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CASE REPORT

INTERMEDIATE

CLINICAL CASE

Reversible Myocardial Injury Associated With SARS-CoV-2 in an Infant

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ABSTRACT

Coronavirus disease-2019 is caused by the severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) and has been associated with myocardial dysfunction and heart failure in adult patients. We report a case of reversible myocardial injury and heart failure in an infant with SARS-CoV-2 infection. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2020;2:2348–52) © 2020 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 2-month-old infant presented with an episode of choking and cyanosis after feeding. There was no history of fever, cough, upper respiratory tract infection symptoms, diarrhea, vomiting, or decreased oral intake prior to the initial presentation. On arrival of emergency medical service, the patient had a pulse but poor respiratory effort and was treated with oxygen and bag mask ventilation. On arrival to the emergency department, non-rebreather mask ventilation (15 l/min, 80% FiO_2) was initiated. On arrival to the pediatric intensive care unit, initial examination revealed a heart rate of 170 beats/min, respiratory rate of 70 breaths/min, a blood pressure of 66/36 mm Hg, and an oxygen saturation of 98%. The weight and height were at 66th and 90th percentile for corrected gestational age, respectively. The examination was significant for a 3/6 holosystolic murmur at the apex radiating to the axilla, liver was palpable 2 to 3 cm below the costal margin and the extremities were cool with 3 to 4 seconds of capillary refill. Initial arterial blood gas was significant for mild metabolic acidosis with a lactate of 2.9 mmol/l (Table 1). On the first day of illness (DOI 1), pertinent laboratory data showed lymphopenia (2.1 K/μl), elevated Troponin-T (TnT) 0.16 ng/ml (normal <0.1 ng/ml), and N-terminal pro-B natriuretic peptide (NT-proBNP) 15,000 pg/ml (normal <450 pg/ml). The C-reactive protein (CRP) level was normal. There were mild elevations in liver function tests, D-dimer, and interleukin-6 levels. Initial assay for severe acute respiratory syndrome-coronavirus-2

LEARNING OBJECTIVES

- To make a differential diagnosis of LV dysfunction in infancy.
- To understand the importance of testing for SARS-CoV-2 in children presenting with signs and symptoms of heart failure and LV dysfunction during the pandemic.

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(SARS-CoV-2) infection was negative. Repeat Cepheid Xpert Xpress polymerase chain reaction assay of the nasopharyngeal sample confirmed SARS-CoV-2 infection. The chest radiograph showed cardiomegaly with bibasilar patchy opacities greater in the left lower lobe and right upper lobe atelectasis (Figure 1). A 12-lead electrocardiogram (ECG) showed sinus tachycardia, nonspecific ST-segment depression, T-wave inversions in the anterolateral and inferior leads, and prominent mid-precordial voltages (Figure 2A).

PAST MEDICAL HISTORY

The patient was born at 33 weeks requiring a 3-week stay in the neonatal intensive care unit with 1 week of nasal continuous positive airway pressure support.

DIFFERENTIAL DIAGNOSIS

Given the initial presentation, ECG findings, troponin, and NT pro-BNP elevation, the differential diagnosis at presentation included primary acute myocardial injury due to the viral infection versus an underlying dilated cardiomyopathy with heart failure symptoms exacerbated by the viral infection and ischemic dilated cardiomyopathy secondary to anomalous left coronary artery.

INVESTIGATIONS

A transthoracic echocardiogram on DOI 1 demonstrated severely depressed left ventricular (LV) systolic function (ejection fraction [EF] 30%), severe mitral regurgitation (MR), and normal right ventricular systolic function. The origins of the coronary arteries were normal. There were no other cardiac abnormalities or pericardial effusion. Multiplex viral panel polymerase chain reaction to rule out other viral etiologies for acute myocarditis was negative.

