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Acute pericarditis and cardiac tamponade after Covid-19 vaccination

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INTRODUCTION

Since December 2019, there has been a rapid and unprecedented spread of the coronavirus disease 2019 (Covid-19) globally. As of 11 May 2021, there have been over 157 million cases and 3.2 million deaths reported globally since the start of the worldwide pandemic.[1]

In order to reduce the morbidity and mortality associated with Covid-19, numerous platforms have been involved in the development of vaccines worldwide. To date, two vaccine efficacy trials have been completed and these vaccines have received Emergency Use Authorization (EUA) from the Food and Drug Administration (FDA),[2] namely the 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 December 30, 2020, starting with healthcare workers. As of May 17, 2021, 3,407,068 doses of vaccination 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 male non-smoker with a background history of hypertension developed exertional dyspnoea two days after the first dose of Pfizer-BioNTech Covid-19 vaccination in late January 2021. On day 7 post vaccination, 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 electrocardiography findings of a right bundle branch block and left posterior fascicular block. He had a low grade fever (37.7 degree Celsius), a blood pressure 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 was reported as cardiomegaly, bilateral lower zone opacities likely consolidation and a small left pleural effusion (Figure 1A). He was treated for a community acquired pneumonia and discharged home with oral antibiotics.

On day 12 post vaccination, 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.

An electrocardiogram (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 five days prior. Of note, there was subtle electrical alternans. In addition, although the amplitude of the QRS complexes were not small, however, when compared to the ECG performed post pericardiocentesis, the QRS complexes were later found to be larger (Figure 2B).

Bedside ultrasonography revealed a large circumferential pericardial effusion and mild bilateral pleural effusions. A formal transthoracic echocardiography (Figure 3) confirmed the presence of a large circumferential pericardial effusion [pericardial effusion seen adjacent to left ventricle wall (30mm), left ventricular posterior wall (22mm), right ventricle (24mm), left ventricular apex (27mm) and right atrium (27mm)] 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 hemoserous fluid. A further 90 mL was drained over the next 12 hours. After the initial drainage of 750 mL of pericardial fluid, the patient's heart rate decreased from 95-115 beats per minute to 85-100 beats per minute.

Computed tomography scan of the neck, thorax, abdomen and pelvis was done which showed non-specific borderline enlarged mediastinal lymph nodes that were likely reactive, bilateral pleural effusions 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 that was in keeping with pericarditis.

Microbiological, viral, autoimmune and serological investigations were performed on his blood and pericardial fluid samples (Table 1) and the results unyielding. 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 three months to reduce the risk of recurrent pericarditis but not a non-steroidal anti-inflammatory drug as his chest pain had resolved immediately after pericardiocentesis.

There was no further pericardial drain output after the first 12 hours. 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 re-accumulation of pericardial fluid and he was discharged well later that day.

A follow-up clinic review 2 weeks post discharge revealed no recurrence of symptoms and repeat electrocardiogram done 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 post discharge 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 affecting millions of people globally. Vaccines have been touted as a means to control further viral spread and a possible solution to the current pandemic. In the recently concluded phase 3 trials, the Pfizer-BioNTech Covid-19 vaccine reported 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 parasthesia 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 available microbiological and molecular examinations were unyielding.

The temporal course and evolution of symptoms shortly after Covid-19 vaccination is suspicious that the underlying mechanism may be related to an immune-mediated process post-vaccination, possibly secondary to molecular mimicry by 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 prior 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^{TM} SARS-CoV-2 Neutralization 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 neutralizing antibodies as suggested by a positive cPass assay (65.62% Inhibition Value), were in keeping with seroconversion from the first dose of the vaccine. This therefore disproved our hypothesis.

