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Myocarditis Associated with mRNA COVID-19 Vaccination

Jitka Starekova, MD • David A. Bluemke, MD, PhD • William S. Bradham, MD, PhD • Thomas M. Grist, MD • Mark L. Schiebler, MD • Scott B. Reeder, MD, PhD

From the Departments of Radiology (J.S., D.A.B., W.S.B., T.M.G., M.L.S., S.B.R.), Medical Physics (D.A.B., T.M.G., S.B.R.), Medicine (W.S.B., S.B.R.), Biomedical Engineering (T.M.G., S.B.R.), and Emergency Medicine (S.B.R.), University of Wisconsin-Madison School of Medicine and Public Health, 600 Highland Ave, Madison, WI 53792. Received June 4, 2021; revision requested June 30; revision received July 2; accepted July 7. **Address correspondence to** J.S. (e-mail: *starekova@wisc.edu*).

Conflicts of interest are listed at the end of this article.

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Mass immunization campaigns have been initiated to contain the ongoing COVID-19 pandemic. COVID-19 vaccines currently authorized for emergency use in the United States include BNT162b2 (Pfizer-BioNTech), mRNA-1273 (Moderna), and JNJ-78436735 (Johnson & Johnson). Recently the lay press has reported concerns for vaccine-associated myocarditis (1). In this work, we describe cardiac MRI findings in patients with myocarditis detected shortly after COVID-19 mRNA vaccination.

Materials and Methods

In this retrospective institutional review board–approved and Health Insurance Portability and Accountability Act–compliant study, cardiac MRI examinations performed at our institution between January 1 and May 25, 2021, were reviewed for MRI findings of myocarditis and pericarditis. Subsequently, electronic health records were reviewed, and all patients who received COVID-19 vaccine preceding cardiac MRI were included (consecutive sample). Informed consent was waived per institutional review board protocol. Patients with a history of prior COVID-19 were excluded.

Cardiac MRI was performed at 1.5 T or 3.0 T (GE Healthcare) and evaluated as recently described (2). Clinical radiology reports were reviewed by three cardiovascular radiologists (J.S., S.B.R., and D.A.B., with 7–27 years of experience) in consensus. Demographic and clinical data including COVID-19 vaccination, 12-lead electrocardiogram finding, and serum markers of cardiac injury were documented.

Results

Five patients (4:1 male:female; age range, 17–38 years) were identified who had abnormal MRI findings and were vaccinated against COVID-19 prior to MRI. Cardiac troponin levels and electrocardiogram findings were abnormal in all patients. All patients were hospitalized due to acute onset of chest pain with diagnosis of acute myocarditis.

Patients 1–3 received their second dose of BNT162b2 vaccine 2 days, 3 days, and 2 days, respectively, before onset of chest pain. Patients 4 and 5 both received their second dose of mRNA-1273 at 3 days before onset of chest pain. In all patients, MRI showed myocarditis-like findings including nonischemic pattern of late gadolinium enhancement, corresponding signal abnormalities on T2-weighted images, and pericardial enhancement (Table, Figure). Diagnostic considerations included pulmonary embolus or acute coronary event with additional imaging-based testing (Table). Ipsilateral axillary lymphadenopathy to the vaccination site was identified in four patients. COVID-19 testing at the time of diagnosis (and history of prior COVID-19) were negative. No respiratory symptoms, prodrome, or skin rash were present prior to vaccination. Furthermore, medical history did not reveal any preexisting cardiac disease in these patients.

Discussion

In this work, we report the MRI findings of myocarditis in five patients who recently received mRNA COVID-19 vaccination. The clinical presentation (acute chest pain, abnormal troponin level, and electrocardiogram finding), temporal relationship, lymphadenopathy, and negative COVID-19 history raises concern for vaccine-related myocarditis. Because vaccine-related myocarditis is expected to be rare compared with typical viral myocarditis, the associations we observed do not indicate causation. However, the cases shown illustrate potential cardiac MRI findings that may be encountered by the imaging physician. Awareness of a possible association of vaccine with the clinical presentation of myocarditis or pericarditis may also be beneficial to reduce other diagnostic testing (eg, CT or MR angiography, scintigraphy).

To date, 627 cases of myocarditis following COVID-19 vaccination have been reported in the Centers for Disease Control and Prevention's Vaccine Adverse Event Reporting System, or VAERS, database (3). Because VAERS requires active reporting, there is a risk of bias, and the confidence in prior reports is unclear. Recently, several cases of acute myocarditis have been reported after receiving one or two doses of BNT162b2 or mRNA-1273 vaccine in adults and adolescents (4–8). The myocarditis-like MRI findings in these studies are consistent with those observed in our patients (5–8). Furthermore, news headlines from Israel have emerged (1), reporting myocarditis in 275 patients, the majority after the second dose of mRNA COVID-19 vaccine.

