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Cardiac Dysfunction and Shock in Pediatric Patients With COVID-19

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ABSTRACT

Coronavirus disease-2019 (COVID-19) has been reported to cause significant morbidity in adults, with reportedly a lesser impact on children. Cardiac dysfunction has only been described in adults thus far. We describe 3 cases of previously healthy children presenting with shock and COVID-19–related cardiac inflammation. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2020;2:1267–70) © 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/).

The pandemic caused by coronavirus disease-2019 (COVID-19) continues to inflict significant morbidity and mortality around the world. Most pediatric infections have been reported to be mild. Cardiovascular complications of COVID-19 have been reported in adult literature, but pediatric data are lacking. With Northwell Institutional Review Board approval, we describe 3 previously healthy children admitted to the pediatric intensive care unit (PICU) for COVID-19–related shock and evidence of cardiac injury.

LEARNING OBJECTIVES

- To recognize that pediatric COVID-19 may present with evidence of shock and cardiac dysfunction independent of lung disease.
- To review the different mechanisms of cardiac injury in pediatric patients with COVID-19.

PATIENT #1

A 13-year-old previously healthy obese male patient presented to the emergency department (ED) with 5 days of fever, headache, and abdominal pain; 2 days of diarrhea; and 1 day of shortness of breath. On initial presentation, he was afebrile, tachycardic (119 beats/min), hypotensive (76/35 mm Hg), and tachypneic (56 breaths/min), with oxygen saturation of 94% on room air. On examination, he had mild crackles at lung bases, a regular heart rhythm with a gallop, hepatomegaly, and delayed capillary refill time of 4 s. A norepinephrine infusion was started for fluid refractory hypotension along with supplemental oxygen therapy via nonrebreather.

Initial laboratory results showed a leukocytosis with neutrophil predominance and bandemia, as well as significant elevation in inflammatory markers that have been associated with COVID-19 (C-reactive protein, procalcitonin, lactate dehydrogenase,

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ABBREVIATIONS AND ACRONYMS

AKI = acute kidney injury

COVID-19 = coronavirus disease-2019

ED = emergency department

FS = fractional shortening

hsTnT = high-sensitivity troponin T

IVIG = intravenous immunoglobulin

LVEF = left ventricular ejection fraction

PCR = polymerase chain reaction

PICU = pediatric intensive care unit

TTE = transthoracic echocardiogram

VIS = vasoactive ionotropic score

triglycerides, ferritin, D-dimer, and fibrinogen). High-sensitivity troponin T (hsTnT) was elevated to 389 ng/l (<6 to 14 ng/l). The patient also had acute kidney injury (AKI) and mild transaminitis. He had a metabolic acidosis with an initial lactate of 6.4 mmol/l. Nasopharyngeal polymerase chain reaction (PCR) testing for COVID-19 returned positive, and a respiratory viral panel was negative. An initial chest x-ray film showed a left basal opacity, with no cardiomegaly.

He was admitted to the PICU, where bedside cardiac ultrasound showed moderately decreased function (fractional shortening [FS] 18%) with no pericardial effusion. Owing to increasing lactate levels, he was intubated, placed on a ventilator, sedated, and chemically paralyzed. Epinephrine and milrinone infusions were initiated. He was treated with tocilizumab, an interleukin-6 inhibitor, and intravenous immunoglobulin (IVIG) on PICU day 1 and transthoracic echocardiography (TTE) showed improvement in left ventricular function with a FS of 32% and left ventricular ejection fraction (LVEF) of 49%. Remdesivir, an antiviral that inhibits COVID-19 replication, and intravenous methylprednisolone were started on PICU day 2.

His course was complicated by brief episodes of atrial tachycardia. By PICU day 4, he was off inotropic infusions and extubated to non-invasive ventilation, and by PICU day 5, he was weaned to room air with downtrending inflammatory markers and troponin levels. A repeat echocardiogram on PICU day 5 showed improved function (FS 45% and LVEF 65%) and he was discharged on PICU day 11 after completing his remdesivir course.

