CASE REPORT

BNT162b2 mRNA COVID-19 vaccine induces recurrent acute coronary syndromes in coronary artery disease patients with coronary stents: a case report

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ABSTRACT

INTRODUCTION: Reports of COVID-19 vaccine-associated adverse events have gradually become widespread. Here, we present a case of recurrent acute coronary syndrome (ACS) after administration of the BNT162b2 mRNA COVID-19 vaccine (Pfizer-BioNTech), speculating that it probably occurs via a micro-emboli formation mechanism. CASE PRESENTATION: We describe a case of recurrent ACS in a 70-year-old man with multiple coronary stents after receiving the BNT162b2 mRNA COVID-19 vaccine (Pfizer-BioNTech). This patient experienced recurrent angina pectoris after the implantation of his third stent. An electrocardiogram (ECG) and elevated serum troponin I levels confirmed myocardial ischemia. The patient's symptoms were partially relieved after his anticoagulation (AC) and antiplatelet (AP) regimen had been

adjusted and disappeared 3 months after the vaccination. CONCLUSION: We speculate that the BNT162b2 mRNA COVID-19 vaccine could increase the risk of recurrent ACS in coronary artery disease (CAD) patients with coronary stents; antithrombotic therapy may need to be strengthened in the case of such patients receiving a vaccination. (Am J Transl Med 2022. 6(4):185-190)

Keywords: Acute coronary syndrome; BNT162b2 mRNA COVID-19 vaccine; microthrombosis; coronary artery disease; antithrombotic therapy.

Manuscript submitted: 10/16/2022; Accepted: 11/22/2022; published: 12/01/2022.

INTRODUCTION

To date, reports have not indicated an association between the recurrence of the acute coronary syndrome (ACS) and COVID-19 vaccines, though cases of thrombosis with thrombocytopenia syndrome (TTS) have been reported rather frequently after COVID-19 infection or the administration of various types of COVID-19 vaccines (Polack et al., 2020; Schultz et al., 2021). The COVID-19 vaccine was approved for emergency use when the Food and Drug Administration released its phase 3 trial results on December 11, 2020 (Tumban, 2020), and reported cases of TTS after COVID-19 vaccination have been made publicly available (Lon et al., 2021). According to the manufacturers' specifications, the COVID-19 vaccine should be administered in two doses separated by a 21-day interval, and its adverse effects (AEs) should be monitored for at least 14 weeks after the booster shot. Systemic AEs of the vaccine, such as fever, headaches, thrombocytopenia, venous and arterial thromboembolic events, and hemorrhagic events, have been reported (Medicherla et al., 2020). To the best of our knowledge, no reports have indicated an association between recurrent ACS and the BNT162b2 mRNA COVID-19 vaccine; thus, the present case provides a useful supplement to the safety information of this COVID-19 vaccine.

CASE PRESENTATION

A 70-year-old man received his second COVID-19 vaccine shot at a Hong Kong community hospital. After the vaccination, he did not exhibit fever, coughing, a runny nose, an abnormal sense of taste and smell, or any other manifestations of COVID-19 infection. Five days later, he began to experience recurrent episodes of angina pectoris, which was manifested as chest pain together with numbness in his four limbs, lasting approximately 70 minutes. His cardiologist arranged a coronary angiography test for him 18 days later, and a third stent was implanted at the stenosis of the first diagonal branch of the left coronary artery (LCA) in case he experiences symptomatic cardiovascular events.

Nonetheless, the recurrence of angina pectoris occurred notably more frequently. The patient decided to return to mainland China to seek a second opinion but experienced successive severe chest pains during a hotel quarantine that could not be relieved by sublingual nitroglycerin. This brought him to our quarantine hospital (a separate temporary hospital providing emergency medical services for inbound patients), as per the border quarantine rules for entry into mainland China. His electrocardiogram (ECG) results could be related to a previous myocardial infarction because the man had received coronary stenting therapy for angina pectoris over 2 consecutive years (in 2007 and 2008). Regarding his medical history, he had been completely symptom-free since the second stenting procedure and had continued to lead a healthy lifestyle and engage in frequent physical activity. We also ruled out myocarditis, pericarditis, and recurrent myocardial infarction in his

medical history. Moreover, he was free of infectious disorders such as syphilis, tuberculosis (TB), and acquired immunodeficiency syndrome (AIDS). Additionally, he had no history of medication sensitivities, parasitic infections, or repeated blood transfusions. Further, he does not have a family history of congenital heart disease (CHD), nor does he smoke, drink, or abuse substances.

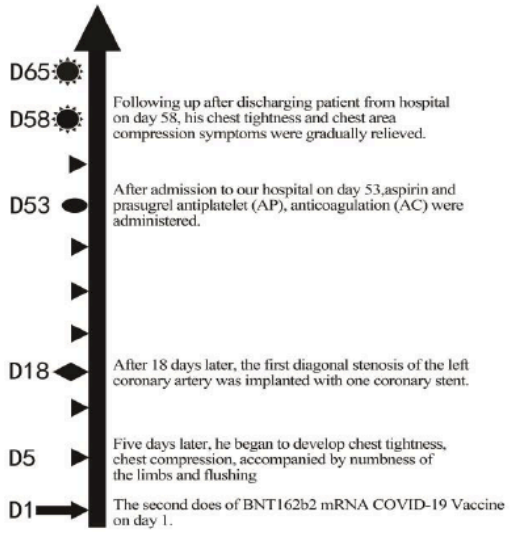

Figure1: BNT162b2 mRNA COVID-19 Vaccine adverse effect time plots.

