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Case Report

Acute Myocarditis After Severe Acute Respiratory Syndrome Coronavirus 2 Infection

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A B S T R A C T

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This case report describes a young adult patient with post-severe acute respiratory syndrome coronavirus 2 acute viral myocarditis who initially presented to a local urgent care center. The patient decompensated and was transferred to our tertiary, intensive care setting.

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We report a case of acute myocarditis after infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in a 20-year-old woman. This case report highlights how SARS-CoV-2 can be associated with acute myocarditis, addresses the distinction from other SARS-CoV-2 complications and vaccine-associated myocarditis, and discusses the importance of early and appropriate management.

History

In November 2020, a 20-year-old woman presented to a local urgent care center with a complaint of dry cough and loss of taste and smell. She was in her usual state of health and had no known past medical history. Her only past surgical history was a tonsillectomy and adenoidectomy. The patient was exposed to SARS-CoV-2 at a campus party and afterward tested positive for the virus. She initially experienced mild symptoms (eg, “tired” and “ill”) without shortness of breath (SOB), rash, fevers, or unusual fatigue. Subsequently, she felt fully recovered. Six weeks later, she experienced a sore throat, SOB, anosmia, and worsening cough. She presented to a community urgent care center and was prescribed a methylprednisolone dose pack and a course of doxycycline and was discharged home.

Her past health and social history included regular exercise (competitive swimming for over 18 years) and living on the college campus. She admitted to drinking alcohol (at times “too much”) and denied tobacco, illicit drug, or substance abuse. She was taking oral contraceptives and denied additional over-the-counter or prescription drug use.

After discharge from urgent care, she initiated the methylprednisolone dose pack, and her symptoms improved, but as the steroid doses decreased, she experienced generalized abdominal discomfort, became increasingly fatigued, and developed new-

onset SOB. Two days later, she became dyspneic and was not able to walk a half block. She went to the local emergency department. When she arrived, her pulse oximetry was less than 90% (> 95%). Her laboratory values were as follows: troponin = 2,273 (0-0.4 ng/nL), white blood cells = 27,000 (4,500-10,000/ μ L in females), and lactic acid = 2.5 (0.5-1 mmol/L). An echocardiogram revealed a left ventricular ejection fraction (LVEF) of 10% (> 55%). A chest computed tomographic scan with pulmonary embolism protocol was negative but revealed left lower lobe pneumonia. She was started on levofloxacin and then transitioned to vancomycin 1.5 g every 12 hours and cefepime 1 g every 8 hours. In the emergency department, she had a syncopal event. She was given 2 L of intravenous fluid and was transferred with direct admission to the cardiac intensive care unit (ICU).

Physical Examination

On admission to our cardiac ICU, the patient was ill appearing, fatigued, diaphoretic, and showing increased work to breathe. She was alert and oriented to time, place, and person. Her vital signs showed the following: temperature of 99.9°F, heart rate of 150 beats/min, blood pressure of 97/53 mm Hg, respiratory rate of 24 breaths/min, and pulse oximetry of 97% on 3 L nasal cannula; her weight was 245 lb. Her skin was warm to the touch, flushed, and diaphoretic. The patient’s cardiovascular examination was significant for S1 and S2 heart sounds with S3 gallop, elevated jugular venous distention to the jaw, and lower extremity pitting edema. She had bilateral pulmonary rhonchi on auscultation.

Diagnostic Testing

The patient’s admission electrocardiogram revealed sinus tachycardia with nonspecific ST- and T-wave abnormalities

