Acute pericarditis and cardiac tamponade after COVID-19 vaccination

INTRODUCTION

Since December 2019, there has been a rapid and unprecedented spread of coronavirus disease 2019 (COVID-19) globally. As of 11 May 2021, over 157 million cases and 3.2 million deaths have been reported globally since the start of the worldwide pandemic.[1] To reduce the morbidity and mortality associated with COVID-19, numerous platforms have been involved in the development of vaccines worldwide. As of this writing, two vaccine efficacy trials have been completed and these vaccines have received emergency use authorisation (EUA) from the Food and Drug Administration (FDA).[2] The vaccines are BNT162b2 mRNA vaccine from Pfizer and BioNTech, and the mRNA-1273 vaccine from Moderna, which showed 95% and 94.1% vaccine efficacy, respectively. Both Phase 3 clinical trials showed good safety profile and low incidence of serious adverse events.[3,4]

In Singapore, COVID-19 vaccination commenced in phases from 30 December 2020, starting with healthcare workers. As of 17 May 2021, 3,407,068 doses of vaccines have been administered in Singapore.[5] As with any vaccine or medication, there are always possible adverse side effects. We report a patient who developed acute pericarditis and cardiac tamponade shortly after receiving the first dose of the Pfizer–BioNTech COVID-19 vaccine.

CASE DESCRIPTION

A 53-year-old Chinese man, a non-smoker with a background history of hypertension, developed exertional dyspnoea 2 days after the first dose of Pfizer–BioNTech COVID-19 vaccination in late January 2021. On Day 7 postvaccination, his symptoms worsened; he had dyspnoea at rest, decreased effort tolerance and left-sided chest discomfort on deep inspiration. He consulted a primary care doctor and was referred to the emergency department for abnormal electrocardiogram (ECG) findings of a right bundle branch block and left posterior fascicular block. He had a low-grade fever (37.7°C), blood pressure readings of 139–155/97–111 mmHg, an elevated heart rate of 105–110 beats per minute and oxygen saturation of 96%–98% on room air. A COVID-19 nasopharyngeal swab was negative. A chest radiograph revealed cardiomegaly, bilateral lower zone opacities (likely consolidation) and a small left pleural effusion [Figure 1a]. He was treated for community-acquired pneumonia and discharged home with oral antibiotics.

On Day 12 postvaccination, the patient presented with worsening dyspnoea and bilateral pleuritic chest pain that was worse in the supine position and better on sitting forward. He was afebrile, with a blood pressure of 148/92 mmHg, heart rate of 105 beats per minute and oxygen saturation of 100% on room air. A repeat chest radiograph [Figure 1b] showed worsening pleural effusions bilaterally. In view of his tachypnoea, lower limb oedema, progression of symptoms and worsening chest radiograph findings, he was admitted for further evaluation. The ECG [Figure 2a] revealed sinus tachycardia, a right bundle branch block and left posterior fascicular block, but no evolution of changes from the recent ECG done 5 days before. Of note, there was subtle electrical alternans. In addition, although the amplitude of the QRS complexes was not small, the QRS complexes were found to be larger when compared to the ECG performed post-pericardiocentesis [Figure 2b].

Bedside ultrasonography revealed a large circumferential pericardial effusion and mild bilateral pleural effusions. Formal transthoracic echocardiography [Figure 3] confirmed the presence of a large circumferential pericardial effusion (pericardial effusion seen adjacent to the left ventricle wall [30 mm], left ventricular posterior wall [22 mm], right ventricle [24 mm], left ventricular apex [27 mm] and right atrium [27 mm]) with echocardiographic features of cardiac tamponade physiology (right atrial and ventricular diastolic collapse, left ventricular septal bounce, 80% respiratory variation of diastolic tricuspid inflow and 37% respiratory variation of diastolic mitral inflow, dilated and non-compliant inferior vena cava). A pericardiocentesis was performed on Day 3 of admission with immediate drainage of 750 mL of haemoserous fluid. A further 90 mL was drained over the next 12 h. After the initial drainage of 750 mL of pericardial fluid, the patient's heart rate decreased from 95–115 to 85–100 beats per minute.

