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Case Report

COVID-19 mRNA vaccine-related myocarditis: A PRISMA systematic review, imaging approach and differential diagnoses ☆,☆☆

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ABSTRACT

We present a case involving a young individual who developed acute myocarditis on the fourth day following administration of a COVID-19 mRNA vaccine. The patient's condition was managed conservatively, resulting in a favorable outcome. This paper extensively discusses the pathogenesis, clinical manifestations, imaging characteristics of COVID-19 mRNA vaccine-related myocarditis and includes a comprehensive review of pertinent literature. Additionally, a systematic review of COVID-19 mRNA vaccine-related myocarditis, conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) principles, is presented. Healthcare professionals should maintain a clinical suspicion for COVID-19 mRNA vaccine-related myocarditis when encountering patients with confirmed myocarditis who have received recent COVID-19 mRNA vaccination, after ruling out other potential causes. The diagnosis of acute myocarditis primarily relies on adherence to the Lake Louise Criteria (LLC) for cardiac magnetic resonance (CMR). Nevertheless, specific CMR features or distinctive patterns indicative of COVID-19 mRNA vaccine-related myocarditis are currently undefined. Among patients with vaccine-related myocarditis, common CMR findings encompass subepicardial late gadolinium enhancement and T2-based myocardial edema, although these findings lack specificity and may resemble other medical conditions. Supportive care involving a short-term regimen of NSAIDs, colchicine, and steroids represents the cornerstone of treatment for this variant of myocarditis, which tends to be self-limiting with favorable short-term prognoses. Timely diagnosis is paramount for optimizing patient care.

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Introduction

The emergence of COVID-19 in December 2019 prompted the development of the Moderna mRNA-1273 vaccine, which entered Phase III trials in July 2020 [1]. By the close of 2020, numerous countries had initiated their vaccination campaigns employing the Moderna mRNA-1273 vaccine. However, a growing body of evidence has pointed to rare adverse events, including myopericarditis, linked to mRNA vaccines on a global scale.

This paper undertakes a systematic review of COVID-19 mRNA vaccine-related myocarditis, adhering to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. Our focus is primarily on the cardiac MRI imaging pattern of late gadolinium enhancement (LGE), treatment modalities, and patient outcomes. Furthermore, we present a case study involving a young individual who developed acute myocarditis 4 days after receiving a COVID-19 mRNA vaccine. The patient received conservative treatment at our institution and exhibited a favorable prognosis.

Additionally, we delve into the pathogenesis, clinical manifestations, and imaging characteristics associated with COVID-19 mRNA vaccine-related myocarditis, while also addressing relevant differential diagnoses.

Materials and methods

We conducted a comprehensive literature search on the PubMed and Cochrane Library databases using the following keywords: "COVID-19 vaccine myocarditis" OR "COVID-19 vaccine myocarditis MRI" OR "COVID-19 vaccine myocarditis cardiac MRI." The search was limited to June 1, 2023, and the results were imported into MEDELEY software for further processing, with duplicate studies removed.

The articles of the relevant studies were retrieved and analyzed in detail. The inclusion criteria for the studies were as follows: (1) original case reports or case series, (2) clinical diagnosis of COVID-19 mRNA (Pfizer/Moderna) vaccine-related myocarditis, and (3) cardiac MRI findings. Exclusion criteria were as follows: (1) publications not in English, (2) duplicated studies, and (3) studies without cardiac MRI data.

Results

Our initial search identified 1101 studies, of which 47 articles were retrieved for full assessment. Twenty three studies were further excluded for the following reasons: (1) cardiac MRI data lacking in relevant details, (2) studies were not relevant to our study, and (3) full text article could not be retrieved. The final 24 articles which fulfilled the inclusion criteria consisted of 17 original case reports and 7 case series. Our flowchart for identification and selection of studies based on the PRISMA principles is demonstrated in Fig. 1. The demographics, cardiac MRI imaging pattern of LGE, treatment and outcomes of patients with COVID-19 mRNA vaccine related myocarditis are summarized in Table 1.

