**A Case Series on Myocarditis after COVID-19 Vaccination**

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**Abstract**

Many efforts have been undertaken to develop a successful vaccine to contain the catastrophe since the COVID-19 outbreak. Early in December 2020, the SARS-CoV-2 vaccine program was initiated, and it significantly reduced transmission and mortality. However, there are cases of cardiac complications like myocarditis that have been encountered in several individuals after administrating the COVID-19 vaccine. Therefore, this present work aims to describe four cases of Myocarditis in the existing literature review. A literature search was carried out using Scopus, Science Direct, PubMed, and other renowned databases for high-quality recent individualized case reports of individuals having myocarditis after receiving the vaccine, research papers, case series, and review articles with no language restriction. The findings from the four cases and rigorous literature review revealed that myocarditis is one of the adverse reactions after COVID-19 vaccination which comes with initial symptoms of chest pain and fever which can further exacerbate if ignored. However, the use of symptomatic relief and anti-inflammatory non-steroidal drugs have been noted to be effective in managing myocarditis induced by COVID-19 Vaccinations.

**Keywords**

Case Report, COVID-19, Myocarditis, SARS-CoV-2, Vaccine

**1. INTRODUCTION**

In Wuhan, China, the “Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)” that is the cause of the “Coronavirus Disease of 2019 (COVID-19)” initially emerged. The “World Health Organization (WHO)” formally classified it as an outbreak in March 2020. All 50 states in the US have been affected by the pandemic as of 2020, which has caused 18,500 deaths and over 490,000 cases. The number of infected individuals has reached over a million. While lung and other respiratory system-related complications have received a lot of attention, emergency clinicians must be mindful of cardiovascular complications as well, since they can play a vital part in the mortality rate of the disease. Patients having acute COVID-19 infection can appear with a wide range of cardiac presentations: a few patients show no symptoms but also have abnormal cardiovascular test results (such as asymptomatic cardiac arrhythmias, abnormalities on cardiac imaging, or elevated serum cardiac troponin), or a few patients do not have any sign when others show clinical symptoms of cardiac issues. Myocardial damage, cardiac arrhythmias, cardiogenic shock, Heart failure (HF), myocarditis, pericarditis, and sudden cardiac arrest are all examples of cardiac complications. In patients having COVID-19, symptoms and signs of cardiac complications can result from the acute progression of the COVID-19 disease [1]–[4].

The body system involved in respiration is the preliminary site of infections for SARS-CoV-2, which can cause a range of clinical manifestations, going from common “asymptomatic subclinical infection” to severe “acute respiratory distress syndrome (ARDS)”; that further necessitates ventilators and admittance to the “intensive care unit (ICU)” [5], [6]. It has been well noted that pulmonary complications are the largest cause of death because of COVID-19, however, cardiovascular complications, such as 1) myocarditis, 2) endothelial dysfunction, 3) dysautonomia, 4) acute myocardial injury, 5) thrombotic events 6) arrhythmias and 7) cardiac fibrosis can also provide a significant contribution in the deaths of COVID-19. There is still much to know about the pathophysiology of cardiac manifestations in patients having COVID-19. The knowledge of heart-related manifestations of “COVID-19” is constrained due to a lack of histological data that is sufficient to fully assess cardiac pathologies, par-
particularly in conditions like myocarditis where a histological investigation is a need for the diagnosis. Additionally, existing COVID-19 therapies may have an impact on the cardiovascular system. Additionally, the existence of cardiovascular manifestations may affect how severe COVID-19 is, and underlying cardiovascular diseases can worsen mortality. Therefore, better patient care and management could result from better knowledge of the processes behind COVID-19-mediated cardiovascular disease. Apart from the cardiac complications during COVID-19 infection, there have been several cases reporting the cardiac complication after COVID-19 vaccination which is one of the main case causes of concern in context with human subjects of the SARS CoV-2 vaccines. Myocardial infarction, heart failure, myocarditis, and pericarditis are among the most observed cardiac clinical symptoms after administering the COVID-19 vaccine especially when an individual is given the COVID-19 mRNA vaccine. Hence, giving an alarm to the manufacturers and the scientist working on the vaccine production, we have reviewed four case studies reporting clinical symptoms after giving the first, second, or another booster dose of the COVID-19 vaccine[7], [8].

