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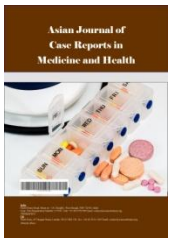

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Case Study of COVID-19 Vaccine-Associated Myocarditis

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

COVID-19 mRNA vaccines have serious side effects, including myocarditis; it's an uncommon but dangerous side effect following mRNA-based COVID-19 immunization. Herein we report a 45-year-old female presenting with myocarditis seven days after the second dose of Pfizer-BioNTech vaccine, yet to recover three months later with guideline-directed medical treatment. COVID-19-associated myocarditis was evaluated and treated similarly to typical myocarditis with reduced ejection fraction heart failure, after exhausting other possible different etiologies. Here we illustrate various causes of myocarditis, contrasting diagnostic approaches, prognosis, and solidating management guidelines.

Keywords: COVID-19 vaccine; COVID-19 induced myocarditis, COVID-19.

1. INTRODUCTION

Myocarditis is an inflammation of the myocardium with necrosis and/or degeneration, which can be caused by infectious or non-infectious causes [1]. The clinical presentation and course of myocarditis are variable, with some patients not requiring therapy. In contrast, others are afflicted with serious cardiac failure necessitating a heart transplant or leading to death [2]. Most myocarditis findings demonstrate a male preponderance and a median age of 42

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for individuals with lymphocytic myocarditis [3-6]. Despite the uncertainty of myocarditis' etiology, several diseases, infections, and drugs can lead to the condition [7]. The COVID-19 mRNA vaccines, including Pfizer-BioNTech and Moderna, cause myocarditis, among other serious side effects. Myocarditis is an uncommon but dangerous side effect, especially in teenage and young men following mRNA-based COVID-19 immunization [8]. COVID-19 vaccine-associated myocarditis cases were first evaluated and treated similarly to typical myocarditis cases. Supportive care was a cornerstone of treatment with particular cardiac or critical care treatments, indicated by the patient's clinical status [9,10,11].

2. CASE REPORT

45-year-old female medically free, presented to the outpatient cardiology clinic, with palpation and dyspnea for three months, worsened for which she sought medical attention. These symptoms were associated with orthopnea, abdominal distention, and lower limb swelling. However, she denied chest pain. These symptoms and signs were noticed after receiving the second dose Pfizer COVID-19 vaccine. The collection of symptoms and signs necessitated urgent admission for further workup and optimal medical care. Her vital signs revealed Blood pressure of 102/73 mmHg, heart rate of 84 beats per minute, regular respiratory rate, temperature, and O2 saturation of 97% on room air; the rest of the physical examination was unremarkable, apart from mild inspiratory fine crackles at the bases of lungs, and bilateral lower limb edema. Electrocardiogram (ECG) (Fig. 1) showed normal sinus rhythm, with left bundle branch block, while Echocardiogram reported severely dilated cardiomyopathy.

(Fig. 2A) with an Ejection fraction of 28%, diastolic dysfunction, moderate mitral insufficiency, severe tricuspid insufficiency, and severe pulmonary hypertension. Laboratory panel, including cardiac markers, thyroid function, complete cell count, renal function, electrolytes, connective tissue work-up, and viral serology within normal limits. COVID-19 antigen test was negative. BNP 791.4 m/mol

Myocardial perfusion imaging was done to exclude the possibility of ischemia-induced cardiomyopathy. There was no evidence of stress-induced ischemia. However, both post-stress and rest scans showed significantly reduced left ventricular function with global hypokinesia and dilated cardiac cavity (Fig. 3). Delayed Myocardial enhancement was reported on Cardiac MRI (CMR), validating the diagnosis of myocarditis. Heart failure with reduced ejection fraction (HF-rEF) guidelines directed medical therapy (GDMT) was initiated achieving symptom control and a euvolemic state with an intravenous diuretic.

The patient dramatically improved clinically and was discharged home, and was seen on regular bases as an outpatient, with close monitoring of GDMT regimen, renal, and electrolyte status. She responded favorably to treatment, and a follow-up Echocardiogram three months later showed restoration of Left ventricular size, function, and valvular lesions (Fig. 2B). She is continued on Heart failure with a preserved ejection fraction (HF-pEF) regimen.

3. DISCUSSION

"Myocarditis, as defined by the World Health Organization (WHO)/International Society and Federation of Cardiology (ISFC) in 1995, is the inflammation of the heart muscle, diagnosed by established histological, immunological, and immunohistochemical criteria" [12]. "Symptoms of myocarditis may vary, from asymptomatic cases to presentations with myocardial infarction to devastating conditions with cardiogenic shock. Moreover, acute or chronic heart failure (HF) and chest pain are possible during the disease" [13]. Our patient came with acute heart failure presentation in the form of orthopnea, ascites, and lower limb swelling.