Case report

A 21-year-old male presented to the emergency department with acute central chest pain radiating to the left shoulder blade 4 days after receiving the second dose of the mRNA-1273 vaccine. The patient had no cardiovascular risk factors or past medical history. He had initially developed myalgia and fever a day after the vaccination. On examination, his vital signs were normal, but his electrocardiogram showed global ST elevation. His initial cardiac markers were elevated, including Troponin T at 705 ng/L, Creatine Kinase (CK) at 516 U/L, and Creatine kinase-MB (CKMB) at 35.8 ug/L, as well as mildly elevated C-reactive protein levels at 8.5 mg/L.

There were concerns for an aortic dissection, but CT Aortogram was negative. A transthoracic echocardiogram showed a normal ejection fraction of 59% with no pericardial abnormalities. Subsequently, contrast-enhanced cardiac magnetic resonance imaging (MRI) revealed myocardial oedema and subepicardial and mid-wall late gadolinium enhancement (LGE) (non-ischemic distribution) in the basal inferior, basal, and mid inferolateral segments (Fig. 2). These findings were suggestive of acute myopericarditis under the 2018 Lake Louise Criteria [26].

As the patient had a recent COVID-19 mRNA vaccine with no other clear etiology, including a negative COVID PCR test, the diagnosis of COVID-19 vaccine-related myocarditis was made. The patient was treated with a week's course of ibuprofen, a non-steroidal anti-inflammatory drug (NSAID), and a 3-month course of colchicine. His symptoms resolved by day 2 of admission, and his cardiac biomarkers normalized on subsequent follow-up.

Discussion

The data from the US Centre for Disease Control and Prevention reveals that the incidence rates of COVID-19 mRNA vaccine-related myocarditis/pericarditis vary between 0 and 35.9 per 100,000 for males and 0 to 10.9 per 100,000 for females across all age groups above 5 [27]. In the local context, the incidence rate was reported to be 0.47 per 100,000 individuals across all age groups following either the first or second vaccine dose. Notably, COVID-19 mRNA vaccine-related myocarditis cases were most prevalent among males aged 12-19 years old, and the majority of these cases occurred within a week after vaccination [28].

Despite ongoing research, the exact mechanism behind COVID-19 mRNA vaccine-related myocarditis remains unclear. Some hypotheses have been proposed, including the possibility that a low-level presence of double-stranded RNA (dsRNA) within the vaccine may trigger an immune or inflammatory response within the myocardium, as suggested by Milano et al. [29]. Other studies have indicated that antibodies generated against the glycoprotein of SARS-CoV-2, which the mRNA vaccine encodes, might cross-react with self-antigens, including α-myosin, potentially leading to an

Table 1 – Summary of the demographics, MRI features treatment and outcomes of Covid-19 mRNA vaccine-related myocarditis.

First Author [Ref]	Case No.	Age/ gdr	Day(s) Post-vac	COVID-19 vac (Brand/types)	Cardiac MRI	Echocardiogram (Echo) or biopsy (Bx)	Treatment	Outcomes
Kojima [2]	1	17/M	2d	BNT 162b2 mRNA vaccine (Pfizer)	Diffuse Ep LGE and LV T2w HI (OE)	1. Positive history of prior myocarditis 3 years ago 2. Bx: normal	Aspirin, Colchicine, IVIG	CR
Suresh [3]	2	22/M	2d	mRNA-1273 vaccine (Moderna)	1. Basal inferolateral LV wall myocardium patchy LGE and T2w HI (OE) 2. Trace Pc fluid	-	Ibuprofen, Colchicine	CR
Nagasaka [4]	3	23/M	3d	BNT 162b2 mRNA vaccine (Pfizer)	Mid inferolateral LV wall Se and Mm LGE	Bx: Small amount of inflammatory cells infiltration (mononuclear cells)	NSAIDs	CR
Singh [5]	4	24/M	3d	BNT 162b2 mRNA vaccine (Pfizer)	Lateral LV wall Se linear LGE	-	-	CR
Tailor [6]	5	44/M	4d	mRNA-1273 vaccine (Moderna)	1. Mid to basal septum and inferior LV walls Mm, Mid to apical lateral LV walls Se and Mm patchy linear enhancement 2. My OE at most of the myocardium 3. Mild Pc enhancement	Echo: Reduced ejection fraction (40%) with global hypokinesis most severe at apex	Colchicine, intravenous diuretics, ACE inhibitor, BB	Ejection fraction improved
Watanabe [7]	6	19/M	2d	mRNA-1273 vaccine (Moderna)	Mid to basal inferolateral LV walls Se LGE and T2w HI (OE)	-	Ibuprofen, ACE inhibitor	CR
	7	20/M	3d	mRNA-1273 vaccine (Moderna)	Basal inferior LV mid wall T2w HI (OE) initially with LGE on subsequent study (47 days later)	-	Ibuprofen, ACE inhibitor	CR
	8	29/M	2d	mRNA-1273 vaccine (Moderna)	Anterior and inferior LV walls mid wall LGE and T2w HI (OE)	-	Ibuprofen, ACE inhibitor	CR
	9	48/M	5d	BNT 162b2 mRNA vaccine (Pfizer)	Basal inferior LV mid-wall, Mid septum and inferoseptum LV walls Se LGE and T2w HI (OE)	1. ECG: Atrioventricular block 2. Echo: Reduced ejection fraction (30%) with diffuse hypokinesis	Dobutamine, diuretics, ibuprofen, ACE inhibitor	CR but longer hospitalization