MANAGEMENT

Patient required fluid resuscitation and inotropic support for hypotension and mechanical ventilation for respiratory failure. On DOI 4, after obtaining approval for compassionate use, the patient was started on remdesivir, a nucleotide analogue prodrug that inhibits viral RNA polymerases, which was continued for 10 days. Intravenous antibiotics, vancomycin and ceftriaxone, were started to cover for possible superinfections until the blood culture showed no growth (DOI 1 to 4). The infant was extubated to noninvasive ventilation on DOI 6. On DOI 8,

ABBREVIATIONS AND ACRONYMS

COVID-19 = coronavirus disease-2019

CRP = C-reactive protein

DOI = day of illness

ECG = electrocardiogram

LVEF = left ventricular ejection fraction

MR = mitral regurgitation

NT-proBNP = N-terminal pro-B natriuretic peptide

SARS-CoV-2 = severe acute respiratory syndrome-coronavirus-2

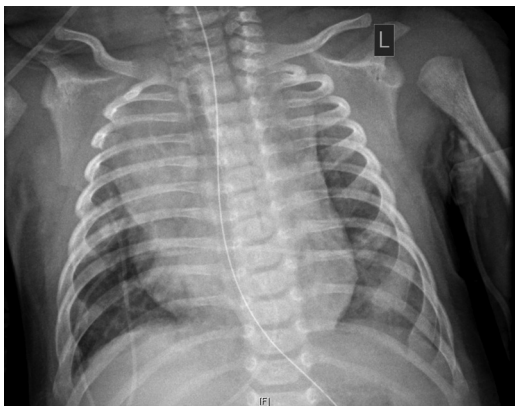
TnT = Troponin T

TABLE 1 Clinical Laboratory Results

Test	Reference Range	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14
WBC count, K/μl	6.0-17.5	9.2	9.8	9.8	6.9	8.7	6.8	5.3	6.9	11.7	6.6	12.3	17.1	18.5	19.2
Lymphocytes, K/μl	4.0-13.5	2.1	4.5	3.8	2.9	3.5	4.9	3.1	1.5	5.0	3.0	6.3	4.7	6.0	9.8
Hemoglobin, g/dl	9.0-14.0	8.9	8.9	14.0	12.8	12.3	11.5	10.3	9.0	8.3	7.9	8.1	10.4	8.6	9.0
Hematocrit, %	28-42	27.8	27.5	42.0	36.9	26.9	31.7	31.6	26.9	21.4	23.7	25.0	31.0	27.9	29.3
Platelets, K/μl	150-400	287	268	194	202	183	179	137	159	122	315	247	259	434	594
TnT, ng/l	<0.10	0.16	0.19	0.05	0.04	0.02	0.02	0.04	0.01	0.09		0.01		0.01	
NT-proBNP, pg/ml	<450	15,000		1,434			1,488			15,000	13,247	3,457	4,931	5,082	678
CRP, mg/dl	>0.5	<0.5		4.6		0.9		4.3	6.9	4.8	1.2	0.6	0.5	<0.5	<0.5
BUN, mg/dl	4.5-20	15	12	14	8	23	24	16	9	11	7	13	18	22	23
Creatinine, mg/dl	<0.7	0.2	0.2	0.3	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.3
Alanine aminotransferase, U/l	<30	31	23	13	17	15	17	14	18	16	14	13	17	20	29
Aspartate aminotransferase, U/l	<50	72	70	36	33	34	31	24	44	35	26	<20	25	25	37
Arterial blood gas (FiO_2%)		80	45	30	25	25	25	30	90	55	35	35	40	35	35
pH	7.35-7.45	7.28	7.40	7.38	7.42	7.41	7.35	7.42	7.11	7.50	7.40	7.40	7.39	7.42	7.36
pCO_2, mm Hg	35-45	48	38	35	46	44	48	40	77	37	39	38	39	38	39
pO_2, mm Hg	80-100	136	79	61	102	107	86	107	240	199	116	166	163	107	203
HCO_3, mmol/L	22-28	23	24	21	27	28	27	26	25	29	25	23	24	25	22
Lactic acid, mmol/L	1.1-1.35	2.9	1	1.3	1.2	1.1	1.1	1.2	1.1	1.1	1.2	1.2	1.2	1.1	1.1
D-dimer, μg/ml FEU	0.0-0.5	3.99	1.78		1.78	1.86	2.35	2.68	1.95	2.69	9.78	6.73	3.08	1.96	2.59
Ferritin, ng/ml	25-270	129		133	189		121	192	209		241		161	146	162
LDH, U/l	<400	486		539		316		410	317	485	389	354	476	411	542
Plasma, IL-6, pg/ml	<14.8	42		9.9											

BUN = blood urea nitrogen; CRP = C-reactive protein; FiO_2 = fraction of inspired oxygen; FEU = fibrinogen equivalent units; HCO_3 = bicarbonate; IL = interleukin; LDH = lactate dehydrogenase; NT-proBNP = N-terminal pro-B natriuretic peptide; pCO_2 = partial pressure of oxygen; pO_2 = partial pressure of carbon dioxide; TnT = Troponin T; WBC = white blood cell.