Infectious agents, systemic diseases, drugs, and toxins may cause myocarditis. Viral myocarditis is often suspected when a recent febrile illness is accompanied by myalgias and is rapidly followed by cardiac symptoms [14].

A multitude of published studies have shown that adolescent and young adult males may experience and develop symptoms of myocarditis following COVID-19 mRNA vaccinations (Pfizer-BioNTech, Comirnaty, Moderna Spikevax), two to seven days after the second dose. As of March 4, 2022, there were 1,886 reports of myocarditis/pericarditis to the Public Health Agency of Canada and Health Canada, of which 1,192 occurred following Pfizer-BioNTech Comirnaty COVID-19 vaccination at a rate of 2.18 events per 100,000 doses [15-17].

Our patient started to have the symptoms after the second dose of the Pfizer-BioNTech vaccine by seven days which is like most published studies.

“Enteroviruses, particularly Coxsackie group B viruses, may cause direct cardiotoxic injuries, cytokine activation, cytoskeletal damage, or autoimmune response” [7]. Approximately 1.6% of people with DCM have HIV type 1 (HIV-1) infection, which causes cytokine activation and progressive tissue damage in myocardial cells [18]. In 75% of people with giant cell myocarditis (GCM), a rare disorder of unknown etiology, heart failure progresses rapidly over days or weeks [5].

