CASE REPORT **DOI: https://doi.org/10.18502/fem.v6i3.9402**

Rare presentation of COVID-19 in 6-year-old girl: myocarditis with severe restrictive diastolic dysfunction

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Published online: 2022-02-27

Cite this article as: Chegini V, Omidi F, Shojaeian F, Hatamabadi H, Farshidgohar M. Rare presentation of COVID-19 in 6-year-old girl: myocarditis with severe restrictive diastolic dysfunction. Front Emerg Med. 2022;6(3):e40.

1. Introduction

Since the emergence of Coronavirus Disease 2019 (COVID-19), critically ill children with COVID-19 made up a small proportion of the patients. Still, recent records of coronavirus infection in children and adolescents have been accompanied by multisystem inflammatory syndrome and Kawasaki-like symptoms (1-3). This new phenomenon, called Multisystem Inflammatory Syndrome in children (MIS-C), seems to be a kind of post-viral inflammatory disease rather than a remitting infection. The most common manifestations of this disease are fever, gastrointestinal symptoms, rash, conjunctivitis, and shock. Myocarditis and myocardial dysfunction have also been reported by performing echocardiography (4-6). It should be noted that there are differences between viral myocarditis and myocarditis following MIS-C in COVID-19. In viral myocarditis, signs and symptoms are due to viral penetration and the immune response; however, in these inflammatory diseases and MIS-C, the manifestations are mainly due to inflammatory infiltration and cytokine storm in interstitial myocardial tissue (5, 7). Even so, myocarditis with severe restrictive diastolic dysfunction is considered a rare presentation of this disease among children.

There has been an increasing number of children with MIS-C reported worldwide in the last six months, including Europe, North America, Asia, and Latin America. Although children are less susceptible to severe COVID-19 symptoms than adults, appearing severe presentations in them should be studied carefully. Here we report a 6-year-old girl with a rare presentation of myocarditis with severe restrictive diastolic dysfunction due to COVID-19 from Iran.

2. Case presentation

A 6-year-old girl was brought to the emergency department (ED) of a children hospital due to cyanosis, diarrhea, fever, and symptoms related to the impaired peripheral perfusion owing to cardiogenic shock. The patient had no history of heart disease and was once hospitalized in 9-month-old due to pneumonia. On physical examination, the patients appeared distressed with gasping respiration, the body temperature was 39°C, pulse was 120/minute, and blood pressure was 80/55 mm Hg with the SpO2 of 50% on admission. She had fine bilateral crackles on the lung, and grade II systolic murmur on heart auscultation, and the liver was 3 cm palpable below the right lower costal margin. The patient was immediately intubated, transferred to the pediatric intensive care unit, and put on a mechanical ventilator. She had a history of COVID-19 exposure by her father.

An electrocardiogram showed sinus tachycardia with tall and wide P wave and low voltage in precordial lids (Figure 1-a). The chest X-ray demonstrated massive cardiomegaly (Figure 1-b).

In her lab study, high cardiac troponin (0.286 ng/mL, normal <0·014 ng/mL), leukocytosis with lymphopenia (WBC: 18000, lymphocyte: 18%), slight increase in her C-reactive protein (38 mg/L) and normal D-dimer level (219 ng/mL, normal <500 ng/ml) was detected. Arterial Blood gases showed mixed metabolic acidosis and respiratory acidosis. Echocardiography findings were as follows: biatrial enlargement and restrictive cardiomyopathy pattern, moderate right ventricular dysfunction (Tricuspid Annular Plane Systolic Excursion (TAPSE) =8 mm), severe left ventricular diastolic dysfunction (restrictive pattern, E/A=2.5, LV E'septal=6, LV E'lateral=7), increased left ventricular filling pressure (E/E' =16), severe mitral regurgitation (MR), severe tricuspid regurgitation (TR) (Pulmonary Artery Pressure (PAP)=55 mmHg), fixed and dilated inferior vena cava (IVC). Her left ventricular Ejection fraction (LVEF) was reduced to 40% (Figure 2).