2. METHODOLOGY

To find publications documenting the prevalence of myocarditis following the COVID-19 vaccine, databases including “Scopus”, “Science Direct”, “Google scholar”, and “PubMed” has been searched from the latest studies from 2018 to Aug 2022. Manual screening from 20 pages of google scholar has also been carried out to search for other important and appropriate papers and then inspected manually. Data mining was then performed using selected keywords including, SARS-CoV-2, COVID-19, Corona Virus, Myocarditis, Vaccine-induced myocarditis, cardiac complications, pericarditis, and Pfizer BioNTech and the combination of the above keyword were used to find and sought on the case studies and case series documenting the cardiac complications induced from COVID-19 vaccine. Below is the block diagram representing the methodology of the present work. Figure 1 details the methodology used to carry out the study.

![Figure 1: Illustrating the Block Diagram of Methodology used to carry out the Study.](image-url)
2.1. Eligibility criteria
The search for relevant publications published between 2018 and August 2022 was conducted in the literature. There were no language limitations and all relevant case series and case reports were included. Patients with COVID-19 vaccine with or without SARS-CoV2 infection that reported cardiac complications met the eligibility requirements for this preset work. Review papers, other research papers and commentaries were also included in this study.

2.2. Study selection
Any duplicate studies were eliminated, and all research found through manual searches were included. The abstracts and titles of the records were initially screened to weed out those that were not relevant to the objective of the study. After screening out based on the abstract and title, the remaining papers were reviewed in accordance with the set exclusion and inclusion criteria.

2.3. Data Extraction
Manual retrieval of the data from selected research studies was then performed. For every record or paper, below details are extracted manually such as the basic information about the study, including title, DOI which is short form of a digital object identifier, name of the first author, and other details of the case studies like age of the presented case, previous medical history, the symptoms on presentation, physical examination findings and advanced laboratory findings, endomyocardial biopsy (EMB) findings, echocardiogram findings, electrocardiogram findings (ECG), in-hospital treatment, other health complication, and outcomes.

3. CASE REPORTS

CASE 1
A 23-year-old male with no history of CVD or other preexisting complications presented to the emergency area three days after taking the 2nd dosage of mRNA vaccine(Pfizer-BioNTech BNT16B2b2) with chest pain and fever but no respiratory problems. It is also worth noting that he was all updated with his vaccines including influenza shot which was not resulted in any kind of adverse reactions. Negative results were also found for different kind of COVID-19 tests including PCR and SARS-CoV-2 antigen.

CASE 2
Immediate, intense chest discomfort that was altered by breathing and posture and was not accompanied by dyspnea or palpitations was experienced by a Caucasian man who is 19-year-old, had no cardiovascular risk factors and prior medical history. The patient had already administered his 2nd dosage of the Pfizer vaccine three days prior. As he presented to the department, he displayed symptoms of influenza-like illness, including asthenia, or headache on the first day after the vaccine.
CRP was somewhat elevated above 50mg/ml (normal level: 6 mg/L). “Hemogram” results were normal. Creatinine phosphokinase was 399 UI/L at arrival compared to a reference level of 300 UI/L for Hs-troponin T, which was high at 600 ng/mL. At 270 ng/mL, NT pro-BNP was only slightly raised compared to the reference level of 125 pg/mL.

