SARS-CoV-2 infection presenting as sustained atrial flutter and advanced ventricular dysfunction

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Abstract
We report a case of a 15-year-old girl who presented with atrial flutter and acute decompensated heart failure ultimately requiring cardiac support with extracorporeal membrane oxygenation (ECMO). While the patient's atrial flutter and cardiac dysfunction are believed to be related, the spontaneous development of atrial flutter is exceedingly rare in teenagers. While both arrhythmia and decompensated heart failure can be seen in fulminant myocarditis, the patient did not have a clinical history or testing consistent with myocarditis or systemic inflammation.

Upon her admission to the intensive care unit, her nasopharyngeal SARS-CoV-2 PCR was negative. However, her anti-SARS-CoV-2 IgG antibody titer was mildly elevated upon admission and increased four-fold within a month during her hospitalization, suggesting recent infection. After 8 days of ECMO support, the patient’s heart function improved, and she was successfully decannulated. She later underwent an electrophysiology study with successful ablation of atrial flutter. She has not experienced further atrial arrhythmias and was ultimately discharged 2 months later with normal ventricular function by echocardiogram. Throughout her lengthy hospitalization she underwent numerous tests to elucidate her unusual clinical picture. Remote COVID-19 infection remains the most likely explanation for the timing and severity of this patient’s clinical course.

Abbreviations: COVID-19: Coronavirus disease of 2019; ECMO: Extracorporeal membrane oxygenation; EF: Ejection fraction; ICU: Intensive care unit; LVIDd: Left ventricular internal dimension in diastole; MIS-C: Multi-system inflammatory syndrome in children; MRI: Magnetic resonance imaging; SARS-CoV-2: Severe acute respiratory syndrome-coronavirus-2; TIC: Tachycardia induced cardiomyopathy.

Introduction
Viral infections may affect the cardiovascular system in various ways. A number of viruses are known to cause myocarditis and pericarditis, which may result in severe impairment of ventricular function leading to decompensated heart failure [1]. Viral infections may also cause systemic inflammatory response syndrome and septic shock from exaggerated immune inflammatory response [2]. Certain viruses have also been linked to development of cardiac arrhythmias [3,4]. In these cases, evidence of myocardial inflammation is often found. However, arrhythmias are sometimes the only indicator of cardiac involvement in viral infections. Additionally, myocardial failure of any cause can raise atrial and ventricular filling pressures, resulting in increased myocardial fiber stress, potentially inducing arrhythmias or triggering arrhythmias.

The coronavirus disease of 2019 (COVID-19), caused by severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), became a worldwide pandemic in March 2020. This disease has already had devastating effects on the adult population, accounting for over 1.5 million fatalities worldwide [5]. Most frequent causes of morbidity and mortality are due to septic shock and respiratory failure [6]. Cardiovascular involvement, such as myocarditis and arrhythmias, is also common [7]. In pediatrics, however, morbidity and mortality from SARS-CoV-2 appears to be attenuated. Much of the current focus of SARS-CoV-2 in pediatrics, in fact, is on its latent effects of multi-system inflammatory syndrome in children (MIS-C) which is a toxic shock-like syndrome [8]. We report here our cautionary experience of a latent SARS-CoV-2 infection complication causing atrial arrhythmia, decompensated heart failure, and severe hemodynamic compromise requiring extracorporeal membrane oxygenation (ECMO) support before cardiac recovery 2 weeks later.

Case report
Our patient is a 15-year-old female with a history of scoliosis, for which she had undergone spinal fusion 8 months prior to presentation. She was brought to the emergency department with a one-day history of shortness of breath and orthopnea. She denied any preceding palpitations, chest pain, viral symptoms, fever, or changes in energy level, and she had no known ill contacts. Initial vital signs revealed tachycardia with a heart rate of 150 bpm, and hypoxemia with an oxygen saturation of 85%. Her chest radiograph was significant for a moderately enlarged heart, patchy infiltrates seen in the left lower lobe, with a trace left-sided pleural effusion. Her laboratory data revealed an elevated brain natriuretic peptide level of 1,503 pg/mL, with normal transaminase, blood urea nitrogen and creatinine levels. Complete blood count revealed total leukocyte count of 8.04 K/µL (62%
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In the ICU, the decision was made to intubate and sedate the patient for DC cardioversion. Upon anesthesia induction, she became hypotensive and bradycardic, then asystolic followed by a wide QRS complex tachycardia with frequency in children or adolescents [9]. TIC can develop as early as 3 days after onset of tachyarrhythmia, and ventricular dysfunction is least in part, by sustained atrial flutter rather than myocarditis. Three scenarios were possible: 1.) SARS-CoV-2 infection resulted in the onset of atrial flutter, with secondary development of tachycardia induced cardiomyopathy (TIC); 2.) COVID-19 caused myocarditis with hemodynamic and electrophysiologic changes resulting in atrial flutter; and 3.) COVID-19 resulted directly in the development of both atrial flutter and myocarditis in the weeks prior to hospitalization, with the combined effects of atrial flutter and COVID-19 resulting in impaired ventricular function.