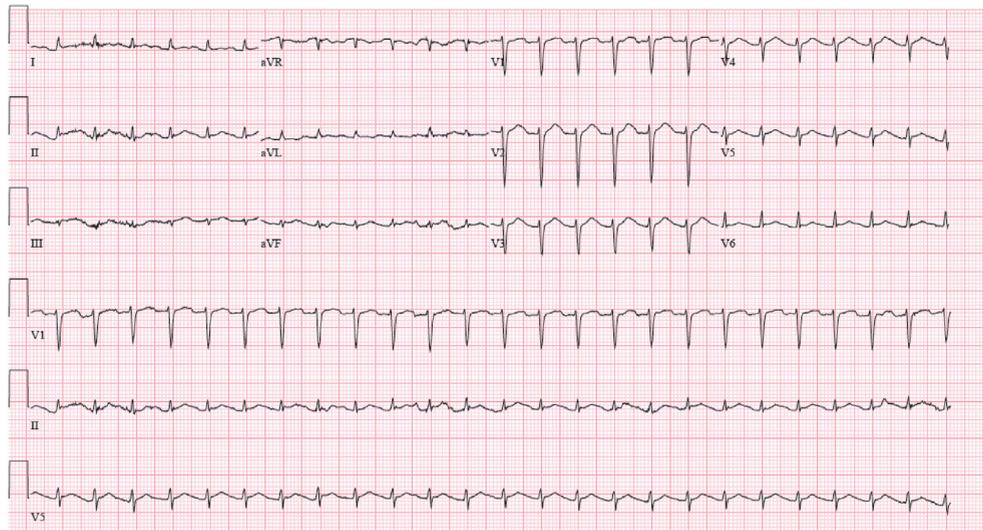


Figure. The patient's admission electrocardiogram.

(Figure). Additional laboratory, blood, respiratory, and stool culture results are found in Table 1.

The patient's chest X-ray revealed decreased lung volumes with bibasilar atelectasis, perihilar haze, and peribronchial cuffing with instances of interstitial septal thickening. Kerley B lines were most notable in the right lung. Additional significant chest X-ray findings included patchy airspace opacities in the right upper lung and the left lower lobe and small left and possible trace right lung pleural effusion.

Cardiac magnetic resonance imaging (CMRI) identified normal size of the right ventricle, normal systolic function, and normal valvular structure and function. No hemodynamically significant intracardiac shunt was detected. Significant positive CMRI findings included a small, circumferential pericardial effusion and a mildly dilated left ventricle with low normal systolic function (LVEF = 55%). No regional wall motion abnormalities or myocardial delayed enhancement were found. Evidence of active myocardial edema or inflammation based on T1 and T2 mapping was noted, and her overall CMRI findings were reported as inflammation likely secondary to recent SARS-CoV-2 infection.

A transthoracic echocardiogram was significant for a 42% LVEF with global hypokinesis and a normal-size right ventricle with borderline decreased function.

Differential Diagnoses and Treatment Decisions

Because she exhibited volume overload, diuresis was initiated along with supportive care. The plan also included right heart catheterization with myocardial biopsy for the assessment of hemodynamics and tissue analysis; however, this was deferred until she was clinically stable.

The infectious disease service was consulted. Because of the patient's recent SARS-CoV-2 infection and presenting symptoms, she was initially diagnosed with post-SARS-CoV-2 multi-inflammatory syndrome in children (MIS-C). The Centers for Disease Control and Prevention criteria for MIS-C include an individual less than 21 years of age, fever, laboratory results indicating elevated inflammatory markers, and severe illness requiring hospitalization including multisystem (greater than 2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, and neurologic). In addition to these clinical criteria, no alternative etiologies should better explain the syndrome.¹ Recommendations

from the infectious disease service included discontinuation of the vancomycin and treatment of possible bacterial pneumonia with 1 dose of 500 mg oral azithromycin followed by 250 mg orally to complete a 5-day course.