Case reports of pericarditis and pericardial effusions after influenza vaccination have been reported, but are uncommon.[7-14] In addition, although pericardial effusions can occur in up to 60 percent of patients with acute pericarditis, the majority of effusions are small or moderate in size (79 and 10 percent respectively) without any haemodynamic compromise, while only 5 percent of effusions result in cardiac tamponade.[15] It is thus very uncommon for pericarditis to occur post vaccination, much less so for it to result in cardiac tamponade.

Our patient had numerous echocardiographic and several ECG features of cardiac tamponade as detailed above, in addition to a tachycardia that was unexplained for 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, however, the tachycardia did improve 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 have been recently reported in a series of mostly younger males, typically 48-72 hours after 2nd dose of Covid-19 mRNA vaccination.[17] In contrast, our patient is a middle aged gentleman (53 year old) who developed pericarditis complicated by cardiac tamponade after his 1st 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. We wish to highlight the possibility of post vaccination 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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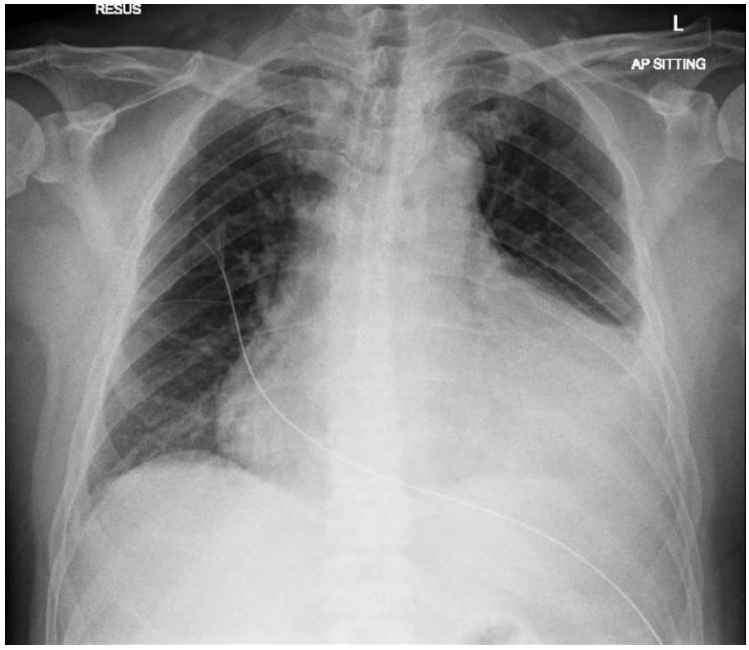

Fig. 1A: Chest radiograph – Day 7 post vaccination on first presentation to the emergency department.

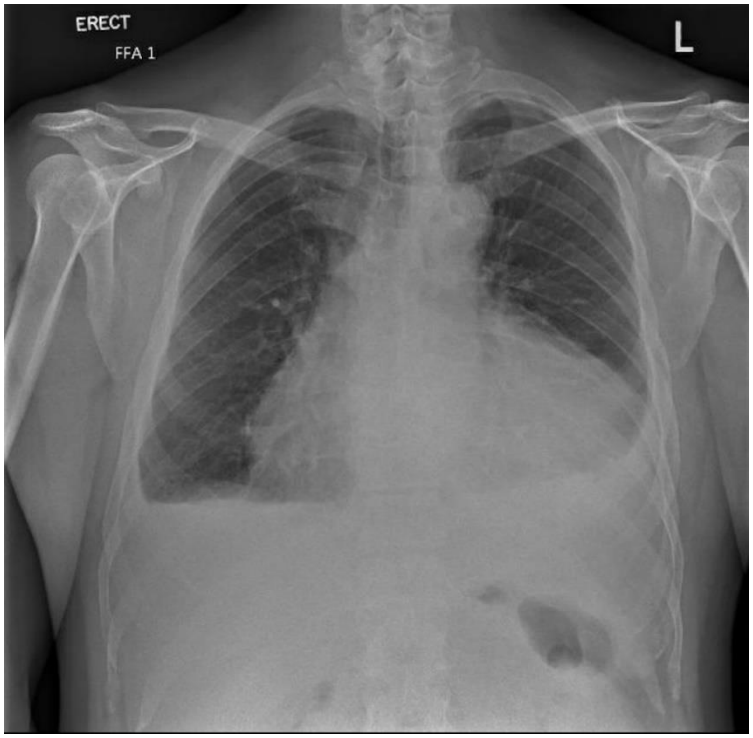

Fig 1B: Chest radiograph – Day 12 post vaccination on second presentation to the emergency department with worsening symptoms.