In general, establishing a causal link between myocarditis and vaccination is difficult (9), especially when the prevalence is rare. However, based on emerging data, pharmacovigilance for myocardial injury related to mRNA-based vaccination should be encouraged during the ongoing vaccination program. Although rare, prior vaccines have also been linked to myocarditis (9).

Results in Five Patients Diagnosed with Acute Myocarditis in Short Temporal Relation to mRNA COVID-19 Vaccine

Clinical Data and Diagnostic Tests	Patient 1 (Male, 21 y)	Patient 2 (Female, 32 y)	Patient 3 (Male, 17 y)	Patient 4 (Male, 18 y)	Patient 5 (Male, 38 y)
Vaccine type administered	BNT162b2, 2nd dose	BNT162b2, 2nd dose	BNT162b2, 2nd dose	mRNA-1273, 2nd dose	mRNA-1273, 2nd dose
Symptoms after vaccination*	Chills, headache, fever, chest discomfort and pain, dyspnea	Headache, body ache, fatigue, chest discomfort and pain	Subjective mild fever, chills, malaise, nausea, chest pain	Subjective mild fever, chills, malaise, chest pain, dyspnea	Myalgias, malaise, nausea, lightheadedness, chest pain
Vaccine, chest pain (d)†	2	3	2	3	3
Vaccine, cardiac MRI (d)†	3	4	5	5	5
Troponin-I level at peak (ng/mL)	3.82	1.02	14.65	4.00	12.19
BNP (pg/mL)	Not obtained	75	Not obtained	38	Not obtained
12-lead electrocardiogram	Diffuse ST-elevations in inferior and anterolateral leads, ST-depression in aVR and V1	Nonspecific T-wave abnormality in anterior leads	Diffuse ST segment elevation in leads I, II, aVL, and precordial leads V3-V6	Nonspecific T-wave abnormality anterolateral leads, RSR' pattern in V1	Inferolateral T-wave inversion
Cardiac MRI, main findings‡	LGE: linear mid myocardial septum, epicardial anterior and lateral LV wall, RV insertion and free wall. T2w signal abnormality in corresponding locations as LGE. Pericardial enhancement and small effusion. LVEF: 30%. RVEF: 42%. Ipsilateral axillary lymphadenopathy††	LGE: epicardial LV along the inferolateral basal wall. T2w signal abnormality in corresponding locations as LGE. Pericardial enhancement and small effusion. LVEF: 64%. RVEF: 60%. Ipsilateral axillary lymphadenopathy††	LGE: epicardial LV inferolateral basal wall. T2w signal abnormality in corresponding locations as LGE. Pericardial enhancement, no effusion. LVEF: 53%. RVEF: 57%. No lymphadenopathy identified on localizers††	LGE: epicardial LV inferior basal wall, lateral wall mid ventricle, anterolateral wall apical. T2w signal abnormality in corresponding locations as LGE. Pericardial enhancement and borderline effusion. LVEF: 57%. RVEF: 54%. Ipsilateral axillary lymphadenopathy††	LGE: epicardial LV inferior and anterolateral basal wall, epicardial and mid myocardial inferior wall mid ventricle and apical. T2w signal abnormality in corresponding locations as LGE. Pericardial enhancement, no effusion. LVEF: 54%. RVEF: 53%. Ipsilateral axillary lymphadenopathy††
Coronary CTA, scintigraphy§‖	Not obtained	Negative§	Not obtained	Negative§	Negative‖
Pulmonary MRA, CTA#**	Not obtained	Negative#	Not obtained	Negative#	Negative**

Note.— COVID-19 testing and history of prior COVID-19 were negative in these patients. All patients were hospitalized. Reference normal values: B-type natriuretic peptide (BNP), ≤99 pg/mL; troponin-I, ≤0.03 ng/mL. aVL = augmented vector left, aVR = augmented vector right, EF = ejection fraction, LGE = late gadolinium enhancement, LV = left ventricular, RV = right ventricular, T2w = T2 weighted.

* Symptoms that occurred following the second COVID-19 vaccination dose.

† Time (days) passed between vaccine administration and *(a)* onset of cardiac symptoms and *(b)* cardiac MRI.

‡ Diagnosis of myocarditis was based on updated Lake Louise criteria.

§ Coronary CT angiography (CTA) performed to exclude coronary artery disease, and evidence of ischemia or infarction.

‖ Scintigraphy performed to exclude coronary artery disease and evidence of ischemia or infarction.

