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CASE REPORT
Cardiovascular surgery

Incessant myopericarditis after mRNA vaccination requiring IL-1 receptor antagonist therapy and pericardiectomy: case report

Michael B. Hay [1], Rahul G. Muthalaly [1,2], Sean Tan [1], and Nitesh Nerlekar [1,2]*

[1]Monash Heart, Monash Health, 246 Clayton Rd, Clayton, 3168 VIC, Australia; and [2]Monash University, Wellington Rd, Clayton, 3800 VIC, Australia

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Background During the COVID-19 pandemic, there has been global administration of novel mRNA vaccines that are effective in reducing the burden of COVID-19. In tandem with this administration, mRNA vaccine-associated complications have been identified. One such complication is mRNA vaccine-associated pericarditis.

Case summary This is a case of a 40-year old male who developed clinical pericarditis 3 days after his first dose of the Pfizer-BioNtech mRNA COVID-19 vaccination. The diagnosis of mRNA vaccine-induced pericarditis was confirmed on cardiac magnetic imaging and was resistant to numerous lines of medical therapy. These included substantial simple and opioid-based analgaesia, colchicine, prednisolone, interleukin-1 receptor antagonist therapy (anakinra), and a ketamine infusion that were all titrated over the course of eight hospital admissions. Ultimately, surgical pericardiectomy was performed that resulted in a favourable outcome.

Discussion This case depicts an example of incessant mRNA vaccine-associated pericarditis, a known complication of the Pfizer-BioNtech mRNA COVID-19 vaccination. There is limited evidence guiding the therapy of mRNA-induced pericarditis especially when recurrent and resistant to simple analgaesia, colchicine, and steroids. Thus, this case represents a potential framework to help future cases of incessant mRNA vaccine-induced pericarditis.

Keywords Pericarditis • mRNA vaccine • Pericardiectomy • Case report

ESC curriculum 2.2 Echocardiography • 2.3 Cardiac magnetic resonance • 6.6 Pericardial disease

Learning points

- Early diagnosis of mRNA-induced pericarditis is important to allow titration of medical therapy.
- While most cases of mRNA-induced pericarditis are self-limiting, some cases can be incessant and resistant to many lines of medical therapy.
- Pericardiectomy should be considered in cases of incessant mRNA vaccine-induced pericarditis that have failed medical therapy.

Introduction

Myopericarditis is a known complication of mRNA vaccination with adolescent males and young men being most at risk.[1,2] The incidence of mRNA vaccine-induced myopericarditis is 12.6 cases per million doses of the second mRNA vaccine, and most commonly individuals will develop symptoms within 1–3 days of the second dose.[1,3] Unsurprisingly, cardiac magnetic resonance imaging (CMR) will demonstrate a similar pattern of myocardial injury when compared with other aetiologies of myocarditis.[4] Both mRNA vaccine-induced myocarditis

* Corresponding author. Tel: +613 9594 6666, Email: Nitesh.nerlekar@monash.edu
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and pericarditis generally demonstrate a mild and self-limiting natural history, however, a minority of cases will progress and require significant medical therapy.[3,5] There is limited evidence guiding the therapy of mRNA-induced pericarditis. The therapies that have been suggested in literature thus far mimic the guidelines for non-mRNA vaccine-induced pericarditis and include supportive therapy as well as colchicine, glucocorticoids, and intravenous immunoglobulin therapy.[3,5]

We present a case incessant mRNA vaccine-induced pericarditis that was resistant to numerous lines of medical therapy, resulted in multiple hospital admissions, and ultimately necessitated surgical pericardiectomy.