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Table 1 (*continued*)

First Author [Ref]	Case No.	Age/ gdr	Day(s) Post-vac	COVID-19 vac (Brand/types)	Cardiac MRI	Echocardiogram (Echo) or biopsy (Bx)	Treatment	Outcomes
Marshall [8]	10	16/M	2d	BNT 162b2 mRNA vaccine (Pfizer)	Apical lateral LV Se LGE and My OE	-	IVIG, IV methyl-prednisolone, PO prednisolone, NSAIDs	CR
	11	19/M	3d	BNT 162b2 mRNA vaccine (Pfizer)	Basal inferolateral LV midwall patchy LGE and My OE	-	Colchicine, Aspirin, NSAIDs	CR, Sinus tachycardia
	12	17/M	2d	BNT 162b2 mRNA vaccine (Pfizer)	1. Basal anterolateral and basal to mid inferolateral LV walls Se LGE with My OE 2. T1w evidence of diffuse fibrosis	-	NSAIDs	CR
	13.	18/M	3d	BNT 162b2 mRNA vaccine (Pfizer)	1. OE, hyperemia and fibrosis 2. Mild mitral regurgitation	-	IVIG, IV methyl-prednisolone, PO prednisolone, NSAIDs	CR
	14	17/M	3d	BNT 162b2 mRNA vaccine (Pfizer)	Anterior and lateral LV walls Ep LGE	-	IVIG, IV methyl-prednisolone, PO prednisolone, Aspirin, NSAIDs	CR
	15	16/M	3d	BNT 162b2 mRNA vaccine (Pfizer)	Diffuse Se LGE and OE	-	IVIG, prednisolone	CR
	16	14/M	2d	BNT 162b2 mRNA vaccine (Pfizer)	Mid to apical free LV walls Se LGE with My OE and hyperemia	Echo: Mildly reduced LV and RV systolic function (LVEF 47%)	Frusemide, NSAIDs	LV and RV function recovered
Park [9]	17	17/M	18d	BNT 162b2 mRNA vaccine (Pfizer)	Mid to basal septum and apex lateral LV walls focal nodular LGE	Echo: hyperechoic nodular lesion at interventricular septal wall (RV side)	ACE inhibitor, aspirin	CR
Albert [10]	18	24/M	4d	mRNA-1273 vaccine (Moderna)	Mid anterolateral and inferolateral LV walls Ep and Mm LGE and T2w HI (OE)	-	BB	CR

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Table 1 (*continued*)

