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Case report

A rare case of COVID-19 vaccine-induced myopericarditis in a young adult ☆,☆☆

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ABSTRACT

Although extremely rare, the COVID-19 mRNA vaccine can induce myopericarditis without left ventricular dysfunction, and there have been rare reports of such incidents. However, these prior cases either did not have pericardial effusion without reduced left ventricular ejection fraction or had a more typical presentation of vaccine-induced myopericarditis such as shortness of breath or tactile temperature. We present a rare case of a 25-year-old man who developed myopericarditis following administration of the second dose of COVID-19 mRNA Vaccine. As vaccination plays a significant role in the fight against the COVID-19 pandemic, it is essential to highlight the physical manifestations of the vaccine's potential adverse effects and risk factors to increase the general population's awareness regarding the importance of emergent medical care.

Introduction

In 2021 FDA has authorized the emergency use of 3 vaccines in the US: Pfizer BioNTech BNT162b2, MODERNA mRNA-1273, and J&J/Jansen Ad26.COV2 [1]. Since 2020, more than 322 million doses of COVID-19 vaccines have been administered, and very few cases have led to severe adverse effects [2]. Headache, fatigue, myalgias, and chills have been most reported among all reported side effects. In the past, there have been sporadic cases of myocarditis reported due to Hepatitis B, Influenza, and some other vaccines [3]. Newest data suggests there have been a total of 3128 cases of mRNA COVID-19 vaccine-induced myocarditis/pericarditis as of December 31, 2021. Among these cases, 560 cases were considered children aged 6-17 years, followed by 903 cases of young adults aged

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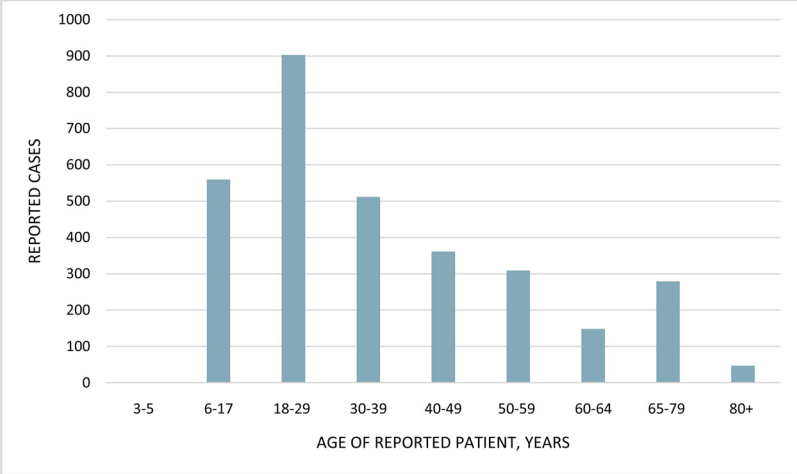

Fig. 1 – Preliminary reports of myocarditis/pericarditis to Vaccine Adverse Event Reporting System (VAERS) after mRNA COVID-19 Vaccination by age (as of December 2021).

18-29 years old (Fig. 1). Myocarditis (inflammation of myocytes) and pericarditis (inflammation of the pericardium) often occur concurrently. Myopericarditis clinically manifests as a pericardiac syndrome with minor myocardial involvement [4]. Acute pericarditis is the presence of 2 or more pleuropericarditis chest pain, diffuse ST elevation, PR depression on electrocardiogram, pericardial effusion, or pericardial friction rub on the exam. Moreover, the diagnostic evaluation algorithm for myopericarditis requires an additional feature involving elevated cardiac biomarkers, left ventricular systolic dysfunction, or myocardial inflammation confirmed by cardiac magnetic resonance [5]. Despite the existence of rare cases of vaccine-induced myopericarditis and pericarditis, the benefit-risk assessment of the COVID-19 vaccine indicates a greater benefit regarding vaccine administration for all age and sex groups [5]. Manifestation of rare side effects resulting from the COVID-19 vaccine should raise awareness and highlight the importance of emergent medical care regarding potential life-threatening vaccine adverse effects.