PATIENT #2

A 6-year-old male patient with history of mild persistent asthma presented to the ED with 6 days of fever, pharyngitis, myalgia, and abdominal pain and 1 day of diarrhea and shortness of breath. On initial presentation, he was afebrile, tachycardic (130 beats/min), hypotensive (71/34 mm Hg), and tachypneic (40 breaths/min), with oxygen saturation of 97% on room air. On examination, he had good air entry bilaterally, with an III/VI systolic murmur appreciated at the left upper sternal border. A norepinephrine infusion was started for fluid refractory hypotension.

Initial laboratory results showed a leukocytosis with neutrophil predominance and bandemia as well as significant elevation in inflammatory markers that have been associated with COVID-19. He had a normal lactate level but was noted to have AKI as well as a mild transaminitis. His hsTnT was elevated to 116 ng/l (<6 to 14 ng/l). A rapid test for COVID-19 returned positive, and respiratory viral PCR panel was negative.

He was admitted to the PICU on room air. Contemporaneous TTE showed low-normal LVEF of 56%, FS of 29%, mild mitral regurgitation, and holodiastolic reversal of flow in the descending aorta. Epinephrine infusion was added at this time because of continued hypotension. He was treated with a 5-day course of hydroxychloroquine, as well as intravenous tocilizumab. By 36 h of admission, all inotropic support had been weaned off and his AKI had resolved. He was discharged on PICU day 3. His inflammatory markers trended down at discharge and his echocardiography showed an LVEF of 57% and an FS of 35%.

PATIENT #3

A 13-year-old female patient with a known small midmuscular ventricular septal defect presented to the ED with 9 days of intermittent fever, headache, and cough and 5 days of abdominal pain and diarrhea. On initial presentation, she was febrile (39.4°C), tachycardic (119 beats/min), normotensive (117/68 mmHg), and mildly tachypneic (18 breaths/min), with oxygen saturation of 100% on room air. On examination, she was awake and alert, and had good air entry with diminished breath sounds at the bases, normal heart sounds, mild epigastric abdominal tenderness, and normal peripheral perfusion with brisk capillary refill. For tachycardia, she received a 10-cm^3/kg fluid bolus with minimal improvement in heart rate. Initial laboratory results showed an elevated white blood cell count with a left shift and bandemia. She also had a significant elevation in inflammatory markers that have been associated with COVID-19. The patient had normal renal function. Her hsTnT was 43 ng/l (<6 to 14 ng/l). Nasopharyngeal PCR testing for COVID-19 returned positive, and a respiratory viral panel was negative.

She was admitted to the pediatric ward, where she received additional fluid boluses for worsening tachycardia (134 beats/min) and hypotension (85/45 mm Hg). Given the abnormal hsTnT and persistent tachycardia, a TTE was performed, which showed moderately decreased left ventricular systolic function with an LVEF of 40%, FS of 21% with mild mitral regurgitation, holodiastolic flow reversal in the descending aorta, and a small pericardial effusion. She was transferred to the PICU, started on a milrinone infusion, and continued treatment with

TABLE 1 Comparison of Presenting Symptoms, Echocardiographic Findings, and Labs Among 3 COVID-19 Patients