FIGURE 1 Chest Radiograph



Chest radiograph showing cardiomegaly, bibasilar opacities, and right upper lobe atelectasis.

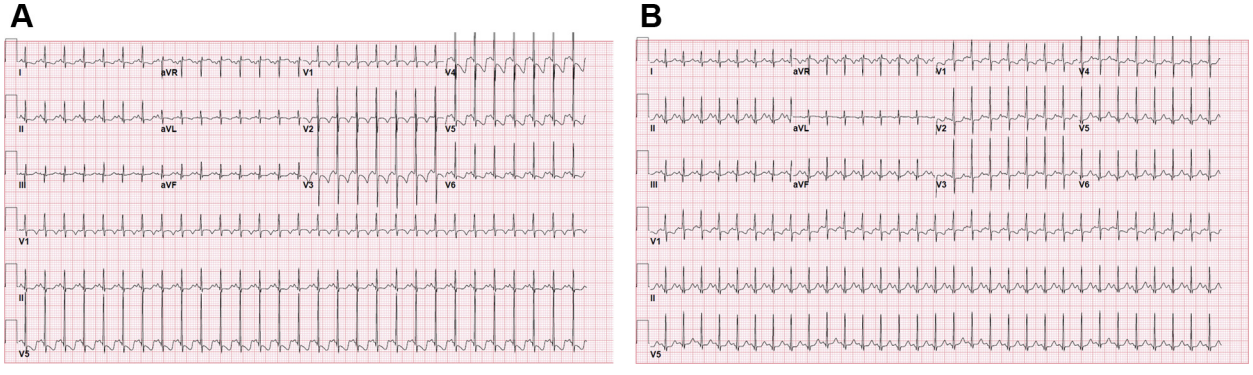
the infant developed acute respiratory distress requiring reintubation. TnT, NT-proBNP, CRP, and D-dimer increased. LV size, ventricular function, and MR remained unchanged. On DOI 8 intravenous methylprednisolone at 2 mg/kg/day was started. D-dimer increased to 9.78 μg/ml on DOI 10 (**Table 1**) and low molecular heparin was initiated at a therapeutic dose with a goal anti-Xa level of 0.6 to 1.0. The patient was extubated on DOI 14 to noninvasive ventilation support. TnT, NT-proBNP, and CRP decreased from DOI 8 to 14. **Figure 3A** shows the trend of selected laboratory values. LV size and function normalized (EF 58%) by DOI 14 and MR remained severe, which subsequently improved. Milrinone was discontinued on DOI 16 and the patient did not require oral heart failure therapies. **Figure 3B** shows the trend of LV size and function over the course of illness.

DISCUSSION

The earliest reports of SARS-CoV-2 from China indicated the presence of myocardial injury in a subset of patients. In a cohort of 416 adult patients hospitalized with confirmed coronavirus disease 2019 (COVID-19), 20% had evidence of myocardial injury defined as serum cardiac biomarkers (high sensitivity TnT) greater than the 99th percentile upper reference limit, regardless of new abnormalities in ECG or on echocardiography (1). Guo et al. (2) reported a slightly higher incidence (28%) of myocardial injury as indicated by elevated TnT levels in hospitalized patients with confirmed COVID-19 resulting in cardiac dysfunction and arrhythmia. Both studies showed that older patients with pre-existing cardiovascular disease were at a higher risk of myocardial injury and at a higher mortality risk.

