

Reviewer: 04323513

Manuscript titled “Pericarditis Following Covid-19 Vaccination: A Review of Two Cases and Current Literature” by authors Justyna Fydrych et al. evaluates 2 cases of pericarditis after Moderna Covid-19 vaccine and reviews the current literature. Authors identify that pericarditis as a complication of COVID-19 vaccines of various brand and technology is not rare; however outcome studies or case series are not available at this moment. Besides, for the second case, there are shortfalls:

1. The electrocardiogram (ECG/EKG) does not show the typical patterns of acute pericarditis i.e. diffuse ST elevations with PR depressions. Comparatively, the ECG of the first case shows diffuse ST elevations with PR depressions in lead II nicely.
 - Normalization of the ST and PR segments occurs within hours to days after the onset of the symptoms. Since the patient presented a week post-vaccine and after several days of symptoms, it’s possible ST elevations and PR depressions had resolved. This is addressed in the discussion on page 11.
2. As the authors also point out in the discussion part, the second case has had a previous diagnosis of Covid-19, so it is possible that myopericarditis is result of active infection, rather than vaccination.
 - As the reviewer states, this is addressed in our discussion on pages 12-13. “Our patient cases do have inherent limitations. In the second case, since the patient reported a previous diagnosis of Covid-19, it is impossible to completely rule out myopericarditis as a complication from acute infection. Covid-19 test results could not be found in the electronic medical record, so the exact date of infection is unknown; however, he tested negative for active infection on admission. To our knowledge, neither patient has received the second immunization in the series; therefore, we are unable to assess outcomes when re-challenged with the second dose.” Additionally, we point out that “...both patients scored a 5 on the Naranjo Algorithm, or Adverse Drug Reaction Probability Scale, resulting in a probable association. The reaction “followed a reasonable temporal sequence after a drug, followed a recognized response to the suspected drug, was confirmed by withdrawal but not by exposure to the drug, and could not be reasonably explained by the known characteristics of the patient’s clinical state.””
3. Beside clinical presentation, ECG and echocardiogram, authors should consider other investigations to further delineate the diagnosis e.g. cardiac MRI shows pericardial oedema and late gadolinium enhancement (LGE) of pericardium in acute pericarditis, or myocardial oedema and LGE of epicardium in acute myocarditis.
 - This is addressed in the discussion on pages 12-13. “Both patients presented to a community hospital where there was not access to cardiac MRI, and based on rapid clinical improvement, myocardial biopsy was not warranted. Furthermore, other causes of pericarditis cannot be completely ruled out. The first patient tested negative for Covid-19, influenza, and RSV. Other infectious causes are less likely but were not tested for. Covid-19, RSV, influenza, bocavirus, adenovirus, parainfluenza, metapneumovirus, rhinovirus, enterovirus, Mycoplasma pneumoniae, and Chlamydia pneumoniae were ruled out for the second patient, making viral and bacterial causes unlikely.

Neither of these patients have a significant past medical history, including no likely medication causes, no trauma, nor autoimmune conditions.

4. In the description of Figure 1 and Figure 2, it should be "Electrocardiogram" instead of "Echocardiogram".
 - Good catch! Thank you. Descriptions corrected to "Electrocardiogram".

Reviewer: 03846666

The manuscript is well-written and concise and could be quite informative to the readers.

- Thank you! We appreciate your feedback.

Reviewer: 03413692

I really appreciate these two case reports as they are updated and in line with the current worries about vaccines for COVID-19. Indeed, I would like that the authors point out a question: beyond the causal link between vaccine and pericarditis, the authors should outline the fear of the population for vaccine-associated symptoms which force individuals to the Emergency Department and second level instrumental evaluations. I mean, most of myocarditis/pericarditis often are underdiagnosed as poorly symptomatic, but the worldwide and unjustified fear for vaccines may exaggerate the need for care. Please outline such a point in the discussion section.

- Thank you for your feedback. We certainly do not want to exaggerate the populations fear surrounding the vaccine and associated symptoms. We have added the following paragraph on page 13-14 of the discussion section. "During the time of these cases, the new mRNA Covid-19 vaccinations were under emergency use authorization (EUA). It is important to note, despite the skepticism and fear surrounding these novel vaccines, the benefits greatly outweigh the risk of rare side effects, including myocarditis. In fact, the CDC has reported the rare incidence of myocarditis/pericarditis as about 12.6 cases per million doses of second-dose mRNA vaccines in those age 12 to 39 years old (0.0000126%).¹² However, a study investigating cardiovascular sequelae in Covid-19 infected patients revealed that 5.0% developed new-onset myocarditis and 1.5% developed pericarditis; therefore, there is much higher risk from active infection than vaccination.²⁴ The Covid-19 mRNA vaccines reduce the rate of severe infections, hospitalizations, and death from Covid-19. In a study conducted at five Veteran Affairs Medical Centers, mRNA vaccines were 86.8% effective at preventing Covid-19 associated hospitalizations in those who were over the age of 18 years old.²⁵ Most episodes of pericarditis are uncomplicated and can be managed in the outpatient setting.¹⁸ Therefore, these patient cases should alleviate the fear of vaccination associated adverse effects and help guide the public on when to seek care."