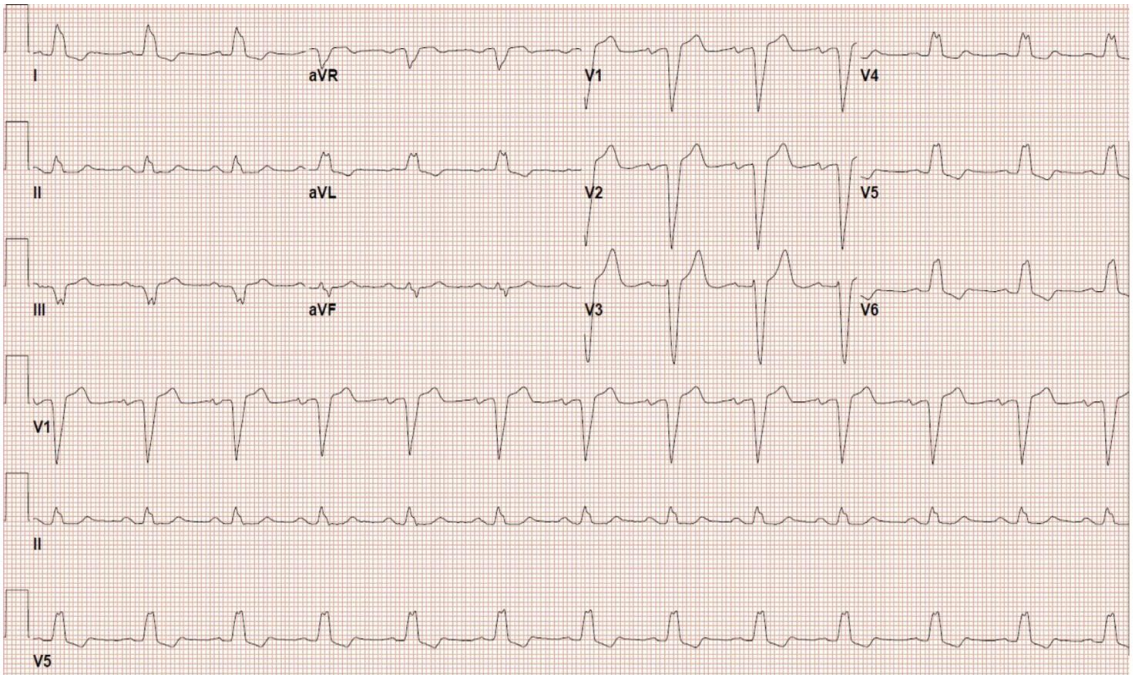

Fig. 1. ECG. with NSR and LBBB/LAD

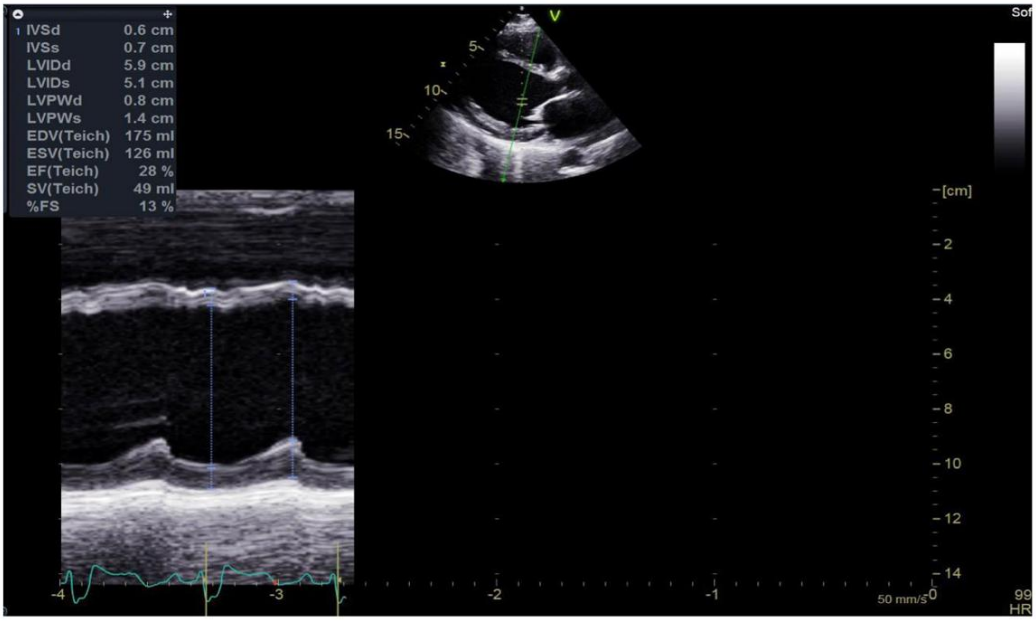

Fig. 2A. M-mode acroos the LV, Dilated LV with reduced EF

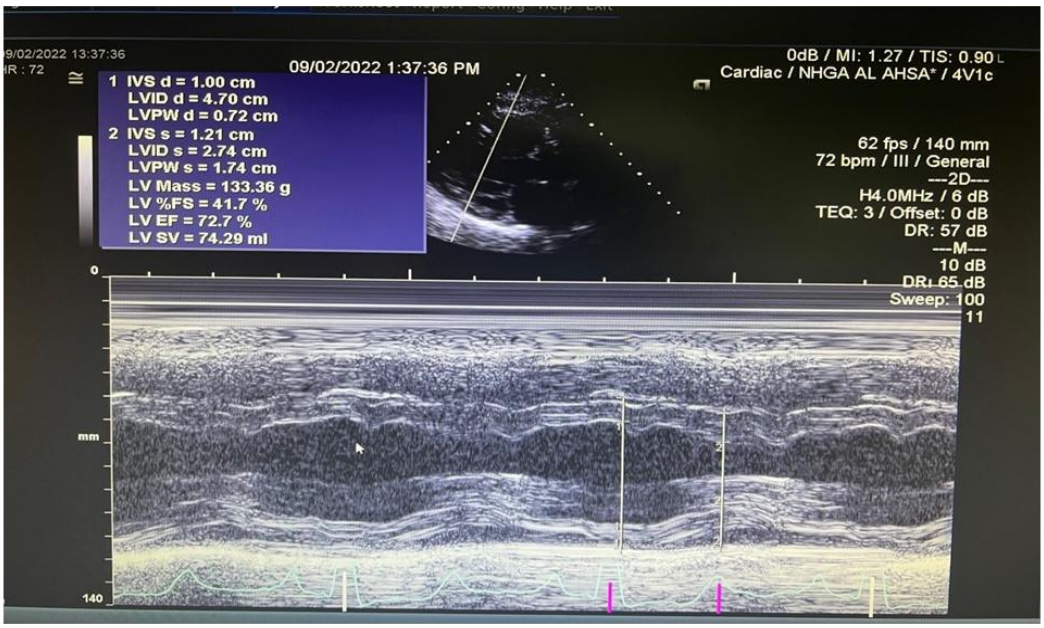

Fig. 2B. M-mode across the LV; Normal LV dimension with normal EF

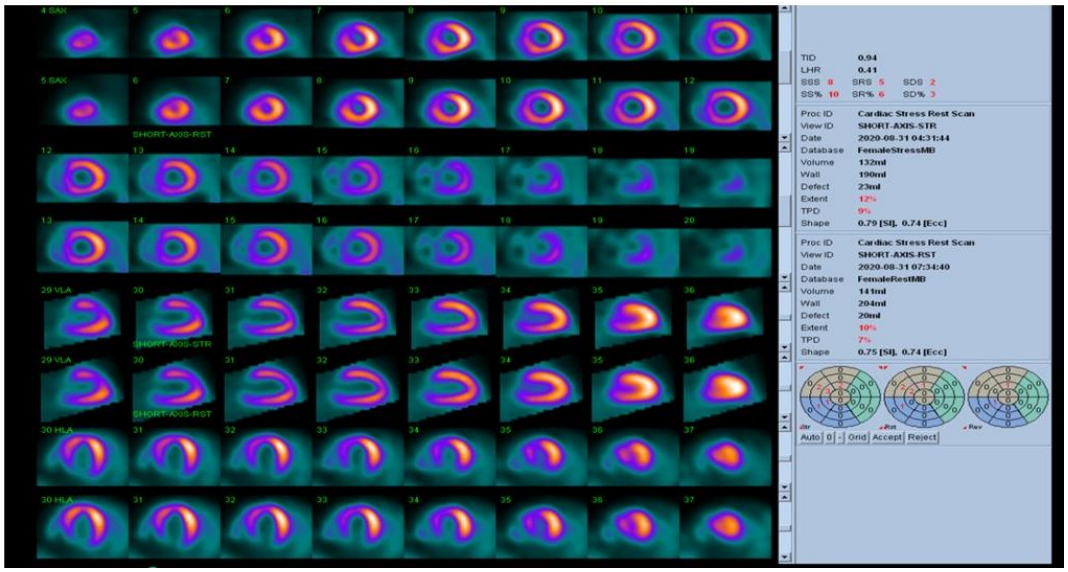

Fig. 3. Myocardial perfusion study; dilated LV in rest and post stress images, no perfusion defect

Idiopathic hyper-eosinophilic syndrome is associated with eosinophilic endomyocardial disease (Loeffler endomyocardial fibrosis), which results from direct eosinophil granule protein damage within the heart [19]. Medical therapy and cardiac transplantation often fail to treat autoimmune disorders that cause myocarditis, such as sarcoidosis, systemic lupus erythematosus, and polymyositis [14]. The incidence of immune checkpoint inhibitor-induced myocarditis is approximately 1.9% among patients treated with ICI, with an onset date of 34 days after treatment [20].

Myocarditis is commonly characterized by leukocytosis (often lymphocytic), although eosinophilia may suggest hypersensitivity (eosinophilic) myocarditis [1]. Furthermore, myocarditis can be detected by elevated acute phase reactants such as erythrocyte sedimentation rate or ultrasensitive C-reactive protein, but they have low specificity [21].

Cardiovascular markers and enzyme elevation such as cardiac troponins and creatine kinase are not specific to myocarditis; however, their absence does not exclude myocarditis [22,23]. Rheumatologic screening to send for antinuclear antibodies and rheumatoid factor is inducted if clinically suspected systemic lupus erythematosus, Polymyositis, Wegener granulomatosis, or Scleroderma [24]. A blood workup screening was ordered for our patient for all suspected viral infections and autoimmune diseases, which returned negative. Inflammatory and cardiac markers were standard as well.