Tachycardia induced cardiomyopathy (TIC) is associated with a number of tachyarrhythmias. In adults, it is diagnosed frequently in the setting of atrial fibrillation and flutter, but is less often encountered in the pediatric population because these tachyarrhythmias do not occur with frequency in children or adolescents [9]. TIC can develop as early as 3 days after onset of tachyarrhythmia, and ventricular dysfunction is often rapidly reversible with appropriate treatment of the arrhythmia [9]. Despite having an abnormally high ventricular heart rate of 150 bpm, our patient did not experience any palpitations, which made it challenging to determine the onset and duration of her atrial flutter. Her rapid cardiac recovery with essentially normal ventricular function two weeks following defibrillation is consistent with the recovery timeline expected of TIC.

Discussion and Conclusion

Our case is unusual in that although COVID-19 has been linked to fulminant myocarditis in numerous reports, our patient did not demonstrate any evidence of active infection or inflammation. She had no history of recent fever or infectious illness, had no elevation of inflammatory markers, no detectable active infection upon laboratory testing, and no inflammation on endomyocardial biopsy. She had no known contact with a person known to have contracted COVID-19. Based on the lack of evidence for myocardial injury, and the electrophysiologic finding of a substrate for atrial flutter, it is possible that the patient's acute decompensated heart failure was caused, at least in part, by sustained atrial flutter rather than myocarditis. Three scenarios were possible: 1.) SARS-CoV-2 infection resulted in the onset of atrial flutter, with secondary development of tachycardia induced cardiomyopathy (TIC); 2.) COVID-19 caused myocarditis with hemodynamic and electrophysiologic changes resulting in atrial flutter; and 3.) COVID-19 resulted directly in the development of both atrial flutter and myocarditis in the weeks prior to hospitalization, with the combined effects of atrial flutter and COVID-19 resulting in impaired ventricular function.

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As part of the evaluation for myocarditis, our patient underwent a battery of infectious tests, all of which were negative for active infection. The patient's cardiac MRI did reveal myocardial edema and inflammation, but interpretation is difficult as the patient had undergone cardiopulmonary resuscitation, defibrillation, and ECMO cannulation shortly before MRI imaging. Although the COVID-19 PCR was negative, an anti-SARS-CoV IgG titer was found to be mildly positive in the early phase of her hospital admission. Repeat testing two- and six-weeks later revealed steady increase in SARS-CoV IgG antibodies, indicating that our patient had likely been infected approximately two to three weeks prior to her acute cardiac presentation [10].

Based on the timeline of our patient's clinical course and the results of tests performed, it seems most likely that our patient suffered a SARS-CoV-2 infection in the weeks prior to hospital admission, which presented with atrial flutter and ventricular dysfunction. While it may be possible that our patient had frank COVID-19 myocarditis manifesting both with arrhythmia and cardiac dysfunction, the absence of inflammation or myocardial damage, and her rapid recovery within two weeks after DC cardioversion are unusual for myocarditis [11]. However, as SARS-CoV-2 is a relatively novel virus, there remains much to be learned, including the expected clinical timeline of SARS-CoV-2 infection as it relates to the heart, particularly in pediatrics.

The majority of current literature and understanding of COVID-19 clinical repercussions draws from adult experience, and much of the pediatric experience with SARS-CoV-2 remains within the context of MIS-C. Continued reporting of unique clinical manifestations of this virus is essential to refine the medical knowledge of our current pandemic.

Competing interests

The authors have no conflicts of interest to disclose.

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