Acute cardiac events following ChAdOx1 nCoV-19 corona virus vaccine: report of three cases

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Case Report

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Abstract

Acute myocarditis following COVID-19 vaccination has been observed majorly following mRNA vaccines. Recently a single case of ChAdOx1 nCoV-19 vaccination induced myocarditis with an ischemic presentation has been reported. Here we report three cases of acute cardiac events following ChAdOx1 nCoV-19 vaccination, in an elderly female, a middle-aged male and a middle-aged female. The first case presented with an ischemic phenotype, the second with acute heart failure, and the third with cardiac symptoms and magnetic resonance imaging evidence of myocardial inflammation. The patients were all managed successfully with conservative treatment and showed symptomatic improvement within few weeks which was further corroborated by improved electrocardiographic and echocardiographic findings in the first two patients. The possibilities of molecular mimicry, autoimmunity and direct S-protein induced toxicity to the heart may need to be evaluated in the future to explain cardiac adverse events of COVID-19 vaccines.

Highlights

1. Acute cardiac events with or without elevated cardiac biomarkers and symptoms suggestive of acute coronary syndrome or heart failure may be a rare complication of chimpanzee adenovirus based COVID-19 vaccines.
2. Antibody-mediated mechanisms characterized by elevated titres of serum anti-Spike antibody may be responsible for acute cardiac events following COVID-19 vaccination.
3. Acute cardiac events including myocarditis may occur after administration of COVID-19 vaccines based on diverse platforms.

Main Text

To curtail the COVID-19 pandemic, several COVID-19 vaccines have been given emergency use approval. Some of these having widespread use in many countries include the recombinant chimpanzee adenovirus (ChAdOx1)-based vaccine (AstraZeneca/Oxford university) and the mRNA-based vaccines from Pfizer and Moderna. COVISHIELD (Serum Institute of India) manufactured in India and imported to several countries, is based on the AstraZeneca/Oxford vaccine platform. Safety wise, these vaccines have demonstrated a favourable profile and majority of adverse events observed in clinical trials have been of mild or moderate severity. In the post approval period, however, some rare but serious adverse events have been reported for each. The prominent ones include cases of vaccine induced thrombosis and thrombocytopenia (VITT), Guillain Barre syndrome (GBS), facial palsy and myocarditis.¹⁻³ Of these, myocarditis has been reported so far mostly with Pfizer's BNT162b2 and Moderna's mRNA-1273 mRNA-based vaccines.^{3,4} Here we report two patients with potentially serious acute cardiac events following vaccination with ChAdOx1 nCoV-19 vaccine (COVISHIELD).

Case 1: A 52-year-old male with bronchial asthma controlled on inhaled steroids and beta agonists was admitted with dyspnea and productive cough of 6 days duration, which developed 6 days following his first dose of ChAdOx1 nCoV-19 vaccine. The patient did not have past history of COVID-19 or other recent acute viral illness. He had bilateral basal crepitations in the chest, pitting pedal edema, and facial puffiness on examination. RT-PCR for SARS-CoV-2 was negative at the time of admission.

Electrocardiography (ECG) showed widespread ST segment depression over chest leads and sinus tachycardia. Serum brain-type natriuretic peptide (BNP) was elevated (2140 pg/mL). 2D echocardiography revealed dilatation of cardiac chambers, moderate left ventricular systolic dysfunction (LVSD) with an ejection fraction of 35%, global hypokinesia and pericardial effusion. A diagnosis of probable myocarditis with heart failure phenotype was made, and the patient was managed with diuretics, antiplatelet drugs, statins, and ramipril. On follow up after 7 weeks, marked clinical improvement was seen and repeat echocardiography showed an ejection fraction of 44% with normal left ventricular dimensions, and absence of pericardial effusion and hypokinesia. Serum anti-Spike IgG antibody tested at follow-up (>10 weeks after first dose) was found to be high (5484.70 AU/mL, positive if > 50AU/mL).

Case 2: A 65-year-old female with hypertension (controlled on metoprolol and amlodipine) and mood disorder (controlled on sertraline), presented with fever, chest pain and exertional dyspnea of 5 days duration, symptoms having started within 24 hours of receiving her 2nd dose of ChAdOx1 nCoV-19 vaccine. There was no history of similar symptoms or SARS-CoV-2 infection in the past and ECG and echocardiogram of the pre-vaccination period were normal. On examination, blood pressure was 150/100 mm Hg and bilateral basal crepitations were present in the chest. Her RT-PCR for SARS-CoV-2 during the present visit was negative. ECG showed ST depression in chest leads (V1-V6) while echocardiogram showed hypokinesia in the territory of right coronary artery (RCA) and left circumflex artery (LCX) and a left ventricular ejection fraction of 49%. Cardiac biomarkers were normal. A diagnosis of probable myocarditis with ischemic phenotype was made, and the patient was managed with oral antiplatelet, statin and nitrate along with continuation of metoprolol and amlodipine. On follow up after 6 weeks, she showed clinical improvement with normalization of ECG and echocardiography findings. Serum SARS-CoV-2 anti-Spike antibody at this time (6 weeks post second dose) was found to be 7959.80 AU/mL.