Summary figure

Time	Event
Days 0–4 (Admission 1)	Admission for pericarditis 3 days post-Pfizer-BioNtech mRNA COVID-19 vaccination. Normal troponin and inflammatory markers. Discharged with simple analgaesia.
Days 5–7 (Admission 2)	Exacerbation of chest pain necessitating invasive coronary angiography that demonstrated smooth coronary arteries. Normal transthoracic echocardiography (TTE). Discharged on colchicine and ibuprofen.
Days 28–35 (Admission 3)	Exacerbation of chest pain. Repeat TTE demonstrating a small pericardial effusion. Discharged on prednisolone 25 mg daily.
Days 38–42 (Admission 4)	Exacerbation of chest pain. Repeat TTE demonstrated features of constrictive pericarditis. C-reactive protein increased to 208 mg/L. Prednisolone was increased to 50 mg daily and subsequently discharged.
Days 53–54 (Admission 5)	Exacerbation of chest pain that improved without alteration of medication.
Days 64–75 (Admission 6)	Exacerbation of chest pain, weight gain, and mood disturbance attributed to steroid use. Cardiac magnetic resonance imaging (CMR) with late gadolinium enhancement (LGE) confirmed the diagnosis of pericarditis. Azathioprine 25 mg daily was introduced.
Days 85–90 (Admission 7)	Exacerbation of chest pain with a C-reactive protein of 103 mg/L. Reviewed by psychiatry team for adjustment disorder. Commenced on anakinra 100 mg daily.
Days 205–240 (Admission 8)	Exacerbation of chest pain while on anakinra, colchicine, azathioprine and naproxen. Repeat CMR demonstrating persistence of pericarditis. A ketamine infusion provided temporary relief. Subsequently, surgical pericardiectomy was performed with tissue demonstrating focal fibrosis. Good clinical response with no subsequent admissions.

Case presentation

Initial presentation (Days 0–4)

A 40-year old male presented to hospital with pleuritic chest pain with radiation to the back 3 days after his first dose of the Pfizer-BioNtech mRNA COVID-19 vaccination. The patient had neither past medical history nor any regular medications. He lived with his wife and was employed as a school teacher.

The patient's initial ECG demonstrated sinus rhythm with PR- and ST-segment changes consistent with acute pericarditis (*Figure 1A*). Initial blood tests revealed a normal high sensitivity troponin level of 4 ng/L (upper limit of normal value of 20 ng/L), C-reactive protein of 2.4 mg/L, and a normal D-dimer level. Viral polymerase chain reaction performed on a nasopharyngeal swab was negative for common respiratory viruses including COVID-19. An echocardiogram demonstrated no pericardial effusion and preserved left and right ventricular functions. The patient underwent CT aortography given the radiation to the back, which was normal. The patient was admitted to the hospital for analgaesia with fentanyl and oxycodone due to the severity of the pain before down-titrating to ibuprofen 400 mg three times a day for one week. Given an improvement in pain and stable vital parameters, the patient was discharged from the hospital after 5 days of admission with the plan for follow-up with his general practitioner.

Presentation 2–5 (Days 5–54)

Within 24 h, the patient represented with chest pain. Repeat ECGs taken in the emergency department demonstrated mild ST-segment elevation in the inferior leads. In light of this, the patient proceeded to emergency invasive coronary angiography that demonstrated angiographically smooth coronary arteries. The patient's repeat blood tests demonstrated a normal troponin level and C-reactive protein. A repeat bedside transthoracic echocardiogram demonstrated no pericardial effusion and a normal left ventricular ejection fraction. The patient was treated for acute pericarditis with colchicine 500 μg twice daily and high dose ibuprofen at 800 mg three times daily. He was discharged after 3 days with decreasing pain.

Over the next 2 months, the patient had three admissions with recurrent chest pain despite good compliance with medications. During these admissions, he had a peak C-reactive protein of 208 mg/L and a transient mild raise in troponin of 42 ng/L. The patient had two further transthoracic echocardiograms, one of which demonstrated early features of constrictive pericarditis manifested by a trace pericardial effusion, interdependence of the ventricular septum, and annulus reversus assessed by tissue Doppler imaging. Subsequent to this, the patient was commenced on immunotherapy and discharged on prednisolone 50 mg daily, trimethoprim–sulfamethoxazole 160–800 mg three times weekly, pantoprazole 40 mg daily, colchicine 500 μg three times daily, and ibuprofen 600 mg three times a day.

Presentation 6–7 (Days 64–90)

One week later, the patient represented with recurrent chest pain as well as significant weight gain, mood disturbance, and insomnia related to glucocorticoids. Repeat TTE demonstrated no features of constriction. Cardiac magnetic resonance imaging with LGE demonstrated extensive pericardial enhancement with no myocardial fibrosis (*Figure 1B and C*) and no features of constrictive physiology. During admission, azathioprine 25 mg was added to his medical regime prior to discharge after a 10-day admission.