The treatment was started with inotropic medications (milrinone and dopamine) and furosemide infusion. Covid-

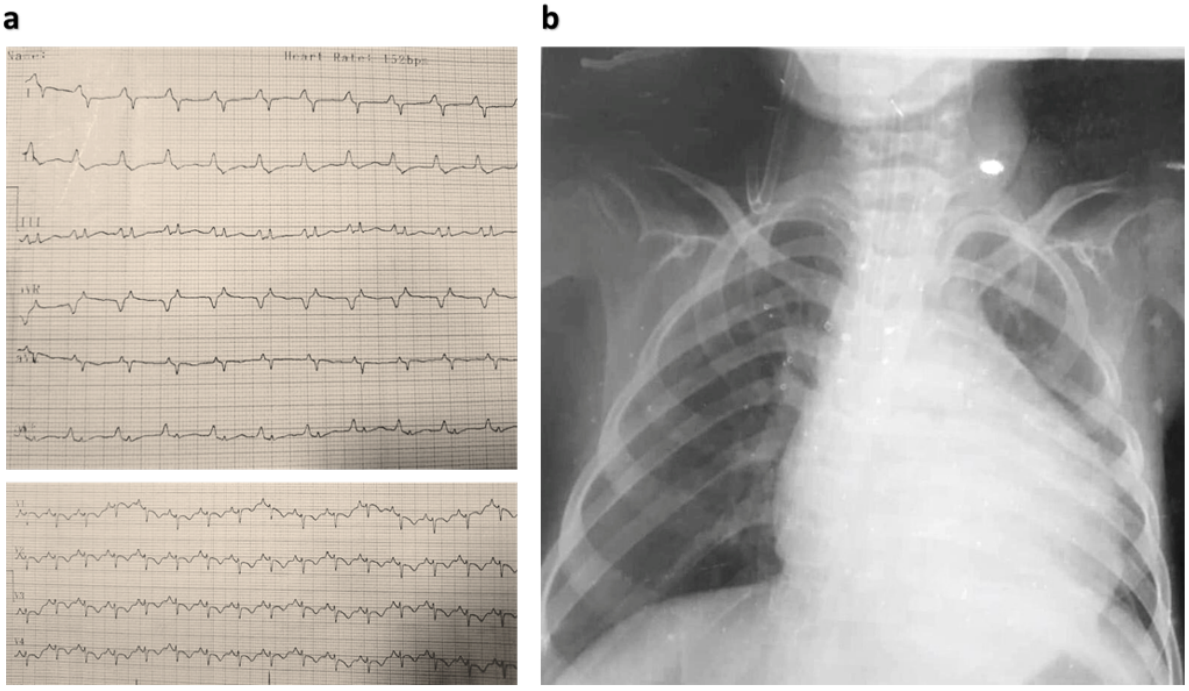

Figure 1 Electrocardiogram (a) and Chest x-ray (b) of the patient, demonstrating tachycardia and massive cardiomegaly

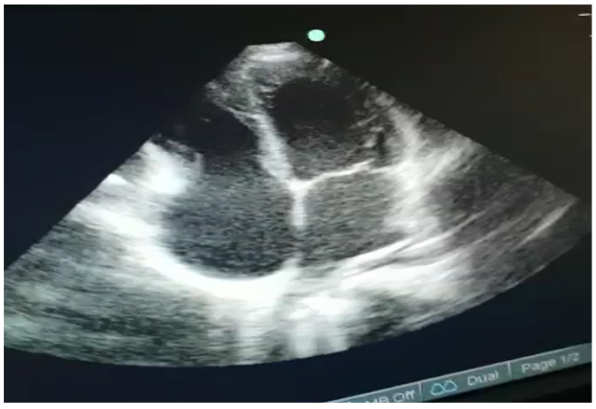

Figure 2 Four chamber echocardiography view of the patient showed biatrial enlargement and restrictive cardiomyopathy pattern

19 reverse transcription-polymerase chain reaction (RT-PCR) detected positive and intravenous immunoglobulin (IVIg), enoxaparin, and methylprednisolone was added to her treatment. The patient was also administered epinephrine due to cardiac dysfunction and hypotension. Repeated daily echocardiography was performed, and no significant improvement was observed. On the fifth day of admission, she had a ventricular tachycardia (VT) attack resistant to direct current (DC) shock and antiarrhythmic drugs. Unfortunately, despite all the efforts for resuscitation, she passed away.