Table 1 delineates characteristics of the two cases.

Discussion

Following emergency use authorisation of COVID-19 vaccines, rare serious adverse events are being reported across the globe. Myocarditis with COVID-19 vaccines so far have been reported majorly with mRNA-based vaccines. Recently, a case of myocarditis associated with hyper eosinophilia in a medical professional, has been reported following inactivated SARS-CoV-2 vaccine (COVAXIN) used in India.⁵ Though reported to pharmacovigilance databases, myocarditis with ChAdOx1 nCoV-19 has been studied definitively in only one patient so far.⁶ In this case, myocarditis occurred in a 68-year-old female within 24

hours of first dose of ChAdOx1 nCoV-19 vaccine, had an infarct like presentation and clinical features similar to case-2 of our study.

Here we presented potentially serious cardiac events in two patients following ChAdOx1 nCoV-19 Corona virus vaccine (recombinant). Though histopathological examination is required for the confirmation of myocarditis, acute onset of cardiac symptoms, deranged cardiac imaging and/or cardiac enzymes in the absence of pre-existing cardiac disease fulfilled the Centers for Disease Control and Prevention (CDC) and U.S. Department of Health and Human Services (DHHS) criteria for 'probable' myocarditis in the two patients.⁷ Symptoms occurred following the second dose in one patient and after first dose in the other. The onset of symptoms varied from 24 hours to 6 days following vaccination. One patient developed acute congestive heart failure like phenotype, and the other had features suggestive of myocardial ischaemia. The course was uneventful in both, patients could be managed conservatively, and the cardiac abnormalities were reversible with improvement noticed clinically as well as on echocardiography. In a recently published safety data on the use of ChAdOx1 nCoV-19 vaccine (n=730) assessed up to seven days following second dose, adverse events of significant severity (FDA grade ≥ 3) were seen in 5 (0.7%) and three out of these five individuals had autonomic and cardiac disturbances in the form of chest discomfort, high blood pressure, tachycardia, and palpitations.⁸

A possible mechanism behind the cardiac manifestations may be molecular mimicry leading to autoimmune phenomena. SARS-CoV-2 has been associated with flares or occurrence of auto immune diseases such as GBS and immune thrombocytopenic purpura (ITP).⁹ Recently varying degree of sequence homology has been shown between SARS-CoV-2 proteins and human proteins, and antibodies against SARS-CoV-2 proteins have been shown to cross react with multiple host proteins.¹⁰ Likewise, one study compared hexa or heptapeptide sequences of SARS-CoV-2 spike (S) protein with the host's proteome and observed many homologies not seen with endemic coronaviruses like HKU1, 229E and OC43.¹¹ Some shared peptide sequences may be epitopes for B and T lymphocytes.¹² As a corollary of these findings, the adaptive immune response generated by vaccine comprising both antibodies and reactive T-cells can be presumed to cross react with host tissue proteins. The presence of high level of antibodies to the S-protein observed in the two cases might suggest the possibility of an antibody dependent mechanism of cardiac injury.

Acute respiratory distress syndrome and diffuse systemic coagulopathy are the primary reasons of COVID-19 associated mortality and with the limited therapeutic options available, the importance of vaccination cannot be denied. However, with the emergence of serious adverse events including but not limited to the cardiac system, the benefits of mass roll out of vaccines should be weighed carefully with the possible risks. Both the cases were atypical in presentation and similar cases were not observed by treating physicians in the previous years. There may also be a possibility of relapsing autoimmune phenomena due to antibody cross-reactivity, for which one needs to be vigilant. Since the S protein is the common agent in various COVID-19 vaccine platforms, the direct pathophysiological impact of this protein on the cardiovascular system also needs to be delineated from future pre-clinical studies.

Declarations

Funding: None

Conflict of Interest: None

Ethical statement: No human experiments were performed. All ethical principles were followed as per the Declaration of Helsinki. IRB permission not required for individual case reports in the institute.

Consent to publish: Written informed consent to publish the cases has been provided by the patients.

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Table 1

Due to technical limitations, table 1 is only available as a download in the supplementary files section.

Figures

Figure 1

Cardiac magnetic resonance imaging- Short-axis T1 (A), Fat suppressed T2 (B,C) and delayed post contrast images (D,E,F) obtained after 10 min of contrast administration shows T2 hyperintensity in subendocardial region (black arrows in B and C) and delayed post contrast enhancement (white arrows in D,E,F).

Supplementary Files

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- [Table1.docx](#)