Case presentation

A 25-year-old Caucasian man with a past medical history of attention deficit hyperactivity disorder presented to the emergency department with flu-like symptoms of fatigue, myalgia, progressive sharp substernal chest pain that started 72 hours after administering the second dose of COVID-19 mRNA-1273 (Moderna, Inc) vaccine. There were no other associated symptoms such as shortness of breath, headache, fever, and sweating. The patient was hemodynamically stable with a temperature of 36.7 Celsius, blood pressure of 144/97 mm Hg, heart rate of 97 bpm, respiration rate of 19 breath/min, and oxygen saturation of 97% on room air. On physical exam, there was periumbilical pain and RUQ tenderness on palpation. There were no concurrent or prior COVID-19 infections as a potential source of his symptoms. The patient denied smoking and drinking with no significant family history claimed. The electrocardiography revealed diffuse ST elevation typical for pericarditis. Troponin levels were 0.75 ng/ml (normal <0.03 ng/mL), and C-Reactive protein level was 322.63 mg/L. Echocardiography revealed small to moderate pericardial effusion measuring up to 1.4 cm (Video 1). Inflammatory markers were elevated. Chest X-ray showed no radiographic evidence of any acute pulmonary disease. RUQ ultrasound was normal. ANA and dsDNA antibodies were measured to rule out any rheumatological disease. He was initially started on 650 mg aspirin TID and 0.6 mg colchicine once a day for 90 days leading to minimal improvement. Aspirin was replaced with Indomethacin with marked improvement of pain. After 5 days of hospitalization, the patient was discharged with 2 weeks of NSAID and 3 months of colchicine. At the follow-up visit 30 days later, all the inflammatory markers, WBC, and Echo were normal (Video 2).

Discussion

Many cardiovascular conditions are known to have emerged from COVID-19 infection. Although it was predicted for COVID-19 to predominantly affect the respiratory system like other types of corona Virus such as severe acute respiratory syndrome (SARS) and Middle East Respiratory Syndrome, numerous cases have been observed to affect the cardiovascular system and cause hypercoagulable state [6]. While the pathogenesis behind cardiovascular adverse effects of mRNA COVID-19 Vaccine remains unclear, it has been established that there is an association between severity and hypercoagulable condition in COVID-19 patients [6]. Moreover, the evidence suggests that immune response through dysregulated T cells can lead to disruptive clearance of SARS-CoV-2 from tissue and lead to an over-activated inflammatory response.

It has been shown that COVID-19 infected patients tend to have a higher cytokine level, suggesting activation of pro-inflammatory T-helper cells such as IFN-γ and IFN-γ inducible protein 10 (IP-10). COVID-19 mRNA vaccines are designed to encode the viral spike glycoprotein located on the virus's surface, stimulating the adaptive immune response to produce spike protein IgG antibodies. Therefore, preventing the attachment of SARS-CoV-2 to its host cell [6].

One of the proposed mechanisms leading to postvaccination myocarditis is the potential immune response to the vaccine's mRNA portion, leading to proinflammatory and immunologic pathways activation. Additionally, molecular mimicry between the spike protein in the COVID-19 virus and self-antigens is another important potential mechanism behind the development of myocarditis as part of a systemic reaction in certain individuals [6]. some researchers believe high testosterone levels among young men enhance the inflammatory response in men, increasing the number of cardiovascular incidents in this population [7]. The gold standard to diagnose myopericarditis would be to perform an endomyocardial biopsy (EMB). Although EMB is the gold standard to diagnose myocarditis, patients considered low risk may be clinically diagnosed due to its invasive nature. In one study, the CRP to troponin ratio of more than 250 was determined to have a specificity of more than 85% in differentiating myopericarditis from acute myocardial infarction. This further emphasizes the validity of myopericarditis as the final diagnosis considering the CRP/Troponin value for this patient was approximately 430 [8].