The patient represented 10 days later with chest pain and a C-reactive protein level of 103 mg/L despite good compliance to medical therapy. After multi-disciplinary discussion, anakinra 100 mg daily was commenced. The patient was also reviewed by the psychiatry team with a diagnosis of adjustment disorder in the setting of multiple

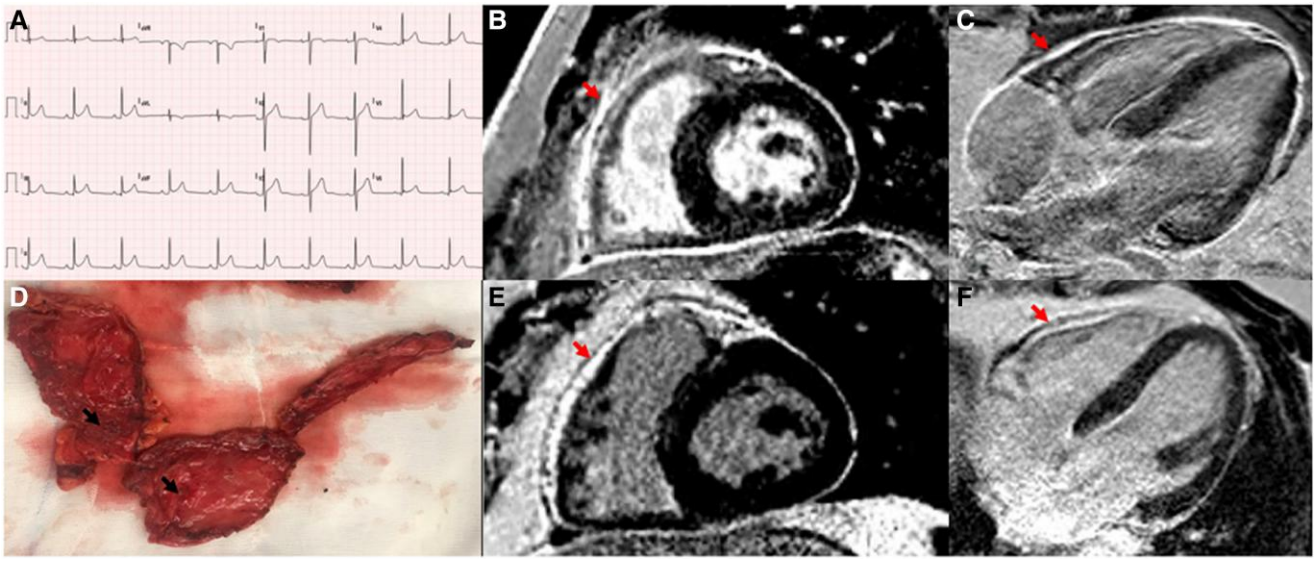

Figure 1 Cardiac investigations demonstrating pericarditis. (*A*) An ECG demonstrating acute pericarditis. (*B* and *C*) Cardiac magnetic resonance (CMR) imaging using gadolinium demonstrating diffuse enhancement of the pericardium (arrows) suggesting inflammation at time of fifth representation (Day 53). (*D*) Tissue samples post-surgical pericardiectomy demonstrating small areas of fibrosis (arrows). (*E* and *F*) Repeat late gadolinium enhancement 4 months after initial CMR demonstrating a mild improvement but persistence in pericardial enhancement (arrows).

hospital presentations. The patient was discharged after a 5-day admission with significant improvement on prednisolone 20 mg daily, anakinra 100 mg daily, trimethoprim–sulfamethoxazole 800 mg/160 mg daily, colchicine 500 µg twice daily, naproxen 1 g daily, pantoprazole 40 mg daily, and a fentanyl transdermal patch.

Final presentation (Days 205–240)

The patient represented with chest pain and dyspnoea after 2 months of only occasional mild chest pain and one presentation to the emergency department that did not require admission. Given the recurrence of pain, despite successful biochemical response, a repeat CMR with gadolinium was performed. Compared to the initial CMR, there was some improvement, however, there was persistence of diffuse pericardial enhancement with mild pericardial thickening (*Figure 1E and F*). There were concerns regarding central sensitization that was treated with a continuous ketamine infusion over 5 days under the guidance of a pain specialist. This therapy provided temporary relief of pain, however, there was recurrence of pleuritic chest pain after cessation of the ketamine infusion despite substantial medical therapy.

Given the case complexity and the persistence of debilitating chest pain despite maximal medical therapy, a heart team decision to proceed with pericardiectomy was reached. This involved a sternotomy that revealed a moderately thickened pericardium with soft adhesions between the pericardium and epicardium over the anterolateral, inferior, and diaphragmatic surfaces (*Figure 1D*). The parietal pericardium and inflammatory tissue attached to the visceral pericardium were subsequently resected prior to two drain tubes being inserted and the chest closed with sternotomy wires. Subsequent tissue histology demonstrated areas of focal fibrosis without features of malignancy. Acid-fast bacillus (AFB) staining was negative.

