | 13.2        | –               | 103           |
| End-systolic volume (mL)                        | 6.4          | 4.5         | –               | 82            |
| Fractional area change (%)                      | –            | –           | 54.2            | 17.9          |
| Maximal area (cm²)                              | 3.2          | 2.3         | –               | –             |
| Minimal area (cm²)                              | 1.4          | 1.9         | –               | –             |
| Peak global longitudinal strain (%)             | −60%         | −10%        | –               | −6.60         |
| Average of peak segmental transverse myocardial strain ± standard deviation (SD) | −22.50 ± 6.84 | −23.50 ± 6.27 | 30.5 ± 50.36 | 15.6 ± 5.57 |
| Average of peak segmental longitudinal myocardial strain ± SD | 12.60 ± 5.31 | 11.40 ± 2.48 | −5.50 ± 15.19 | −7.10 ± 3.57 |
| Average of peak segmental radial strain ± SD    | −           | –           | 6.8 ± 6.75      |               |
| Average of peak segmental myocardial circumferential strain ± SD | −           | –           | −5.80 ± 1.87    |               |
| Average of peak segmental transverse myocardial strain rate ± SD | 2.4 ± 1.39 | 2.50 ± 1.07 | 1.70 ± 1.56 | 0.90 ± 0.22 |
| Average of peak segmental longitudinal myocardial strain rate ± SD | −0.80 ± 0.26 | −1.10 ± 0.36 | −1.20 ± 0.36 | −0.50 ± 0.20 |
| Average of peak segmental radial myocardial strain rate ± SD | −           | –           | 0.60 ± 0.22     |               |
| Average of peak segmental circumferential myocardial strain rate ± SD | −           | –           | −0.40 ± 0.16    |               |
| Average of time to peak segmental myocardial transverse strain ± SD | –           | –           | 227.80 ± 92.27 | 329 ± 76.28 |
| Average of time to peak segmental myocardial longitudinal strain ± SD | –           | –           | 266.70 ± 88.65 | 349.30 ± 88.38 |
| Average of time to peak segmental radial strain ± SD | –           | –           | 284.70 ± 87.41 |               |
| Average of time to peak segmental circumferential strain ± SD | –           | –           | 254.80 ± 41.86 |               |
| Maximal opposing wall delay for transverse strain | 0           | 18          | 161             | 125           |
| Maximal opposing wall delay for longitudinal strain | 0           | 35          | 232             | 71            |
| Maximal opposing wall delay for transverse strain rate | 36          | 36          | 196             | 36            |
| Maximal opposing wall delay for longitudinal strain rate | 107         | 0           | 304             | 107           |
| Apical rocking –epicardial layer                 | +0.39        | +0.28       | –               | −0.05         |
| Apical rocking –myocardial layer                 | +0.61        | +0.12       | +0.84           | −0.23         |
| Apical rocking –endocardial layer                | +0.72        | +0.22       | +0.29           | −0.17         |
signaling of angiotensin II by SARS-CoV-2 [4]. Genetic characteristics may play a role in various clinical features of COVID-19 infection [17, 18].

Although we performed a comprehensive strain analysis including longitudinal, circumferential, radial, and transverse strain imaging in this patient, transverse and radial strains are reported to be less reliable [5, 7].

The presence of four-chamber-apical rocking with opposite direction of rocking in the failed left ventricle compared to the three other cardiac chambers has not been reported before. Apical rocking or transverse motion of the apex is recognized as a marker of left ventricular dyssynchrony. It has been reported as a parameter that predicts response to cardiac resynchronization therapy [19–22]. We may speculate that all three other chambers are working together to compensate for abnormal left ventricular apical rocking.

Moreover, his child had prestretch and rebound stretch in the left ventricular longitudinal strain imaging. Gorcsan et al., in a study on 422 patients with heart failure, reported the presence of systolic stretch as an indicator of favorable response to cardiac resynchronization therapy in patients with a QRS duration of 120 149 ms or absent left bundle branch block [23]. Thus, the septal flash, apical rocking, and the peculiar strain pattern in this patient may predict a potential favorable response to CRT [22].

Evaluation of left atrial strain is a necessity in patients with heart failure. It provides information regarding the left atrium’s reservoir, conduit, and booster function and is considered a parameter for assessing left ventricular diastolic function. Left atrial reservoir strain of less than 23% is abnormal [9, 24–28].

Cardiac magnetic resonance imaging is a robust gold standard tool for diagnosis, follow-up, and prognostication of myocarditis in acute, chronic, and healed states [29, 30]. The diagnosis of definite myocarditis was established for this patient by fulfilling the two major (myocardial edema and myocardial injury) and the two minor (pericarditis and left ventricular systolic dysfunction) criteria of the updated Lake Louise criteria [10]. Georgiopoulos and colleagues reported that late gadolinium enhancement (LGE) and anteroseptal location portend a worse prognosis in patients with acute myocarditis [31]. Myocardial edema may be seen in acute and chronic

![Cardiac magnetic resonance imaging of the patient. A: Pericardial effusion, B: Indicates diffuse myocardial edema, C: Depicts late gadolinium enhancement, and D: Shows a severe enlargement of the left ventricle.](image-url)
myocarditis. However, the scar is a feature of healed myocarditis [10]. Furthermore, persistent myocardial edema has been reported in 25% of patients with COVID-19 myocarditis [1].

