Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letters

Patients With Myocarditis Associated With COVID-19 Vaccination

mRNA vaccines against COVID-19 have demonstrated excellent efficacy and have been well tolerated. Myocarditis has been reported as a rare, but serious, complication associated with vaccination.[1] The overall incidence has been observed to be approximately 2 cases per 100,000 adults vaccinated, with an observed incidence of 11 cases per 100,000 among recently vaccinated young men.[2] The early clinical course has been reported to be favorable, with the majority recovering quickly.[3] The intermediate-term clinical course after this vaccine-associated complication remains unknown but is of public health interest and for informing clinical decision-making among those with this complication.

We report the results of prospectively planned, research-based cardiac magnetic resonance imaging (CMR), electrocardiogram (ECG), laboratory testing, and clinical follow-up for 7 patients who were hospitalized for myocarditis following COVID-19 vaccination, from 2 U.S. medical centers in Falls Church, Virginia, and Dallas, Texas. Institutional Review Board approval and written informed consent were obtained from all participants undergoing research procedures. The initial presentation and management of 5 of the cases were previously published, and baseline data are included for comparison.[4]

All subjects were White or Hispanic men between the ages of 19 and 39 years. Median time from vaccination to presentation was 3 days (range 2-5 days). Repeat CMR, ECG, and measurement of high-sensitivity cardiac troponin I (hs-cTnI), N-terminal pro-B-type natriuretic peptide (NT-proBNP), and COVID-19 nucleocapsid serology were obtained at a median time of 189 days (range 164-322 days) from vaccination. **Table 1** shows baseline characteristics, index and follow-up imaging, ECG, and laboratory results. At the time of follow-up, all participants denied activity intolerance, chest pain, shortness of breath, or palpitations, and there were no interim major adverse cardiac events or hospitalizations. Follow-up ECG showed resolution of ST abnormalities in 6 of the 7 cases. On the initial CMR, all patients had evidence of late gadolinium enhancement (LGE) and on follow-up, 2 had complete resolution, and the other 5 had interval improvement. Two participants' CMR initially met criteria for myocardial edema, but no edema was present in any subject at follow-up by T2 mapping. The left ventricular ejection fraction increased in all participants from a median of 52% (IQR: 50%-61%) to 60% (IQR: 56%-62%), and end-systolic volume index decreased in all 7 from a median of 32 mL (IQR: 32-44 mL) to 24 mL (IQR: 20-33 mL). There were no regional wall motion abnormalities noted on initial or follow-up CMR. Two participants also had evidence of pericardial inflammation on their initial CMR, which had resolved at follow-up. cTnI, which had been markedly elevated during index hospitalization, was now within normal limits for all. COVID-19 nucleocapsid serology was negative at follow-up in 6 of 6 participants, indicative of no interval infection, and all 7 participants denied symptoms or diagnosis of COVID-19 infection. At the date of follow-up, no participant eligible for the COVID-19 vaccine booster had received it. All cases were reported to the vaccine adverse event reporting system (VAERS).

This intermediate-term follow-up report of a convenience sample of 7 men who were hospitalized with myocarditis following COVID-19 vaccination builds on our prior description of a favorable short-term course for those who experienced this rare adverse COVID-19 vaccination side effect.[4] There are several important findings: 1) follow-up CMR demonstrated improved or resolved LGE in all cases; 2) left ventricular ejection fraction improved and end-systolic volume index decreased in all subjects; 3) there was no evidence of ongoing active myocardial injury by CMR (edema) or hs-cTnI; and 4) there were no interim symptoms, impaired activity tolerance, or hospitalizations. Although these findings are all favorable, it is important to note that while there was interval improvement, 5 of the cases did show evidence of persistent LGE on follow-up CMR, potentially indicative of myocardial fibrosis. Given the possible of risk

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TABLE 1 Patient Characteristics and Outcomes