As the patient continued to experience chest pain after admission, his serum troponin I level was monitored and a series of ECG examinations were conducted. Though changes associated with myocardial infarction were shown on the ECGs, the serum troponin I level fluctuated in the range of 0.0353–0.444 ng/ml (reference range ≤0.032 ng/ml). After also performing 64-MSCT coronary computed tomography angiography (CTA), only a shallow myocardial bridge and old myocardial infarction in the left ventricular anterior wall, left ventricular septal wall, and left ventricular apex were identified; no obvious stenosis was detected in the major epicardial coronary arteries. After the administration of a COVID-19 antibody test, the patient tested positive for IgG but negative for IgM. His routine blood tests yielded essentially normal results, with a platelet count of 190×10^9 platelets/L and normal coagulation function.

Considering all the data, we inferred that the patient was suffering from recurrent myocardial ischemia, that is, ACS. Accordingly, after adjustments to his anticoagulation (AC) and antiplatelet (AP) regimen, the recurrence of angina pectoris gradually decreased, as revealed by a telephone follow-up (**Figure 1**). A follow-up after 2 months of the percutaneous coronary intervention indicated no obvious abnormalities (Supplemental material 1), and the symptoms of recurrent angina pectoris disappeared after 3 months, as per a telephone follow-up.

DISCUSSION

As the patient displayed recurrent angina pectoris after receiving the second dose of the COVID-19 vaccine – a previously unreported response to vaccination – with ECG abnormalities and elevated serum troponin I levels, the diagnosis of ACS seems reasonable. However, the mechanism by which the vaccine leads to recurrent events remains unclear. The patient has not received any other vaccine in the past few months, nor is he predisposed to any condition that could lead to ACS. On the other hand, the association between the vaccination and the recurrence of ACS seems rather strong in regard to the timing of the recurrence (Figure 1), and the patient himself continued to complain that the vaccination was causing the re-emergence of his symptoms. Furthermore, according to a nationwide safety evaluation of the BNT162b2 mRNA COVID-19 vaccine conducted in Israel, systemic thrombosis and cerebral venous sinus thrombosis (CVST) can be induced by COVID-19 vaccination (Barda et al., 2021; Tan et al., 2021). Possible mechanisms include the formation of an antibody against the antigenic complexes of platelet

factor 4 (PF4), which triggers substantial platelet activation, aggregation, and depletion, thereby reducing the platelet count and causing thrombosis, similar to heparin-induced thrombocytopenia (Greinacher ET A., 2017; Greinacher et al., 2021; Schultz et al., 2021). Microembolization and microvascular dysfunction can sensitize the coronary microcirculation and contribute to angina in the absence of major epicardial coronary obstruction, especially in combination with the release of thrombogenic, vasoconstrictor, and inflammatory substances (Heusch, Skyschally., 2018). Meanwhile, antibody-mediated procoagulant platelets in SARS-CoV-2-vaccination-associated immune thrombotic thrombocytopenia (VITT) have been previously reported (Althaus et al., 2021). Therefore, it is more likely that the COVID-19 vaccine induces ACS recurrence via recurrent microthrombosis, and a follow-up coronary digital subtraction angiography (DSA) conducted in another institute further excluded the involvement of the major coronary artery. This case thus warns of a potential adverse effect of the COVID-19 vaccine in CHD patients, which is worth monitoring after vaccination.

The main limitation of this case report is that we only identified a closely timed relationship between the recurrence of ACS and the administration of a COVID-19 vaccine. Furthermore, the present study did not test antibodies against PF4 or whether the vaccine activated platelets in the patient due to the limited availability of facilities for this type of investigation and the limited time for the patient to remain in the quarantine area.

In summary, due to the lack of alternative explanations for the recurrent ACS episodes and the closeness of the timing between the ACS attacks and the vaccination in this case study, we speculated that the BNT162b2 mRNA COVID-19 vaccine could increase the risk of recurrent ACS for CAD patients with coronary stents. Temporary strengthening of anticoagulation or antiplatelet therapy may be necessary for vaccinations of this patient group.

ABBREVIATIONS

ACS: acute coronary syndrome;
AC: anticoagulation;
AP: antiplatelet;
CAD: coronary artery disease;
TTS: thrombosis with thrombocytopenia syndrome;
AEs: adverse effects;
LCA: left coronary artery;
TB: tuberculosis;
AIDS: acquired immunodeficiency syndrome;
CHD: congenital heart disease;
CTA: computed tomography angiography;
ECG: electrocardiogram;
CVST: cerebral venous sinus thrombosis;
PF4: platelet factor 4;
VITT: immune thrombotic thrombocytopenia.

ETHICAL STATEMENT

The studies involving human participants were reviewed and approved by The Seventh Affiliated Hospital, Sun Yat-sen University.

INFORMED CONSENT AND PATIENT DETAILS

Written informed consent to participate in this study was provided by the participant, who consented to the publishing of this manuscript.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

AVAILABILITY OF DATA AND MATERIALS

The original contributions presented in the study are included in the article material/supplemental material; further inquiries can be directed to the corresponding author.

FUNDINGS

None.

AUTHORS' CONTRIBUTIONS

JQX and CL wrote the manuscript; QHH conceived of the study and thoroughly revised the manuscript; and SYL, HZL, CLZ, LFC, TB, GNL, CC, and ZHZ acquired and analyzed the information related to the case. All authors approved the final version of the manuscript.

ACKNOWLEDGEMENTS

Not applicable.

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