Testing for the influenza RT-PCR and PCR of COVID-19 were negative. The possible tool for confirmation of myocarditis after EMB, “Cardiac magnetic resonance imaging (CMR)” revealed “lateral sub-epicardial high signal intensity (SI)” and myocardial wall edema in the “LV myocardium on T2 short tau inversion recovery image”, confirming myocarditis. Additionally, the “middle to apical lateral LV segments” showed a sub-epicardial late gadolinium enhancement which was also noted in the case 1. A total of 2 of 3 Criteria of Lake Louise tissue for diagnosis of myocarditis were met by these observations. The patient had a normal ECG and echocardiogram during the one-month evaluation and further follow up, and no symptoms were present [10].

CASE 3
A 33-year-old man who had previously been in good health arrived to the emergency room reporting of recently developing substernal chest discomfort. The Janssen Ad26.COV2S vaccine had been given to him two days earlier. His chills and myalgias first disappeared 24 hours following the vaccine. What followed was a prolonged retrosternal, non-radiating chest ache, and non-exertional. The pain was determined to be positional, exertional, and not pleuritic. He had a remarkable previous medical history for obstructive sleep apnea and asthma, but no well-known heart history.

The electrocardiogram (ECG) revealed a sinus rhythm with regular times. Readings in the lab were remarkable for “High-sensitivity troponin T” which was found to be 0.041 ng/mL (reference value: 0.014 ng/mL). The CRP was revealed elevated to 40.4 mg/L (normal value, 3.0 mg/L), differential CBC was found to be normal level, and both were within the normal range. Troponin reached its highest level of 10.2 ng/mL throughout the course of 24 hours. In the left ventricle, where the scar is 2 % in size, a tiny focal area of myocarditis was seen using gadolinium-enhanced CMR imaging. No hypokinesis was observed, and overall left ventricular systolic performance was normal. Because of the high temporal correlation, myocarditis was considered to be a result of the vaccine that was given [11].

CASE 4
A 16-year-old male who had previously been in good condition arrived at the emergency department (ED) complaining of 36 hours of stabbing, acute chest discomfort. About 60 hours before his presentation, the patient had his second dosage of the “Pfizer” vaccine. The patient experienced myalgias and tactile fevers around 12 hours after the vaccine, which went away in a day. A day after taking the vaccination, the patient subsequently had sudden, severe mid sternal chest pain.

When the patient arrived at the emergency department, his clinical findings of symptoms and signs involved a BP of 112/70 mmHg, an HR of 80 bpm, a RR of 18, a temperature of 37.5 °C, and a pulse oximetry reading of 98 % on room air. Cardiovascular and respiratory tests were both normal during the physical examination. On electrocardiogram (ECG), generalized ST elevation was seen in V-2 to V-6 and I and a VL, along with normal sinus rhythm. Troponin T was increased to a level of 1,018 ng/L, creatinine kinase increased to a level of 699 U/L, and CK-MB to a level of 47.7 g/L in laboratory findings. At 111 pg/mL, the “B-type natriuretic peptide” was only slightly bitted over typical. When compared to the rest of his complete metabolic panel, his creatinine level was raised to 1.17.

Rapid SARS CoV-2 and influenza tests revealed negative outcomes. He was then diagnosed with myo-pericarditis(suspected) and hospitalized in ICU because of the risk of cardiac shock and collapses that necessitated tracking and monitoring systems of his physiological parameters while a workup and treatment were performed. The CT angiography showed mild sub-epicardial hyper-enhancement on the lateral wall, which is indicative of myocarditis. Additionally, it was discovered that he had an accidental benign coronary artery abnormality that was thought to be unconnected to his disease. CMR imaging revealed “morphology”, “normal biventricular volumes”, and “systolic function”. The presence of “myocardial fibrosis” symptoms, “myocardial fibrosis”, and a little “pericardial effusion” that may have been caused by myopericarditis were present, though.

