

# Acute Fulminant Myocarditis in a Pediatric Patient With COVID-19 Infection

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The majority of patients with coronavirus disease 2019 (COVID-19) display pulmonary disease; however, a significant portion of patients have cardiac injury as well, with a high incidence of myocarditis documented in the adult population. Pediatric disease from COVID-19 has been relatively rare, and no cases of virus-related cardiac disease have been published. We present a case of an adolescent girl with fulminant myocarditis with complete heart block, elevated troponin I levels, and severely depressed systolic function in the setting of COVID-19 infection.

On March 11, 2020, coronavirus disease 2019 (COVID-19), the disease caused by the novel human coronavirus severe acute respiratory syndrome coronavirus 2, was declared a pandemic. COVID-19 has primarily pulmonary manifestations, but studies have also revealed a relatively high incidence of related cardiac disease in adults.<sup>1,2</sup> Specifically, myocarditis and acute cardiac injury have been shown to be common in patients with COVID-19.<sup>3,4</sup> The pediatric population has been largely spared in the pandemic, with few cases of severe disease and no documented cases of COVID-19-related myocarditis.<sup>5,6</sup> We review the case of an adolescent girl with fulminant myocarditis in the setting of COVID-19 infection.

## CASE

The patient is a 12-year-old previously healthy Asian American girl. She was in her usual state of health until 3 days before admission (early April 2020) when she developed fatigue. The next day, she developed a fever of 101°F. The day before admission, she

developed diffuse abdominal pain; nausea; nonbloody, nonbilious emesis; and no diarrhea. The morning of admission, she appeared unwell, with new pallor and blue discoloration of her lips. She was evaluated by her pediatrician who found her to be hypothermic and bradycardic, so she was sent to a local emergency department. In the emergency department, she was noted to be afebrile, bradycardic with a heart rate in the 40s (beats per minute), and normotensive (116/69 mm Hg), with a respiratory rate of 24 and normally saturated. She was ill appearing, awake but irritable, with no murmur, no organomegaly, with cool extremities and a delayed capillary refill time of 4 seconds. An electrocardiogram revealed complete heart block with an atrial rate of 150 beats per minute and a ventricular escape rate of 43 beats per minute. Laboratory analysis revealed evidence of acute cardiac, kidney, liver injury (troponin 38.4 mg/mL,  $\beta$ -natriuretic peptide 953 pg/mL, creatinine 1.5 mg/dL, aspartate aminotransferase 710 U/L, alanine aminotransferase 485 U/L) and

## abstract

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metabolic acidosis (carbon dioxide 15 mmol/L). A complete blood count was unremarkable, with a white blood cell count of 8.75 k/ $\mu$ L (granulocytes 58%, lymphocytes 30%), hemoglobin of 14.5 g/dL, and a mildly elevated platelet count of 379 k/ $\mu$ L. Her chest radiograph was normal. While awaiting transport to a tertiary care facility, she developed worsening bradycardia (beats per minute in the 30s) and hypotension (60/30 mm Hg). She was endotracheally intubated and had a subsequent cardiac arrest requiring 2 minutes of cardiopulmonary resuscitation with return of spontaneous circulation. There was improvement in the heart rate on an epinephrine infusion. She had a second short episode of cardiac arrest during transport. She had no known exposure to COVID-19, but a family member is a frontline health care professional. A qualitative polymerase chain reaction result for COVID-19 was positive. A respiratory infection panel result was also positive for adenovirus. The patient's heart rate and blood pressure responded well to a low-dose epinephrine infusion; the intensive care, cardiology, and cardiac surgery teams evaluated the patient for possible mechanical support including a temporary pacemaker or extracorporeal circulatory support. Happily, she returned to sinus rhythm with episodes of accelerated ventricular and junctional rhythm. She had high troponin I levels peaking at >50 ng/mL. Her serum  $\beta$ -natriuretic peptide peaked at 2652 pg/mL. An echocardiogram revealed no chamber dilation, normal valvular

function, severely diminished left ventricular systolic function with an ejection fraction (Simpson 4 chamber) of 27%, and moderately diminished right ventricular systolic function. A milrinone infusion was added given her depressed systolic dysfunction. Because of the severity of the patient's disease, intravenous immunoglobulin (IVIg) was given (2 g/kg).

Steroid therapy was considered but decided against given the risk of becoming immunocompromised in the setting of 2 viral infections. A cardiac MRI and endomyocardial biopsy were deferred given the patient's instability and the fact that they would not change acute management. Experimental COVID-19 therapies were considered (eg, hydroxychloroquine, azithromycin, remdesivir, toilizumab), but given the lack of evidence of their effectiveness or safety and her clinical improvement, they were not used. The patient responded well to the IVIg therapy with a rapid decrease in her troponin levels and recovery of atrioventricular conduction over the course of 4 days and improvement in her renal (4 days) and liver function (10 days). She was extubated on hospital day 4. Her left ventricular systolic function steadily improved and she had normal cardiac function after discharge on hospital day 10 (Table 1).

