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Acute myocarditis after a second dose of the mRNA COVID-19 vaccine: a report of two cases

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ABSTRACT

We report two cases of myocarditis, in two young and previously healthy individuals, temporally related to the second dose of the mRNA-COVID-19 vaccine. Both patients developed acute chest pain, changes on electrocardiogram (ECG), and elevated serum troponin within two days of receiving their second dose. Cardiac magnetic resonance (CMR) findings were consistent with acute myocarditis.

1. Introduction

Myocarditis encompasses a broad range of immune processes that may cause functional and/or structural abnormalities in the myocardium. The majority of cases of myocarditis result from viral infections. Non-infectious etiologies of myocarditis are rare and have been reported with systemic inflammatory conditions and after drugs and vaccinations.[1] While myocarditis after vaccination has been reported in the literature, establishing causality remains elusive.[2] There have been a few reports of myocarditis after the mRNA COVID-19 vaccine.[3–5] Herein, we report two cases of myocarditis occurring after the second dose of the mRNA COVID-19 vaccine.

2. Case description

2.1. Case 1

A previously healthy 25-year-old man presents to the hospital after receiving the second dose of the mRNA-1273 SARS-CoV-2 immunization (Moderna). On the first day after the second dose the patient developed subjective fever and chills. Six hours after the onset of fevers, the patient noticed substernal chest pain and as result reported to the hospital. His physical examination revealed a fever of 39.1 °C, blood pressure of 129/75 mmHg, pulse of 76 bpm, a respiratory rate of 20, and oxygen saturation of 98% on room air. An electrocardiogram (ECG) revealed diffuse mild concave ST elevations with no reciprocal changes. Initial laboratory evaluation showed an elevated troponin I of 14 ng/mL (normal <0.032 ng/mL), an elevated C-reactive protein (CRP) of 25 ng/mL (normal 0–0.5 ng/mL), and erythrocyte sedimentation rate (ESR) of 25 mm/h (normal <15 mm/h). Nasopharyngeal SARS-CoV-2 PCR was performed twice and was negative; the patient also denies any history of infection with COVID-19. The patient was admitted and underwent coronary angiography that showed normal coronary arteries. An echocardiogram showed normal function and no significant valvular disease; ejection fraction was 55%. Troponin levels continued to rise, peaking at 20.4 ng/mL on hospital day 2 and declined to 9.5 ng/mL by the time of discharge on the morning of hospital day 3, at which point his chest pain had resolved.

The patient was referred for cardiac magnetic resonance imaging (MRI) to evaluate for myocarditis. Cardiac MRI (Fig. 1) was performed on a 3-T scanner [Magnetom Vida, Siemens Healthcare] six days after the second dose of vaccine. Cine images showed normal left ventricular function. Short axis (A) and four-chamber long axis (B) post-contrast inversion recovery images showed subepicardial late gadolinium enhancement in the anterolateral wall of the mid and apical left ventricle. Short axis native T1 (C) and T2 (E) maps showed corresponding increased T1 (1450–1550 ms; *normal: 1100–1300*) and T2 (54–60 ms; *normal: 40–50*[6]) signal intensity, respectively. Measured T1 (D) and T2 (F) values of the normal intraventricular septum was 1200–1300 and 43–46 ms, respectively. Per the 2018 Lake-Louise

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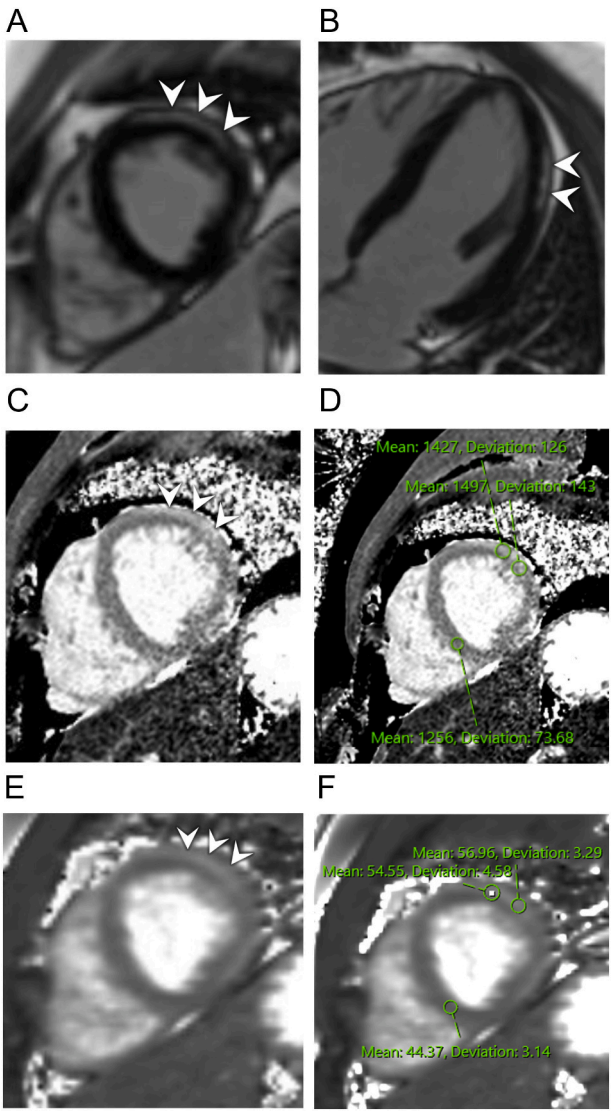

