

# Multimodality imaging and histopathology in a young man presenting with fulminant lymphocytic myocarditis and cardiogenic shock after mRNA-1273 vaccination

Mazhar Kadwalwala,<sup>1</sup> Bhawneet Chadha,<sup>1</sup> Jamel Ortoleva,<sup>2</sup> Maurice Joyce<sup>2</sup>

<sup>1</sup>Department of Medicine, Tufts Medical Center, Boston, Massachusetts, USA

<sup>2</sup>Department of Anesthesiology and Perioperative Medicine, Tufts Medical Center, Boston, Massachusetts, USA

## Correspondence to

Dr Maurice Joyce;  
mjoyce@tuftsmedicalcenter.org

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## SUMMARY

A 38-year-old man presented with several days of chest pain and shortness of breath 8 days after receiving the first dose of an mRNA-1273 vaccine. The patient was found to have new left ventricular ejection fraction of 10% in the setting of hypotension and cardiogenic shock requiring mechanical support with an axial flow catheter pump. The presentation was concerning for acute fulminant myocarditis secondary to an inflammatory response from the recent mRNA-1273 vaccine. The patient was treated with pulse dose steroids for 3 days, ultimately leading to haemodynamic recovery and removal of mechanical circulatory support. Endomyocardial biopsy was performed and showed focal lymphocytic interstitial infiltrate with myocyte damage consistent with lymphocytic myocarditis. The patient had improvement of cardiac function which was seen on serial imaging.

and acetaminophen. On day 4 postvaccination, he developed generalised malaise and headaches that resolved 2 days after onset. He continued to have intermittent chills, fevers and diaphoresis, with a reported maximum temperature of 38.9 degrees Celsius. These symptoms continued into day 5 postvaccination, when he also began to have pleuritic chest pain, worse on lying supine. On day 6 postvaccination, he presented to the emergency department of a local hospital.

At the local hospital, he underwent left heart catheterisation with a coronary angiogram revealing no epicardial coronary disease. At that time, due to an acute worsening of the left ventricular ejection fraction (LVEF) from 30% to 10%, shortness of breath, ST changes on ECG and increasing norepinephrine requirements, an axial flow catheter pump (Impella CP, Abiomed, Danvers, Massachusetts) was placed for mechanical circulatory support and the patient was transferred to a tertiary care centre.

On initial evaluation at the tertiary care centre, his temperature was 37.8°C, heart rate was 133 beats per minute, blood pressure was 99/78 mm Hg (Mean Arterial Pressure of 85 mm Hg), respiratory rate was 33 breaths per minute and oxygen saturation was 90% on 5 L oxygen administered via nasal cannula. His physical examination after transfer to the tertiary care facility and placement of a mechanical circulatory support device was significant for crackles in the left lower lung field and trace bilateral lower extremity non-pitting oedema. His neurological examination was significant only for left-sided visual field loss, which was known and stable since his GBM diagnosis and treatment. His ECG (figure 1) demonstrated sinus tachycardia with a right bundle branch block. Initial laboratory values are illustrated in table 1. A transthoracic echocardiogram (TTE) was performed and showed LVEF of 10%, severely reduced left ventricular systolic function with apical akinesis and hypokinesis at the mid and basal left ventricle. Left ventricular global strain analysis was not performed. The right ventricle was normal with mildly reduced right ventricular function (figure 2). He initially required a low-dose infusion of norepinephrine, which was subsequently weaned and discontinued. He was started on pulse dose steroids with 1 g Methylprednisolone daily for 3 days to treat presumptive myocarditis as the cause of his cardiogenic shock. Pulmonary artery catheterisation using central

## BACKGROUND

As the vaccination against SARS-CoV-2 for prevention of COVID-19 has extended to younger and healthier patient populations, the profile of potential adverse events has evolved. A rare potential adverse event of myocarditis has been temporally associated with messenger RNA (mRNA) vaccination for COVID-19 prevention, particularly in adolescent and young adult men.<sup>1–3</sup> Majority of reported cases have described haemodynamically stable presentations with no histopathological confirmation.<sup>1–3</sup> In this case report, we describe a young man presenting with cardiogenic shock requiring temporary mechanical circulatory support secondary to biopsy-proven lymphocytic myocarditis after the first dose of the mRNA-1273 vaccine (Moderna, Cambridge, Massachusetts, USA).