	Patient #1	Patient #2	Patient #3
Presenting symptoms	Fever, headache, abdominal pain, diarrhea, dyspnea	Fever, pharyngitis, myalgia, abdominal pain, diarrhea, dyspnea	Fever, headache, cough abdominal pain and diarrhea
Cardiac rhythm	Sinus tachycardia Nonspecific ST- and T-wave abnormalities Atrial tachycardia on PICU day 3	Sinus tachycardia Nonspecific T-wave abnormalities	Sinus tachycardia Right axis deviation Nonspecific T-wave abnormalities
Initial LVEF/FS, %	—/18	56/29	40/21
Discharge LVEF/FS, %	65/45	57/35	54/28
Initial descending aortic Doppler	N/A	Holodiastolic flow reversal	Holodiastolic flow reversal
Peak VIS	26	18	5
Peak lactate, mmol/l	11	1.5	2.8
Peak hsTnT, ng/l	475	116	43
Peak ferritin, ng/ml	1,426	1,985	375.8
Peak WBC count, K/μl	28.1	15.8	10.3
Peak D-dimer, ng/ml	1,973	2,829	508
Peak LDH, U/l	313	300	347
Peak fibrinogen, mg/dl	1,145	582	771
Peak triglycerides, mg/dl	987	813	191
Peak C-reactive protein, mg/l	425.3	361.1	216.3
Peak procalcitonin, ng/ml	4.4	35	2.45
COVID-19 therapies received	Tocilizumab Remdesivir IVIG Steroids	Tocilizumab Hydroxychloroquine	Hydroxychloroquine
Anticoagulation	Enoxaparin (therapeutic)	Enoxaparin (therapeutic)	None
Length of PICU stay, days	11*	4	4

*Patient was stable for discharge on hospital day 7 but remained in hospital to complete the 10-day course of remdesivir.

COVID-19 = coronavirus disease-2019; FS = fractional shortening; hsTnT = high-sensitivity troponin T; IVIG = intravenous immunoglobulin; LDH = lactic dehydrogenase; LVEF = left ventricular ejection fraction; N/A = not assessed; PICU = pediatric intensive care unit; VIS = vasoactive ionotropic score; WBC = white blood cell.

hydroxychloroquine. By PICU day 2, her inflammatory markers and hsTnT had improved. A repeat echocardiogram on PICU day 3 showed improved LVEF to 54% and FS to 28%, and milrinone was discontinued. She was discharged on PICU day 4.

DISCUSSION

Studies suggest a milder clinical course in children, with very few requiring intensive care (1). There are currently limited data regarding cardiovascular and myocardial involvement in pediatric patients with COVID-19, although anecdotal reports of a shock-like presentation with features of Kawasaki disease with myocarditis exist (2). We present 3 pediatric patients admitted to intensive care with shock and evidence of cardiac injury (**Table 1**).

The mechanism for COVID-19-related cardiac injury and shock is unclear. One proposed theory is cytokine-mediated myocardial inflammation (3). Cytokine release appears to be a major causative etiology in the multiorgan dysfunction seen in COVID-19 patients and can adversely impact myocardial function along with the function of other vital organ systems (4). All 3 of our patients presented with features of distributive shock and cytokine release syndrome, with elevated troponin levels and inflammatory markers. Two demonstrated holodiastolic flow reversal in the descending aorta, suggestive of severe vasodilation, which appears to support this hypothesis. None of our patients had other symptoms of classic Kawasaki disease or evidence of coronary involvement.

The other postulated theory of cardiac injury is direct viral infection causing myocarditis. A report on endomyocardial biopsy in COVID-19 has shown both viral particles and inflammatory infiltrate in the myocardium (5).

Currently, there are no established treatment recommendations for cardiac injury and inflammation related to COVID-19 infection. Steroids and IVIG have been described as treatments in adult COVID-19 myocarditis with unclear benefit (6). Both IVIG and steroids were utilized to treat patient 1, our patient with the most severe clinical presentation. Tocilizumab, an interleukin-6 inhibitor, was used in Patients #1 and #2 per an institutional guideline (7). Antiviral therapies were also used.

These cases demonstrate that COVID-19 infection can cause severe illness in previously healthy

children. Shock and cardiac dysfunction can be a significant component of illness independent of lung disease. Further studies are ultimately needed to determine the optimal treatment for these patients. Long-term follow-up is important to understand the pathophysiology and long-term prognosis of children with cardiac injury resulting from COVID-19. As this case series goes to press, our hospital has admitted more than 100 children with COVID-19-related illnesses, including more than 30 children with various cardiac manifestations of COVID-19. Of these children admitted with cardiac manifestations, a large proportion have required intensive care. We anticipate addressing this growing patient population in more detail in future papers, and hope that this case series will raise awareness of a particular subset of cardiac dysfunction and shock associated with COVID-19.

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