First Author [Ref]	Case No.	Age/ gdr	Day(s) Post-vac	COVID-19 vac (Brand/types)	Cardiac MRI	Echocardiogram (Echo) or biopsy (Bx)	Treatment	Outcomes
Starekova [11]	19	21/M	2d	BNT 162b2 mRNA vaccine (Pfizer)	1. Septal LV wall Mm LGE. Anterior, lateral, RV insertion and free LV walls Ep LGE. 2. Pc enhancement and small effusion. 3. Reduced LVEF (30%)	-	-	-
	20	32/F	3d	BNT 162b2 mRNA vaccine (Pfizer)	1. Basal inferolateral LV wall Ep LGE and T2w HI (OE) 2. Pc enhancement and small effusion	-	-	-
	21	17/M	2d	BNT 162b2 mRNA vaccine (Pfizer)	1. Basal inferolateral LV wall Ep LGE and T2w HI (OE) 2. Pc enhancement	-	-	-
	22	18/M	3d	mRNA-1273 vaccine (Moderna)	1. Basal inferior, mid lateral and apical anterolateral LV walls Ep LGE with T2w HI (OE) 2. Pc enhancement and borderline effusion	-	-	–
	23	38/M	3d	mRNA-1273 vaccine (Moderna)	1. Basal inferior and anterolateral LV walls Ep, Mid to apical inferior LV wall Ep and Mm LGE with T2w HI (OE) 2. Pc enhancement	-	-	-
Mouch [12]	24	24/M	3d	BNT 162b2 mRNA vaccine (Pfizer)	Basal septum and inferolateral LV walls Se and Mm LGE with mild T2w HI (OE)	-	NSAIDs, Colchicine	CR
	25	20/M	1 day	BNT 162b2 mRNA vaccine (Pfizer)	Basal to mid anterolateral and inferolateral LV walls Se LGE with mild T2w HI (OE)	-	NSAIDs, Colchicine	CR
	26	29/M	2 days	BNT 162b2 mRNA vaccine (Pfizer)	1. Basal anteroseptal, anterolateral and inferolateral LV walls Mm LGE 2. Diffuse My OE	-	NSAIDs, Colchicine	CR

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Table 1 (*continued*)

First Author [Ref]	Case No.	Age/ gdr	Day(s) Post-vac	COVID-19 vac (Brand/types)	Cardiac MRI	Echocardiogram (Echo) or biopsy (Bx)	Treatment	Outcomes
	27	45/M	16d	BNT 162b2 mRNA vaccine (Pfizer)	Mid anterolateral and inferolateral, Apical anterior LV walls Se LGE with T2w HI (OE)	-	NSAIDs, Colchicine	CR
	28	16/M	1d	BNT 162b2 mRNA vaccine (Pfizer)	Basal inferolateral and Mid anterolateral LV walls Se and Mm LGE with T2w HI (OE)	-	NSAIDs, Colchicine	CR
	29	17/M	3d	BNT 162b2 mRNA vaccine (Pfizer)	1. Basal inferolateral, Mid inferolateral and infero-septal, Apical lateral, anterior and inferior LV walls Se LGE with T2w HI (OE) 2. Mid inferolateral and anterolateral, Apical anterior and lateral LV walls Mm enhancement	-	NSAIDs, Colchicine	CR
D'angelo [13]	30	30/M	3d	BNT 162b2 mRNA vaccine (Pfizer)	1. Diffuse Se LGE with sparing of basal and mid septal segments. 2. Basal inferolateral LV wall Se T2w hyperintensity 3. Pc thickening and enhancement	Echo: Mild Pc effusion, segmental wall motion abnormality at apical interventricular septum	NSAIDs, BB	CR
Garcia [14]	31	39/M	1d	BNT 162b2 mRNA vaccine (Pfizer)	Lateral wall Se enhancement and OE	-	-	CR
Kim [15]	32	36/M	3d	mRNA-1273 vaccine (Moderna)	Apical lateral LV wall Ep LGE	-	Colchicine, NSAIDs	CR
	33	23/M	5d	BNT 162b2 mRNA vaccine (Pfizer)	1. Multifocal Ep LGE with T2w HI (OE) 2. Small Pc effusion	-	Corticosteroids, Colchicine	CR
	34	70/F	1d	mRNA-1273 vaccine (Moderna)	1. Multifocal patchy and diffuse My LGE with T2w HI (OE) 2. Small Pc effusion	-	-	CR
	35	24/M	2d	BNT 162b2 mRNA vaccine (Pfizer)	Lateral LV wall Ep patchy LGE with T2w HI (OE)	-	Colchicine, NSAIDs	CR

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Table 1 (*continued*)