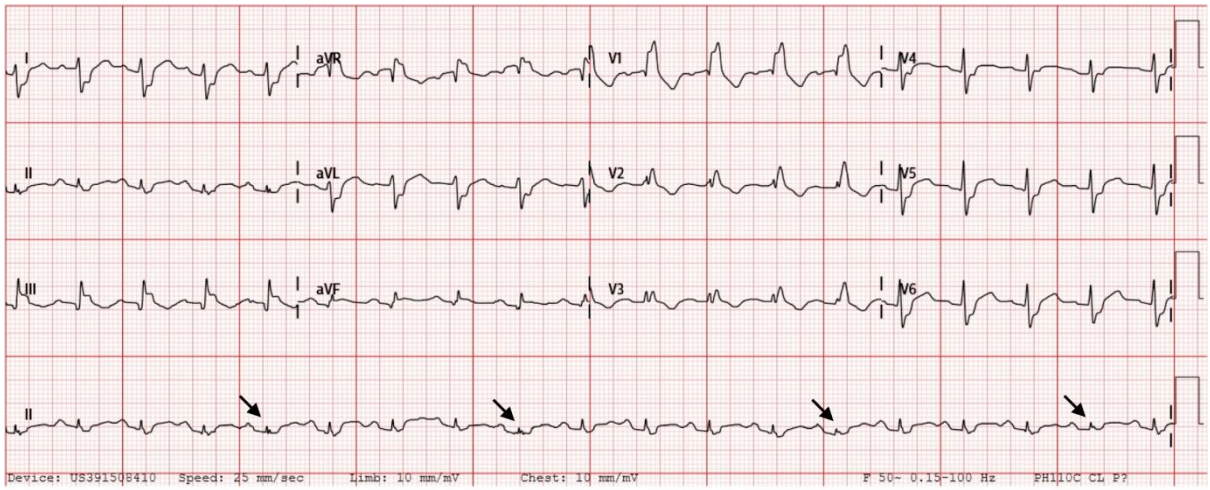

Fig. 2A: ECG – Day 12 post vaccination on admission; arrows showing QRS complexes of smaller amplitude signifying electrical alternans.