According to the American College of Cardiology, Cardiac Magnetic Resonance is recommended to confirm suspected myocarditis in patients with a higher pretest likelihood [9]. In this case, the patient was 25 years old with no significant past medical history placing him in the low-risk category. The most established risk factors associated with vaccine-induced myopericarditis are age and gender so far. According to CDC, as of December 31, 2021, there has been a total of 3128 reports of myocarditis and pericarditis on the VAERS, with most cases in the adult male of 18-29 years old and mainly after the second dose of mRNA Vaccine. It is observed that although myocarditis tends to develop more frequently in younger patients after the second dose of vaccine, pericarditis affects older patients after either the first or second dose (Fig. 2). Furthermore, in 1 study that compared the risk of cardiac events between different vaccine products, it was found that while myocarditis is potentially a life-threatening condition, most vaccine-induced myocarditis events tend to be mild and self-limited as it is in this case [10]. Data from the same study suggests that the risk of myocarditis incidence after the first and second dose of mRNA vaccine is approximately anywhere between 1 to 6 per million and 10 per million persons vaccinated, respectively. In contrast, the incidence of myocarditis following the infection with SARS-CoV-2 is estimated to be 40 per million [10]. Additionally, there has been no evidence suggesting an increased risk of postvaccination pericarditis or cardiac arrhythmias, with the exception of those who received their second dose of the mRNA-1273 vaccine [11]. However, the risk of myocarditis, pericarditis, and cardiac arrhythmia was increased following SARS-CoV-2 infection in the same population [10]. Therefore, the risk observed is much lower following mRNA vaccine administration than substantial lifetime increased risk of morbidity and mortality following SARS-CoV-2 infection [10].

Sixty-nine peer-reviewed case reports and case series published in 2021 were analyzed, among which there were 207 cases of myocarditis/myopericarditis reported. One hundred ninety-nine cases (96.1%) presented with chest pain in approximately 3 days (median time from vaccination to symptom onset) along with the feeling of fever (79 cases) and headache (38 cases), unlike this case that presented with isolated chest pain. The majority of reported cases had increased troponin (99.5% of cases), white blood cells, C-reactive protein levels (90.1% of cases), and diffuse ST-segment elevation on ECG, as observed in this case. While transthoracic echocardiogram showed normal left ventricular ejection fraction (LVEF) in most cases, 38 cases reported LVEF$<$50%, and only 10 cases reported minimal or mild pericardial effusion [5]. Although myopericarditis, in this case, manifested with normal ejection fraction (65%), it also showed moderate pericardial effusion of up to 1.4 cm that is not observed in other reported cases with LVEF$>$50% [5].

In the case report by Badshah et al., myopericarditis has been reported after the injection of the second dose of the MODERNA mRNA-1273 Vaccine in a patient with a subclinical autoimmune predisposition [12]. This autoimmune predisposition was suggested by elevated anti-nuclear antibodies (ANA) and anti–Sjogren's syndrome-related antigen A autoantibodies titers. Interestingly, the case being reported mutually showed elevated ANA titers, but unlike Badshah et al.'s case, it was negative for all other possible autoimmune disease antibody markers ruling out the potential impact of subclinical autoimmune predisposition on vaccine-induced myopericarditis in this case. In another recent case report from Korea, a 29-year-old male was diagnosed with myopericarditis after the second dose of the Pfizer-BioNTech COVID-19 vaccine [13]. According to Kim et al., this is "the second recognized case of Pfizer-BioNTech COVID-19 vaccine-induced myopericarditis in Korea and the first to have recovered from it" [13]. This case is similar to the case being reported in the sense that both patients revealed pericardial effusion with normal LVEF. Although Kim et al.'s case also reveals a pericardial effusion of 3.5 mm (vs 14 mm in this case), the patient has received the Pfizer-BioNTech COVID-19 vaccine, which makes it different from the case being reported. Data suggests individuals who received the BNT162b2 vaccine, especially the second dose, are more susceptible to myopericarditis than those who received the mRNA-1273 Vaccine, unlike this case [5].