First Author [Ref]	Case No.	Age/ gdr	Day(s) Post-vac	COVID-19 vac (Brand/types)	Cardiac MRI	Echocardiogram (Echo) or biopsy (Bx)	Treatment	Outcomes
Rosner [16]	36	39/M	3d	mRNA vaccine (Moderna or Pfizer)	Anterior and lateral LV walls Se LGE	Echo: Reduced ejection fraction (35-40%) and mild global left ventricular hypokinesis	BB, Angiot3ensin receptor blocker	CR
	37	39/M	4d	mRNA vaccine (Moderna or Pfizer)	1. Multifocal Se and Mm LGE 2. Anterior LV wall Pc enhancment	-	IV steroids	CR
	38	24/M	7d	mRNA vaccine (Moderna or Pfizer)	1. Septal and inferior LV walls Mm LGE 2. Anterior, lateral and inferior LV walls Se LGE 3. Lateral and inferior LV walls My OE	-	Colchicine, Ibuprofen	CR
	39	19/M	2d	mRNA vaccine (Moderna or Pfizer)	1. Lateral and inferolateral LV walls multifocal patchy Se and Mm LGE 2. Basal lateral LV wall My OE	-	Colchicine, Ibuprofen	CR
	40	20/M	3d	mRNA vaccine (Moderna or Pfizer)	1. Lateral, inferolateral and anterolateral LV walls Se LGE 2. Inferior LV wall My OE	-	Ibuprofen	CR
	41	23/M	3d	mRNA vaccine (Moderna or Pfizer)	1. Basal to mid anteroseptal wall LGE 2. Trace Pc enhancement	-	BB, colchicine	CR
Isaak [17]	42	15/M	2d	BNT 162b2 mRNA vaccine (Pfizer)	Basal lateral and inferior LV walls Se LGE and OE	-	-	CR
Ammirati [18]	43	56/M	3d	BNT 162b2 mRNA vaccine (Pfizer)	Basal and mid inferolateral LV walls Se and Mm LGE	-	-	CR
Muthukumar [19]	44	52/M	3d	mRNA-1273 vaccine (Moderna)	Basal inferior and mid lateral LV walls Se and Mm LGE	-	BB, ACE inhibitor	CR
Minocha [20]	45	17/M	1d	BNT 162b2 mRNA vaccine (Pfizer)	Mid lateral and apical lateral LV walls Se LGE	-	NSAIDs	CR

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Table 1 (*continued*)

First Author [Ref]	Case No.	Age/ gdr	Day(s) Post-vac	COVID-19 vac (Brand/types)	Cardiac MRI	Echocardiogram (Echo) or biopsy (Bx)	Treatment	Outcomes
Williams [21]	46	34/M	1d	mRNA-1273 vaccine (Moderna)	Mid anterolateral and inferolateral LV walls Se LGE and patchy My OE	Echo: Reduced ejection fraction (43%)	Aspirin, Colchicine, BB, ACE inhibitor	CR
Kim [22]	47	24/M	1d	BNT 162b2 mRNA vaccine (Pfizer)	Basal inferior and inferolateral LV walls Se LGE and OE	-	-	CR
King [23]	48	23/F	5d	mRNA-1273 vaccine (Moderna)	Basal inferior, basal to mid inferolateral, mid anterolateral, apical lateral, apical septal, and apical inferior LV walls Se LGE	Echo: Basal inferior and basal inferolateral hypokinesis	-	CR
Patel [24]	49	22/M	2d	BNT 162b2 mRNA vaccine (Pfizer)	Basal inferior, basal inferolateral and apical lateral LV walls Se LGE and My OE	-	Aspirin, Colchicine	CR
	50	19/M	1d	BNT 162b2 mRNA vaccine (Pfizer)	Basal inferolateral LV wall Se LGE	-	Ibuprofen, Colchicine	CR
	51	25/M	3d	mRNA-1273 vaccine (Moderna)	Lateral LV walls Se LGE and My OE	-	Colchicine	CR
	52	37/M	2d	BNT 162b2 mRNA vaccine (Pfizer)	Basal anteroseptal LV wall Se LGE and My OE	-	-	CR
	53	20/M	3d	BNT 162b2 mRNA vaccine (Pfizer)	1. Lateral LV walls Se and Mm LGE 2. Mid and apical lateral LV walls My OE	-	Colchicine, Ibuprofen, BB, ACE inhibitor	CR
Hasnie [25]	54	22/M	3d	mRNA-1273 vaccine (Moderna)	1. Mid and apical lateral and inferior LV walls Se LGE. 2. Mild adjacent Pc LGE	Echo: Mid to apical anterior and anterolateral LV hypokinesis	Aspirin, Colchicine, BB	CR
Current	55	21/M	4d	mRNA-1273 vaccine (Moderna)	Basal inferior, basal inferolateral, mid inferolateral LV walls Se and Mm LGE	-	Colchicine, Ibuprofen	CR

BNT, BioNTech; CR, complete recovery; d, day/days; gdr, gender; F, female; M, male; MRI, Magnetic resonance Imaging; LV, left ventricle; vac, vaccination; My, myocardial; Mm, mid-myocardial; Ep, epicardial; Se, subepicardial; Pc, pericardial; LGE, late gadolinium enhancement; OE, oedema; HI, hyperintensity; BB, beta-blocker.