The patient was discharged Day 7 post-pericardiectomy with mild sternal pain but resolution of his pericardial pain. He was discharged on anakinra 100 m daily, azathioprine 175 mg daily, colchicine 500 µg, gabapentin 600 mg three times daily, indomethacin 50 mg three times daily, tapentadol 100 mg twice daily, and paracetamol 1000 mg four times a day.

Follow-up

The patient has now been managed in the community for 4 months since the previous admission with complete resolution of chest pain. He has begun down-titration of immunosuppression. Exercise capacity is now unlimited, and there is no current analgaesia requirement.

Patient experience

The patient described this experience as immensely frustrating with a clear impact on his mental health, and loss of independence as well as inability to remain employed. This was compounded by the temporary benefit and then relapse of attempted therapies. Relief of symptoms has resulted in a slow and steady improvement in his mental health (*Figure 2*).

Discussion

A case report by Hysi *et al.*[6] described a case of severe constrictive pericarditis post-mRNA COVID-19 vaccination that ultimately required surgical pericardiectomy. Furthermore, within the current literature, there are case reports of myopericarditis post-mRNA vaccination for COVID-19.[3,7]

There is otherwise minimal published experience regarding immunosuppressive or surgical treatment in of mRNA vaccine-induced pericarditis especially without features of constrictive pericarditis. However, it seems that a minority of patients may require such advanced therapies.

Unfortunately, there is insufficient evidence to understand risk factors for identifying treatment refractory cases that would allow us to better counsel patients. At the time of presentation, rilonacept that has now been used in recurrent pericarditis was not available for use, and it remains uncertain whether this may have been a beneficial step in therapy. However, the use of anakinra had limited effect on our

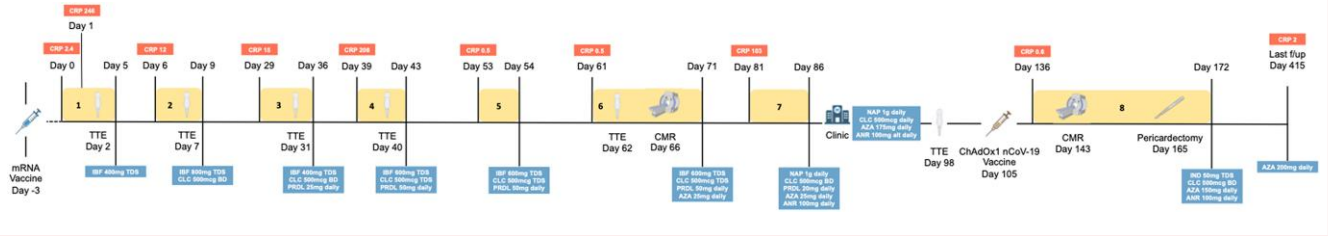

Figure 2 Timeline of investigations and management.

patient. To our knowledge, this is the first report of incessant pericarditis without constrictive physiology following mRNA vaccination necessitating surgical pericardiectomy and resulting in complete resolution of symptoms.

Interestingly, it was expected that this patient's symptoms would have improved as the inflammation was resolved as identified through the improved biochemical response; especially given the lack of constrictive physiology on imaging. This however did not occur, hence the need to proceed to pericardiectomy.

Conclusion

This report demonstrates a case of incessant mRNA vaccine-induced pericarditis that required pericardiectomy due to failure of significant immunosuppression and analgaesic therapy. This management regime appears to have resulted in a favourable outcome and provides a potential framework to base the management of future incessant mRNA-induced pericarditis cases. Despite this potential complication, it is clear that COVID-19 vaccination provides a clear overall benefit and it is of the belief of the authors that COVID-19 vaccine should not be avoided due to this rare complication.

Lead author biography

Michael Hay completed his MBBS at Monash University in 2016 and is a current cardiology advanced trainee based in Melbourne, Australia. He has interests in cardio-metabolic medicine as well as preventative cardiology.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports*.

Consent: The authors confirm that written consent for submission and publication of this case report, including images and associated text, has been obtained from the patient.

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Data availability

The data underlying this article are available in the article and in its online supplementary material.

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