3. Discussion

Here, we presented a 6 -year-old girl with no history of cardiac disease, infected with COVID-19. Her echocardiography findings showed myocarditis with severe restrictive diastolic dysfunction, a rare cardiac presentation in children. The severe restrictive diastolic dysfunction can be characterized by impaired diastolic relaxation, abnormal ventricular compliance, elevated left and right ventricular end-diastolic pressure, and biatrial dilatation (8).

In comparison to adults, the incidence of clinically symptomatic COVID-19 infection in children is low (1–2%), with the great majority of children experiencing relatively mild or no symptoms. However, during the current pandemic, a new MIS-C has been discovered, appearing after the peak of COVID-19 infection in adults. There was no indication of active COVID-19 infection in these children, and multisystem inflammation was thought to be driven by cytokine activation (3-5). Adult COVID-19 patients have been demonstrated in to have cardiovascular problems, including the possibility of direct cardiomyocyte damage due to viral invasion or indirect myocardial injury due to severe acute inflammation, disrupting the pulmonary endothelium (9, 10). Cardiovascular involvement and clinical characteristics overlapping with other acute inflammatory syndromes such as toxic shock syndrome and macrophage activation syndrome have been documented in children with MIS-C. However, discrepancies in clinical presentation and test data suggest a particular investigation in vulnerable people. Clinical observations from a diverse geographical and population mix are critical when dealing with a novel disease, especially during a global pandemic emergency, to further refine the case definition and develop management strategies, initially from expert consensus and hopefully later from controlled trials (1-3, 7).

As a result, we discussed the first child with a new cardiac

complication from Iran, whose COVID-19 resulted in myocarditis with a restrictive pattern. Echocardiography findings demonstrated tran's mitral doppler inflow characteristics such as an elevation in the E: A ratio and increased E wave deceleration, as well as severe biatrial enlargement, elevated pulmonary arterial and right ventricular systolic pressure. It seems that myocarditis due to COVID-19 was the etiology of this condition in this patient. Although in most cases of the MIS-C, the COVID-19 PCR test has been reported negative, our patient was detected positive (3).

Myocarditis can have a variety of clinical presentations ranging from mild symptoms such as fatigue, chest pain, and palpitations to life-threatening manifestations such as cardiogenic shock or sudden cardiac death associated with ventricular arrhythmias (3, 8). Here, COVID-19 caused a restrictive heart pattern with increased myocardial stiffness and abnormal myocardial relaxation. The myocardial injury might be due to direct invasion of covid-19 or myocardial inflammation due to cytokine storm response, affected ventricular compliance, and its stiffness and relaxation. COVID-19 has a broad spectrum of cardiovascular complications, including heart failure, arrhythmias, acute coronary syndrome, myocarditis, and cardiac arrest; this presentation of myocarditis with the restrictive diastolic dysfunction is pretty rare.

In this case, COVID-19 caused myocarditis with severe and restrictive diastolic dysfunction that, despite standard treatment of myocarditis and supportive care, unfortunately she passed away. Therefore, it seems necessary to precisely follow different cardiac presentations and cardiac consequences of the pandemic in children.

4. Conclusion

COVID-19 might cause multisystem inflammatory syndrome in children (MIS-C), which presented with different manifestations. In this study, we described a young girl with myocarditis and severe restrictive diastolic dysfunction due to COVID-19.

5. Declarations

5.1. Acknowledgement

The authors would like to thank the Imam Hossein Hospital personnel, doctors, and nurses for all their efforts to save people's life, especially during the pandemic.

5.2. Authors' contribution

MF and VCh: conceived of the presented idea; MF, HH, and FSh: wrote the manuscript in consultation with all authors; VCh, FO, MF, and HH: conceived the study and were in charge of overall direction and planning; VCh, MF, HH, and FO: were directly involved in the treatment plan of the patients; All authors discussed the results and commented on the manuscript.

5.3. Conflict of interest

The authors know of no conflicts of interest associated with this publication.

5.4. Funding

There has been no financial support for this work.

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