Additional input was also obtained from the rheumatology service. After evaluating the patient, providers from the rheumatology service concluded that her symptoms were less indicative of MIS-C and more consistent with a diagnosis of multi-inflammatory syndrome in adults (MIS-A). Although the exact etiology is unknown, the suspected pathophysiology of MIS-A includes endothelial dysfunction, thrombotic inflammation, and dysregulated immune responses.² The key characteristics include fever, elevated troponins, cardiogenic shock, and biventricular heart failure developing 2 to 5 weeks after a SARS-CoV-2 diagnosis.² The current criteria include severe illness requiring hospitalization in a person greater than 21 years old with a positive test for SARS-CoV-2 (ie, nucleic acid, antigen, or antibody within the previous 12 weeks). The criteria also include severe dysfunction of 1 or more organ systems (eg, hypotension, cardiac dysfunction, arterial or venous thromboembolism, and acute liver injury) with elevated inflammatory markers (eg, elevated C-reactive protein, ferritin, D-dimer, and interleukin) with the absence of severe respiratory illness.³

Kawasaki disease was also included in the differential diagnosis because of the reported similarities between MIS-C, MIS-A, myocarditis, and Kawasaki-like disease.^{4,5} The criteria include a febrile illness for at least 5 days, a rash with cervical lymphadenopathy greater than 1.5 mm, bilateral conjunctival injections, oral mucosal changes, and peripheral extremity changes.⁶ Our patient did not exhibit any of the features of Kawasaki disease; therefore, this diagnosis was eliminated from the differential early in her ICU admission. Moreover, although she met some of the criteria for MIS-C and MIS-A, her presentation and course during hospitalization led the team to conclude that her final, primary diagnosis was most likely post-SARS-CoV-2 acute viral myocarditis.

Over the following 3 days, all inflammatory markers normalized or were trending toward normal. Because of diuresis, the patient's weight decreased to 215 lb. Symptomatically, she was feeling much better. The rheumatology service advised that they did not endorse further inpatient treatment, and there was no indication for intravenous immunoglobulin or intravenous corticosteroids.

The team began preparations for discharge with close outpatient follow-up. Based on the timing of recovery, the cardiology

Table 1
The Patient's Laboratory, Blood, Respiratory, and Stool Culture Results^a

Diagnostic Test	Results	Normal Values/Range
White blood cell count	27.6 thousands/ μ L	4.0-11.0 thousands/ μ L
Ferritin	389.1 ng/mL	10-306.8 ng/mL for females
Lactic acid dehydrogenase	281 U/L	98-102 U/L
Eosinophil sedimentation rate	99	0-25 for females
C-reactive protein	> 160 mg/L	< 7.50 mg/L
Lactic acid	1.9 mmol/L	0.5-2.2 mmol/L
D-dimer	4.91 μ g/mL	< 0.5 μ g/mL
Interleukin 6	89.7	2.0 ng/mL or less
Procalcitonin	4.58	For adults, normal = below level of detection
Troponin T	0.582 ng/mL	0.00 = 0.030 ng/mL
N-terminal pro-B-type natriuretic peptide	> 35,000 pg/mL	0-12 pg/mL
International normalized ratio	2.0 seconds	.08-1.1 seconds
Blood cultures	Negative	No growth at 2 days
Respiratory viral panel and sputum culture	Negative	No growth
Stool studies	Negative for <i>Clostridium difficile</i> and all enteric pathogens	Negative

^a All results in this table are from the patient's admission to the tertiary care intensive care unit.

service revised their initial diagnosis and concluded this was more likely a case of acute viral myocarditis rather than a multi-inflammatory syndrome.

The day before discharge she had an elevation in aspartate aminotransferase to 103 (15-41) and alanine aminotransferase to 126 (14-54). The gastroenterology service concluded that these changes were likely from recent antibiotic therapy and suggested outpatient monitoring of these enzymes 1 week postdischarge because SARS-CoV-2 is also known to cause hepatocellular injury. She was discharged from the ICU to her parent's home with plans for a follow-up visit in 1 month.

At the patient's 1-month follow-up visit, she was feeling well and was starting to increase her activity daily with plans to return to school. Her laboratory values, electrocardiography, and LVEF had returned to normal.

Discussion

Myocarditis can be a sequela of SARS-CoV-2. This case demonstrates the significance of early recognition, public health implications of differentiating SARS-CoV-2 myocarditis from vaccine-associated myocarditis, and effective management.

It is critical to identify post-SARS-CoV-2 cardiac symptoms early to optimize treatments and achieve a successful outcome. This includes an awareness that adolescents and young adults may experience these symptoms as well as an understanding of the primary differential diagnoses.