Ibuprofen for symptom relief and the cure of chest pain was given to the patient along with a four-dose
intravenous immunoglobulin series. Other than that, he didn’t require any more treatments during his hospitalization or any supporting measures for his heart or lungs. On day three in the hospital, his ECG indicated that the ST elevation had resolved. On the sixth day in the hospital, he was released with a troponin level of 45ng/L—down from 1,693ng/L—and a downward trend (Figure 2). He was sent back to the house with just a prescription of ibuprofen and famotidine for seven days and a follow-up visit with pediatric cardiology for two weeks [12]. An overview of the findings from four detailed cases is given in Table 1.

![Figure 2: Illustrating the electrocardiograph of the 4 detailed cases of Myocarditis after COVID-19 vaccinations.](image)

Table 1
Overview of clinical, laboratory, and imaging data of the four cases.

<table>
<thead>
<tr>
<th>DETAILS</th>
<th>CASE 1</th>
<th>CASE 2</th>
<th>CASE 3</th>
<th>CASE 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Author</td>
<td>Takashi Nagasaka[9]</td>
<td>Schmitt Paul</td>
<td>Imran Sulenmankhil</td>
<td>Kelsey McLean</td>
</tr>
<tr>
<td>Age</td>
<td>23</td>
<td>19</td>
<td>33</td>
<td>16</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>Male</td>
<td>Male</td>
<td>Male</td>
</tr>
<tr>
<td>Vaccine</td>
<td>Pfizer-BioNTech</td>
<td>Pfizer-BioNTech</td>
<td>Janssen Ad26.COV2-S</td>
<td>Pfizer-BioNTech</td>
</tr>
<tr>
<td>Time from vaccination to Presentation</td>
<td>3 Days</td>
<td>3 Days</td>
<td>2 Days</td>
<td>2.5 days</td>
</tr>
<tr>
<td>Preexisting Relevant Conditions</td>
<td>None</td>
<td>None</td>
<td>Asthma, Obstructive sleep apnea, No cardiac history</td>
<td>None</td>
</tr>
<tr>
<td>Presenting Symptoms</td>
<td>Fever, chest pain</td>
<td>Acute sharp chest pain</td>
<td>Acute onset substernal chest pain</td>
<td>Sharp/stabbing chest pain</td>
</tr>
<tr>
<td>Physical Examination Findings</td>
<td>Temp; 37.8°C , BP; 106/70 mmHg RR; 18 br/min</td>
<td>Normal temperature with Normal Heart rate Others; Not Specified</td>
<td>Not Specified</td>
<td>Temp; 37.5°C HR; 80 Beats/min BP; 112/70 mmHg RR; 18 br/min</td>
</tr>
<tr>
<td>Time from Admission to Discharge or normalization of symptoms</td>
<td>7 Days</td>
<td>1 Month</td>
<td>-</td>
<td>7 days</td>
</tr>
</tbody>
</table>
Heart inflammation known as myocarditis is characterized by myocardial damage without inflammatory infiltrates and ischemic etiology. Acute myocarditis following COVID-19 vaccines was the clinical diagnosis for the above-presented cases. The diagnosis of Myocarditis in the above cases was made through EMB, cardiac MRI, or troponin levels [13]–[16]. Additionally, adverse reactions to the vaccine have been documented in some earlier studies. Numerous case reports published recently suggest that the COVID-19 vaccine may act as a myocarditis trigger. The real incidence of myocarditis cannot be accurately estimated because of differences in diagnostic criteria and case reporting. Given the decreased overall prevalence of endomyocardial biopsies in COVID-19 patients, the identification of myocarditis depends more largely on indications of CMR and myocardial damage in addition to clinical manifestations to meet the definition of myocarditis given by the CDC [17]–[19].