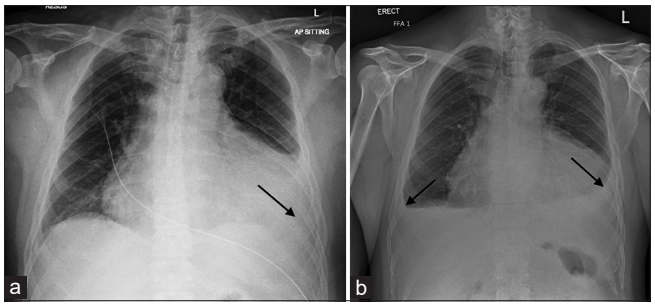

Figure 1: (a) Chest radiograph taken on first presentation to the emergency department (ED) (Day 7 postvaccination) shows a small left pleural effusion (arrow). (b) Chest radiograph taken on second presentation to ED (Day 12 postvaccination) shows worsening pleural effusions bilaterally (arrows).

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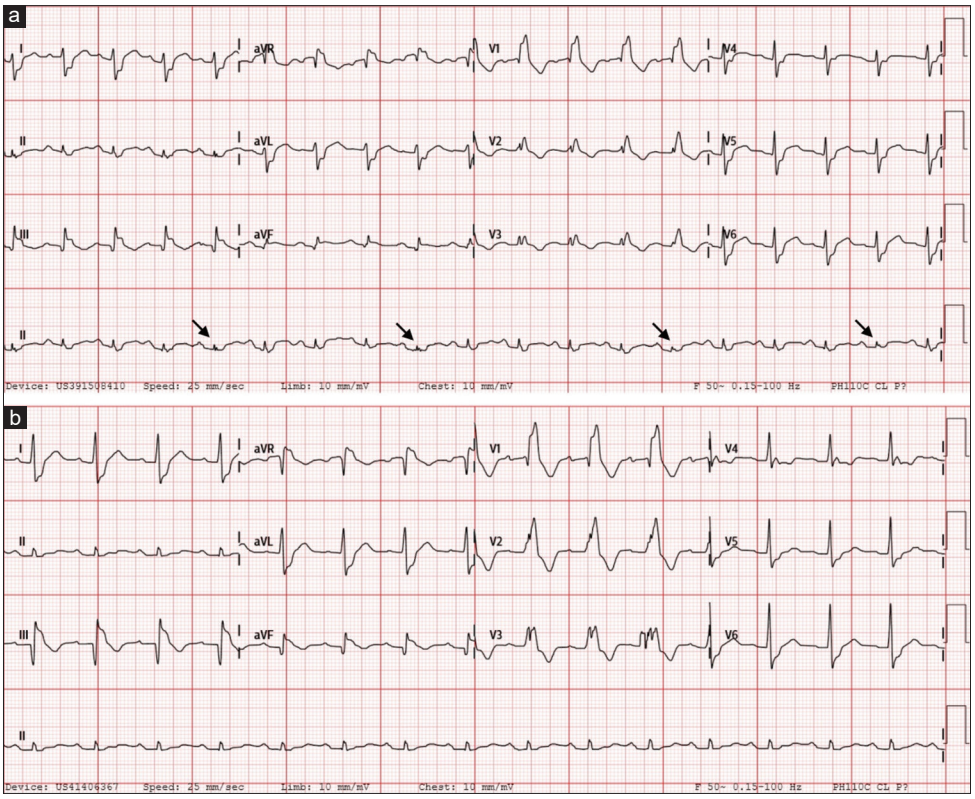

Figure 2: (a) ECG taken upon admission (Day 12 postvaccination) shows QRS complexes of smaller amplitude, signifying electrical alternans (arrows). (b) ECG taken post-pericardiocentesis shows that the QRS complexes are now of larger amplitude with resolution of electrical alternans.

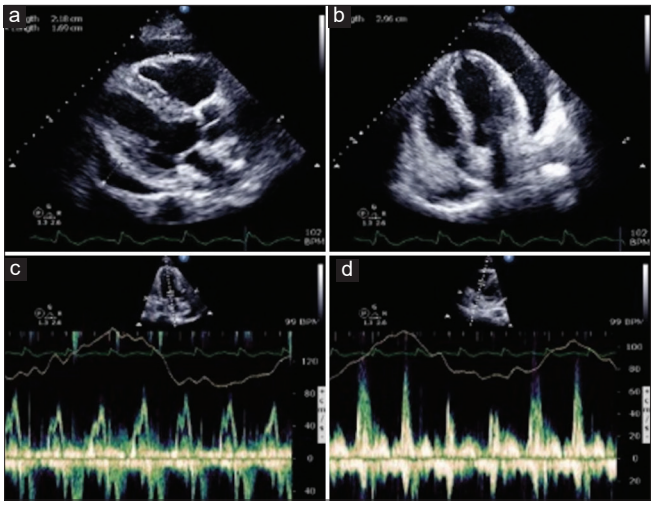

Figure 3: Echocardiograms before pericardiocentesis show (a & b) circumferential pericardial effusion measuring up to 2.96 cm, (c) respiratory variation of diastolic mitral inflow, and (d) respiratory variation of diastolic tricuspid inflow.