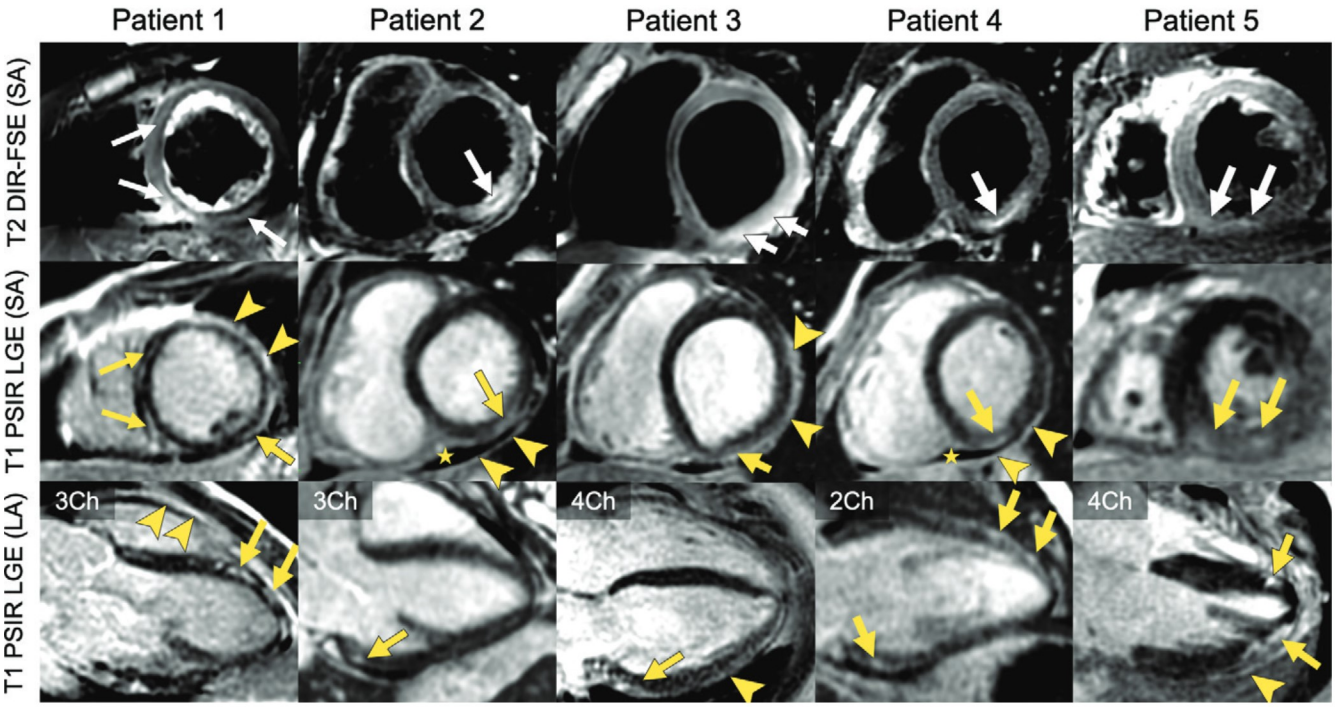
Pulmonary MR angiography (MRA) performed to exclude pulmonary embolus.

** CTA performed to exclude pulmonary embolus.

†† Visualized on localizer images.

Myocardial biopsy was not performed in our patients per local standard of care for mild uncomplicated myocarditis. Viral serologies were not performed, and are typically only recommended for fulminant myocarditis (10).

In conclusion, vaccine-related myocardial injury should be considered in the differential diagnosis in patients recently vaccinated against COVID-19 who present with acute chest pain.



Cardiac MR images in five patients diagnosed with acute myocarditis 3–5 days after a second dose of mRNA vaccine. Yellow arrows depict myocardial late gadolinium enhancement in a nonischemic pattern, white arrows depict corresponding T2 signal abnormalities, arrowheads depict pericardial enhancement, and stars depict pericardial effusion. Patient 1 (male, age 21 years) 3 days after vaccination with BNT162b2. Patient 2 (female, age 32 years) 4 days after vaccination with BNT162b2. Patient 3 (male, age 17 years) 5 days after vaccination with BNT162b2. Patient 4 (male, age 18 years) 5 days after vaccination with mRNA-1273. Patient 5 (male, age 38 years) 5 days after vaccination with mRNA-1273. 4Ch = four-chamber view, LA = long axis, PSIR LGE = phase-sensitive inversion recovery late gadolinium enhanced imaging, SA = short axis, T2w DIR-FSE = T2-weighted double inversion recovery fast spin echo, 3Ch = three-chamber view, 2Ch = two-chamber view.

Author contributions: Guarantors of integrity of entire study, J.S., T.M.G., S.B.R.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; agrees to ensure any questions related to the work are appropriately resolved, all authors; literature research, J.S., D.A.B., W.S.B., T.M.G., S.B.R.; clinical studies, all authors; and manuscript editing, all authors

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