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Myopericarditis After the Pfizer Messenger Ribonucleic Acid Coronavirus Disease Vaccine in Adolescents

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Reports have emerged of myocarditis and pericarditis predominantly after the second dose of the coronavirus disease messenger ribonucleic acid vaccine. We describe 13 patients aged 12-17 years who presented with chest pain within 1 week after their second dose of the Pfizer vaccine and were found to have elevated serum troponin levels and evidence of myopericarditis. *(J Pediatr 2021;238:317-20).*

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On May 10, 2021, the US Food and Drug Administration extended the Emergency Use Authorization of the Pfizer-BioNTech messenger ribonucleic acid (mRNA) coronavirus disease (COVID-19) vaccine for adolescents aged 12-15 years.[1] Following this authorization, large numbers of adolescents across the country began to receive immunization. As of June 21, 2021, 98 008 adolescents aged 12-15 years and 69 489 adolescents aged 16 and 17 years in Washington state completed the 2-dose schedule of the mRNA COVID-19 vaccine.[2]

Reports of post-COVID-19 vaccine myocarditis and pericarditis have emerged, particularly after the second dose of the mRNA vaccine. Initial cases were noted predominantly in male adolescents and young adults in the Israeli military.[3] Subsequently, US institutions have reported 7 cases in adolescents aged >16 years[4] and 7 cases in young adults.[5] As the age range of eligibility for the COVID-19 vaccine has broadened in Washington, we have cared for a cohort of younger patients with postvaccination myopericarditis. Here we describe clinical and cardiac magnetic resonance imaging (CMR) findings for 13 patients aged 12-17 years seen at our center.

Methods

With Institutional Review Board approval, we performed a retrospective electronic medical record review. Inclusion criteria were patients aged <18 years presenting with severe chest pain and signs of myopericarditis within 1 week of receiving the second dose of the Pfizer COVID-19 vaccine between April 1, 2021, and June 21, 2021.

Results

Clinical and laboratory findings are presented in **Table I**. We identified 13 patients with myopericarditis, with a median age of 15 years (range, 12-17 years). The majority of patients were male (n = 12; 92%), and non-Hispanic white (n = 10; 76.9%). The median time to presentation from the second dose of the Pfizer COVID-19 mRNA vaccine was 3 days (range, 2-4 days). According to the inclusion criteria, all patients had sudden onset of intense, persistent chest pain that was not exacerbated by movement or activity. The most common accompanying symptoms were shortness of breath (n = 6; 46.2%), tactile temperature (n = 5; 38.5%), and myalgias (n = 4; 30.7%).

All patients had an elevated serum troponin level (median, 9.18 ng/mL; range, 0.65-18.5 ng/mL). The median serum brain natriuretic peptide level was 37.5 pg/mL (range, 7-87 pg/mL). C-reactive protein was elevated in patients in whom it was measured (n = 10; median, 3.7 mg/dL; range, 1.4-6.5 mg/dL). COVID-19 nucleocapsid immunoglobulin G antibody was measured in 9 patients and was negative in all 9.

Cardiac testing results are presented in **Table II**. Nine patients had an abnormal electrocardiogram, with ST segment elevation the most common finding. All patients underwent echocardiography on admission; 11 patients had normal left ventricular (LV) systolic function, and 2 patients demonstrated mildly reduced LV systolic function as well as regional LV wall motion abnormalities. The median LV ejection fraction (LVEF) was 60% (range, 45%-69%; normal defined as >55%). No patients had significant pericardial effusion. One patient had an incidental finding of bicuspid aortic valve without regurgitation or stenosis.

All patients underwent CMR within 1 week of presentation. All CMRs performed were abnormal, showing late gadolinium enhancement in a patchy subepicardial to transmural pattern with predilection for the inferior LV free wall (**Figure**). In addition, all CMRs had evidence of edema in corresponding segments by T2-weighted CMR and met the Lake Louise criteria[6] for myocarditis. LV regional wall

CMR	Cardiac magnetic resonance imaging
COVID-19	Coronavirus disease
LV	Left ventricular
LVEF	Left ventricular ejection fraction
mRNA	Messenger ribonucleic acid

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Table I. Demographic features and clinical findings in adolescents following receipt of the Pfizer mRNA COVID-19 vaccine