Computed tomography of the neck, thorax, abdomen and pelvis showed non-specific borderline enlarged mediastinal lymph nodes that were likely reactive and bilateral pleural effusion that was worse on the left with passive atelectasis of the left lower lobe, but no evidence of malignancy. Of note, there was marked thickening of the pericardium associated with pericardial enhancement, which was in keeping with pericarditis.

Microbiological, viral, autoimmune and serological investigations were performed on his blood and pericardial fluid samples, and the results were unyielding [Table 1]. The patient was administered empirical broad-spectrum antibiotics, which were ceased on Day 4 of admission when bacterial infection was ruled out. He was prescribed colchicine for 3 months to reduce the risk of recurrent pericarditis but not a nonsteroidal anti-inflammatory drug, as his chest pain had resolved immediately after pericardiocentesis. There was no further pericardial drain output after the first 12 h. The drain was clamped on Day 5 of admission and eventually removed on Day 7, as serial transthoracic echocardiograms did not show any pericardial effusion. A repeat transthoracic echocardiogram on Day 11 of admission did not show any reaccumulation of pericardial fluid, and he was discharged well later that day. A follow-up clinic review 2 weeks postdischarge revealed no recurrence of symptoms, and repeat electrocardiogram showed sinus rhythm with right bundle branch block and left posterior fascicular block [similar to the ECG in Figure 2b]. A transthoracic echocardiogram done 2 months postdischarge showed normal left ventricular ejection fraction with no regional wall motion abnormalities. There was no recurrence of pericardial effusion.

DISCUSSION

Since the outbreak of viral pneumonia was identified in Wuhan in December 2019, COVID-19 has escalated into a pandemic

Table 1. Results of investigations — blood, pericardial fluid and respiratory swabs.

Test	Result (RR)	Test	Result (RR)
Blood		Anti-ENA profile	Negative
Biochemistry		Anti-double-stranded DNA antibody (IU)	5.41 (<25: negative)
Troponin T (ng/L)	7, 7[a] (0–29)	*Others*	
ProBNP (pg/mL)	70.9 (<125.0)	General lymphoma screen panel	Negative[c]
Creatinine (μmol/L)	73 (65–125)	**Pericardial fluid**	
Albumin (g/L)	43 (37–51)	*Biochemistry*	
Haemoglobin (g/dL)	13.4 (13.0–17.0)	Appearance	Heavily blood stained and turbid (NA)
WBC count ($\times 10^3/\mu$L)	10.4 (4.0–10.0)	Total protein, fluid (g/L)	54.0 (NA)
Platelet count ($\times 10^3/\mu$L)	580 (150–450)	Total protein, serum (g/L)	79 (62–82)
TSH (mIU/L)	1.34 (0.10–4.00)	Glucose, fluid (mmol/L)	4.6 (NA)
Thyroxine (T4) Free (pmol/L)	14.46 (10.00–20.00)	Lactate dehydrogenase, fluid (U/L)	2,387 (NA)
Microbiology		Lactate dehydrogenase, serum (U/L)	424 (90–190)
Blood culture aerobic & anaerobic	Negative	Neutrophil (%)	15 (NA)
QuantiFERON®-TB Gold In-tube	Negative	Lymphocyte (%)	85 (NA)
VDRL and *Treponema pallidum* particle agglutination	Negative	*Microbiology*	
Rickettsia serology	Negative	Aerobic and anaerobic culture	Negative
Epstein–Barr virus Capsid IgM antibody	Negative	Acid-fast bacilli smear	Negative
Cytomegalovirus IgM antibody	Negative	Acid-fast bacilli culture	Pending
Parvovirus B19 PCR	Negative	Fungal microscopy	Negative
Hepatitis A IgM antibody	Negative	Fungal culture	Pending
Hepatitis B Surface antigen & antibody	Negative	SARS-CoV-2 PCR	Negative
Hepatitis C antibody screen (EIA)	Negative	Enterovirus RNA	Negative
HIV screen	Negative	Adenovirus PCR	Negative
Roche spike antibody (U/mL)	46.71 (NA)	*Others*	
Roche nucleocapsid antibody	Negative	Cytology	Negative[d]
cPass assay™ SARS-CoV-2 neutralisation antibody	Positive[b]	General lymphoma screen panel	Negative[c]
Autoimmune		**Respiratory swabs**	
Anti-neutrophil cytoplasmic antibody EIA profile	Negative	SARS-CoV-2 PCR	Negative
Antinuclear antibody	Negative	Respiratory pathogens multiplex PCR	Negative