Clinicians should be alert for reports that a patient may have been exposed to SARS-CoV-2, may have symptoms or be asymptomatic, or may have a positive SARS-CoV-2 test result before developing postinfection symptoms. In addition, early recognition is an important strategy for preventing or minimizing the spread of SARS-CoV-2 because individuals under age 30 currently account for more than 20% of the cases in the United States.⁷ Moreover, younger individuals are more likely

than older persons to spread SARS-CoV-2 to others because they more often work in industries such as restaurants, retail shops, and childcare centers.⁸

Case reports and emerging data suggest that an association exists between SARS-CoV-2 and acute viral myocarditis.⁹ This is not vaccine-associated myocarditis but rather an acute myocardial injury that develops after SARS-CoV-2 and often presents with symptoms of heart failure.¹⁰ Myocarditis is a rare adverse event after vaccines, and the resolution of symptoms occurs in most cases. The messenger RNA SARS-CoV2 vaccine has been implicated in myocarditis, which is characterized as a primarily mild presentation mainly occurring in young males. In contrast, the incidence of myocarditis after SARS-CoV-2 is estimated as 100 times greater than vaccine-associated myocarditis and carries a 10% to 30% incidence of long-term cardiovascular complications (eg, 10%-30% of patients report long-term tachycardia, decreased exercise tolerance, chest pain, SOB, and atrial fibrillation).¹¹ Our patient exhibited classic heart failure symptoms including SOB, S3 gallop, edema, and low LVEF. Acute and chronic inflammatory heart conditions may be diagnosed via myocardial biopsy. Noninvasive tests (CMRI is the gold standard, Table 2) may also be used in patients like the one in our case, who was too unstable to undergo biopsy.¹²

Because the patient rapidly improved once she was admitted to the ICU, we focused on acute viral myocarditis and initiated evidence-based supportive care. Effective management strategies included treatments to optimize hemodynamic stability and systemic perfusion (eg, diuresis and fluid management) and appropriate antibiotic therapy to treat her possible pneumonia. The treatment of myocarditis after SARS-CoV-2 mirrors the treatment of viral myocarditis and is based on symptoms, hemodynamic status, and the progression or resolution of symptoms. Patients should also be followed closely in a critical care setting where the development of arrhythmias and cardiac and other organ system decompensation can be quickly detected and treated because these

Table 2
Diagnostic Tests for Post-Severe Acute Respiratory Syndrome Coronavirus 2 Myocarditis

Diagnostic Test	Positive Findings
Troponin (high-sensitivity assay)	Elevated
Electrocardiogram	Diffuse T-wave inversion, ST-segment elevation without reciprocal ST-segment depression, prolongation of the QRS complex duration)
Transthoracic echocardiogram	Ventricular wall motion abnormalities often in a noncoronary distribution, abnormal ventricular strain
Cardiac magnetic resonance imaging	Myocardial inflammation, nonischemic epicardial scar, pericardial effusion/enhancement
Endomyocardial biopsy	Increased CD68+ macrophage or monocytic infiltration, endothelialitis, microvascular dysfunction, cell necrosis

indicate poor outcomes.¹³ Although our patient responded quickly to supportive measures, unstable patients with post-SARS-CoV-2 myocarditis may require additional intensive care with extracorporeal membrane oxygenation or a ventricular assist device followed by cardiac transplantation.¹²

Conclusion

The SARS-CoV-2 pandemic remains an ongoing threat. Health care providers are likely to encounter patients with post-SARS-CoV-2 infection symptoms for the foreseeable future. Our case draws attention to symptoms that overlap with several syndromes and the potentially life-threatening cardiac manifestations of SARS-CoV-2.⁶ Furthermore, because of confusion about the incidence of vaccine-associated myocarditis (and, in turn, the potential for vaccine hesitancy), our case highlights the important fact that SARS-CoV-2 infection itself may have significant or even fatal cardiac complications.

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