Fig. 1. Magnetic Resonance Imaging of Case 1. Post contrast magnitude inversion recovery (MAG-IR) images in short axis (A) and four-chamber long axis (B) views show subepicardial enhancement in the anterolateral wall of the mid ventricle and apex (arrowheads). Native T1 map shows corresponding abnormality (arrowheads in C) with elevated values (D) in the anterolateral wall as compared to the interventricular septum. T2 mapping also showed abnormality in this region (arrows in E) with elevated values (F) when compared to the interventricular septum.

criteria, these findings are diagnostic of myocarditis.[7,8] A respiratory viral panel was performed and was negative.

2.2. Case 2

A 21-year-old woman with no underlying health conditions presents as a transfer from an outside hospital for chest pain. The patient received the second dose of the mRNA-1273 SARS-CoV-2 immunization (Moderna) vaccine and developed lightheadedness the next day while exercising, such that she was unable to complete her usual exercise routine. Two days after the vaccine, the patient developed sharp retrosternal chest pain that radiated to her left jaw and woke her up from sleep for which she presented to an outside hospital. Her vital signs were normal with a temperature of 36.5 °C, blood pressure of 110/70 mmHg, heart rate of 70 bpm, respiratory rate of 18, and oxygen saturation of 99% on room air. Initial ECG showed diffuse, mild concave ST elevations and PR depressions without reciprocal changes. Her initial laboratory results showed an elevated troponin I of 2.3 ng/mL (normal <0.3 ng/mL), and elevated D-Dimer of 640 ng/mL (normal <500 ng/mL), an ESR of 7 mm/h (normal 1–20 mm/h), and a CRP of 8 ng/mL (normal <10 ng/mL). A nasopharyngeal SARS-CoV-2 PCR was negative and the patient denies past history of infection with COVID-19. The patient reported a family history of long QT syndrome in three of her siblings and her mother for which she has received work-up consisting of echocardiography, a stress test, and genetic testing 4 years prior, all of which were negative; the patient's QT and QTc at the time of presentation were 384 and 428 ms, respectively.

A CT pulmonary angiogram performed to exclude pulmonary embolism was negative. The coronary arteries were visualized on the CT and appeared normal with no abnormal course or origin. A transthoracic echocardiogram showed a mildly reduced LVEF of 50% with no wall motion abnormalities or significant valvular disease.