[a]Results of troponin T were 24 h apart. [b]Positive at 65.62% inhibition value. [c]No evidence of atypical B or T lymphocytes with aberrant expression in blood sample. [d]No malignant cell is seen. BNP: B-type natriuretic peptide, EIA: enzyme immunoassay, ENA: extractable nuclear antigen, HIV: human immunodeficiency virus, NA: not applicable, PCR: polymerase chain reaction, RR: reference range, SARS-CoV-2: severe acute respiratory syndrome coronavirus 2, TSH: thyroid stimulating hormone, VDRL: venereal disease research laboratory, WBC: white blood cell

affecting millions of people globally. Vaccines have been touted as a means to control further viral spread and as a possible solution to the current pandemic. In the Phase 3 trials, the Pfizer–BioNTech COVID-19 vaccine showed a good safety profile with low rates of adverse events. Serious adverse events reported included shoulder injury related to vaccine administration, axillary lymphadenopathy, paroxysmal ventricular arrhythmia, lower limb paraesthesia and two deaths (one from arteriosclerosis and one from cardiac arrest).[4]

To the best of our knowledge, this is the first reported case of Pfizer–BioNTech COVID-19 vaccine-related acute pericarditis complicated by cardiac tamponade. Despite the extensive investigations, we acknowledge that there is a possibility of an undiagnosed acute viral pericarditis. However, the patient did not complain of viral prodromal symptoms, and the available microbiological and molecular examinations were unyielding.

The temporal course and evolution of symptoms shortly after COVID-19 vaccination raises suspicion that the underlying mechanism may be related to an immune-mediated process postvaccination, possibly secondary to molecular mimicry by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral spike protein triggering an autoinflammatory response.[6] We also postulated that the mechanism could be a result of an enhanced immune response in a host with previous asymptomatic COVID-19 infection. Therefore, serology tests were sent to assess for previous COVID-19 infection; this included Roche S and N antibodies, as well as cPass™ SARS-CoV-2 neutralisation antibody detection. However, the results of detectable S antibody levels (46.71 U/mL) in the absence of N antibodies, as well as the presence of neutralising antibodies as suggested by a positive cPass assay (65.62% inhibition value) were in keeping with seroconversion from the first dose of the vaccine. Therefore, this disproved our hypothesis.

Cases of pericarditis and pericardial effusions after influenza vaccination have been reported, but they are uncommon.[7-14] In

addition, although pericardial effusions can occur in up to 60% of patients with acute pericarditis, the majority of effusions are small or moderate in size (79% and 10%, respectively) without any haemodynamic compromise, while only 5% of effusions result in cardiac tamponade.[15] It is thus very uncommon for pericarditis to occur postvaccination, much less so for it to result in cardiac tamponade.

Our patient had numerous echocardiographic and several ECG features of cardiac tamponade, in addition to a tachycardia that was unexplained, given his clinical picture. Although he did not have other clinical features such as hypotension, an elevated jugular venous pressure, muffled heart sounds or a weak peripheral pulse, the tachycardia improved after pericardiocentesis, indicating that there was some haemodynamic effect from the large pericardial effusion. In addition, he has a history of hypertension, and it has been reported that elevated blood pressure may occur in some patients with cardiac tamponade who have pre-existing hypertension.[16]

Myocarditis after BNT162b2 and mRNA-1273 vaccination has been reported in a series of mostly younger males, typically 48–72 h after they received the second dose of COVID-19 mRNA vaccination.[17] In contrast, our patient is a middle-aged man (aged 53 years) who developed pericarditis complicated by cardiac tamponade after his first dose of Pfizer–BioNTech COVID-19 vaccine. Healthcare providers should, therefore, be vigilant in assessing for rare but severe reactions from COVID-19 vaccination in patients of all age groups, regardless of the dose of the vaccine administered.

Given that this is the first report of pericarditis resulting in cardiac tamponade after COVID-19 vaccination, this case should not negate the benefits of mass COVID-19 vaccination. This case highlights the possibility of postvaccination serositis as a differential when evaluating patients who present with dyspnoea and chest pain with cardiomegaly on chest radiograph after COVID-19 vaccination.

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Conflicts of interest

There are no conflicts of interest.

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