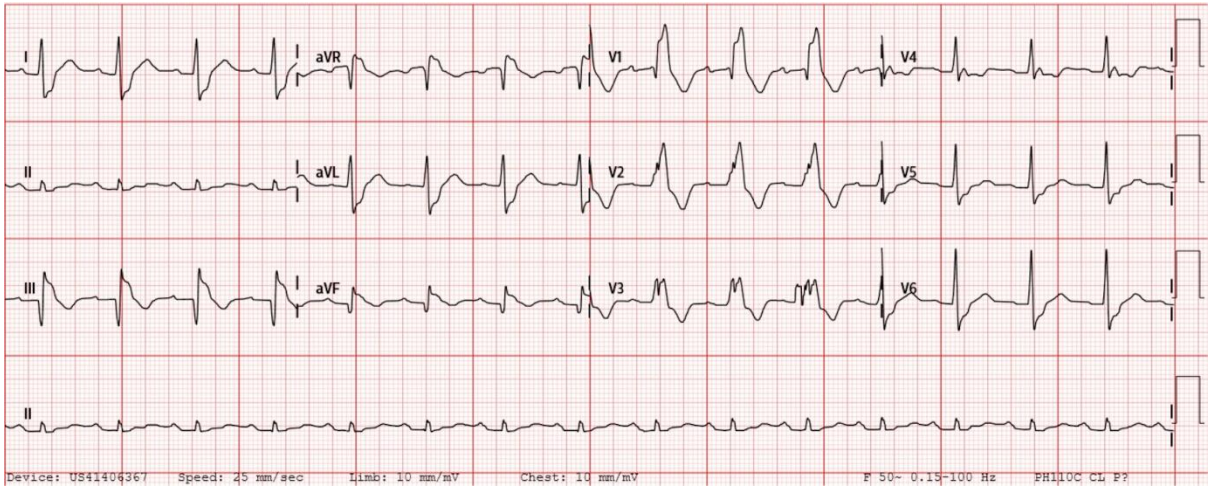

Fig. 2B: ECG – Post pericardiocentesis showing QRS complexes are now of larger amplitude with resolution of electrical alternans.