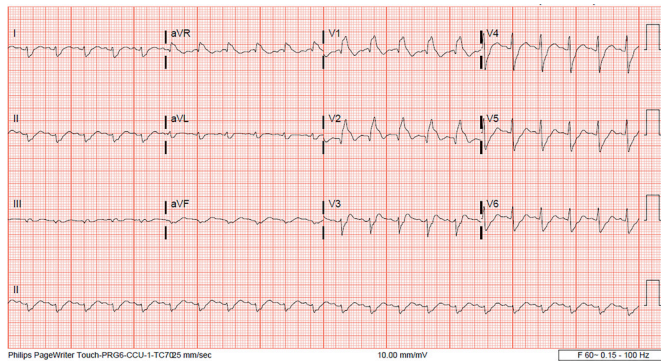
## CASE PRESENTATION

A 38-year-old man with a medical history significant for glioblastoma multiforme (GBM) in 2018 presented with several days of chest pain and progressive dyspnoea. The patient had received the first dose of the mRNA-1273 vaccine (Moderna) 8 days prior to presentation at a tertiary care centre. The evening after vaccine administration, he reports upper extremity pain which quickly resolved. On day 2 postvaccination, he started having fatigue and fevers intermittently associated with diaphoresis, which he treated with ibuprofen



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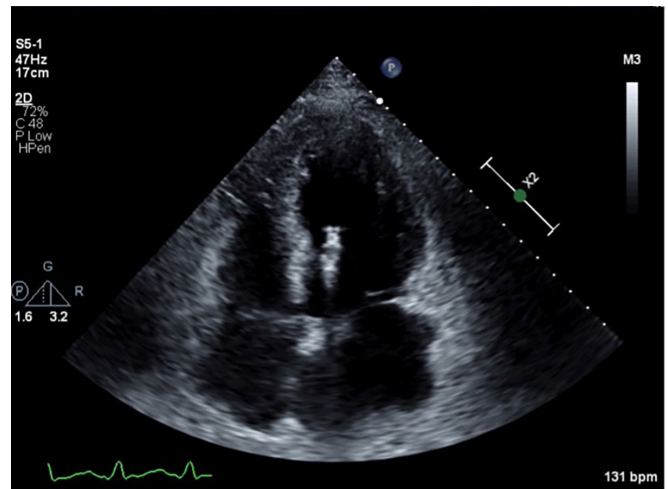
**Figure 1** ECG taken on presentation to tertiary care centre with sinus tachycardia and right bundle branch block. aVR, augmented Vector Right; aVL, augmented Vector Left; aVF, augmented Vector Foot.

venous pressure (CVP), pulmonary artery pressure, pulmonary capillary wedge pressure (PCWP) and mixed venous cardiac output (Mixed venous oxygen saturation) calculations were used to guide therapy. The Impella was placed as high as P8 to reduce vasopressor requirements. A maximum Lactate dehydrogenase of 494 and no creatinine elevation were reported. After weaning off all pharmacological haemodynamic support, the axial flow catheter pump was placed on a performance level of P3 for over 16 hours and a preremoval haemodynamic analysis found the following: CVP of 4, pulmonary artery systolic of 18, pulmonary artery diastolic of 10 and a PCWP of 5 with an accompanying cardiac index of 3.03. Given the improvement in his haemodynamic status, the decision was made to remove the device. The axial flow catheter pump was weaned and then removed after 6 days of support. Given the absence of acute kidney injury, after removal of the pump, nitroprusside was initially used to optimise afterload. This was subsequently weaned in favour of low-dose oral captopril. Next, spironolactone and finally metoprolol extended release were instituted prior to discharge without incident.

This patient's medical history was significant for a diagnosis of GBM and no cardiovascular issues. He was diagnosed with GBM in 2018 when he presented to a local hospital with right-sided frontal headaches and associated nausea and vomiting. A CT scan of the head showed a 6 cm × 5 cm right temporal mass, with mass effect and cerebral oedema causing midline shift, effacement of the lateral ventricles and uncal herniation. This was confirmed by brain MRI. He subsequently developed a dilated right pupil with decreased responsiveness and was transferred to a tertiary medical centre for acute neurosurgical intervention and resection of the mass. The pathology was consistent with GBM, WHO grade IV. Isocitrate dehydrogenase-1 mutated, O-6-methylguanine-DNA methyltransferase methylated and

**Table 1** Initial laboratory values on presentation to tertiary care facility

|                                     |        |
|-------------------------------------|--------|
| Haemoglobin (g/L)                   | 102    |
| Lactate Dehydrogenase (IU/L)        | 434    |
| Ferritin (ng/mL)                    | 1245   |
| Brain Natriuretic Peptide (pg/mL)   | 1636   |
| Troponin I (mg/mL)                  | 8.3    |
| D-dimer (ng/mL)                     | 384    |
| Erythrocyte Sedimentation Rate (mm) | 78     |
| C-Reactive Protein (mg/L)           | 236.07 |