All patients with clinically suspected myocarditis should undergo a 12-lead ECG. Although the ECG is only approximately 47% sensitive to detecting myocarditis, it may uncover sinus tachycardia or other ischemia-related abnormalities, non-specific ST-segment and T-wave [1,24]. Transthoracic echocardiography should also be performed for the purpose of excluding alternative causes of heart failure, detecting intracardiac thrombi and associated valvular disease, and assessing left ventricular dysfunction (LVD). During hospitalization, if the patient's hemodynamic status worsens, the echocardiogram should be repeated [7,25]. In addition, nuclear imaging antimyosin scintigraphy (indium III monoclonal antimyosin antibodies) is effective at detecting myocardial inflammation with 91% sensitivity and 93% negative predictive value, but has low specificity (32%) [7].

Our patient's ECG upon diagnosis showed normal sinus rhythm, with left bundle branch block. At the same time, Echocardiogram reported severely dilated cardiomyopathy (Fig. 2A) with an Ejection fraction of 28%, diastolic dysfunction, moderate mitral insufficiency, severe tricuspid insufficiency, and severe pulmonary hypertension. Myocardial perfusion imaging was done to exclude the possibility of ischemia-induced cardiomyopathy. There was no evidence of stress-induced ischemia. However, both post-stress and rest scans showed significantly reduced left ventricular function with global hypokinesia and dilated cardiac cavity (Fig. 3).