Further investigation is required to identify the vaccines association with the severity of pericardial effusion in vaccine-induced myopericarditis. CDC advises against receiving a subsequent dose of mRNA COVID-19 Vaccine (eg, Booster shot) in individuals with a history of mRNA Vaccine-induced myocarditis/pericarditis. This is due to the lack of sufficient safety data available [14]. However, administration of a subsequent dose of mRNA COVID-19 vaccine may be considered in certain circumstances for this population, such as the increased personal risk of severe acute COVID-19 or increased level of COVID-19 community transmission [14]. Myopericarditis due to the COVID-19 vaccine is treated with empirical anti-inflammatory therapies. It is suggested to treat myopericarditis in these cases with doses typically recom-

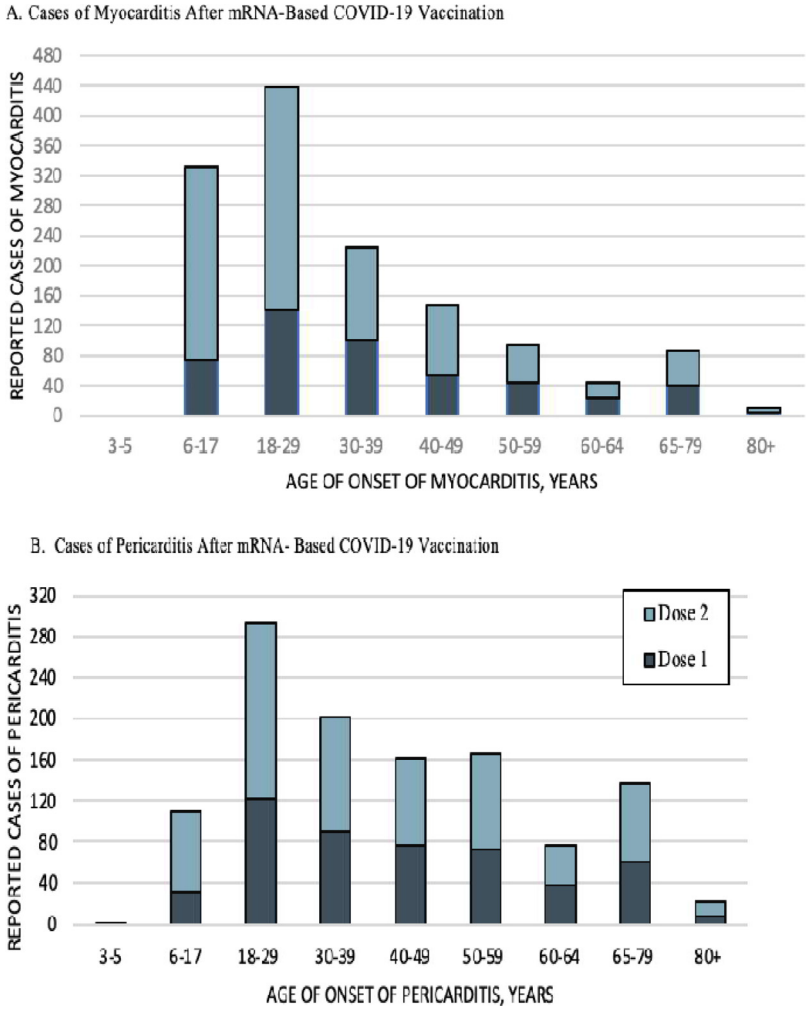

Fig. 2 – The reports to the VAERS met the case definition of myocarditis and pericarditis (reported cases). Among individuals older than 80 years of age, there were no more than 5 reports of myocarditis for any individual age and there were no more than 14 reports of pericarditis for any individual age.

mended for acute pericarditis. The first line of treatment for most patients is a combination of Aspirin (650-1000 mg) or Ibuprofen (600-800 mg), or Indomethacin (25-50 mg) for 1-2 weeks plus Colchicine (0.5-0.6 mg) for 3 months [15].

Conclusions

In summary, the important implication from this case as the adverse effects of mRNA Vaccines are being further investigated is to highlight the low incidence of myopericarditis due to COVID-19 vaccination. This means the benefit of vaccination is far greater than the risk of such a cardiovascular condition [6]. With that being said, the health care community and the people receiving the vaccine should have a very low tolerance for any adverse event post-vaccination. It is critical to report any adverse reaction due to vaccination to investigate further the association between the COVID-19 vaccine and the risk of myopericarditis in adults and any long-term outcome associated with this incident.

Patient consent

Written informed consent for publication was obtained from the patient.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.radcr.2022.03.039.

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