Myocardial injury, as evidenced by increased blood cardiac troponin levels, has been documented in up to 36% of individuals hospitalized with severe COVID-19 infection [20]–[22]. Yet, even in severe cases of myocarditis that are not related to COVID-19 and its vaccination, normal serum troponin levels have been recorded, restricting the use of troponin levels as a primary diagnostic criterion for myocarditis. The criterion for myocarditis diagnosis continues to be an endomyocardial biopsy (EMB) or direct histological examination. Myocyte injury or damage in the presence of inflammatory infiltrates is the overall definition of myocarditis according to the Dallas criteria. The incidence of myocarditis is predicted to be significantly lower than that of the reported incidence of myocardial injury based on scant histopathology research in severe COVID-19 infections [23].

In April 2021, a few rare examples of Israeli young men who developed myocarditis just after being given the “Pfizer-BioNTech mRNA” vaccine for “SARS-CoV-2” were first reported by international news networks. Since that time, several observational studies from the Europe, Asia, the Middle East, and North America have shown a connection between the mRNA vaccine and a transiently higher risk of myocarditis. What is the molecular basis connecting the SARS-CoV2 vaccine to this uncommon pericarditis and acute myocarditis cases? In addition to that, are there any effects of vaccine-induced myocarditis that are long-term in nature? Even though the effects of myocarditis and pericarditis that are long-term in nature, and associated with the vaccine are unknown, the existing understanding of the short-term clinical trajectories is comforting. After receiving the mRNA vaccine, the clinical manifestations of myocarditis have mostly been mild, and only a small number of patients have needed intensive care [24], [25]. However, one case series of adolescent patients revealed that radiographic abnormalities persisted during follow-up examinations, which might be worrying.

However, the individuals that were monitored had excellent clinical results, indicating that there was little chronic morbidity related to vaccine-associated myocarditis. However, it is essential to constantly monitor such patient groups for any increase in the number of sudden cardiac death, heart failure, or associated cardiac problems.

Although CMR is recommended for patients with normal coronary arteries, acute chest pain, and a recent systemic viral infection, the majority of cases did not receive the experiment despite showing signs of myocarditis on ECG, serology, and echocardiogram due to the challenges of getting the scan during an infectious disease outbreak. For COVID-19 vaccine-associated myocarditis patients, there are currently no long-term outcome statistics available. The CDC has launched intensive follow-up monitoring in young adults and adolescents to evaluate cardiac outcomes at 3 to 6 months as well as health and functional status.

As per the above reports and the review of existing literature, it can be seen that men are more prone to develop myocarditis post-COVID-19 vaccination than women. This suggests that the development of myocarditis associated with COVID-19 is sex more sex-dependent, therefore highlighting the need for the male community to take more and more precautions 15 days after COVID-19 vaccinations. In addition to that, it has also been observed that the Pfizer-BioNTech vaccine resulted in more cases of vaccine-induced myocarditis than other vaccines. However, normalization of the statement is still not possible because of the limitations of the study that has been used in the present work. Sharp chain pain and stubbing were found to be the most presenting symptoms in cases with probable vaccination-induced myocarditis and the most common duration after taking vaccination and the development of chain was found to be 3-5 days.
To conclude, noting the findings of vital signs and other laboratory tests, Myocarditis can be considered one of the adverse reactions to the vaccine suggesting the need to recall and validate the effectiveness and safety of the COVID-19 vaccination regardless of the manufacturer.

In addition to the above observation and findings, we can further conclude that myocarditis, an adverse reaction can further be managed by a close follow upon male individuals having COVID-19 vaccination. The most commonly used drugs to treat myocarditis are restricted to symptomatic treatments and other range of anti-inflammatory drugs.

5. CONCLUSION

Myocarditis may be an extremely unusual consequence following SARS-CoV-2 immunization. The instances mentioned herein had a moderate clinical course. The diagnostic procedures followed current recommendations and confirmed the suspicion of cardiac involvement. Based on what is now known, the advantages of vaccination exceed the hazards. As a result, widespread immunization is advised. Nonetheless, we encourage more research into the negative consequences of the new technology for the mRNA vaccine, which might be employed for the majority of vaccinations in the future.

References