	Demographics			Clinical information			Laboratory tests			
Patient	Age, y	Sex	Race	Length of stay, d	Time from vaccination to presentation, d	Other symptoms	Peak troponin, ng/mL (normal <0.05 ng/mL)	Peak BNP, pg/mL (normal <55 pg/mL)	Peak CRP, mg/dL (normal <0.08 mg/dL)	COVID-19 immunoglobulin G nucleocapsid antibody testing
1	16	M	White non-Hispanic	1	2	Fever, chills, myalgias, headache, shortness of breath	8	15	4.3	Negative
2	16	M	Asian non-Hispanic	1	2	Fever, myalgias	11.1	28	3.5	Not tested
3	16	M	White non-Hispanic	3	3	Myalgias, headache	10.9	<10	3.6	Negative
4	17	M	American Indian/Alaska Native non-Hispanic	1	3	Fever, malaise	9.18	14	–	Negative
5	15	M	White non-Hispanic	2	2	Myalgias, shortness of breath	4.95	13	5.5	Negative
6	15	F	White non-Hispanic	1	3	Vomiting	0.65	7	1.4	Negative
7	15	M	White non-Hispanic	3	3	Fevers, shortness of breath	9.12	74	3	Negative
8	15	M	White non-Hispanic	3	3	Chills	13.2	87	6.2	Negative
9	12	M	White non-Hispanic	2	3	None	13	37	–	Negative
10	14	M	White non-Hispanic	3	3	Fever, headache	18.5	66	–	Negative
11	14	M	Asian non-Hispanic	2	4	Malaise, shortness of breath	6.08	55	3.7	Not tested
12	16	M	White non-Hispanic	2	2	Shortness of breath	16.4	38	6.5	Not tested
13	15	M	White non-Hispanic	2	3	None	7.89	86	3.4	Not tested

BNP, brain natriuretic peptide; *CRP*, C-reactive protein; *F*, female; *M*, male.

Table II. Cardiac testing results and treatment in adolescents following receipt of the Pfizer mRNA COVID-19 vaccine

	Cardiac testing							Treatment		
		Echocardiography		CMR						
Patient	ECG findings	LV wall motion abnormalities	LVEF, % (normal ≥55%)	LVEF, % (normal ≥55%)	Edema	LGE	LV focal hypokinesis	IVIG	Corticosteroids	NSAIDs
1	Normal	No	66	50.8	Yes	Yes	No	No	No	Yes
2	ST elevation	No	59	51.1	Yes	Yes	No	No	No	Yes
3	ST elevation	No	69	56.6	Yes	Yes	No	Yes	No	Yes
4	ST elevation	No	58	49.4	Yes	Yes	No	No	No	Yes
5	Normal	No	58	52	Yes	Yes	No	No	No	Yes
6	Nonspecific T-wave changes	No	58	48	Yes	Yes	No	No	No	Yes
7	T-wave inversion	No	61	61	Yes	Yes	No	No	No	Yes
8	ST elevation	Yes	45	46	Yes	Yes	Yes	Yes	Yes	Yes
9	Normal	No	64	54	Yes	Yes	No	No	No	Yes
10	ST elevation	No	62	55	Yes	Yes	Yes	No	No	Yes
11	ST elevation	No	60	58	Yes	Yes	No	No	No	Yes
12	ST elevation	Yes	53	58	Yes	Yes	No	Yes	Yes	Yes
13	Normal	No	61	53	Yes	Yes	No	No	No	Yes

ECG, electrocardiography; *IVIG*, intravenous immunoglobulin; *LGE*, late gadolinium enhancement; *NSAID*, nonsteroidal anti-inflammatory drug.

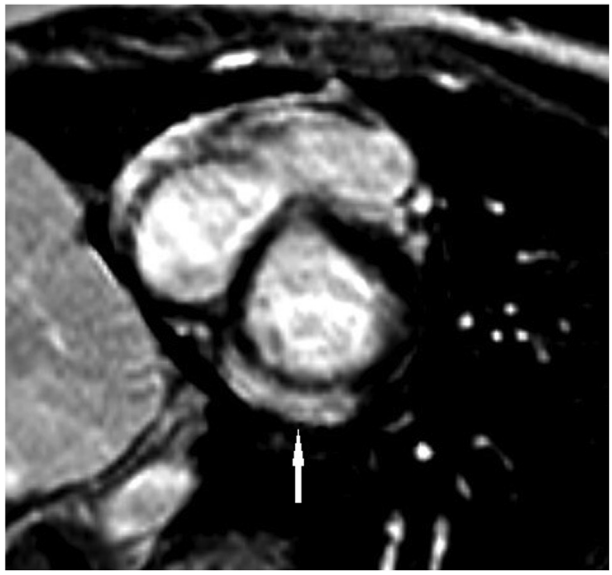

Figure. Short-axis CMR image with an arrow showing delayed enhancement in the inferior and inferolateral basal segments of the LV free wall.