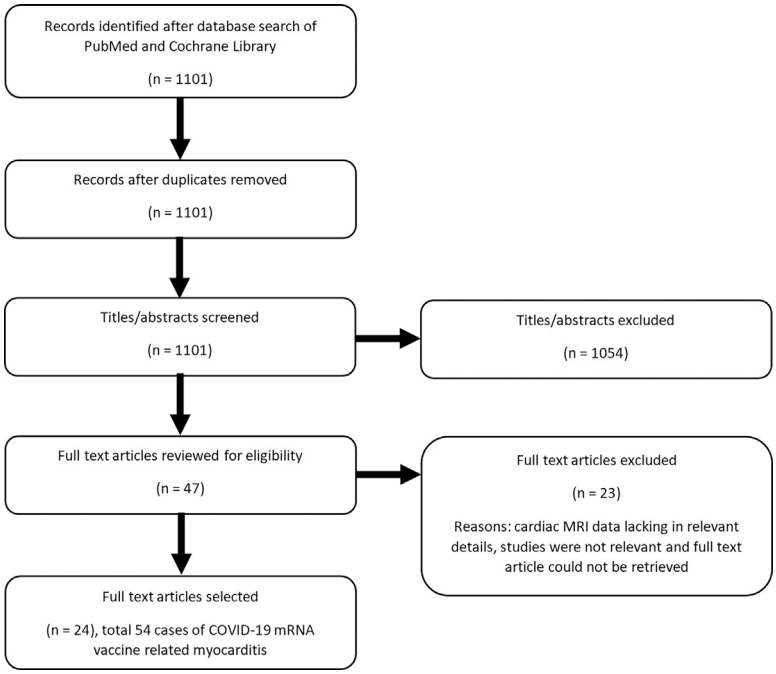

Fig. 1 – PRISMA flowchart for identification and selection of COVID-19 mRNA related myocarditis studies.

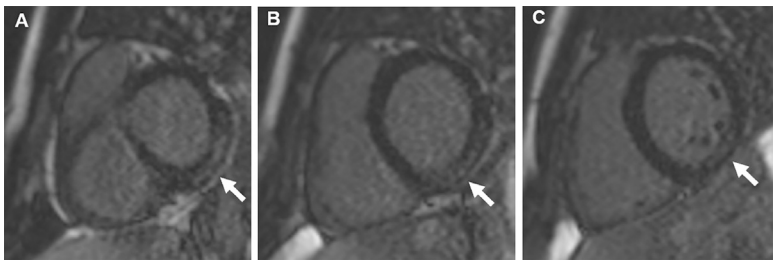

Fig. 2 – A 21-year-old male diagnoses with COVID-19 mRNA vaccine-related myocarditis. Representative images of Late Gadolinium Enhancement (LGE) phase of the short axis views of conventional cardiac magnetic resonance reveal LGE of the subepicardial and mid-wall of the basal inferolateral (A), basal inferior (B) and mid inferolateral (C) segments of the left ventricle.

immune-mediated reaction [30]. Additionally, researchers have suggested that genetically predisposed individuals may exhibit an immune response to the mRNA components, although modifications in the nucleosides of the mRNA vaccine have been shown to reduce its immunogenicity [31].

In terms of imaging, diagnosing myocarditis is crucial for effective management, and typical tissue characteristics observed in cardiac MRI (CMR) are considered one of the diagnostic criteria [32]. CMR is a non-invasive and low-risk alternative to endomyocardial biopsy, which is the gold standard for diagnosing myocarditis. CMR is also valuable for ruling out other conditions with similar presentations, such as ischemic heart disease or stress-induced cardiomyopathy [33]. While CMR is the primary imaging modality for myocarditis diagnosis, dual-energy iodinated contrast-enhanced cardiac CT scans can also be useful. Late iodine enhancement on CT has been found to correspond well with delayed contrast enhancement observed in CMR, which can aid in evaluating myocardial delayed enhancement patterns in cardiomyopathies, including myocarditis [34].