Conclusions
This is the first case report that indicates COVID-19 can induce silent myocarditis with progression to dilated cardiomyopathy and newly developed systemic hypertension. Accordingly, this case encompasses several critical lessons for primary care physicians and pediatric cardiologists. First and foremost, a thorough examination of the heart and measurement of blood pressure are mandatory in every child with COVID-19 infection. Second, the role of cardiac MR with appropriate sequences in the diagnosis, follow-up, and prognostication of myocarditis should not be underestimated. Third, four-chamber speckle tracking strain imaging showed apical rocking in all the four chambers of the heart in this child with secondary dilated cardiomyopathy with opposite direction in the failed left ventricle compared with other cardiac chambers. Fourth, the presence of septal flash on M-mode echocardiography, apical rocking, and prestretch–rebound stretch patterns on longitudinal strain imaging of the left ventricle may be of predictive value for response to CRT in these patients.

Abbreviations
CMR: Cardiac magnetic resonance imaging; CRT: Cardiac resynchronization therapy; LA: Left atrium; LV: Left ventricle; RA: Right atrium; RV: Right ventricle.

Supplementary Information
The online version contains supplementary material available at https://doi.org/10.1186/s43044-022-00282-w.

Acknowledgements
None.

Author contributions
The first author contributed to the concept, patient management, data collection, echocardiographic examinations, preparing, editing, and critical review of the draft. The second author contributed to data collection and preparation, editing, and critical review of the draft. Both the authors have read and approved the final manuscript.

Funding
None.

Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations
Ethics approval and consent to participate
Not applicable.

Consent for publication
Written informed consent was obtained from the parents.

Competing interests
The authors have no conflict of interest to declare.

Author details
1 Department of Pediatric Cardiology, Children’s Medical Center (Pediatric Center of Excellence), Tehran University of Medical Sciences, Tehran, Iran. 2 School of Medicine, Tehran University of Medical Sciences, Tehran, Iran.

Received: 28 January 2022 Accepted: 17 April 2022

Published online: 31 May 2022

References
1. Li DL, Davogustto G, Soslow JH, Wassenaar JW, Parikh AP, Chew JD, Dendy JM, George-Durrett KM, Parra DA, Clark DE, Hughes SG (2022) Characteristics of COVID-19 myocarditis with and without multisystem inflammatory syndrome. Am J Cardiol 168:135–141
2. Kohli U, Meinert E, Chong G, Tesher M, Jani P (2020) Fulminant myocarditis and atrial fibrillation in child with acute COVID-19. J Electrocardiol 50(22–07):305.71–305.79
3. Azeka E, Arshad A, Martins C, Dominguez AC, Siqueira A, Loss AS, Jatene M, Miura N (2021) Case report: dilated cardiomyopathy in a newborn, a potential association with SARS-COV-2. Front Pediatr 9:674300
4. Chen G, Li X, Gong Z, Xia H, Wang Y, Wang X, Huang Y, Barajas-Martinez H, Hu D (2021) Hypertension as a sequel in patients of SARS-CoV-2 infection. PLoS ONE 16(4):e0250815
5. Dallaire F, Slorach C, Bradley T, Hui W, Sarkola T, Friedberg MK, Jaeggi E, Dragulescu A, Mahmud FH, Daneman D, Mertens L (2016) Pediatric reference values and Z score equations for left ventricular systolic strain measured by two-dimensional speckle-tracking echocardiography. J Am Soc Echocardiogr 29(8):786–793.e8
6. Marcus KA, Mavinkurve-Groothuis AM, Barends M, van Dijk A, Feuth T, de Korte C, Kapusta L (2011) Reference values for myocardial two-dimensional strain echocardiography in a healthy pediatric and young adult cohort. J Am Soc Echocardiogr 24(6):625–636
7. Marwick TH, Kosmala W (2022) Strain imaging applications and techniques. In: Marwick HH (ed) ASE’s comprehensive strain imaging. Elsevier, Philadelphia, pp 1–19
8. Tsugu T, Postolache A, Dulgheru R, Sugimoto T, Tridetti J, Nguyen Trung ML, Pitte C, Moonen M, Manganaro R, Iardi F, Chitroceanu AM, Sperlongano S, Go YY, Kacharava G, Athanassopoulos GD, Barone D, Baroni M, Cardim N, Hagendorff A, Hristova K, Lopez T, de la Morena G, Popescu BA, Penicka M, Ozyigit T, Rodrigo Carbonero JD, van de Veire N,