"Myocarditis may mimic myocardial infarction (pseudoinfarct pattern) in its clinical presentation, especially if there are focal wall motion abnormalities and localizing electrocardiographic changes. Thus, Coronary angiography is often indicated to exclude coronary artery disease as the cause of new-onset heart failure" [24]. "The American Heart Association recommends the use of CMR imaging to diagnose myocarditis as a noninvasive method in its scientific statement as Class IIB, level of evidence C" [26] "which was conducted in our patient and supported myocarditis as a primary diagnosis and cause of patient's presentation. Endomyocardial biopsy (EMB) is not a routine practice. Still, it remains the gold standard in diagnosing myocarditis, identifying the underlying etiology and the type of inflammation (e.g., giant cell, eosinophilic myocarditis, sarcoidosis). Results frequently impact the therapy of the patient" [4]. EMB should be considered when cardiac function quickly deteriorates for unknown reasons and standard medical therapy does not seem to help [7]. EMB was not considered in our patient as her clinical condition improved, and she responded to treatment.

Depending on the etiology, clinical presentation, and disease stage, myocarditis outcomes and prognoses can be very different. In the acute phase, patients are advised to avoid vigorous exercise for at least six months, if not longer depending on the LV function. Although the duration of abstinence from competitive sports after recovery from acute myocarditis is still debatable [27].

"Patients with myocarditis and acute dilated cardiomyopathy should be managed according to the current guidelines from the American Heart Association, the American College of Cardiology, and the European Society of Cardiology. Angiotensin-converting enzyme inhibitors, beta-blockers, and aldosterone antagonists are standard treatments for heart failure" [9]. "Patients with apical aneurysms with thrombus (e.g., Chagas disease, atrial fibrillation, and prior embolic episodes) usually receive anticoagulation to prevent thromboembolic events" [28]. "First-line therapies for arrhythmia management include b-blockers, amiodarone, and sotalol. Permanent pacemakers are used for heart block or bradyarrhythmia" [29]. "The insertion of implantable cardioverter-defibrillators (ICDs) is indicated for patients in the chronic phase with persistently low ejection fraction and those with malignant arrhythmias that are refractory to medical therapy. Cardiac resynchronization therapy with defibrillator function is indicated for patients with impaired LV function (ejection fraction <_ 35%) and left

bundle branch block in New York Heart Association (NYHA) functional class II-IV" [9].

In cardiogenic shock due to acute myocarditis, particularly in fulminant myocarditis, where the hemodynamic status of the patient is severely compromised, inotropic therapy with milrinone, dobutamine, or mechanical circulatory support, including extracorporeal membrane oxygenation (ECMO) or mechanical assist devices (LV assist devices) for hemodynamic support and afterload reduction may provide a bridge to transplant or recovery [27].

"The vast majority of patients with myocarditis recover completely, but the prognosis depends on several factors, including clinical presentation, clinical parameters, and EMB findings. Myocarditis with preserved LV function has a good prognosis and is associated with a high rate of spontaneous recovery" [13]. "Current guidelines for myocarditis recommend discharging patients when cardiac markers have normalized, while high-risk patients may be observed slightly longer and followed as outpatients in shorter intervals, as we have recently demonstrated that disease activity may persist even when cardiac markers have normalized" [30]. "One- to three-month clinical follow-up examinations are recommended after diagnosis to adjust standard heart failure medication. Serial echocardiographic assessment of ventricular structure and function is often performed, although there are no definitive guidelines regarding the required intervals of echocardiographic estimates after myocarditis" [9,24,27]. Our case improved clinically and was seen on regular out-patient follow-up, closely monitoring GDMT regimen, renal, and electrolyte status.

4. CONCLUSION

COVID-19 mRNA vaccinations (Pfizer-BioNTech, Comirnaty, Moderna, and Spikevax) have demonstrated myocarditis as an apparent side effect, with profound heart failure symptoms and signs. Most of these patients with myocarditis recover completely. While the outcome and prognosis of myocarditis depend solely on etiology, clinical presentation, and disease stage, adopting Heart failure reduced ejection fraction management guidelines substantially impacts myocarditis outcomes. We add another case of COVID-19 myocarditis to the literature, with complete restoration of Left ventricular size, function, and valvular lesions after three months of treatment.

CONSENT

Written informed consent was obtained from the patient for publication.

ETHICAL APPROVAL

The study was approved by King Abdullah International Medical Research Center (KAIMRC).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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