The MRI features of acute myocarditis are based on the Lake Louise Criteria (LLC), which were revised in 2018 [35]. These criteria involve T2-based markers of myocardial edema and T1-based markers of myocardial damage. These include regional high T2 signal intensity, a global T2 signal intensity ratio of $\geq$2.0 on T2-weighted images, and regional or global increases in myocardial T2 relaxation time. T1-based criteria encompass regional or global increases in intrinsic T1 myocardium or extracellular volume, or late gadolinium enhancement in a non-ischemic distribution. These criteria have demonstrated a sensitivity of 87.5% and specificity of 96.2% for acute myocarditis [26]. However, specific CMR features or patterns unique to COVID-19 mRNA vaccine-related myocarditis have not yet been conclusively identified.

Regarding treatment and prognosis, COVID-19 mRNA vaccine-related myocarditis is typically self-limiting, with

supportive care as the primary treatment, as indicated by recent case series [30]. Treatment often involves a short course of nonsteroidal anti-inflammatory drugs (NSAIDs), colchicine, and steroids, with only a few cases requiring aspirin and intravenous immunoglobulins [30]. Most patients remain hemodynamically stable, without significant left ventricular systolic dysfunction or arrhythmias [30]. However, for those with left ventricular systolic dysfunction, β-blockers and angiotensin-converting enzyme inhibitors are initiated, following current heart failure guidelines [31–32]. Although rare, cases complicated by hemodynamic compromise or new-onset arrhythmias may require cardiac or intensive care support [32]. It is generally recommended to limit physical or sporting activities for at least 3 to 6 months after the resolution of clinical symptoms [23].

While long-term data on COVID-19 mRNA vaccine-related myocarditis is limited, short-term outcomes appear more favorable compared to viral-related myocarditis. Symptoms in mRNA vaccine-related cases have a shorter onset and faster recovery [36]. In contrast, viral myocarditis often follows a variable and unpredictable course, with a study by Ghelani et al. reporting that nearly 6% of adolescents with viral myocarditis resulted in mortality or necessitated heart transplantation [37].

Finally, differential diagnoses for myocarditis include other conditions such as viral myocarditis, acute giant cell myocarditis, eosinophilic myocarditis (EM), autoimmune myocarditis, and cardiac sarcoidosis. While CMR features for COVID-19 mRNA vaccine-related myocarditis are mostly nonspecific, these other differential diagnoses may exhibit specific patterns of distribution based on clinical presentation and CMR findings [26].

Viral myocarditis

Viral myocarditis predominantly affects young individuals and exhibits a particular vulnerability in children, pregnant women, and immunocompromised individuals [38]. Patients often report a preceding viral syndrome involving the respiratory or gastrointestinal tract before the onset of cardiac symptoms [39]. While most cases remain benign and subclinical, some may present as severe acute heart failure or infarct-like acute myocarditis, with a higher incidence in males, ST-elevation on ECG, and elevated cardiac biomarkers [26]. Cardiac magnetic resonance imaging (CMR) findings in viral myocarditis frequently reveal myocardial damage (T1-based) and edema (T2-based) in the subepicardial layers, primarily affecting the lateral and inferolateral wall of the left ventricle [26]. In cases of infarct-like acute myocarditis, MRI typically displays widespread myocardial edema and often presents with patchy late gadolinium enhancement (LGE) in the inferolateral distribution [40].

Acute giant cell myocarditis

Acute giant cell myocarditis is characterized by its rapid progression and can necessitate heart transplantation in severe cases [41]. Clinical features encompass acute heart failure, cardiogenic shock, ventricular arrhythmias, and atrioventricular block [42]. Timely diagnosis is paramount, as immediate treatment with immunosuppressive agents can potentially improve patient outcomes [41]. A published case series on cardiac magnetic resonance (CMR) findings in giant cell myocarditis has revealed a widespread pattern of late gadolinium enhancement (LGE) affecting all layers of the myocardium [43]. This pattern appears to correspond to the extensive inflammation and fibrosis observed histologically. Additionally, CMR may reveal a moderate to severe reduction in left ventricular systolic function, consistent with the clinical presentation of heart failure [43].