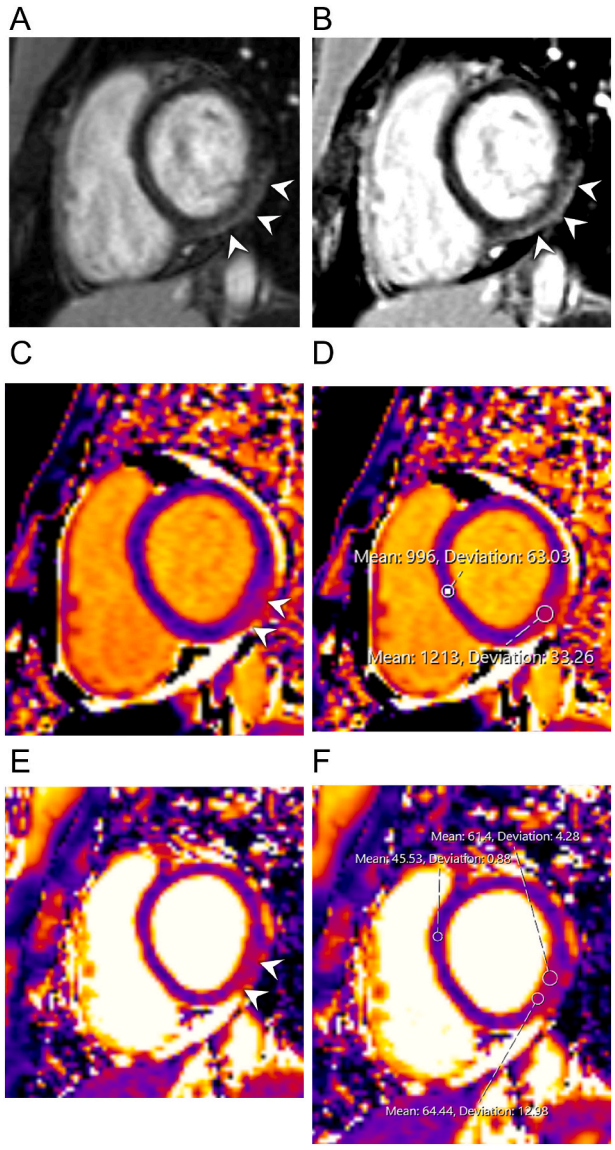

Fig. 2. Magnetic Resonance Imaging of Case 2. Post-contrast magnitude inversion recovery (MAG-IR) (A) and phase sensitive inversion recovery (PSIR) (B) images in short axis views show subepicardial enhancement in the inferolateral wall at the base (arrowheads). Native T1 map shows corresponding abnormality (arrowheads in C) with elevated values (D) in the inferolateral wall as compared to the interventricular septum. T2 mapping also showed abnormality in this region (arrows in E) with elevated values (F) when compared to the interventricular septum.

Repeat testing showed the troponin I had increased to 4.4 ng/mL. A CMR (Fig. 2) was performed on a 1.5-T scanner [Magnetom Vida, Siemens Healthcare] four days after the second dose to evaluate for possible myocarditis. Cine images revealed normal left ventricular size and function. Short-axis post-contrast images (A) showed subepicardial enhancement in the inferolateral wall at the base. T1 (B) and T2 (D) maps showed corresponding elevated values of 1200 ms for T1 (normal 950–1050 ms), as opposed to 950–980 for the septal wall (C), and 59–63 ms for T2 (normal 45–55 ms[6]) as opposed to 44–48 ms for the septal wall (E). Per the 2018 Lake-Louise criteria, these findings are diagnostic of myocarditis.[7,8] A respiratory viral panel was also performed on this patient and was negative.

The patient's symptoms resolved the next day and her troponin declined to 1.3 ng/mL. The patient improved clinically and was discharged home on metoprolol.

3. Discussion

On December 11 and December 18, 2020, the United States Food and Drug Administration (FDA) issued Emergency Use Authorization (EUA) for the Pfizer-BioNTech[9] and Moderna[10] mRNA-COVID-19 vaccinations, respectively. A rapid vaccination rollout is now underway and, as of May 31, 2021, more than 285 million doses of both mRNA-COVID-19 vaccines have been administered in the United States alone.[11] These vaccines are generally well-tolerated with mostly self-limited, mild side effects including pain at the injection site, myalgias, and fever, with the reactions potentially being more severe after the second dose.[12,13] In April 2021, the Center for Disease Control and Prevention (CDC) issued recommendations for clinicians regarding reported cases of myocarditis and pericarditis after the mRNA COVID-19 vaccines stating that most cases responded well to medical therapy and rest, and that most occurred in young male adolescents and young adults, more commonly after the second dose.[14] The CDC is currently investigating these reports, but continues to recommend the vaccine for everyone aged 12 years or older[14].

Post-vaccination myocarditis has been reported, most notably after the smallpox vaccine,[15] with a prospective study suggesting a relative risk of clinical myopericarditis of greater than 200-times higher than published background rate.[16] Cases have also been reported after the influenza, tetanus, human papillomavirus, and hepatitis B vaccines, among others[17]; however, the association is not as strong as with that of the smallpox vaccine.[15] While the pathophysiology of this entity is unclear, limited endomyocardial biopsy and autopsy case reports show lymphocytic and eosinophilic infiltration adjacent to necrotic myositis suggestive of a maladaptive immune-mediated injury or hypersensitivity reaction.[2,18] The gold standard to determine the underlying etiology in the case of post-vaccination myocarditis would be to perform an endomyocardial biopsy; this was not performed in the cases reported as both patients had rapid clinical improvements.

We have reported two cases of acute myocarditis, both in young, previously healthy individuals with a temporal relation to the second dose of the mRNA-COVID-19 vaccine. In the vaccine trials, younger patients developed a stronger immune response to the vaccine and the second dose produced more severe symptoms when compared to the first. If the myocarditis in these two cases was related to an immune response, this could explain why it occurred after the second dose in both cases. Work-up with a respiratory viral panel was negative for both patients and the panel includes the most common viruses that cause myocarditis in the general population, most notably adenovirus and coxsackie virus. It is important to note, however, that any notion of a causal relationship between the mRNA-COVID-19 vaccine and myocardial inflammation in this case remains speculative. As the rapid vaccine rollout continues, further data may help shed new light on whether myocarditis could be an adverse effect of mRNA-COVID-19 immunization. Both mRNA-COVID-19 vaccines have so far shown to be relatively safe and effective. The benefits of administering the vaccine will still overwhelmingly outweigh the risk of developing myocarditis, if such an association was to be established; however, clinicians and radiologists alike should be aware of this potential relationship.

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