**Figure 2** Transthoracic echocardiogram four-chamber view showing apical akinesis and hypokinesis at the mid and basal left ventricle, left ventricular ejection fraction of 10%, normal right ventricle and mildly reduced right ventricular function. The axial flow catheter pump (Impella CP, Abiomed, Danvers, Massachusetts) device can be seen.

a 1p/19q co-deletion was not present. He was treated with 24 cycles of Temodar from 2018 to 2020 and initiated on Optune therapy, which has continued up until and beyond his presentation with acute myocarditis. He had unremarkable family history and works part-time as a clinical pharmacist. He does not use nicotine or nicotine-containing products, nor does he drink alcohol or use any recreational/illicit drugs.

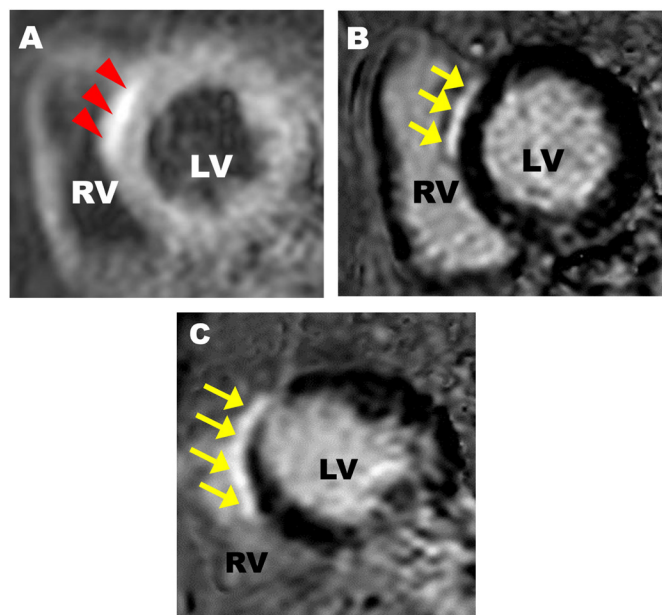
## INVESTIGATIONS

His haemodynamic status improved after initiation of pulse dose steroids and the axial flow catheter pump was weaned and then removed after 6 days of support. After axial flow catheter pump removal, a cardiac MRI (figure 3) was performed and showed left ventricular dysfunction with global hypokinesis and LVEF of 27% and areas of septal late gadolinium enhancement (LGE) in a non-coronary vascular distribution. The presence of high T2 signal intensity plus LGE is consistent with acute myocarditis.<sup>4</sup> Right ventricular ejection fraction was normal at 47%.

To further understand the aetiology of the cardiogenic shock and to exclude infiltrative aetiologies of myocarditis such as giant cell myocarditis, an endomyocardial biopsy was performed after mechanical circulatory support was discontinued. This biopsy showed focal lymphocytic interstitial infiltrate with myocyte damage, consistent with lymphocytic myocarditis (figure 4). Immunohistochemistry for cytomegalovirus (CMV), herpes simplex virus (HSV) 1 and 2, varicella zoster virus (VZV) and adenovirus was performed and was negative. CD3 and CD68 immunostains labelled a vast majority of the infiltrate. There were a small population of CD20 cells. C4d stain was negative and non-contributory. Of note, the biopsy was done 7 days after the initiation of steroids. This is a potential confounder in the interpretation of these results.

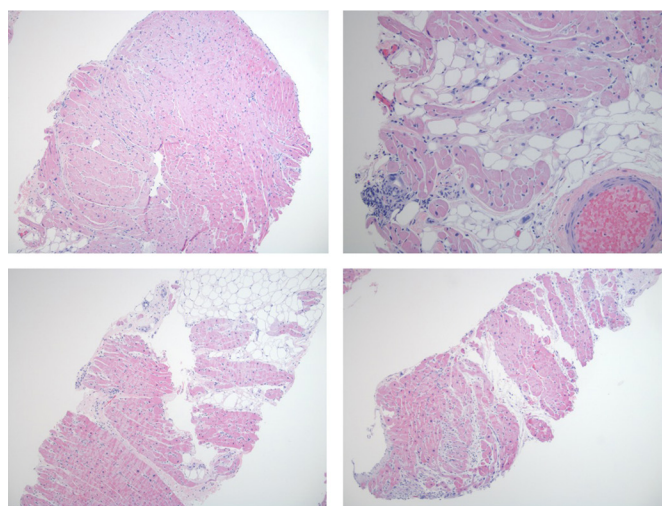
## DIFFERENTIAL DIAGNOSIS

Viral infections are the most common cause of lymphocytic myocarditis. Various viruses have been implicated in the aetiology of myocarditis, including parvovirus B19, coxsackie B virus, adenovirus and CMV. Bacteria and fungi have also been implicated in causing myocarditis, but much less commonly