Eosinophilic myocarditis

EM constitutes a rare subtype of myocarditis, accounting for only 0.1% of biopsied myocarditis cases. Treatment for EM depends on its underlying cause, which may include hypersensitivity or allergic reactions, drug-induced reactions, infections, malignancies, vasculitis, and hypereosinophilic syndromes [44]. While the presence of eosinophilia may strongly suggest EM, definitive diagnosis relies on endomyocardial biopsy, which typically exhibits eosinophilic infiltration of the myocardium. CMR findings in EM usually show subendocardial late gadolinium enhancement (LGE), which can manifest as patchy or diffuse in a non-ischemic distribution. These findings may correspond to areas of subendocardial hypodensities visible on cardiac CT scans [44].

Autoimmune myocarditis

Autoimmune myocarditis can manifest either with exclusive cardiac involvement or within the context of autoimmune diseases presenting with extracardiac manifestations. It is common in conditions such as sarcoidosis, systemic sclerosis, rheumatoid arthritis, and systemic lupus erythematosus (SLE) [32]. A negative viral PCR, with or without the presence of serum cardiac antibodies, is a key diagnostic criterion. In rheumatoid arthritis, CMR typically reveals diffuse or focal fibrosis and myocardial inflammation, resulting in larger areas of T2-based markers for myocardial edema, elevated native T1 and ECV, and focal mid-wall LGE [45]. Similarly, CMR can detect early myocardial fibrosis in systemic sclerosis, featuring mid-wall LGE primarily in the basal and mid-septal regions and at right ventricular insertion sites, as well as pericardial involvement, such as pericardial effusion or pericardial LGE [46]. In SLE, high T2 signal intensity ratio and early gadolinium enhancement demonstrate significant correlations with disease activity [47]. Furthermore, CMR angiography can assist in detecting abnormal coronary arterial wall contrast enhancement [48].

Cardiac sarcoidosis

Cardiac sarcoidosis arises when sarcoidosis involves the heart. Although autopsy studies have found cardiac involvement in 25% of sarcoidosis cases, only 5% appear to be symptomatic [49]. Clinically significant cardiac sarcoidosis carries high mortality rates, accounting for 13%-25% of sarcoidosis-related deaths in the United States [50]. CMR findings are contingent on the disease's time course, which holds clinical relevance since early-phase treatment with steroids or

immunosuppressive agents can improve patient outcomes. In the acute phase of myocardial inflammation, typical CMR manifestations include thickened myocardium with high T2 signal intensity indicating myocardial edema, mid-wall and subepicardial LGE at the basal septal and lateral segments as dominant features [51]. In the chronic phase, noncaseating granulomas form in the myocardium, accompanied by patchy and nodular areas of LGE with less intensity than the acute phase [51]. Myocardial thinning may also be observed in some cases. 18F FDG PET is a useful imaging modality, often revealing focal FDG uptake indicative of active inflammatory sarcoidosis. Conversely, the presence of a perfusion defect without FDG uptake suggests myocardial fibrosis and scarring [50].

Other less common causes of myocarditis encompass bacterial or fungal infections, drug-induced myocarditis, and idiopathic (unknown) etiologies. The diagnosis of myocarditis can be intricate, often necessitating a combination of clinical, laboratory, imaging, and histological findings.

Conclusion

In conclusion, COVID-19 mRNA vaccine-related myocarditis should be considered in patients presenting with myocarditis symptoms shortly after receiving a COVID-19 mRNA vaccine. While characteristic CMR findings, such as subepicardial LGE and T2-based myocardial edema, are often observed, they lack specificity and can mimic other myocardial conditions. The primary treatment approach involves supportive care, typically including a short course of NSAIDs, colchicine, and steroids, with some cases requiring aspirin and intravenous immunoglobulins. Fortunately, most patients with vaccine-related myocarditis exhibit a self-limiting clinical course and achieve favorable short-term outcomes.

However, it is essential to acknowledge that other forms of myocarditis may manifest with more severe or unpredictable courses. Therefore, ensuring a timely and accurate diagnosis remains critical for the optimal management of these patients. As our understanding of COVID-19 mRNA vaccine-related myocarditis continues to evolve, ongoing research and surveillance are necessary to refine diagnostic criteria and treatment strategies for this condition.

Patient consent

Informed consent was obtained from the patient for publication of this case report and accompanying images.

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