motion abnormalities were noted in 2 patients; CMR-based LV systolic function was mildly decreased in 8 patients. The CMR-detected LVEF ranged from 46% to 61% (median, 53%). No significant pericardial effusions were seen on CMR.

All patients received scheduled doses of nonsteroidal anti-inflammatory agents (ie, ibuprofen every 8 hours, with dose dependent on patient weight). Three patients received intravenous immunoglobulin, 2 of whom were the patients with decreased LV function on echocardiography. These 2 patients also received corticosteroids according to our institutional pathway for treatment of myocarditis. One patient had isolated premature ventricular contractions on telemetry; no other patient had evidence of arrhythmia. The median hospital length of stay was 2 days (range, 1-4 days) with no intensive care unit admission, significant morbidity, or mortality. All patients had resolution of chest pain and a falling serum troponin level before discharge.

Discussion

We report 13 adolescents with myopericarditis after the second dose of the Pfizer mRNA COVID-19 vaccine. This cluster of cases was identifiable as the age of eligibility for vaccination broadened with Emergency Use Authorization by the Food and Drug Administration. Our hospital is the only freestanding children's hospital in Washington and serves as a tertiary referral institution. To our knowledge, at least 3 other cases in this age group have been cared for at other hospitals in the state. Using these numbers and Washington Department of Health data on immunization,[2] we estimate a possible incidence of 0.008% in adolescents aged 16-17 years and 0.01% in those aged 12-15 years following the second dose.

All patients had evidence of myocardial inflammation and edema on CMR, similar to findings in limited case series of adults with post–COVID-19 vaccine myocarditis.[7] Although the symptoms resolved rapidly in all patients, their CMR findings indicate the potential for myocardial fibrosis and unknown long-term impact. Accordingly, we are following the American Heart Association/American College of Cardiology recommendations for exercise restrictions in acute myocarditis for up to 6 months and long-term cardiac surveillance.[8] In addition, follow-up CMR is planned for all patients at 3 months, which may allow us to shorten the period of exercise restriction.

We speculate that a hyperimmune response to the second dose of the vaccine is plausible. Children have demonstrated a more robust immune response to severe acute respiratory syndrome coronavirus 2 infection than adults, as observed in multisystem inflammatory syndrome in children.[9] For noninferior immunogenicity, it is possible the interval between doses 1 and 2 should be longer in children than in adults or that a reduction in the content of dose 2 may be appropriate in individuals aged <18 years.

It is noteworthy that 2 of our cases had a family history of myocarditis in first-degree relatives. There is evidence that genetics may play a role in the susceptibility of patients to myopericarditis.[10] This predisposition may increase the likelihood of inflammation and cardiac effects after the vaccine.

The Pfizer Phase 2/3 clinical trial included only 754 participants in the 16 to 17-year-old age group and 2260 in the 12- to 15-year-old age group. Approximately 50% were males.[11] As noted earlier, we have estimated the incidence of myopericarditis in the younger group as nearly 0.01% of those receiving the second dose of vaccine. Owing to reporting issues, delays, and early inability of practitioners to associate myopericarditis with vaccine, this is likely an underestimate. Moreover, our Washington Department of Health vaccine data for these age groups are not segregated by sex. This adverse event likely would not be detected in the small population of males who received the study vaccine and highlights the need for aggressive postauthorization surveillance.

Although a causal relationship between vaccination and the development of myopericarditis cannot be concluded from a case series, the clustering in time as well as the uncommon occurrence of myopericarditis and the rapid resolution of symptoms and findings likely make this a unique vaccine-related event. Identification of myopericarditis as an adverse event should have high priority during investigations before and after authorization of COVID-19 vaccines and be considered by policy makers in the risk/benefit ratio in adolescents and children. ■

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