**Figure 3** (A) T2-weighted images in basal short-axis view demonstrating increased signal intensity (arrowheads) in the basal septum consistent with oedema. (B) Late gadolinium enhancement images in the same view as (A) demonstrating epicardial late gadolinium enhancement (arrows) in the basal septum in the same area as oedema. (C) Late gadolinium enhancement images in apical short-axis view demonstrating epicardial late gadolinium in the apical septum (arrows). LV, left ventricle; RV, right ventricle.

than viruses. The diagnostic work-up includes testing serology, examining cardiac biopsy specimens and PCR testing for viral genomes. In our patient, the sample from the cardiac biopsy was tested with immunohistochemical stains for CMV, HSV 1, HSV 2, VZV and adenovirus. These tests were all negative. In our patient, the vast majority of the lymphocytic infiltrates consisted of CD3 and CD68 cells, with a small proportion of CD20 cells. C4d staining was negative. Treponemal antibody, toxoplasma IgM, Lyme serologies, parvovirus, respiratory viral panel and COVID-19 testing were all within normal ranges or



**Figure 4** Myocardial tissue fixed on formalin showing focal lymphocytic interstitial infiltrate with myocyte damage consistent with myocarditis.

were negative. He was found to be CMV IgG-positive and CMV IgM-negative. His SARS-CoV-2 IgG was found to be negative. Echocardiographic analysis at our institution did not show any apical ballooning, making the diagnosis of Takotsubo cardiomyopathy less likely.

### TREATMENT

On initial presentation, the patient was found to be hypotensive, with examination consistent with cardiogenic shock. An axial flow catheter pump (Impella CP, Abiomed) was placed for mechanical circulatory support. This was subsequently removed after 6 days once his haemodynamic status improved.

Consistent with guidelines, various reports and case series for the management of lymphocytic myocarditis, he was supported with mechanical circulatory support.<sup>5</sup> In addition, he was started on a 3-day course of pulse dose steroids with Solumedrol 1000 mg intravenously every day. This was followed by a rapid 5-day taper. He was ultimately discharged on lisinopril 10 mg daily, spironolactone 25 mg daily and metoprolol succinate 25 mg daily.

### OUTCOME AND FOLLOW-UP

The patient was seen via telehealth visit for follow-up 1 week after discharge from the hospital. At that time, he reported only mild lingering fatigue. Otherwise, he had no cardiopulmonary symptoms. He had not yet resumed regular exercise. The patient was also advised against getting the second vaccine in the series and recommended to continue practising social distancing, masking and hand hygiene.

One month after discharge he underwent a TTE which showed improvement in his LVEF from 10% to 30%. The left ventricular systolic function also improved. He was maintained on goal-directed medical therapy at this time. He was also seen in person in clinic 1 month after discharge. He had gradually resumed exercising, after consultation with his cardiologist, which involved rowing for 20 min and riding a stationary bicycle for 20 min daily. He did not have any limitations in his activity. He denied chest pain or significant shortness of breath during his exercises. He denied lower extremity swelling, paroxysmal nocturnal dyspnoea, orthopnoea, light-headedness, syncope, fever, chills, nausea or vomiting. His appetite had improved and he was eating well. The case was reported to the Vaccine Adverse Events Reporting System.

### DISCUSSION

Myocarditis is an inflammatory disease of cardiac myocytes with a wide array of causes. The 2019 Global Burden of Disease reports the rate of myocarditis at 6.1 per 100 000 in men and 4.4 per 100 000 in women.<sup>6</sup> The clinical presentation of myocarditis is highly variable, ranging from symptoms such as palpitations to shortness of breath from heart failure to cardiogenic shock. Our patient had no known cardiac history or exposures other than the mRNA-1273 vaccine (Moderna), which could have led to fulminant myocarditis based on emerging data. Symptom onset 8 days after receiving the vaccine also raised the question of whether symptoms were in fact related to an inflammatory response from vaccine exposure. The mRNA COVID-19 vaccine operates by exposing cells to mRNA which encodes for the 'spike protein', which will subsequently be expressed on the cell surface. Immune cells recognise this protein and engage in the production of antibodies to protect against exposure to COVID-19.<sup>7</sup> The inflammatory response which results from this immune amplification and antibody production can elicit substantial

inflammation in the body, potentially leading to myocarditis. Our patient presented with fever and elevated Erythrocyte Sedimentation Rate and C-Reactive Protein, indicative of him being in an inflammatory state.