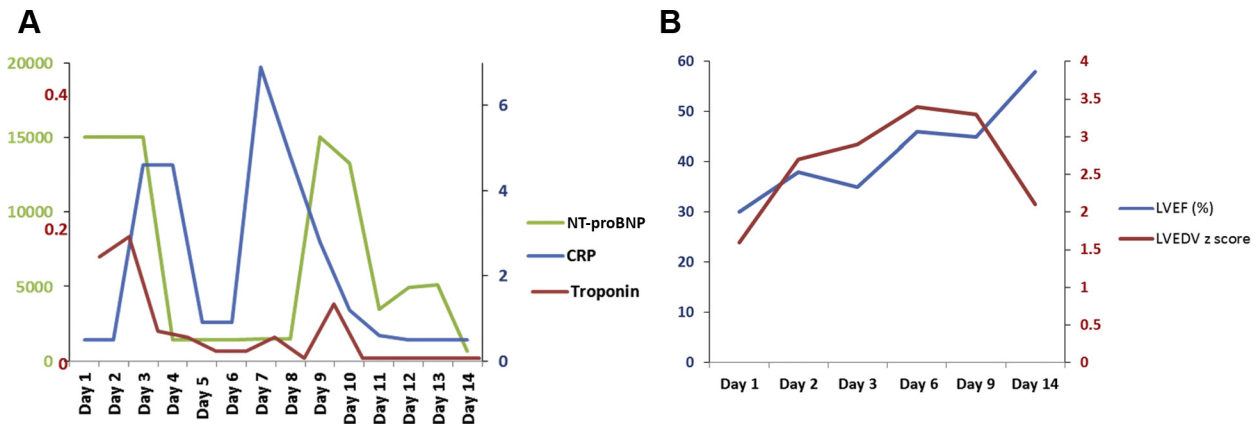
Most children with SARS-CoV-2 infection are either asymptomatic or have mild symptoms (3,4). We report a case of reversible myocardial injury and acute decompensated heart failure associated with documented SARS-CoV-2 infection in an infant. Echocardiographic evaluation demonstrated normal coronary artery origin and flow. The infant's presentation was atypical for a dilated cardiomyopathy because of the absence of a prior history of respiratory illnesses or poor feeding and the infant's normal height and weight-for-age *z* scores (5). The absence of significant LV dilation commonly seen in

FIGURE 2 Electrocardiograms



(A) 12-lead electrocardiogram with sinus tachycardia, nonspecific ST-segment depression and T-wave inversions in anterolateral and inferior leads and prominent mid-precordial voltage. **(B)** Follow-up electrocardiogram showing sinus rhythm, and normalization of T waves in anterolateral and inferior leads.

FIGURE 3 Clinical Data Trends



(A) Selected laboratory trends from admission day of illness 1 through day of illness 14. **(B)** Trends of left ventricular end diastolic volume (LVEDV) *z* scores and left ventricular ejection fraction (LVEF) on echocardiogram. CRP = C-reactive protein; NT-proBNP = N-terminal pro-brain natriuretic peptide.

pediatric patients presenting with dilated cardiomyopathy was also atypical (6). Normalization of LV size and function within 2 weeks of presentation argues strongly for reversible acute myocardial injury associated with SARS-CoV-2.

The presentation and clinical course of this patient mirrors 4 case reports of acute myocardial injury reported in adult patients with COVID-19 (7–10). All 4 cases presented with severe LV dysfunction and elevated cardiac biomarkers (TnT, NT-proBNP), which subsequently normalized. One 63-year-old patient required extracorporeal membrane oxygenation support and had normalization of his LVEF from 32% to 68% but died at DOI 36 (7). Three patients survived and had normalization of LV systolic function. Cardiac magnetic resonance imaging was performed in 2 patients and demonstrated myocardial edema and a nonischemic pattern of late gadolinium enhancement consistent with acute myocarditis (9,10). Coronary angiography was normal in 2 patients with ST-segment elevation on ECG and regional wall motion abnormality (8,9).

FOLLOW-UP

At the time of this submission, the patient has recovered and was discharged home on no oral heart failure therapy with a close follow-up. The LV size and systolic function have remained normal and the MR has resolved.

CONCLUSIONS

Acute myocardial injury as an atypical presentation of SARS-CoV-2 infection is currently being recognized in the adult population. Our case highlights the potential for myocardial involvement in infants with SARS-CoV-2 infection.

AUTHOR DISCLOSURES

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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KEY WORDS coronavirus disease-2019, pediatrics, reversible myocardial injury