## DISCUSSION

Cardiac involvement in patients hospitalized with COVID-19 infection is common, likely present in one-third

of hospitalized adults. Guo et al<sup>2</sup> revealed that 28% of the patients studied had evidence of acute myocardial injury (defined as an elevated troponin T greater than the 99th percentile upper limit). Chen et al<sup>1</sup> showed elevated levels of troponin I in 10% of the patients studied and elevated pro-B-type natriuretic peptide (BNP) in 27.5% of patients. Patients with evidence of cardiac involvement have a higher mortality.<sup>7</sup>

There are several possible etiologies for this cardiac involvement. A systemic inflammatory response, preexisting illnesses like coronary artery disease, diabetes mellitus and hypertension, and multiorgan system failure can all contribute to cardiac injury in the setting of COVID-19 infection. Cardiovascular side effects of therapies and electrolyte derangement are also possible etiologies.<sup>8</sup>

Both the original severe acute respiratory syndrome coronavirus seen in China in 2003 and severe acute respiratory syndrome coronavirus 2 use the angiotensin converting enzyme 2 molecule as their receptor.<sup>9,10</sup> This protein is present in the lungs, heart, and gastrointestinal tract. Oudit et al<sup>9</sup> found that 35% of patients who died of the original severe acute respiratory syndrome outbreak had evidence of direct myocardial injury on autopsy. The authors also found that there is decreased expression of ACE2 in infected individuals. One of the functions of ACE2 is to degrade angiotensin II into byproducts that have vasodilatory and

**TABLE 1** Laboratory Values and Systolic Function Over Time

	Admission	IVIg Administration (Hospital Day 2)	Return of Consistent Sinus Rhythm (Hospital Day 4)	Discharge (Hospital Day 10)
Creatinine, mg/dL	1.5	1.2	0.8	0.7
AST, U/L	522	501	392	57
ALT, U/L	167	334	466	174
LV ejection fraction, %	27	30	33	67
Troponin I, ng/mL	38.400	46.965	6.037	0.037

ALT, alanine aminotransferase; AST, aspartate aminotransferase; LV, left ventricular.

antiinflammatory effects.<sup>9</sup> The overabundance of angiotensin II and lack of its byproducts create a milieu that increases the risk of cardiac injury.

The clearest evidence for direct myocardial involvement seems to be in the cases of myocarditis in otherwise healthy patients with no other organ system involvement. Hu et al<sup>11</sup> describe the case of a previously healthy 37-year-old woman with COVID-19 and suspected myocardial infarction but normal coronary arteries on computed tomography angiogram. She had significantly elevated troponin T and BNP and an abnormal echocardiogram with marked ventricular dilation and severely depressed systolic function. She was treated with IVIg, steroids, norepinephrine, and milrinone infusions and improved over 2 weeks.<sup>11</sup> Inciardi et al<sup>12</sup> treated a healthy 53-year-old woman with COVID-19 infection and myocarditis. She too had elevated troponin and BNP levels as well as decreased systolic function. She was treated with steroids, antiviral medications, chloroquine, and a dobutamine infusion. She also improved with time.<sup>12</sup> Data from the National Health Commission of the People's Republic of China revealed that of those who died of COVID-19, 11.8% who did not previously have underlying cardiac disease had substantial cardiac damage defined as elevated troponin levels or cardiac arrest during hospitalization.<sup>4</sup>

One of the limitations of this study is the lack of cardiac MRI to definitively diagnose myocardial inflammation; our diagnosis of myocarditis was based on clinical and laboratory findings. We plan to perform cardiac

MRI soon. Our case is further complicated by the patient's concurrent adenovirus infection, and we cannot definitively link her COVID-19 infection with her myocarditis. Adenovirus is a common pathogen causing myocarditis. However, there are no large studies published in which authors link adenovirus as the causative agent of acute fulminant myocarditis. Coinfection is common in pediatric patients with COVID-19 (40% documented in 1 study) and deserves further study.<sup>13</sup> With this case, we highlight the fact that cardiac injury is an important feature of patients with COVID-19 and may be present in the pediatric population. Pediatric providers should not dismiss COVID-19 as a causative agent of disease, even with lack of respiratory symptoms.

#### ABBREVIATIONS

BNP: B-type natriuretic peptide

COVID-19: coronavirus disease 2019

IVIg: intravenous immunoglobulin

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