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Age, y	28	39	39	19	23	33	23
Vaccine	J&J	Pf, 2nd	Mod, 2nd	Pf, 2nd	Pf, 2nd	Mod, 2nd	Pf, 2nd
Initial ECG	ST-segment elevation	PR depression	No ST abn	Nonspecific ST-T changes	ST-segment elevations	ST-segment elevations	ST-segment elevations
Follow-up ECG	New LBBB No ST abn	No ST abn	No ST abn	No ST abn	No ST abn	New RBBB No ST abn	Nonspecific ST-T abn
Initial CMR[a]	32 days	11 days	5 days	4 days	17 days	57 days	3 days
LVEF	50%	56%	52%	50%	61%	61%	50%
ESVI, 17-37 mL/m^2	44 mL/m^2	32 mL/m^2	33 mL/m^2	48 mL/m^2	34 mL/m^2	32 mL/m^2	30 mL/m^2
LGE	Patchy LGE mid to apical segments	LGE along A and L segments	Multifocal diffuse LGE	Patchy LGE in the L and IL segments	Patchy LGE A/IL segments	LGE apical S/IL/I segments	LGE basal/mid AS segments
Follow-up CMR[a]	214 days	200 days	322 days	183 days	164 days	189 days	177 days
LVEF	54%	58%	60%	56%	62%	63%	60%
ESVI	40 mL/m^2	20 mL/m^2	24 mL/m^2	33 mL/m^2	25 mL/m^2	19 mL/m^2	28 mL/m^2
LGE	Improved with LGE in I/L segments	Resolved LGE	Near resolution, LGE in IL segments	Improved with LGE in the basal/mid L/IL segments	Near resolution, LGE in mid AL segments	Improved with LGE in A/I segments	Resolved LGE
T1/T2,[b] ms	978, 48	970, 47	937, 51	840, ND	953, 45	950, 47	975, 43
Initial labs							
Peak cTnI, ng/mL	17.1	11.0	13.0	44.8	16.6	38.8	7,000 ng/L[c]
BNP, pg/mL	–	22	97	57.2	12.1	25.4	68
Follow-up labs							
hs-cTnI ng/L, <60.4	6.4	3.5	4.0	54.6	5.2	8.7	6
NT-proBNP, pg/mL	16.6	9.6	11.0	9.3	6.2	32.2	<10

[a]Refers to days from vaccination. [b]T1 normal = (850-1,050 ms), T2 normal = (45-55 ms). [c]hs-cTnI.

A = anterior; Abn = abnormality; AL = anterolateral; AS = anteroseptal; BNP = B-type natriuretic peptide; CMR = cardiac magnetic resonance; cTnI = cardiac troponin I; ECG = electrocardiogram; ESVI = end-systolic volume index; hs-cTnI = high-sensitivity cardiac troponin I; I = inferior; IL = inferolateral; J&J = Johnson & Johnson vaccine; L = lateral; LBBB = left bundle branch block; LVEF = left ventricular ejection fraction; LGE = late gadolinium enhancement; Mod = Moderna (mRNA-1273) vaccine; ND = not done; NT-proBNP = N-terminal pro-B-type natriuretic peptide; Pf = Pfizer-BioNTech COVID-19 (BNT162b2) vaccine; RBBB = right bundle branch block; S = septum.

of arrhythmias, cardiac dysfunction, or recurrent myocarditis, patients should continue to undergo close clinical follow-up.[5]

Myocarditis is a rare, but serious, side effect associated with COVID-19 vaccination. The clinical course of vaccine-associated myocarditis appears favorable, with resolution of presenting symptoms in all patients. Although there were no instances of severe impairment of ventricular function at baseline in this series, all patients had LGE, and several had mild LV dilation. Intermediate-term (6-month) follow-up demonstrated improvement or resolution of CMR findings of myocarditis in all cases. There was no evidence of myocardial dysfunction or ongoing myocardial injury at intermediate-term follow-up and no subsequent adverse cardiac events. Several questions remain regarding the clinical course and management of patients with COVID-19 vaccine myocarditis, including recurrence risk with COVID-19 infection, safety of vaccine boosters, and any long-term sequelae. However, given the potential morbidity of COVID-19 infection, the risk-benefit decision for vaccination remains favorable. Vaccine adverse event reporting remains of high importance, and long-term longitudinal follow-up is needed.

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