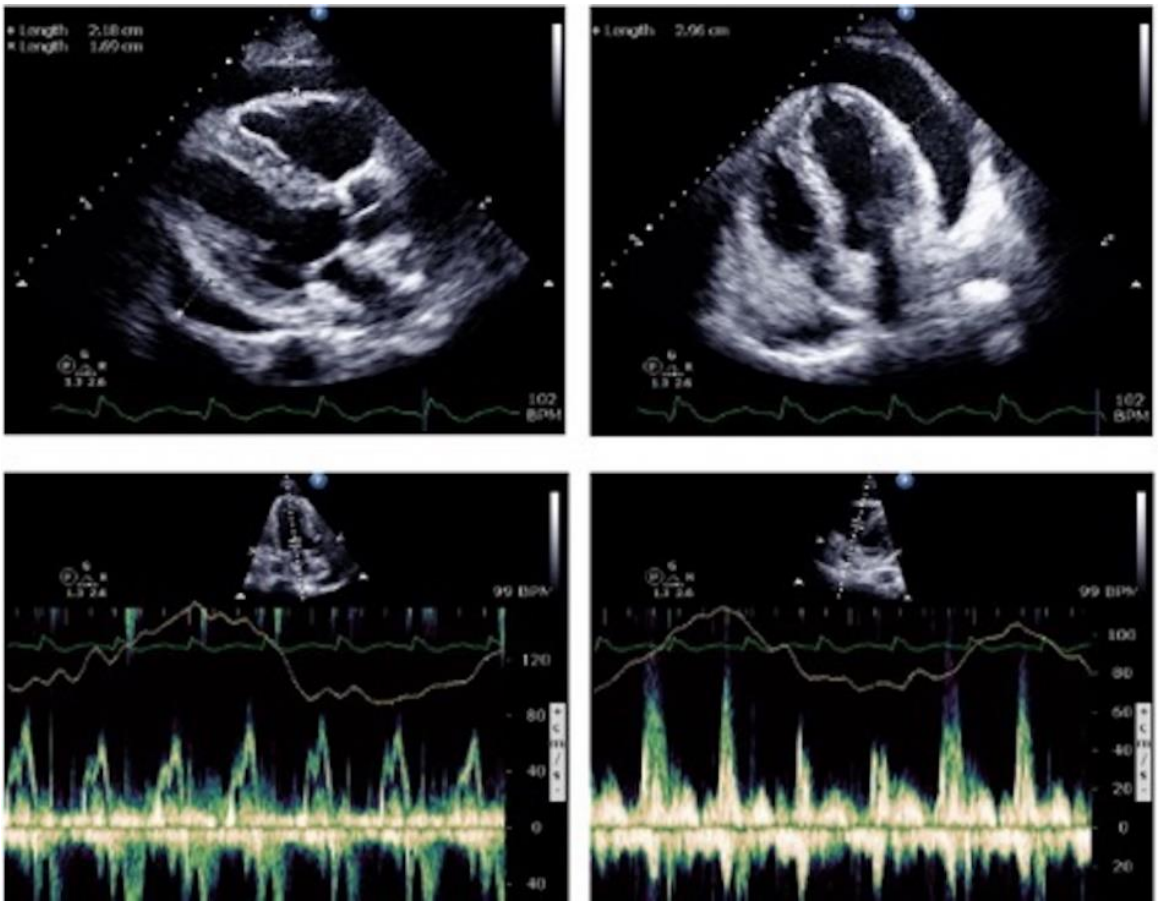

Fig. 3: Echocardiogram prior to pericardiocentesis – Top panels: circumferential pericardial effusion measuring up to 2.96 cm. Bottom left panel: respiratory variation of diastolic mitral inflow. Bottom right panel: respiratory variation of diastolic tricuspid inflow.

Table 1

Blood		
Biochemistry		
Test	Values	Reference range
Troponin T [ng/L]	7, 7 (24 hours apart)	0-29
ProBNP [pg/ml]	70.9	<125.0
Creatinine [umol/L]	73	65-125
Albumin [g/L]	43	37-51
Hemoglobin [g/dL]	13.4	13.0-17.0
WBC Count [$x10^3$/uL]	10.4	4.0-10.0
Platelet Count [$x10^3$/uL]	580	150-450
Thyroid stimulating Hormone [mIU/L]	1.34	0.100-4.00
Thyroxine (T4) Free [pmol/L]	14.46	10.00-20.00
Microbiology		
Test	Result	
Blood culture aerobic & anaerobic	Negative	
QuantiFERON®-TB Gold In-Tube	Negative	
VDRL and Treponema Pallidum particle agglutination	Negative	
Rickettsia serology	Negative	
Epstein-Barr Virus Capsid IgM antibody	Negative	
Cytomegalovirus IgM antibody	Negative	
Parvovirus B19 PCR	Negative	
Hepatitis A IgM antibody	Negative	
Hepatitis B Surface antigen & antibody	Negative	
Hepatitis C antibody screen (EIA)	Negative	
HIV screen	Negative	
Roche Spike antibody (U/ml)	46.71	
Roche Nucleocapsid antibody	Negative	
cPass assay™ SARS-CoV-2 Neutralization antibody	Positive (65.62% inhibition value)	

Autoimmune		
Test	Result	Reference range
Anti Neutrophil Cytoplasmic Antibody EIA profile	Negative	
Antinuclear antibody	Negative	
Anti-ENA profile	Negative	
Anti Double-stranded DNA antibody [IU]	5.41	< 25: negative
Others		
Test	Result	
General lymphoma screen panel	No evidence of atypical B or T lymphocytes with aberrant expression in blood sample	
Pericardial fluid		
Biochemistry		
Test	Values	Reference range
Appearance	Heavily blood stained and turbid	NA
Total protein, fluid	54.0 g/L	NA
Total protein, serum	79 g/L	62 – 82 g/L
Glucose, fluid	4.6 mmol/L	NA
Lactate dehydrogenase, fluid	2387 U/L	NA
Lactate dehydrogenase, serum	424 U/L	90 – 190 U/L
Neutrophil	15%	NA
Lymphocyte	85%	NA
Microbiology		
Test	Result	
Aerobic and anaerobic culture	Negative	
Acid fast bacilli smear	Negative	
Acid fast bacilli culture	Pending	
Fungal microscopy	Negative	
Fungal culture	Pending	
SARS-CoV-2 PCR	Negative	

Enterovirus RNA	Negative
Adenovirus PCR	Negative
Others	
Cytology	No malignant cell is seen
General Lymphoma Screen Panel	No evidence of atypical B or T lymphocytes with aberrant expression in blood sample
Respiratory swabs	
Test	Result
SARS-CoV-2 PCR	Negative
Respiratory pathogens multiplex PCR	Negative