Cardiac disease manifestations such as acute myocarditis have been associated with SARS-CoV-2 exposure. Although no direct correlation has been identified between vaccine exposure and the development of myocarditis, there has been recognition of cases worldwide in which patients have developed myocarditis after vaccination. In Israel, there have been reports of young men developing myocarditis after receiving the Pfizer-BioNTech COVID-19 vaccine, although there were only approximately 60 reported cases out of over 5 million individuals who received the vaccine.<sup>8</sup> Another recently published case report described eight patients diagnosed with acute myocarditis after receiving the currently approved mRNA vaccines.<sup>3</sup> On average, symptoms started 2–4 days following vaccination. Although alternative aetiologies for the development of myocarditis could exist, the presentation of symptoms in proximity to receiving vaccination raises further suspicion that the inflammatory response to immunisation was the aetiology.

The Centers for Disease Control and Prevention has also recognised that there have been reports of young adult men who have developed myocarditis and pericarditis after receiving mRNA COVID-19 vaccines. A recent case study described seven male adolescents who developed symptoms of acute myocarditis within a few days of receiving the second dose of the Pfizer-BioNTech COVID-19 vaccination.<sup>2</sup> These patients all had abnormal cardiac MRI with patchy delayed gadolinium

enhancement consistent with myocarditis. Alternative causes for the development of myocarditis were also excluded by the work-up much like in our patient, with the addition that in our patient a cardiac biopsy helped to further rule out an infectious or inflammatory aetiology, such as sarcoidosis or giant cell myocarditis.

In conclusion, providers should be aware of the extremely rare but non-zero possibility of myocarditis related to COVID-19 vaccination. Additionally, we, the authors, all strongly support vaccination as the most important countermeasure to addressing the pandemic and strongly endorse vaccination in all populations that are currently eligible to be vaccinated.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

### Learning points

- ▶ As vaccination against the SARS-CoV-2 virus ramps up across the world, a small number of cases of myocarditis are being reported.
- ▶ Acute onset of chest pain progressing towards cardiogenic shock and temporally associated with the vaccine should raise suspicion for vaccine-induced myocarditis.
- ▶ Messenger RNA (mRNA) vaccine-associated myocarditis would likely be a diagnosis of exclusion once infectious and infiltrative causes of myocarditis have first been ruled out.
- ▶ Although no management guidelines exist for treatment of vaccine-induced myocarditis, our patient had good outcome with supportive management of cardiogenic shock with mechanical circulatory support and pulse dose steroids followed by a rapid taper.
- ▶ Patients found to have complications after receiving the first dose of an mRNA vaccine should be advised to not receive the second dose or any future doses of an mRNA vaccine and should be further advised to continue practising social distancing, masking and proper hand hygiene.

### REFERENCES

- 1 Montgomery J, Ryan M, Engler R, *et al*. Myocarditis following immunization with mRNA COVID-19 vaccines in members of the US military. *JAMA Cardiol* 2021;6:1202.
- 2 Marshall M, Ferguson ID, Lewis P, *et al*. Symptomatic acute myocarditis in 7 adolescents after Pfizer-BioNTech COVID-19 vaccination. *Pediatrics* 2021;148:e2021052478.
- 3 Larson KF, Ammirati E, Adler ED, *et al*. Myocarditis after BNT162b2 and mRNA-1273 vaccination. *Circulation* 2021;144:506–8.
- 4 Ferreira VM, Schulz-Menger J, Holmvang G, *et al*. Cardiovascular Magnetic Resonance in Nonischemic Myocardial Inflammation. *J Am Coll Cardiol* 2018;72:3158–76.
- 5 Kociol RD, Cooper LT, Fang JC, *et al*. Recognition and initial management of fulminant myocarditis: a scientific statement from the American heart association: a scientific statement from the American heart association. *Circulation* 2020;141:e69–92.
- 6 Roth GA, Mensah GA, Johnson CO, *et al*. Global burden of cardiovascular diseases and risk factors, 1990–2019: update from the GBD 2019 study. *J Am Coll Cardiol* 2020;76:2982–3021.
- 7 CDC. Understanding mRNA COVID-19 Vaccines [Internet]. Cdc.gov, 2021. Available: <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines/mrna.html> [Accessed 19 Jul 2021].
- 8 Vishnupriyan. Israel examines myocarditis linked to Pfizer-BioNTech Covid-19 vaccine [Internet]. Pharmaceutical-technology.com, 2021. Available: <https://www.pharmaceutical-technology.com/news/israel-myocarditis-pfizer-vaccine/> [Accessed 19 Jul 2021].

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